SEGMENTATION OF NEUROANATOMY IN MAGNETIC RESONANCE IMAGES

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ABSTRACT

Segmentation in neurological Magnetic Resonance Imaging (MRI) is necessary for volume measurement, feature extraction and for the three-dimensional display of neuroanatomy. This thesis proposes several automated and semi-automated methods which offer considerable advantages over manual methods because of their lack of subjectivity, their data reduction capabilities, and the time savings they give. Work has concentrated on the use of dual echo multi-slice spin-echo data sets in order to take advantage of the intrinsically multi-parametric nature of MRI. Such data is widely acquired clinically and segmentation therefore does not require additional scans. The literature has been reviewed. Factors affecting image non-uniformity for a modern 1.5 Tesla imager have been investigated. These investigations demonstrate that a robust, fast, automatic three-dimensional non-uniformity correction may be applied to data as a pre-processing step. The merit of using an anisotropic smoothing method for noisy data has been demonstrated.

Several approaches to neurological MRI segmentation have been developed. Edge-based processing is used to identify the skin (the major outer contour) and the eyes. Edge-focusing, two threshold based techniques and a fast radial CSF identification approach are proposed to identify the intracranial region contour in each slice of the data set. Once isolated, the intracranial region is further processed to identify CSF, and, depending upon the MRI pulse sequence used, the brain itself may be sub-divided into grey matter and white matter using semi-automatic contrast enhancement and clustering methods. The segmentation of Multiple Sclerosis (MS) plaques has also been considered.

The utility of the stack, a data driven multi-resolution approach to segmentation, has been investigated, and several improvements to the method suggested. The factors affecting the intrinsic accuracy of neurological volume measurement in MRI have been studied and their magnitudes determined for spin-echo imaging. Geometric distortion - both object dependent and object independent - has been considered, as well as slice warp, slice profile, slice position and the partial volume effect. Finally, the accuracy of the approaches to segmentation developed in this thesis have been evaluated. Intracranial volume measurements are within 5% of expert observers' measurements, white matter volumes within 10%, and CSF volumes consistently lower than the expert observers' measurements due to the observers' inability to take the partial volume effect into account.

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Word up to Jon, Alice the bairn, Mum and Dad, Cephas, Mercedes, the Institute of Neurology NMR Research Group and the UC Academic Radiation Physics Group.

DEDICATION

To my friends who believed, and to my grandparents.

INTRODUCTION.

Magnetic Resonance Imaging (MRI) or Nuclear Magnetic Resonance (NMR) Imaging is a modality that can be considered to be in its adolescent years. The initial research and development has given way to consolidation and increasingly diverse clinical applications. MRI already produces vast amounts of data and this looks set to increase in the future. Technical improvements are allowing volume data, fast pulse sequences and NMR angiography to be used in routine clinical work. Real time clinical 4-D imaging such as Echo Planar Imaging (EPI) cardiac studies are on the horizon whilst MRI's ever-increasing clinical acceptance is producing large amounts of temporal data from lengthy serial studies. It is against such a background that the importance of segmentation, the decomposition of an image into natural units, can be judged.

The successful segmentation of magnetic resonance images is dependent upon three separate stages. Initially, attention must be paid to the image acquisition in choosing appropriate pulse sequences to enhance neurological contrast - possibly using several such sequences. Secondly, the images require preprocessing which in this thesis includes correction for image non-uniformity and image smoothing to reduce the effects of noise. The corrected image is then ready for processing. The segmentation method must take into account the characteristics of NMR data and, as such, may have to rely on methods constructed particularly to take account of this - for example specifically developed brain isolation algorithms.

It is generally thought possible to divide segmentation into three levels of processing, although opinions differ. Low level approaches (or pre-processing) involve image enhancement, smoothing, resolution changes etc.; medium level approaches are segmentation methods such as region-growing, clustering, edge-detection etc.; whilst high-level approaches are methods such as knowledge-based processing and elastic matching to an atlas. This thesis concentrates on the low and medium level approaches in order to produce a number of methods which are appropriate for use on their own, but which could also be the basis for a higher level approaches. Such taking into account the strengths and weaknesses of the various medium level approaches. Such higher level work will not be dealt with in this thesis.

Three approaches to medium level processing have been considered: edge-based processing, region-based processing and the stack - a data driven image description and segmentation scheme. A variety of approaches have been chosen in order to investigate a range of general and more specific tasks. The stack, for instance, is claimed to be a completely general method of segmentation applicable to any image and the region based methods should be applicable to a variety of tissues. Aspects of the edge-based processing will also be generally applicable. Performance has been improved by using a variety of domain specific processing approaches such as search spaces. Although these methods are not directly applicable to other anatomical regions, the ideas behind them remain valid. Finally it is pertinent to note that true 3-D methods ensure coherence in the third dimension, which is not the case for a 2-D slice by slice approach. It will be argued, however, that multi-slice data is often not suitable for certain types of 3-D processing.

The images considered for this work have to a large extent been dual-echo multi-slice head data sets (in order to take advantage of the intrinsically multi-parametric nature of MRI data), and to a lesser extent, images of the head acquired with a variety of other sequences. The availability of two registered images of the same region demonstrating different image contrast gives more information which can make data processing more easy. The dual-echo images were acquired with a spin echo sequence in near transverse oblique slices (the orientation of over 95% of the head data acquired by the Institute of Neurology NMR Research Group) on a 1.5 T General Electric Signa Advantage scanner (GE, Milwaukee, USA) using a TR of 2000 - 4000 ms, echo times of 30 ms and 80 ms, 3-5 mm slice thickness with a 256x192 acquisition matrix (frequency encoding x phase encoding steps) and a 256x256 display matrix. The early echo data is proton density weighted whilst the late echo data is T_2 -weighted. Other data were acquired from a 0.5 T Picker scanner. Careful data collection is a very important part of the segmentation process and hence great care must be taken with quality assurance work [BARKER92], sequence design, movement restraint such as the Nasal Orientation Device (NOD) [TOFTS90], image acquisition, parameter determination and cardiac gating where appropriate. Typical early and late echo images are illustrated by Figure 1 and Figure 2. The use of dual echo images which are widely acquired clinically does not require the acquisition of any other data. This is very important in terms of patient tolerance, data quality and cost, and is discussed in more detail in section 7.10.1.



Figure 1 - Early echo image (SE/3000/30)



Figure 2 - Late echo image (SE/3000/80)

1.1 Medical Imaging

A variety of medical imaging methods exist for visualising anatomy, pathology and function of the human body in-vivo. They vary greatly in their cost, effectiveness and utilisation for a given clinical situation. Roentgen's discovery of X-rays in 1895 quickly led to their use as the major method of medical imaging. Planar X-ray imaging is relatively cheap and is used widely for a large range of applications both with and without contrast media (ie radiography). Such planar techniques may be contrasted to tomographic techniques which produce an image of a slice through the subject.

The concept of Digital Subtraction Angiography (DSA) was first proposed a few years after the discovery of X-rays, and is a technique widely used for the visualisation of fine vessels. The technique relies on the subtraction of an X-ray image acquired prior to the injection of contrast media from one acquired after the injection of contrast media.

Modern nuclear medicine developed shortly after the second world war with the availability of radio-isotopes, following war time nuclear research. Planar nuclear medicine is used widely for

imaging of the central nervous system, cardiovascular system, lungs, hepato-biliary system, gastrointestinal tract, vascular and lymphatic system, the urinary tract, the skeletal system, thyroid, parathyroid and adrenal gland and tumour imaging. There is currently great interest in the use of labelled white blood cells and monoclonal antibodies for targeting infection.

Ultrasound began to be used clinically in the 1960s, with its non-ionising nature making it suitable for foetal imaging. It is the imaging modality which is most operator dependent and requires a prolonged period of training. Ultrasound is widely used in prenatal medicine, vascular disease, cardiac diagnosis and abdominal investigations.

X-ray Computed Tomography (X-ray CT, or CT) was introduced in 1972 by Hounsfield and provided for the first time cross-sectional tomographic slices with high quality anatomical detail. CT is important in neurology and oncology, lung disease, orthopaedics, whole body diagnostics and with fast CT, cine cardiac studies.

Single Photon Emission Computed Tomography (SPECT) and Positron Emission Tomography (PET) began making an impact during the 1970s, in a manner similar to that in which X-Ray CT followed from planar X-Ray imaging. It should be noted that PET is not a widely available technique as it requires an on site cyclotron. The two techniques are used for functional imaging of the brain, heart, liver and kidneys. Recently, there has been great interest in cerebral metabolism for the detection and localisation of cerebral abnormalities producing metabolic and perfusion defects through abnormal isotope uptake.

MRI is the newest of the major imaging techniques having been developed in the 1970s. It is widely used for investigations of the central nervous system, particularly for demyelinating diseases such as multiple sclerosis. It has important uses in imaging parts of the musculoskeletal system, cardiovascular work and bone marrow imaging. Vascular studies are of high quality and MRI angiography shows promise. The clinical realisation of sub-second fast imaging and Echo Planar Imaging (EPI) may lead to increased chest and abdominal applications, although questions of efficiency and cost have yet to be satisfactorily answered.

The tomographic imaging modalities have in the past been considered in two broad groups with CT and MRI providing anatomical and pathological detail, whilst PET and SPECT provide functional and pathological detail. Recently though, the use of MRI angiography, diffusion and

perfusion imaging and paramagnetic contrast agents (both manufactured and 'natural' agents such as the oxygen in haemoglobin), amongst others, have begun to provide MRI with a new functional role.

1.2 Magnetic Resonance Imaging

Magnetic Resonance Imaging (MRI) is an imaging modality of vast flexibility which can produce extremely detailed cross-sectional images of the human body depicting normal and pathological anatomy. The technique is dependent upon the magnetic properties of atomic nuclei, with hydrogen nuclei (protons) being most commonly considered because of their high concentration in the human body, both in water and in fats. When such protons are placed in a magnetic field, they can absorb radio waves of a characteristic frequency, which depends on the magnetic field strength and the physical and chemical environment of the nuclei. The application of a number of pulses of radio waves to a sample is known as a pulse sequence. The absorption and re-emission of such radio waves is the underlying phenomenon utilised in MRI. The technique produces images relating to three main parameters - proton density, transverse relaxation and longitudinal relaxation (which depend upon the proton's environment), as well as a number of other parameters such as flow. Added to this are noise and instrumental effects such as magnetic field and RF non-uniformities. MRI is therefore multi-parametric by its very nature and the choice of appropriate pulse sequences and acquisition parameters allows the relative contrast between normal and pathological anatomy to be varied greatly.

Despite MRI's position as the most expensive common imaging modality, it is widely available in the USA and is becoming more widespread in Europe. It is currently rare in the third world apart from a few isolated sites. In 1992 an MRI system costs from approximately $\pounds 0.75 - \pounds 2$ million. By comparison, X-ray Computed Tomography equipment is approximately 1/2 - 2/3 the price of MRI equipment, and ultrasound equipment 1/10 - 1/20 the price, for example.

In the field of anatomical and pathological neurological imaging, the source of the data for this work, MRI has a number of advantages over its closest rival, CT. MRI does not suffer from the beam hardening found in CT, so regions of the brain abutting the skull are shown clearly. MRI's non-ionising nature is generally advantageous, but makes MRI a particularly attractive alternative to CT for patients requiring many examinations, paediatrics, and pregnant patients past the first
trimester. MRI uses contrast agents minimally compared to CT due to its intrinsically superior soft tissue contrast, although more contrast studies may well be performed in the future. Minimal use of contrast agents is advantageous because of the possibility of adverse patient reaction, the generally invasive nature of administration and the cost. In addition to this, MR contrast agents are much less prone to causing adverse reactions than are CT contrast agents. MRI has the ability to vary the many acquisition parameters to optimise image content and contrast and can also acquire multiple slices simultaneously at any arbitrary angle. However it is an expensive modality and inherently more complex than CT. MRI is not suitable for the visualisation of hard bone and generally suffers more from motion artifacts than CT. The narrow bore of the magnet can cause claustrophobia, and the interaction of the magnetic or RF fields with pacemakers, metallic implants, ventilators and anaesthetic equipment may cause problems.

1.3 Image Segmentation

Image segmentation is the decomposition of an image into natural units and is commonly accomplished with respect to intensity, texture or colour. There are many applications for image segmentation - for robot vision, satellite imaging, geophysical seismic surveys, materials analysis, medical imaging, microscopy and image coding to name but a few. The field of segmentation is a particularly challenging one to work in because as Haralick [HARALICK85] states so well "there is no theory of segmentation". Despite this, however, approaches to segmentation may often be judged by either their broad applicability or ad hoc nature. The literature on segmentation relevant to MRI may be considered as divided into computer science based papers where a method is often applied to several classes of images and clinical papers which evaluate the application of a method to a particular class or sub-class of medical images. A valid criticism of some image processing and artificial intelligence approaches to segmentation is that the authors choose a solution and force it onto a problem, rather than analysing the problem and looking for an appropriate solution. This is the difference between a concept driven and a goal driven approach.

Most MRI data are currently acquired as a series of slices and are therefore three dimensional in nature. Either true volume data, where each voxel is approximately cubic, or multi-slice data with the slice thickness typically being from 3 to 10 times the in-slice voxel dimension for neurological MRI, may be acquired. The acquisition of three dimensional data raises the possibility of using three dimensional segmentation. The majority of the work in the field of segmentation is two dimensional and is concerned with robot vision, military applications and remote sensing. It is therefore often not directly applicable to three dimensional medical datasets. There are major implications for speed associated with true 3-D processing and currently techniques are often carried out slice by slice and in two dimensions because of memory limitations. The true 3-D methods ensure coherence in the third dimension which is not the case for slice by slice approaches.

1.4 Clinical Requirement for Segmentation in MRI

Automatic or semi-automatic segmentation in MRI is important because of the vast amounts of data generated (up to 16 Mbytes per dataset typically); to be able to display only the anatomical, pathological or functional regions of interest, and to quantify volumes of structures would save clinicians time and allow new approaches to the staging and following of neurological diseases. The importance of an automated or semi-automated approach to segmentation may be appreciated by considering the experience of Stimac *et al.* [STIMAC88] who took 4-6 hours to trace contours of the skin, bone, ventricles and optic nerves for a 12 slice 256² dataset. Measurement of the volume of brain parenchyma, grey matter, white matter, cerebrospinal fluid (CSF), the intracranial region, head, individual lesions and total lesion load are important in dementia, Multiple Sclerosis (MS), Acquired Immune Deficiency Syndrome (AIDS) and other diseases with neurological symptoms. Tracking changes in volume temporally would be an aid to following the natural history and response to therapy of such diseases.

Segmentation is often a necessary step in 3-D Medical Imaging (the display of multislice and volume data in a 3-D format using shading and transparency techniques). It allows the visualisation of neuroanatomy such as the skin, bone, brain, grey matter, white matter, lesions, the ventricles and eyes with all the benefits to clinicians that have been reported in the literature [eg HERMAN90]. It is widely believed that segmentation is a weak link in the steps necessary for such display [STIEHL90, COATRIEUX90]. There is somewhat of a division between qualitative 3-D display oriented segmentation techniques where display techniques can compensate to a certain extent for misclassified boundary pixels etc., and volume oriented segmentation techniques. Kohn *et al.* [KOHN91] give an example of four visually similar shaded surface images of the brain, where the volume of the brain varies by 25% within the set of images. Segmentation is the first stage in image analysis. An initial segmentation could provide the input to a feature classification system or expert system. More pertinently, an expert system could be used to interactively drive the segmentation using an anatomical model, modality specific knowledge, information about the possible pathology, a task plan and performance data for various stages of the segmentation. Segmentation is useful for image registration and can be very advantageous in some forms of image compression [KUNT85], an application which may increase in importance with the current interest in Picture Archiving and Communications Systems (PACS). It is also necessary for surgery planning and radiotherapy planning and evaluation [TOONKEL88, JUST91], the following of disease course, and response to therapy. Anatomical segmentation can be used as an aid to functional imaging, either to allow reference to anatomical structures or for image reconstruction using prior knowledge about the structures being imaged [LEAHY91, GINDI91]. Segmentation can also be used to identify key structures for temporal and intra-modality registration. This allows multi-modality image fusion and display.

Automated and semi-automated approaches to segmentation of MRI images have a number of advantages over conventional mouse or tracker ball work, because they provide a non-subjective method of object definition, reduce the volume of data a clinician encounters, and by off-loading much of the work onto computer hardware produce a subsequent saving in time. This work concentrates on the automatic and semi-automatic segmentation of gross normal anatomy. It aims to identify skin, brain, grey matter, white matter, CSF external to the brain, the ventricles (CSF within the brain) and the eyes. Some work on lesion segmentation has also been carried out.

1.5 <u>Neuroanatomy</u>

The human neuroanatomy comprises the central nervous system which consists of the brain and spinal cord, and the peripheral nervous system consisting of spinal and cranial nerves. Only the brain has been considered in this work. The nervous system consists of a vast number of units called neurones which consist of a cell body, axons and dendrites. Neurones are commonly referred to simply as nerves. The nerve cell bodies predominantly form the grey matter of the nervous system and are found in the periphery of the brain, whilst the axons and dendrites form the white matter of the nervous system deep in the brain. Myelin is a sheath of

fatty material which is wrapped around most axons and gives them a white appearance, the origin of the term white matter. The myelin sheath

- acts as an insulator
- protects the axon from injury
- speeds the flow of nerve impulses through the axons

The brain and spinal cord are completely surrounded by three membranes known as the meninges. The innermost two of these membranes are separated by cerebrospinal fluid (CSF), a clear fluid consisting mainly of water, mineral salts, glucose and plasma proteins. Within the brain there are four irregular shaped cavities termed the right and left lateral ventricles, the third ventricle and the fourth ventricle, which also contain CSF. The cerebrospinal fluid

- supports and protects the brain and spinal cord
- acts as a cushion and shock absorber between the brain and cranial bone
- may allow interchange of substances with the nerve cells

The CSF moves within the ventricles in an oscillatory motion, the precise cause of which has yet to be ascertained. The brain is protected by the cranium (part of the skull) which is surrounded by a layer of subcutaneous fat. Bone does not show up well using MRI because it contains few mobile protons, but the signal from the fatty bone marrow is often evident. The brain surface is highly convoluted and demonstrates many infoldings or furrows of varying depth. The exposed areas of the folds are termed gyri or convolutions and are separated by sulci or fissures which are filled with CSF. The term lesion is used to describe an abnormality, such as a tumour or area of demyelination (also known as a plaque in multiple sclerosis).

Figure 3 illustrates a sagittal image of the head of a normal volunteer, with the position of four oblique planes illustrated. Images corresponding to these four planes along with diagrams of the main features are illustrated by figures 1.4 - 1.11. These images are representative of those used in this thesis, with the whole brain typically being covered by 10-20 slices.



Figure 3 - Sagittal slice illustrating typical oblique slice positions for data used in this thesis (SE/3000/30).



Figure 4 - Legend for oblique slice passing through nose and ears.



Figure 5 - Oblique slice passing through the nose and ears (SE/3000/30).

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Figure 6 - Legend for oblique slice passing through the eyes and bridge of the nose.



Figure 7 - Oblique slice passing through the eyes and bridge of the nose (SE/3000/80).



Figure 8 - Legend for oblique slice at the level of the lateral ventricles.



Figure 9 - Oblique slice at the level of the lateral ventricles (SE/3000/80).



Figure 10 - Legend for oblique slices superior to the level of the lateral ventricles.



Figure 11 - Oblique slice superior to the level of the lateral ventricles (SE/3000/30).

1.6 <u>The Use of Prior Knowledge in Segmentation.</u>

It is possible to consider segmentation approaches as being divided into three groups on the basis of their use of prior knowledge. Knowledge can be used intensely, as in the case of Artificial Intelligence Knowledge Based approaches, minimally as done in many medium level segmentation approaches, or not at all as with data-driven approaches.

1.6.1 Knowledge-Based Approaches

Artificial Intelligence (AI) is the emulation of mankind's intelligence using computer hardware and (often) specific AI languages. The vast majority of knowledge-based approaches to MR segmentation initially use weak unsophisticated region-based segmentation techniques (such as a split and merge approach, region growing, simple edge detection or thresholding following crude anisotropic smoothing) to produce an over-segmented image. The small regions are then pieced together using knowledge about region size, surface area, intensity etc., and knowledge about anatomical regions, such as spatial relationships and intensity characteristics. Many methods simply demonstrate various artificial intelligence techniques on a limited sub-set of specially chosen key slices. Dellepiane *et al.* [DELLEPIANE89] acknowledge the poor segmentation of their work and others when they state that

"in the recognition process, the so-called low-level (LL) processing (ie filtering, segmentation, and feature extraction) still plays a key role:<u>Many unsatisfactory</u> results obtained in the final interpretation stage (ie, high-level (HL) stage) may be ascribed to an inappropriate selection of LL algorithms, or to their low performances."

The highlighting is this author's. As demonstrations of AI techniques, many of the methods are very interesting, but unfortunately, their claims to be accurate segmentation methods can be dubious.

This author believes that a more appropriate method would be to use an AI approach to interactively drive the segmentation using an anatomical model, modality specific knowledge, information about the possible pathology, a plan of actions and performance data for various stages of the segmentation. (See for example [MATSUYAMA89] on this last point). This author believes that several methods of segmentation (perhaps several edge-detectors for example) may be necessary for a full accurate result. Artificial Intelligence can provide a very good framework for a knowledge-based approach, but the systems that have been applied to MRI segmentation to date have suffered from poor segmentation.

1.6.2 Medium Level Segmentation Approaches.

These are region or edge-based approaches such as thresholding, clustering, regiongrowing, edge-detection and some multi-resolution approaches. These approaches use knowledge in various ways. For example, applying an intensity threshold or a threshold to an edge requires some knowledge of the scene. These parameters need to be varied depending on the particular scene.

1.6.3 Data Driven Approaches

Data driven methods do not utilise any prior knowledge. The form of the data completely determines the form of the segmentation obtained. The stack and DOLP transform, as discussed in sections 3.6.3 and 3.6.4, are examples of such approaches.

The work in this thesis concentrates on applying a little basic knowledge to low and medium level segmentation methods, and to investigating one particularly attractive data-driven approach - the stack. Low and medium level segmentation methods require adaptation to imaging modality, the anatomy to be imaged and in the case of MRI, even the scan orientation and other parameters. Data-driven approaches, however, are claimed to be independent of such effects.

1.7 <u>Hardware and Software</u>

Work has been carried out using the C and C++ programming languages under Unix along with programs and subroutines from the University of North Carolina's /usr/image/ package (University of North Carolina, Chapel Hill, NC, USA) and to a lesser extent Synoptic's programming language Semper 6+ (Synoptics Ltd., Cambridge UK). The Mayo Clinic's Analyze package [ROBB90] (Bio-dynamics Research group, Mayo Clinic, Rochester, MN, USA) has also been used for image visualisation. Image analysis and display has primarily used xdispunc, part of the dispim suite of programs written by Dave Plummer in the Department of Medical Physics, University College London, UK. The program provides a variety of image display and analysis facilities which include: image intensity scaling, linear profiles, zooming, statistics on regions of interest, simple linear measurements, histograms, colour scale manipulation and some elementary image editing such as windowing and masking. Graphs have been produced using xvgr - a data plotting tool for workstations written by Paul Turner (Oregon Graduate Institute, Oregon, USA).

Sun Workstations (Sun Microsystems, Mountain View, California, USA) have been used exclusively for image handling and processing because of their widespread use in the Medical Imaging community.

During the period of this work, two MRI scanner were used for imaging, both belonging to the NMR Research Group at the Institute of Neurology, Queen Square, London, UK. The first of these scanners was a Picker 0.5 T superconducting machine which was used from October 1989 - October 1991. From November 1991 onwards a GE 1.5 T Signa Advantage scanner was used. The Picker scanner was not suitable for multi-image segmentation, as detailed in section 7.2.1, and therefore images produced by it were not used for this work.

1.8 <u>Summary of Approach to Segmentation Developed</u>

The aim of this work is to develop automatic and semi-automatic methods for segmentation of regions of the neuroanatomy. The work initially concentrates on acquiring high quality dual-echo data which may be acquired in the same time as the equivalent single-echo data, and on techniques appropriate to processing full brain datasets rather than a limited subset of specially chosen key slices. Data is pre-processed to correct for image non-uniformity and anisotropic smoothing is applied to noisy data. It has been found that a variety of techniques must be used to segment the neuroanatomy of interest. Both edge and region based processing have been utilised to this end. Edge-based processing is used to identify the skin, to isolate the eyes, and the intracranial region (the brain parenchyma and CSF). The CSF can be separated from the brain by dual-echo clustering, thresholding or contrast enhancement involving a linear combination of images. If the contrast between grey matter and white matter is adequate then

it may be possible to further subdivide the brain parenchyma into grey and white matter using the same methods. The accuracy of segmentation may often be traded off against processing time. More robust methods tend to take longer. Fast methods can often be applied to a limited subset of key slices, but this work deals with multi-slice datasets.

Such a multi-step approach to segmentation may be contrasted to the use of the stack, a data driven approach which is claimed to be a natural method of segmentation. The applicability of the stack is evaluated in this thesis and several methods of improving the results from the stack are proposed.

1.9 Overview of Thesis

Chapter 2 discusses the essential NMR theory including basic principles, common pulse sequences and image contrast.

Chapter 3 reviews the wide variety of approaches to segmentation. These may be characterised as edge-based methods, region based methods such as thresholding, clustering, region growing and region split and merge, and multi-resolution approaches.

Chapter 4 reviews the literature on magnetic resonance imaging segmentation noting particularly the common split of papers into those with clinical applications, where a goal driven approach has been adopted, and the more abstract concept driven approach.

Chapter 5 discusses the various factors affecting non-uniformity in MRI, the magnitude of these factors for the GE 1.5 T Signa Advantage scanner, and compares several methods of correction for these non-uniformities.

Chapter 6 discusses the use of edge detection in neurological MRI. Edge detection has been used to identify the strong edges associated with the skin and brain. The skin is identified as being a strong outer contour on an early-echo image. The brain is identified as a strong contour in a late-echo image which is long-lived in scale-space. The eyes are identified by their shape from an edge image, using knowledge of anatomy to restrict the search area to the anterior region of the head. The ventricles are identified once a focus of attention within the brain has been established. A comparison of two and three dimensional edge detection methods has also been carried out.

Chapter 7 discusses the use of region-based segmentation. An accurate three-dimensional fully automatic non-uniformity correction is used as a pre-processing step. Anisotropic blurring is proposed as a second pre-processing method, with the degree of smoothing depending upon the particular approach. It is noted that the use of 5 mm thick slices with a 2.5 mm slice skip (as widely acquired clinically) means that 3-D processing is often not appropriate. Thresholding, contrast enhancement and dual-echo clustering approaches for the segmentation of brain, CSF, grey matter, white matter and multiple sclerosis lesions are described. Multi-parametric approaches to segmentation are particularly appropriate where large partial volume effects are apparent, where edge strengths vary greatly and where the border is highly convoluted containing thin strands of tissue.

Chapter 8 discusses the use of the stack - a data-driven multi-resolution approach to segmentation. Such an approach may be contrasted to the highly tuned series of steps considered in chapters 5-7. The stack has been claimed to be a totally general approach to segmentation, but it is demonstrated that this is not the case. The applicability of the stack for neurological MRI segmentation is discussed, and several improvements to the approach suggested.

Chapter 9 discusses volume measurement in neurological MRI, one of the most important reasons for segmentation. Clinical need is reviewed, the magnitude of geometric distortion and methods for its correction discussed, the partial volume effect considered and the results of automatic and semi-automatic segmentation compared to those of experts.

Finally, chapter 10 summarises the work, discusses future directions for research and draws conclusions.

CHAPTER 2

NUCLEAR MAGNETIC RESONANCE THEORY.

2.1 <u>Principles of Nuclear Magnetic Resonance.</u>

2.1.1 Introduction.

Nuclei with non-zero nuclear-spin possess a magnetic moment aligned along the axis of the spin. The spin is quantised and is characterised by the spin quantum number, I, which may be integer or half-integer. The most common nuclei used in Nuclear Magnetic Resonance (NMR) are hydrogen (¹H), phosphorous (³¹P) and carbon (¹³C). All of these isotopes have I=1/2, but further discussions will be limited to the specific case of nuclei consisting of a single proton (¹H). The angular momentum <u>p</u> of a nucleus is given by

$$\underline{p} = -\frac{h\underline{I}}{2\pi} \tag{1}$$

and is related to the magnetic moment $\underline{\mu}$ by

$$\underline{\mu} - \underline{\gamma}\underline{p} \tag{2}$$

/

where h is Planck's constant and γ is the gyromagnetic ratio - a constant for a given nucleus.

If a nucleus has a magnetic dipole then it will interact with an externally applied

magnetic field - the basis of NMR. The application of an external magnetic field \underline{B}_{o} , leads to (2I + 1) nuclear energy levels which correspond to the allowed orientations of the dipole. An isolated proton can take up one of only two stable states when placed in an external magnetic field, usually referred to as 'spin up' and 'spin down'. As with any physical system, the nucleus prefers the low-energy state, in this case 'spin up'. The energy difference between the higher and lower states is given by

$$\Delta E = \frac{\mu B_0}{I} \tag{3}$$

Now the Bohr relationship for a photon of frequency υ is

$$E = hv = \hbar w_0 \tag{4}$$

where $v = w_o/2\pi$, so a photon of energy $\hbar w_0$ will be absorbed when a nucleus transfers from a low-energy to a high-energy state, and conversely, a photon of the same energy will be emitted when a nucleus transfers from a high-energy to a low-energy state. Equating (3) and (4), and substituting from (1) and (2) gives

$$w_0 - \gamma B_0 \tag{5}$$

2.1.2 <u>The Boltzmann Distribution.</u>

At thermal equilibrium, the nuclear spins in a large sample are distributed amongst the energy levels according to a Boltzmann distribution. For I=1/2, the ratio of nuclei in the two states is given by

$$\frac{N_{sp}}{N_{down}} - \exp\left(\frac{\hbar w_0}{kT}\right)$$
(6)

where $N_{Total} = N_{up} + N_{down}$, k is Boltzmann's constant and T the absolute temperature of the sample.

$$\frac{N_{up}}{N_{down}} \approx 1 + \frac{\hbar w_0}{kT} \quad if \ \hbar w_0 << kT \tag{7}$$

The fractional excess of spins in the up-state (low-energy state) is given by,

$$\frac{N_{sp} - N_{down}}{N_{down}} - \frac{\hbar w_0}{kT}$$
(8)

For a proton at 300°K, and a medium MRI field strength of 1 Tesla

$$\frac{\hbar w_0}{kT} = \frac{\hbar \gamma B_0}{kT} = \frac{1.055 \times 10^{-34} \cdot 2.675 \times 10^8 \cdot 1}{1.381 \times 10^{-23} \cdot 300} = 6.812 \times 10^{-6}$$
(9)

This fraction means that approximately 1 in 100,000 nuclei will contribute to an NMR signal. NMR is hence a rather insensitive technique, with sensitivity increasing with field strength.

2.1.3 <u>Classical description of an isolated proton in an externally applied magnetic</u> <u>field.</u>

The interaction between the magnetic field and the nuclear magnetic moment acts to align the magnetic moment with the field. The nuclear angular moment means that the nuclei experience a torque given by

$$\underline{L} - \underline{\mu} \wedge \underline{B}_0 \tag{10}$$

From classical mechanics, the rate of change of angular momentum equals the applied torque.

$$\therefore \qquad \frac{dp}{dt} - \mu_{\wedge} \underline{B}_{0} \tag{11}$$

As
$$\underline{p} = \frac{\mu}{\gamma}$$
 it follows that $\frac{d\mu}{dt} = \gamma \mu A \underline{B}_0$ (12)

which is the equation of motion of an isolated nucleus in a magnetic field. This can be rewritten as

$$\frac{d\mu}{dt} - \gamma \underline{B}_0 \, , \, \underline{\mu} \tag{13}$$

or

$$\frac{d\mu}{dt} - \frac{w_0}{h} \wedge \mu \tag{14}$$

where $\underline{w}_0 = -\gamma \underline{B}_0$ the Larmor frequency. The nucleus will precess about \underline{B}_0 with frequency given by the Larmor frequency, w_0 . The classical spin behaves like a gyroscope or spinning top and the two are often used as models for the behaviour of a single proton in a magnetic field.

2.1.4 Bulk Magnetisation.

Up to this point, only a single magnetic moment has been considered. The bulk magnetisation is given by

$$\underline{M} - \sum \underline{\mu}$$
(15)

and is the response of a large collection of magnetic moments. In zero magnetic field, the nuclei are randomly oriented. (i.e. there is no phase coherence between the individually precessing nuclei) If a magnetic field is applied, the nuclei precess at the same rate - the Larmor frequency. There will be no net contribution to the magnetisation in the direction perpendicular to the field, but due to the slight excess of nuclei in the low-energy state there will be a component of \underline{M} in the direction of B_0 .

2.1.5 <u>The Classical Model as an idealised generalisation of the quantum-</u> mechanical description.

The classical model which has been adopted to this point, and will be further utilised, is a convenient model to adopt in order to appreciate some of the phenomena of NMR. However it should be noted that a quantum-mechanical model should strictly be used to investigate all NMR phenomena, but that for spins of I=1/2, the classical model agrees with the predictions of the quantum model for an isolated nucleus. This is not the case for spins of I=1 and greater.

2.2 <u>The Rotating Frame.</u>

In order to detect <u>M</u>, the bulk magnetisation, it is necessary to perturb the magnetic moment. <u>M</u> will then precess around the main field at a frequency \underline{w}_0 in a similar way to $\underline{\mu}$. If a second rotating field <u>B</u>₁ is applied perpendicularly to <u>B</u>₀ at a frequency \underline{w}_0 , the rotating <u>B</u>₁ field causes <u>M</u> to tilt away from its equilibrium position <u>M</u>₀. In the lab frame, <u>M</u> will follow a complex (spiral) path and so it proves convenient to transform to a frame of reference rotating in synchronism with the rotating <u>B</u>₁ field. Any Cartesian frame of reference is defined by the position of its axes x,y,z. Let $\underline{\hat{i}}$, $\underline{\hat{i}}$, <u>k</u> be the unit vectors defining the directions of the x,y,z axes in our arbitrary rotating frame. Then

$$\underline{M} - M_{x}\underline{\hat{i}} + M_{y}\underline{\hat{j}} + M_{\underline{k}}\underline{\hat{k}}$$
(16)

The time derivative of \underline{M} is

$$\frac{d\underline{M}}{dt} = \frac{\partial M_x}{\partial t} \hat{\underline{i}} + M_x \frac{\partial \hat{\underline{i}}}{\partial t} + \frac{\partial M_y}{\partial t} \hat{\underline{j}} + M_y \frac{\partial \hat{\underline{j}}}{\partial t} + \frac{\partial M_z}{\partial t} \hat{\underline{k}} + M_z \frac{\partial \hat{\underline{k}}}{\partial t}$$
(17)

$$-\left(\frac{\partial M_{x}\hat{l}}{dt} + \frac{\partial M_{y}\hat{l}}{dt} + \frac{\partial M_{z}\hat{k}}{dt}\hat{k}\right) + \left(M_{x}\frac{\partial\hat{l}}{dt} + M_{y}\frac{\partial\hat{l}}{dt} + M_{z}\frac{\partial\hat{k}}{dt}\right)$$
(18)

Now $\hat{1}, \hat{1}, \hat{k}$ can, by definition, only change direction, and not length. Hence

$$\frac{\partial \hat{i}}{\partial t} - \underline{w}_{\lambda} \hat{i} \quad , \quad \frac{\partial \hat{j}}{\partial t} - \underline{w}_{\lambda} \hat{j} \quad , \quad \frac{\partial \hat{k}}{\partial t} - \underline{w}_{\lambda} \hat{k}$$
(19)

i.e. the frame rotates at w radians/s about an axis given by the vector w.

$$\therefore \left(\frac{d\underline{M}}{dt}\right)_{lab} - \left(\frac{d\underline{M}}{dt}\right)_{rot} + \underline{w}_{\Lambda}\underline{M}$$
(20)

but we know that

$$\left(\frac{d\underline{M}}{dt}\right)_{lab} - \underline{\gamma}\underline{M}_{\underline{A}}\underline{B}_{\underline{0}}$$
(21)

SO

$$\underline{\gamma M}_{\underline{A}} \underline{B}_{\underline{0}} = \left(\frac{d\underline{M}}{dt}\right)_{rot} + \underline{w}_{\underline{A}} \underline{M}$$
(22)

$$\Rightarrow \left(\frac{\dot{d}M}{dt}\right)_{rot} - \gamma M_{\Lambda} \left(\frac{B_0}{t} + \frac{w}{\gamma}\right)$$
(23)

$$\Rightarrow \quad \left(\frac{d\underline{M}}{dt}\right)_{rot} - \underline{\gamma}\underline{M}_{\underline{A}}\underline{B}_{eff} \tag{24}$$

where

$$\underline{B_{eff}} - \underline{B_0} + \frac{w}{\gamma}$$
(25)

and \underline{w}/γ is a fictitious field which appears in the rotating frame as a result of the transformation. In the rotating frame of reference, <u>M</u> precesses about <u>B_{eff}</u>, the effective magnetic field. Exactly on resonance, $\underline{w} = -\gamma \underline{B}_0 \implies \underline{B}_{eff} = 0$ (i.e. <u>M</u> remains stationery). The rotating frame is illustrated by Figure 12.

2.2.1 90 and 180 degree pulses.

As stated before, the application of a \underline{B}_1 field causes \underline{M} to tilt away from the equilibrium position \underline{M}_0 . The time for which \underline{B}_1 is applied (and also the strength of \underline{B}_1) will determine the final orientation of \underline{M} . The pulse length to allow \underline{M} to tip through 90° is known as a 90° pulse. A pulse time of double this gives a 180° pulse. In the rotating frame \underline{B}_1 is stationary and is arbitrarily set as lying on the x' axes. (In the rotating frame, $\underline{B}_{eff} = 0$, so that \underline{B}_1 is the only field, and \underline{M} therefore precesses around it. A 90° pulse is just long enough for \underline{M} to precess through a quarter turn before \underline{B}_1 is removed whilst a 180° pulse is long enough for \underline{M} to precess through a half turn.) Such pulses are important, because they can bring the magnetisation into the transverse plane, which is the only way of detecting the magnetization.

A 90° pulse will take \underline{M}_0 down onto the y axis as in Figure 13

An arbitrary pulse, with the system in equilibrium before the pulse will turn \underline{M}_0 through an angle α from z', where α is known as the flip angle, as illustrated by Figure 14



Figure 12 - The rotating frame.



Figure 13 - The effect of a 90° pulse in the rotating frame.



Figure 14 - The effect of an arbitrary pulse in the rotating frame.

2.2.2 <u>The Bloch equations, relaxation processes, T_{11} , T_{2} and T_{2}^{*} .</u>

Once <u>M</u> has been tipped away from its equilibrium state <u>M</u>₀, the exchange of energy between nuclei and from nuclei to the bulk of the material will cause <u>M</u> to return to <u>M</u>₀. Two types of decay of <u>M</u> can be distinguished.



Figure 15 - Transverse (spin-spin) relaxation.



Figure 16 - Longitudinal (spin-lattice) relaxation.

Transverse or spin-spin relaxation (Figure 15) occurs as the individual magnetic moments $\underline{\mu}$ which contribute to \underline{M} dephase under the influence of fluctuating local fields. A splitting up or fanning out of magnetisation occurs, causing M_{xy} to decay to zero with time constant T_2 . In longitudinal or spin-lattice relaxation (Figure 16) the nuclear magnetic moments lose energy to their surroundings, causing M_z to decay back to M_0 with time constant T_1 . In reality, both events occur simultaneously, although obviously $T_2 \leq T_1$ (as if $M_z \Rightarrow M_0$, then $M_{xy} = 0$). It should be noted that T_1 is a function of B_0 , whereas T_2 is approximately constant with field strength.

2.2.3 Bloch Equations

Relaxation modifies equation (24) so that

$$\left(\frac{d\underline{M}}{dt}\right)_{ot} = \underline{\gamma}\underline{M}_{\underline{A}}\underline{B}_{eff} - \frac{1}{T_2}\left(M_x\underline{\hat{i}} + M_y\underline{\hat{j}}\right) - \frac{1}{T_1}\left(M_z - M_0\right)\underline{\hat{k}}$$
(26)

which gives three simultaneous differential equations in \underline{M}_x , \underline{M}_y and \underline{M}_z describing the timevariation of the magnetization. The equations are greatly simplified if the pulse length $\ll T_1$ or T_2 , which is generally the case, so the relaxation can be neglected during the application of a \underline{B}_1 pulse.

2.2.4 Pseudo Relaxation

After the application of a 90[°] pulse to a system initially in equilibrium, <u>M</u> lies in the x-y plane. If there is some variation of <u>B</u>_o with position then <u>B</u>_{static} = <u>B</u>₀ + Δ <u>B</u>₀. Where Δ <u>B</u>₀ \neq 0, the magnetisation will precess in the rotating frame about Δ B₀ once <u>B</u>₁ has been switched off (Figure 17)



Figure 17 - Precession in the rotating frame.

If ΔB_0 is negative then precession will occur in the opposite direction. The net effect is to reduce the transverse component of magnetization and hence the NMR signal. A simple experiment would measure the signal decaying at a rate T_2^* where

$$\frac{1}{T_2^*} - \frac{1}{T_2} + \frac{1}{T_2^{inhom}}$$
(27)

so to measure T_2 it is necessary to remove or determine the effect of T_2^{inhom} given by

$$\frac{1}{T_2^{\text{inhom}}} - \gamma \Delta B_0 \tag{28}$$

2.3 <u>Measurement of NMR Parameters</u>

It is desirable to measure the relaxation times T_1 , T_2 (but generally not T_2^*) and the Proton Density (PD), which gives information about the amount of water in the sample. The basic NMR experiment is to apply a 90° pulse to a sample and then examine the returned NMR signal, as illustrated by Figure 18.



Figure 18 - Examining the FID

The B_1 signal is applied with a coil through which an alternating current is passed at what turns out to be a Radio Frequency (RF). In the simple case, the same coil will pick up the RF signal emitted by the sample as <u>M</u> dephases. The signal induced in the coil by the rotating transverse magnetisation following the B_1 pulse is known as the Free Induction Decay (or FID).

2.3.1 Proton Density

The initial height of the FID is proportional to the proton density. In imaging, a string of 90° pulses is applied separated by a time t_r. The pulse sequence is known as a saturation recovery (SR) pulse sequence (Figure 19). For a true Proton Density image (as opposed to a Proton Density weighted image), a t_r of \geq 5*T₁ seconds is required to allow full relaxation to occur. Since T₁ is typically of the range 100-400 ms, t_r will typically be of the range 0.5-2s. With shorter repetition times, the image will have some degree of T₁ weighting. For technical reasons there is always a short Spin-Echo inserted in the sequence, although this is not shown in Figure 19.



Figure 19 - The Saturation Recovery spin-sequence.

2.3.2 T₁ Measurement

A 180- τ -90 or Inversion Recovery (IR) pulse is used for T₁ measurement (Figure 20). The 180° pulse flips <u>M</u> onto the z-axis, and after a delay the recovered <u>M</u> is then flipped into the x-y plane and its magnitude measured. To measure T₁ accurately, the experiment is carried out several times with varying τ , to allow a decay curve to be built up for the M_z magnetization. A least squares fit is then carried out to give T₁. In imaging, it is common to simply use two points. For technical reasons, the sequence normal contains a spin-echo with a short echo time.



Figure 20 - The Inversion-Recovery spin-sequence.

2.3.3 T, Measurement

In order to measure T_2 values, it is necessary to separate the irreversible decay of M_{xy} caused by spin-spin relaxation from the reversible decay caused by main-field non-uniformity (ΔB_o) . This is achieved by the Hahn spin-echo [HAHN50] which, in its simplest form, is a 90- τ -180- τ -echo as illustrated by Figure 21.



Figure 21 - The Spin Echo spin-sequence.

In the rotating frame, six key events can be identified, as shown by Figure 22

- (1) magnetization in phase
- (2) magnetisation dephasing leading to an FID signal

- (3) magnetisation flipped through 180°
- (4) build up of echo
- (5) magnetization back in phase at echo peak
- (6) decay of echo

The 180° pulse reverses the sign of ΔB_0 , cancelling out the effect of T_2^* , but has no effect on T_2 . The faster and slower precessing spins are compensated for by the 180° pulse.



Figure 22 - The Spin Echo sequence in the rotating frame.

2.3.4 Gradient Echo Imaging

The conventional spin echo experiment acquires one line of data using a 90°/180° pulse pair. The 90° pulse generates transverse magnetisation, which is subsequently read in the form of a spin-echo created by the subsequent 180° pulse. Transverse magnetisation may of course, be generated by pulses with flip angles much smaller than 90°. Such pulses allow the spin system to relax back to a given degree of magnetisation more quickly than a 90° pulse since most of the magnetisation is never disturbed. This therefore allows the use of shorter repetition times (TR) without obtaining only heavy T₁-weighting. To do this a 180° pulse can not be used, so a gradient echo is used, rather than a spin echo as described in section 2.4.4.

2.3.5 Sequence Notation.

The sequence notation that I intend to use is largely based on the American College of Radiology glossary of NMR terms [ACR83] and is one that has evolved in recent years, although it is not complete (for example the duration of data collection is not included). Its form is A /t_r /t_I /t_{e1}, t_{e2}, t_{e3},... / θ where A is a two letter sequence code (eg PS for Partial Saturation sequence etc.), t_r (ms) is the repetition time of the sequence, t_I (ms) is the time between the magnetization inversion pulse and the 90° data interrogating pulse (this term is only used for IRs), t_e (ms) is the time to echo, whether a gradient echo (field-echo) or spin-echo and θ is the flip angle (for sequences where angles other than 90° are utilised, such as gradient echo sequences etc.)

Several acronyms are used to describe Signa spin echo imaging. MEMP (Multiple Echo Multi-Planar) is a sequence with 1, 2 or 4 echoes, where each echo is separated from the previous echo by a delay equal to the first echo time (eg SE/3000/20,40,60,80 for a 4 echo train with the first echo at 20 ms). VEMP (Variable Echo Multi-Planar) is a two echo sequence for which the second echo time is independent of the first echo time (eg SE/3000/32,87). The shape of the slice profiles (see section 2.4.2) for MEMP and VEMP means that a slice skip equal to half the slice width is recommended to avoid crosstalk. CSMEMP (Contiguous Slice Multiple Echo Multi-Planar) and CSVEMP (Contiguous Slice Variable Echo Multi-Planar) are versions of MEMP and VEMP which have squarer slice profiles than MEMP and VEMP and are designed to be used for contiguous slice acquisition. Crosstalk is discussed in more depth in section 5.6, and Signa slice profiles in section 9.5.1.

2.4 Obtaining Spatial Information.

2.4.1 The Field Gradient

An essential part of any NMR imaging system is the magnetic field gradient since it allows spatial information to be obtained from analysis of the NMR signal. The field gradient is simply an additional magnetic field, whose amplitude varies linearly with position along a chosen axis. Field gradients are generated by passing currents through specially constructed 'gradient coils'. An imager has three pairs of gradient coils to generate magnetic field gradients along the three orthogonal axes x,y and z. Consider two bottles in an imager, with the direction of the field gradient as illustrated by Figure 23. The field gradient means that the resonant frequency will vary with x.



Figure 23 - The field gradient.

Frequency analysis of the total signal received following an NMR excitation leads to two amplitude pulses representing the positions of the two bottles. This is known as frequency encoding. Frequency encoding gives 1-D information, but at least 2-dimensions are required for

imaging. In the early days of NMR, reconstruction from projection methods were utilised such as those used in X-Ray Computed Tomography. Fourier Transform methods are now more common. [See section 2.4.3]

2.4.2 <u>Selecting a Tomographic Slice.</u>

If a slice through a sample is required instead of a shadowgram (as in a conventional X-Ray), only spins within a narrow slice should be excited (i.e. subject to a RF pulse). This can be achieved by a method known as selective excitation as illustrated below by Figure 24. Suppose it is desired to produce a slice in the x-z plane. A field gradient, G_y , is applied to the sample at the same time as a spectrally-shaped RF pulse. Only the spins within the narrow shaded strip are excited because only they have Larmor frequencies within the RF pulse's bandwidth.



Figure 24 - Slice selection.

For most NMR studies, the ideal slice is assumed to be parallel-sided and of rectangular section with its surfaces being positioned exactly along the required image plane. Non-uniformities of both main and gradient fields are major causes of non-ideality of the profile and RF non-uniformity is also of importance. These are generally minimised in the centre of the image plane, but can be considerable at the outer edges of the slice. Several RF envelope shapes are commonly used. A Gaussian RF envelope yields a near-Gaussian profile (the discrete Fourier transform of the RF envelope) which is not a good approximation of a rectangular profile. A

truncated sinc shaped RF profile provides a more rectangular profile, but one which has side lobes. These can be reduced by cosine apodization. Slice width is often defined by the FWHM of the slice profile, but it should be noted that this figure may be misleading in the case of some profiles, such as a Gaussian which possesses large side wings. A poor slice profile leads to signal from outside the desired area contaminating a slice and hence means that sharp edges are less well defined.

2.4.3 Fourier Transform Methods

The Fourier Transform (FT) group of imaging techniques derives from an idea presented by Kumar *et al.* [KUMAR75]. The fundamental idea is that a simple 1-D projection is the Fourier Transform of the FID as it evolves with time in the presence of a field gradient. If a second 'dimension' of time could be introduced, in which the FID effectively evolved in the presence of a second gradient at right angles to the first, then a 2-D Fourier Transform of the signal, expressed as a function of ordinary time and pseudo-time (the second dimension), would produce a 2-D image. The array of raw FID data is often referred to as Fourier space, or k-space. A useful approximation of pseudo-time can be obtained by subdividing real-time. This is illustrated by Figure 25. In FT imaging, the real-time evolution of the signal in one gradient is repeated many times. The second field gradient is applied in such a way that its effect increases with each repetition, thereby simulating the progress of pseudo-time. This second field gradient can be considered to introduce a phase 'twist' into each column of spins prior to collecting the FID. Hence this second field gradient is sometimes referred to as the phase-encoding gradient, whilst the first field gradient is referred to as the frequency-encoding gradient.

In Fourier zeugmatography the second field gradient has a constant amplitude with the pulse duration increasing with each successive pulse-FID (ie with the progress of pseudo-time). This has since been superseded by spin-warp imaging [EDELSTEIN80] in which the second field gradient is applied for a fixed duration, but its amplitude varies linearly with the progress of pseudo-time. The spin warp image-forming procedure can be (and is) incorporated into any of the pulse sequences described above.



Figure 25 - FID as a function of real time and pseudo-time.

2.4.4 <u>The Gradient Echo</u>

Consider the use of fast imaging techniques utilising small flip angles. A 180° pulse is not appropriate for echo generation in this situation because it would invert the longitudinal magnetization producing a non-equilibrium situation similar to that in an inversion-recovery pulse sequence. Instead, an echo can be generated by applying a negative gradient in the readout direction to dephase spins, immediately followed by a positive gradient which causes re-phasing. The signal is then sampled as illustrated by Figure 26. The echo is not a spin echo and any main field (B₀) non-uniformities will cause imperfect refocusing. This leads to T_2^* instead of T_2 weighting when using gradient echo sequences. The absence of a 180° pulse allows shorter echo times to be utilised. The speed of this approach means that volume data may be acquired where data are collected simultaneously from a slab of tissue using phase-encoding in a second dimension to encode for the different slices. Such an approach allows isotropic data to be acquired, and it is possible to have the "slice thickness" smaller than the in-slice voxel dimension.



Figure 26 - The gradient echo in a perfect field

2.5 Image Contrast

Image contrast in magnetic resonance imaging is a very complex and subtle process. NMR images may contain PD, T_1 and T_2 information. As well as this, flow, chemical shift, paramagnetic contrast agents, perfusion and diffusion also affect the image contrast, although this discussion will be limited to PD, T_1 , T_2 and contrast agents. The amount of contribution of each characteristic is determined by the nature and timing of the pulse sequence used to collect the NMR signal. Differences in main field strength and the RF will make small differences in the effects of a given pulse-sequence timing between imagers. Image intensity is linearly related to both spin density and receiver coil sensitivity. It should be noted that protons in various types of homogeneous tissue that differ in their molecular environments will exhibit characteristically different values of their relaxation constants T_1 and T_2 because of the difference in proton mobility.

2.5.1 Contrast in Common Sequences.

The most commonly used imaging sequences are Inversion Recovery (IR), Saturation Recovery (SR), Spin Echo (SE) and Rapid Imaging techniques. Although the precise details of sequences differs between imagers, the basic form of the sequences is as shown in Figure 19 - Figure 21. Briefly the contrast dependency of the main sequences are as follows. **Inversion Recovery** : the signal produced by the Inversion Recovery sequence is dependent on PD and T_1 , but not greatly on T_2 . The NMR signal can be positive or negative, although it is not possible to determine which, and therefore the signal modulus is often displayed. **Saturation Recovery** : the signal contains PD information weighted by the amount of T_1 relaxation which has occurred

during the interval T_r . If T_r is long then the relaxation will be complete and only PD information will be available. **Spin Echo** : the SE sequence provides PD information which can be weighted by T_1 , and/or T_2 relaxation. **Rapid Imaging** : gradient echo sequences such as FLASH, SSFP, FISP and GRASS produce images weighted with a mixture of PD, T_1 and T_2 .

2.5.2 Contrast Media

The contrast between tissues can be varied by administering various external agents either orally or intravenously. Generally, contrast media are based on paramagnetic materials of some type which reduce relaxation times due to the fact that they are strongly paramagnetic with one or more free electrons - which have a much larger magnetic moment than is associated with hydrogen nuclei. Gadolinium-DTPA usage has been widely used for diverse investigations.

2.5.3 **Quantitative Images**

It is possible to produce quantitative images, where the image brightness is simply proportional to T_1 , T_2 or PD, by using self normalising sequences and analysis methods. Such sequences allow correction for non-uniformity (primarily RF) in the images by varying the parameter of interest (such as T_R or T_E) whilst retaining the non-uniformity. [See section 2.6 on artifacts.] Quantitative T_2 images can be generated by incorporating more than one echo into a spin-echo sequence (ie a multiple-echo sequence). In general it is necessary to acquire a number of images to calculate quantitative images. If one parameter can be held constant, it is usually possible to obtain T_1 or T_2 images from two standard images. To obtain T_1 , T_2 and PD images, three standard images are required. It is important to distinguish carefully between such $T_1/T_2/PD$ calculated images and $T_1/T_2/PD$ weighted images.

2.5.4 Synthetic Images.

Knowing PD, T_1 and T_2 for a sample from a set of images, it is possible to synthesise other images with different timing parameters, by using knowledge of the spin sequence and the Bloch equations. This has proved useful in deciding upon which sequences to use for new applications.

2.6 Artifacts

A good definition of an artifact is given by Foster and Hutchinson [FOSTER87]. They state that "in imaging technology, an artifact is a feature appearing on the image which does not correspond to the properties of the subject in the corresponding region." An artifact may arise from the equipment itself, from some unwanted interaction between the subject and the imaging equipment, or from an external cause. In NMR, artifacts manifest themselves as local errors such as stripes or single pixel errors, or features displaced from their 'correct' position, the latter commonly being known as aliases.

Respiratory and cardiac motion lead to regular aliases. Irregular motion such as single patient movements cause a more featureless smear in the phase-encoding direction. Spin sequence artifacts and machine imperfections may lead to ghosting, lines or incorrect contrast. Flow artifacts from blood and CSF show up as streaks inside and outside the sample in the phase-encoding direction often at the level of the ears in brain scans. (This is different from the contrast due to flow.) It should be noted that the phase-encoding direction is technically different from the other two orthogonal directions.

There are various types of non-uniformities to which NMR images are susceptible. The non-uniformity of the main field B_0 has an important effect on gradient-echo images, whilst RF non-uniformity affects Spin-Echo images adversely. RF non-uniformities are of particular importance in quantification. Particular emphasis should be placed upon the difference between transmission and reception non-uniformity. This will depend upon whether the same coil is used to transmit and receive the RF signal (such as most body-coils) or not. Surface coils tend to be receive coils only and are particularly susceptible to receive non-uniformity. There are various types of correction that can be used for non-uniformity which are discussed in chapter 5.

Other problems include the ringing at sharp edges known as the Gibbs artifact, which is a feature of the Fourier Transform image reconstruction, mis-registration of image slices and distortions of the main magnetic field by ferromagnetic materials.

2.7 Properties Of NMR Image Data

2.7.1 <u>Noise</u>

In NMR images the noise is generally independent of signal strength. With reasonable amplification circuitry the amplifiers add little noise and the main source will be Johnson noise due to the thermal motion of ions in the body. There is a slight difference at zero signal where rectification may lead to negative values of noise being inverted. In this case, the noise is described by a Rayleigh rather than a Gaussian distribution.

2.7.2 Edge Response

The step-edge is often proposed as a model for an ideal edge in an image. There are a number of factors which mean that edges in an NMR image will not be an ideal step-edge.

The image slice is not (in general) perpendicular to the tissue border.

• The finite size of a pixel/voxel leads to a slight curve being introduced at the first and last pixels of an edge.

• The actual slice profile is imperfect as already discussed.

• The pixel profile in the x and y directions is also imperfect. The phase-encode direction is worse, with some of the signal being contributed from several pixels away. The more phase-encode steps there are, the closer the profile is to the ideal. The difference between phase-encode and read direction comes from the fact that the phase-encoding process starts and ends abruptly, effectively multiplying the time domain response in the phase encode direction, by a top-hat function which becomes a sinc function following a Fourier Transform. In the read direction, the top-hat in the time domain is softened by the (physical) filtering that takes place.

- Noise.
- Tissue inhomogeneity will affect an extended step edge.
- RF non-uniformity will affect a largely extended step-edge.

■ The lack of a classic border between some tissue types (i.e. the lack of a sharp boundary between tissues, for example in the case of grey and white matter where the two tissue types may coexist at the cellular level.)

• The T_2^* effect may lead to a gaussian blurring because of the shape of the FID envelope. This
2.8 Instrumentation.

Most imagers use similar basic hardware. Figure 27 shows a general block diagram of the essential components of an NMR imager. The principal items of hardware are

■ The magnet - magnets for NMR imaging are generally of two distinct types, namely air-cored resistive or superconducting, although permanent magnets are infrequently used.

• Three sets of field gradient windings and their drivers. In most imaging systems, three orthogonal field gradients must be provided.

• The RF transmitting and receiving coil(s) and their electronics. The radiofrequency system is designed to apply RF electromagnetic field pulses to the appropriate region of the patient, and to receive the weak FID emanating from the patient. One coil may be used for transmitting (emitting) and receiving the signals. Often, however, RF pulses are applied via a large 'body-coil', with the receiver being any one of a large number of different coils especially designed to receive signals from particular parts of the body. In the study of multiple sclerosis, head coils, spinal coils and optical coils are commonly used. A Faraday shield surrounds the entire imager coil in order to stop external RF interference reaching the receiver coil.

A reference oscillator operating at or near the Larmor frequency.

A timing controller.

■ A data acquisition and processing system. The data processing is required to collect the incoming data, perform the various Fourier Transforms and other calculations, and to file and archive the images. It also translates the user's commands and set up the appropriate pulse sequences as required.

■ an image display.

.



Figure 27 - Block diagram of basic components of an NMR imager.

CHAPTER 3

MAJOR CATEGORIES OF IMAGE SEGMENTATION

3.1 Introduction

Image segmentation has been approached in numerous ways by various authors in an attempt to produce practical solutions to problems in image analysis. The aim of segmentation is to isolate objects. A region that corresponds to a physical entity, has borders and exhibits contrast between the interior and the surrounding grey levels is often referred to as an object. The basic approaches to segmentation may be considered to be divided into three main categories of medium level approaches. Region-based methods make use of similarities between pixels and may be divided into thresholding, region growing and clustering. Such approaches may be contrasted to edge detection which focuses on the changes which occur at the boundaries between regions. The final category is multi-resolution algorithms which often produce a hierarchical description of an image. The major approaches within each category of segmentation are considered within this chapter.

3.2 <u>Thresholding</u>

Thresholding is most commonly used to separate an object from a background. Several methods of thresholding are also applicable to images containing three or more homogeneous regions and these methods will be dealt with later. Thresholding is commonly applied to cytology images, images of printed or written documents and cloud cover images. Thresholding works well in situations where object and background are homogeneous or smooth, but tends to yield poor results when applied to textured images. In its most general form, thresholding can be mathematically described as

$$S(x,y) - k \text{ if } T_{k-1} \le g(x,y) < T_k \quad k=0,1,...,m$$
 (29)

where (x,y) are the pixel coordinates, S(x,y) and g(x,y) are the segmented and the grey level functions of (x,y) respectively, $T_0 \dots T_m$ are threshold levels with T_0 equal to the minimum and T_m the maximum grey levels in the image and m is the number of distinct labels assigned to the segmented image. It should be noted that although thresholding with respect to grey level is common, thresholding may be carried out with respect to texture or other local properties.

Weszka's early work (WESZKA78), widely acknowledged in the literature as one of the classic survey articles in image processing literature and recently updated by Sahoo *et al.* (SAHOO88), gives a general form for a threshold operator. The form is as a test involving a function T of the form T(x,y,N(x,y),g(x,y)) where (x,y) are the coordinates of the pixel, N(x,y) represents the neighbourhood of (x,y), and g(x,y) denotes the grey level of pixel (x,y). This notation aids the division of thresholding into three categories - global, local and dynamic thresholding. A global threshold is one where the threshold is chosen only on the grounds of the value g(x,y) at (x,y). If the threshold depends on both g(x,y) and N(x,y) then the operation is local. Finally if T depends upon (x,y) as well as g(x,y) and N(x,y) then the thresholding is termed dynamic.

3.2.1 Global Threshold Selection.

3.2.1.1 <u>Techniques Based on Grey Level Histograms.</u>

The p-tile method (an abbreviation for percentile) was one of the earliest automatic thresholding methods and was first suggested by Doyle (DOYLE62). This method uses the grey-level histogram to threshold simple images in situations where the object grey-levels are distinct from the background grey-levels and occupy a known fraction of the area of the image. For example if the object were known to occupy 70% of the image and the background 30% and the object has higher grey levels than the background, then a threshold is chosen so that 30% of the pixels in the output image are below the threshold and 70% above.

Prewitt and Mendelsohn (PREWITT66) suggested using the valleys in the histogram to define a threshold. Their method is known as the mode method. It is based upon the assumption that the white blood cells in the cytological images they were working with could be assumed to represent one peak in the grey-level histogram, the background a second peak and the edge pixels the valley in between these peaks. This yields a histogram termed as bimodal as opposed to a unimodal histogram with a single peak. In unimodal histograms pixels are most often presumed to be due to either the object, the background or the edge pixels alone. The mode method works well for images of white blood cells, but not so well for images with extremely unequal peaks or with broad and flat valleys in their histograms.

Ostu (OSTU78) suggested a global thresholding method based on discriminant analysis. With the pixels of an image divided into two classes at a threshold, three variances can be calculated - the within-class variance, the between class variance and the total variance. An optimal threshold can be determined by minimising the ratio of class variance to total variance where σ_B^2 and σ_T^2 are the between class variance and the total class variance respectively. These are given by

$$\sigma_T^2 - \sum_{i=0}^{l-1} (i - \mu_T)^2 p_i \qquad \qquad \mu_T - \sum_{i=0}^{l-1} i p_i \qquad (30)$$

$$\sigma_B^2 - w_0 w_1 (\mu_1 \mu_0)^2 \qquad w_0 - \sum_{i=0}^t p_i \qquad w_1 - 1 - w_0 \qquad (31)$$

$$\mu_{1} - \frac{\mu_{T} - \mu_{t}}{1 - w_{0}} \qquad \mu_{0} - \frac{\mu_{t}}{w_{0}} \qquad \mu_{t} - \sum_{i=0}^{t} i p_{i} \qquad (32)$$

where t is the proposed threshold, 1 the total number of grey levels in the image and $p_i = n_i / n$.

Several authors have recently suggested methods where the optimal threshold is obtained by applying information theory. These include Pun [PUN80 and PUN81], Kapur [KAPUR85] and Johannsen and Bille [JOHANNSEN82]. Other methods include a moment preserving method where the moments of an image to be thresholded are preserved in the binary output image [TSAI85] and the minimum error method [KITTLER86] which is based upon the minimisation of a criterion representing the probability distribution function of the object and background, their standard deviations, means and a priori probabilities.

3.2.1.2 The Use of Edge Strengths to 'Improve' Histograms.

The methods discussed to this point have been global methods where the grey level histogram is used to determine a global threshold. However local properties have also been used to this end. Two groups have used edge detectors to determine edge pixels and hence 'improve histograms'. Mason *et al.* [MASON] have used a gradient image to weight non-edge pixels in the histogram so as to make histogram valleys deeper and allow the use of a mode method. This has proved fairly successful, although not all valleys are considerably deepened. Weszka *et al.* [WESZKA73a] have suggested another gradient method, based on the Laplacian operator. This has proved advantageous in situations where the histogram valley is broad and the peaks are unequal in size where it is often difficult to choose a threshold. The grey level values of the edge pixels give a more strongly bimodal histogram than the original image, again allowing the use of a mode method.

3.2.1.3 Edge Strengths as an Aid to Threshold Selection.

Instead of using a gradient operator to improve histograms, other authors have used values of local properties to directly compute a threshold for an image. These techniques involve taking a histogram only of pixels which have a high gradient value. As before, these pixels lie on or near the borders of objects, and tend to have a bimodal grey level histogram. However if less and less pixels are used to determine the histogram (i.e. if pixels with higher and higher values

of gradient are used) then a single mode is produced. If a low number of pixels is used, then whether the edge histogram is bimodal or unimodal, the average grey-level of the filtered points should be a reasonable place to threshold the image because this corresponds to the most likely edge position. Both Katz [KATZ65] and Weszka and Rosenfeld [WESZKA75] used this method. Further work using differencing operators was also carried out by Watanbe [WATANBE74] and Weszka *et al.* [WESZKA73b] which achieved good results with cell images, but poor results with images of chromosomes, handwriting and cloud cover.

3.2.1.4 The Co-Occurrence Matrix and Thresholding.

One of the drawbacks of the techniques so far described is that apart from the gradient methods, they calculate a global threshold based solely on first-order grey level statistics (i.e. the grey level histogram). Several methods improve on this by using second-order grey-level statistics. Haralick [HARALICK73] introduced the co-occurrence $M_{(d,\phi)}$ matrix for texture analysis, whose entries are the relative frequencies of occurrence of two neighbouring pixels with grey levels i and j separated by a distance d with an orientation ϕ . Ahuja and Rosenfeld [AHUJA78] used the 4-connected neighbours of a pixel to construct a co-occurrence matrix. Because of homogeneity, pixels interior to objects or background should contribute mainly to the neardiagonal entries of M, whilst pixels near an edge should contribute mainly to the off-diagonal entries of M because of the grey-level change near an edge. Therefore the matrix M can be used to define histograms from the near-diagonal and off-diagonal entries of M, which should have the appearance of a deep valley between object and background grey levels and a sharp peak between the object and background grey levels respectively. A threshold for the image is then chosen from the grey level range in which the valley from the near-diagonal pixels overlaps with the peak in the off-diagonal pixels. Two similar methods are Kirkby and Rosenfeld's (Grey level, local average) scatter plot method [KIRKBY79] and a method by Deravi and Pal [DERAVI83].

3.2.1.5 <u>Relaxation Methods.</u>

Southwell first introduced the idea of relaxation to improve the convergence of recursive solutions for systems of linear equations [SOUTHWELL40, SOUTHWELL46]. When relaxation is applied to thresholding, the pixels of an image are first probabilistically classified into object and background on the basis of their grey level. Then the probability of each pixel

is adjusted according to the probabilities of the neighbouring pixels. One attractive feature of relaxation methods is that they are parallel-processing techniques as opposed to the sequential techniques described so far. This approach has been researched by Rosenfeld and Smith and others [ROSENFELD81, FEKETE81, PAVLIDIS77, PELEG80]. Bhanu and Feugaras [BHANU82] have used a similar method with gradients by maximising a criterion function with gradient optimization.

3.2.2 Local Thresholding Methods.

Local threshold selection techniques have been widely used for optical character recognition which must deal with a wide variation in print quality distortion over a single document, and even a single character. Bartz [BARTZ69] used the average contrast over previously scanned characters, whereas Wolfe [WOLFE69] and Ullmann [ULLMANN74] both used local neighbourhoods, Wolfe of 4x4 and Ullmann of 5x5 pixels to select a threshold. Researchers have also used the gradient, calculated over a local neighbourhood. Both Morrin [MORRIN74] and Panda [PANDA77] have used this method. Panda has also suggested several segmentation procedures that yield tri-modal distributions in the plot of frequency of occurrence as a function of grey level and edge value. The three modes in this joint histogram correspond to points interior to the object, points interior to the background and points on the border between the two.

3.2.3 Dynamic Thresholding.

A dynamic thresholding technique widely quoted in the literature has been suggested by Chow and Kaneko [CHOW72] for detecting boundaries in radiographic images. Their method was designed for low quality radiographic images where the contrast varies across the image, making a global threshold inappropriate. A local histogram and a variance are calculated for overlapping 7x7 windows in the image and the histogram classed as bimodal or unimodal depending upon how well it fits a model of one or two normal distributions. Bimodal distributions are likely to occur on the boundaries of objects. The threshold for each pixel is determined by interpolation between the nearest windows, the threshold value depending on the pixels proximity to boundary points (or their neighbours). Thresholds for boundary points are determined from the model of the two normal distributions in the appropriate local window. Fernando and Monro [FERNANDO82] have used 16 non-overlapping regions and applied the entropic thresholding technique of Pun [PUN80] in each of these regions to determine a threshold value. The entire thresholded image is then finally processed by a low-pass filter to eliminate the grey level discontinuities at region borders. Yanowitz and Bruckstein [YANOWITZ89] propose a method where the threshold level varies over different image regions to fit the spatially changing background and lighting conditions as illustrated by Figure 28 - in other words a threshold surface. This is necessary for automated visual inspection where it is required to separate objects from the background in conditions of poor and nonuniform illumination. This surface is determined by interpolating between points of the original image where the gradient is high, indicating probable edge points. The threshold surface thus obtained is used to segment the image.



Figure 28 - Yanowitz and Bruckstein's Method of Threshold Determination.

3.2.4 Multithresholding Methods.

Many of the methods previously mentioned can be extended to the case of multi-thresholding. These include the methods of Ostu [OSTU78], Pun [PUN80, PUN81], Kapur *et al.* [KAPUR85], moment preserving [TSAI85] and minimum error [KITTLER86]. Other multi-thresholding approaches include that due to Boukharouba *et al.* [BOUKHAROUBA85] where the intrinsic properties of cumulative distribution frequencies (the integral of the histogram) are utilised. Zeroes of the curvature of the cumulative distribution function determine the thresholds as well as the grey level to be assigned to each class. The curvature will be noisy

and oscillatory and should therefore be smoothed and approximated for thresholding. Wang and Haralick [WANG84] propose a recursive technique where pixels are initially classed as edge or non-edge, and edge-pixels classed as dark or relatively dark according to their local neighbourhood, and two edge histograms constructed. A threshold is selected from the higher peak of the two histograms. The procedure is recursively applied using only those pixels whose intensities are smaller than the threshold first and then using only those pixels whose intensities are larger than the threshold. Uniform contrast is another recursive selection procedure which was proposed by Kohler [KOHLER81]. The method is based on the idea that the optimum threshold for image segmentation is that threshold which detects more high contrast edges and less low contrast edges than any other. A histogram of the average contrast for each possible threshold, $\mu(t)$ is constructed where $\mu(t) = C(t) / N(t)$, C(t) being the total contrast detected by threshold t and N(t) the number of edges detected by t. The peak of the histogram is taken as the threshold. For multi-thresholding, any initial threshold is first selected and then a new histogram of $\mu(t)$ computed by removing the contribution of the already detected edges by the initial threshold. The procedure continues until the maximum average contrast for any threshold falls below some minimum average contrast $\theta > 1$.

3.3 Edge detection.

3.3.1 Introduction.

No single mathematical definition of an edge exists that covers all images, because of factors such as edge shape, sampling, noise and blur etc., and hence verbal definitions are often kept informal deliberately. A description as the boundary between two adjacent extensive homogeneous regions, where an image property changes abruptly as the border between the two regions is crossed, is perhaps as good a description as any. The image property is often grey level and sometimes texture, but is not limited to a choice of these two. Edge detection is of interest for applications other than segmentation. It is efficiently implemented in biological visual systems, and so a significant part of the advances in edge detection are provided by research work in this field. Edge detection from this viewpoint has been reviewed by Brady [BRADY82]. It is also of interest for image registration, stereo vision and inference of 3-D structure from motion, for example the determination of 3-D structure of an object from a series of natural

scene images in which the object moves. These applications will not be discussed any further, however.

3.3.1.1 <u>The Ideal Step Edge.</u>

Many papers model an edge as an ideal step edge, as shown in Figure 29. Depending upon the class of image being analyzed, it is possible to encounter a range of edge cross sections such as roof and spike edges. For example spike edges are obtained from lines in an image, and roof edges appear in natural scene images of solid objects which contain surfaces at different orientations meeting at sharp angles. However the step edge is normally the model of interest for most edges. Even if an ideal step-edge does occur in the original 'scene' from which the image is taken, the edge would be subject to the effects of sampling, noise, blurring and other application specific degradations. Hence the edge in the image is often a noisy ramp. If edges are diffuse as in the case of a roof edge, it is impossible to locate them sharply by means of a small operator. It should be noted that edge operators are generally designed to give a maximal response for the edge model they are based upon. However factors such as noise etc., may lead to a high response from areas of the image which do not correspond to edges.

3.3.1.2 <u>Problems Associated with Edge Detection.</u>

There are many inherent problems associated with edge detection. First only rarely can an adequate model of an edge be defined that will hold over the whole image (since most images are not homogeneous) or over all images of a given application. Boundary placement also presents problems in environments with noise, texture, slowly varying gradients etc. Finally since edge detection does not necessarily produce a complete segmentation, further procedures for edge linking and edge cleaning are required to organise the resulting edges. Many dozens of edge-detection methods have been proposed in the literature and this is not the place for an extensive review of these. Instead the basic approaches behind a large number of these edge-detectors will be presented, a few of the more popular methods focused on and some commonly applied methods of post-processing for edge-images presented. Davis *et al.* [DAVIS75], Riseman *et al.* [RISEMAN77], Rosenfeld *et al.* [ROSENFELD82], Pavlidis [PAVLIDIS77] and Fu and Mui [FU81] have all reviewed a number of edge-operators in greater detail.



Figure 29 - Edge types.

3.3.2 Parallel Edge Detectors.

The following methods can all be described as parallel methods because each pixel could be independently processed. This has advantages in that given a suitable architecture, each pixel could be processed in parallel. This is as opposed to the sequential methods such as surface tracking and contour following where pixels are processed in order. These are reviewed later.

3.3.2.1 <u>High Emphasis Spatial Filtering.</u>

One approach to edge detection is the use of a spatial frequency filter [DUDA73]. A basic result from Fourier analysis is that high spatial frequencies are associated with sharp changes in intensity. So by multiplying in the Fourier domain or convolving in the spatial domain with a high pass filter (i.e. one that attenuates the low spatial frequencies and enhances the higher ones) the high frequencies which correspond to edges will be enhanced. One problem is that noise dominates the very high frequencies, so a filter must also attenuate these frequencies. Hence low frequencies corresponding to background structure and extremely high frequencies corresponding to noise are attenuated, whilst the high frequencies corresponding to edges are enhanced. The problem becomes one of optimum filter design.

3.3.2.2 Directional Derivative Methods.

The idea underlying a large number of edge detectors is the computation of a local derivative operator. If f(x,y) represents the grey-level of an image at (x,y) then the simplest edge detector for say horizontal edges would be to compute |f(x,y) - f(x,y+1)|. If this value is high, then there is a horizontal edge between the two points. This is the digital analog of the directional derivative of the picture along the direction orthogonal to the edge we are looking for. Many methods of edge detection use small spatial masks to compute a discrete approximation of a local derivative.

The Gradient.

If a directional derivative were to be used as a measurement of edge strength, its response would vary with the orientation of the edge. To avoid this the magnitude of the gradient is usually used, since this automatically gives the rate of change in the direction of greatest steepness. The Gradient of an image f(x,y) at (x,y) is defined in two dimensions as the vector.

$$\underline{G}[f(x,y)] = \begin{bmatrix} G_x \\ G_y \end{bmatrix} = \begin{bmatrix} \frac{\partial f}{\partial x} \\ \frac{\partial f}{\partial y} \end{bmatrix}$$
(33)

 \underline{G} is orientated in the direction of maximum rate of change of f at (x,y). For edge detection the magnitude of this vector is of interest, generally referred to as the gradient and denoted under a Euclidean metric by

$$G[f(x,y)] = [G_x^2 + G_y^2]^{1/2}$$
(34)

which is often approximated by the City Block Magnitude Gradient (CBMG)

$$G[f(x,y)] \approx |G_x| + |G_y|$$
(35)

The orientation of the gradient is given by

$$\alpha(x,y) - \tan^{-1} \left[\frac{G_y}{G_x} \right]$$
(36)

Computation of the gradient is based on obtaining the partial derivatives $\partial f/\partial x$ and $\partial f/\partial y$ at every pixel location. For a digital picture, first differences rather than first derivatives are used. i.e. the difference in grey levels between neighbouring pixels.) Therefore

$$\Delta x_f(x,y) \equiv f(x,y) - f(x-1,y) \tag{37}$$

and

$$\Delta y_f(x,y) \equiv f(x,y) - f(x,y-1) \tag{38}$$

These are digital convolutions which convolve f with the patterns

.....

$$\begin{bmatrix} -1, 1 \end{bmatrix} \quad and \begin{bmatrix} 1 \\ -1 \end{bmatrix} \tag{39}$$

 Δx_f and Δy_f could be combined by taking $(\Delta x_f^2 + \Delta y_f^2)^{1/2}$ but this would not strictly be a correct approach, since the differences these operators measure are not symmetrically located with respect to (x,y).

The Roberts operator is given by |f(x,y) - f(x+1,y+1)| + |f(x,y+1) - f(x+1,y)|[ROBERTS65] and detects horizontal or vertical edges. Both of these operators compute the finite differences about (x+1/2, y+1/2). A small operator such as this is very susceptible to the effects of noise. A simple extension of this is to compute the difference of the average greylevels of two one-dimensional neighbourhoods on opposite sides of a point, to measure 'central differences' as below.

$$\left| \frac{1}{\Delta} \sum_{n=1}^{\Delta} g(i,j+n) - \frac{1}{\Delta} \sum_{n=1}^{\Delta} g(i,j-n) \right| = \frac{1}{\Delta} \left| \sum_{n=1}^{\Delta} (g(i,j+n) - g(i,j-n)) \right|$$
(40)

This avoids the problem of having an approximation to the gradient at a point between pixels. For n=1 the values of the edge operators are the convolution of f with

$$\begin{bmatrix} -1 & 0 & 1 \end{bmatrix} \quad and \begin{bmatrix} 1 \\ 0 \\ -1 \end{bmatrix} \tag{41}$$

Averaging over many points reduces the effect of noise to a great extent and is also more appropriate for detecting broader edges. However there is a trade off with the localisation ability of larger operators. Many such operators have been suggested. ([HUECKEL73], [BULLOCK74], [FRAM75], [McKEE75], [MARR75])

The Laplacian.

The Laplacian is a second-order derivative operator defined as

$$L[f(x,y)] - \sum_{i=0}^{n} \frac{\partial^2 f}{\partial x_i^2}$$
 (42)

in n-dimensions, where x_i represents a dimension. Since peaks in the first-order derivative of a function correspond to zeroes in the second-order derivative of this function, edge detectors can

be designed by computing an approximation to the second order derivative and looking for zerocrossings. The Laplacian is an orientation-invariant derivative operator. Its analogue for digital pictures is given by

$$(\nabla^2 f)(i,j) \equiv [f(i+1,j) + f(i-1,j) + f(i,j+1) + f(i,j-1)] - 4f(i,j)$$
(43)

which is the digital convolution of f with

$$\begin{bmatrix} 0 & 1 & 0 \\ 1 & -4 & 1 \\ 0 & 1 & 0 \end{bmatrix}$$
(44)

It is of particular interest to construct directional derivative operators that are isotropic i.e. rotation invariant (in the sense that rotating f and then applying the operator gives the same result) as such operators will detect edges of any orientation. The Laplacian is seldom used by itself for edge-detection because a second derivative is typically unacceptably sensitive to noise. The effects of noise on the responses of a difference operator can be reduced by smoothing the image before applying the operator, and this approach has been successfully applied by Marr and Hildreth [MARR80].

3.3.2.3 Edge Matching.

Gradient operators estimate the edge magnitude and direction at a point using difference operators in two perpendiculars directions. Another approach is to match local patterns or fit surfaces to the image at the given point.

Mask Matching.

In choosing edge patterns or masks to match with a picture, it is customary to use masks that represent second differences of step edges. In a 3x3 neighbourhood a second-difference mask for a vertical step edge would have values

$$\begin{bmatrix} -1 & 0 & 1 \\ -1 & 0 & 1 \\ -1 & 0 & 1 \end{bmatrix}$$
(45)

which is the Prewitt operator Δ_{3x} [PREWITT70]. To detect edges by mask matching, a set of difference-operator-like masks are convolved, in various orientations, with the image. The mask giving the highest value at a given point determines the local edge orientation, and the value

determines the edge strength. Both Sobel [SOBEL] and Prewitt have presented masks of this type. For example, Sobel's operator corresponds to the following convolution masks.

$$\frac{1}{4} \begin{bmatrix} 1 & 2 & 1 \\ 0 & 0 & 0 \\ -1 & -2 & -1 \end{bmatrix} \qquad \frac{1}{4} \begin{bmatrix} 2 & 1 & 0 \\ 1 & 0 & -1 \\ 0 & -1 & -2 \end{bmatrix} \qquad \frac{1}{4} \begin{bmatrix} 1 & 0 & -1 \\ 2 & 0 & -2 \\ 1 & 0 & -1 \end{bmatrix} \qquad \frac{1}{4} \begin{bmatrix} 0 & -1 & -2 \\ 1 & 0 & -1 \\ 2 & 1 & 0 \end{bmatrix}$$
(46)

$$\frac{1}{4} \begin{bmatrix} -1 & -2 & -1 \\ 0 & 0 & 0 \\ 1 & 2 & 1 \end{bmatrix} \qquad \frac{1}{4} \begin{bmatrix} -2 & -1 & 0 \\ -1 & 0 & 1 \\ 0 & 1 & 2 \end{bmatrix} \qquad \frac{1}{4} \begin{bmatrix} -1 & 0 & 1 \\ -2 & 0 & 2 \\ -1 & 0 & 1 \end{bmatrix} \qquad \frac{1}{4} \begin{bmatrix} 0 & 1 & 2 \\ -1 & 0 & 1 \\ -2 & -1 & 0 \end{bmatrix}$$
(47)

It is not necessary to use all eight masks in practise, since the second four masks are simply the negative of the first four.

Step Fitting.

Another approach to edge detection is based on fitting an ideal step edge to the given picture f(x,y) at a point P. For simplicity take P to be the origin. A step edge of slope θ through P, having values a and b on its two sides is defined by the function

$$s(x,y) - \begin{cases} a & \text{if } x \sin \theta \ge y \cos \theta \\ b & otherwise. \end{cases}$$
(48)

It is necessary to find a,b, and θ that minimise some measure of the difference between f(x,y) and s(x,y). These values then provide estimates of the contrast |b-a| and slope θ of the edge at P if one exists.

Image Expansion in Terms of Basis Functions.

Hueckel [HUECKEL71] used an orthogonal set of eight basis functions defined in a circular neighbourhood around each point of the image. His method for edge detection was as follows. He expanded both the image and a certain number of basic step functions in terms of the chosen orthogonal set locally at each point; the best-fitting step edge was taken to be the step edge minimizing the differences between corresponding coefficients in the expansions of edge and images in the least-squares sense. The multidimensional edge operator of Zucker and Hummel [ZUCKER81] followed on from Hueckel's work. They expanded the grey-level function in terms of an orthogonal set of basis functions (using Karhuven-Loeve basis functions) locally at each point. Expansions in terms of the same functions were found for a certain number of step functions and again, the best-fitting step, if any, was the one which minimized the differences

between the coefficients of the expansions in the least squares sense. They found that the discrete approximation to the operator they derived was a generalisation of the Sobel operator into higher dimensions.

Surface Fitting.

One way to define operators for detecting edges is to fit a surface to a neighbourhood of each image point using a simple function, for example a polynomial. In two dimensions, a surface would be fitted to the data using the grey level of the pixels as a third dimension. The function can then be used for a number of purposes. For example, the function's gradient and Laplacian can be taken as approximations to the digital gradient and digital Laplacian of the image at the given point. The derivation of digital approximations for the gradient and Laplacian from least-squares fitting of polynomials is due to Prewitt [PREWITT70] and has been very influential. More recently surface fitting has been extended to 3D images by locally fitting hypersurfaces to the image data. e.g. [MORGENTHALER81]

3.3.2.4 <u>Canny's Approach to Edge Detection.</u>

Canny's [CANNY81, CANNY86] work has been very influential. His theoretical approach defines three common criteria relevant to edge detector performance in general.

(1) Low error rate - edges that occur in the image should not be missed by the operator and there should be no spurious responses.

(2) Edge points be well localised, so the edge marked in the output image and the centre of the true edge should be coincident.

(3) There should not be multiple responses to a single edge.

Canny derives terms for each of the criteria and combines these terms. He discovers an uncertainty principle relating detection and localisation of noisy step edges and that there is a direct trade off between the two. One consequence of this relationship is that there is a single unique "shape" of impulse response for an optimal step edge detector, and that the trade off between detection and localisation can be varied by changing the spatial width of the detector. Canny derives optimal operators for ridge and roof edges using numerical optimisation. The optimal detector has a simple approximate implementation in which edges are marked at maxima in gradient magnitude of a Gaussian-smoothed image.

The impetus behind Marr and Hildreth's theory of edge detection [MARR80] was an attempt to develop a computational theory of vision. Their operator has been derived to optimise the enhancement of edges from clearly defined constraints. Marr and Hildreth note that intensity changes tend to occur over a wide range of scales and they suggest that one should therefore first take the local averages of the image at various resolutions and then detect the changes that occur at each one. They select the Gaussian distribution [MARR82] as an optimal smoothing filter based on the argument that

"it has the desirable characteristic of being smooth and localises in both the spatial and frequency domains and, in a strict sense, being the unique distribution that is simultaneously optimally localized in both domains. And the reason in turn why this should be a desirable property of the [Gaussian] blurring function is that if the blurring is as smooth as possible, spatially and in the frequency domain, it is least likely to introduce any changes that were not present in the original image."

The non-directional Laplacian operator was selected to localise the intensity changes because it is more computationally efficient than the use of a range of directional derivative operators. As the Laplacian is a second derivative, the zero crossings of $\nabla^2 G(x,y)*I(x,y)$ are detected for image I(x,y), where G(x,y) is a two-dimensional Gaussian, ∇^2 is the Laplacian and * indicates the convolution operation. The theory explains several basic psychophysical findings, and the operation of forming oriented zero-crossings segments from the output of $\nabla^2 G$ filters acting on the image forms the basis for a physiological model of simple cells.

The Laplacian of Gaussian (LoG) operator as it is commonly known is often implemented with large (30x30 for example) digital convolution masks. It has proven an effective edge detector in a wide range of images, although the vast majority of researchers only calculate the edge positions for one variance of the Gaussian, in contrast to the approach which Marr and Hildreth used when deriving the operator. The operator is also often approximated by the Difference of Gaussians (DoG) filter which has the advantage of being separable into 1-D filters, with a consequential saving in terms of both memory and time requirements. The DoG function may be written as

$$DoG(\sigma_{e},\sigma_{i}) = \frac{1}{\sqrt{2\pi}\sigma_{e}}e^{\frac{-x^{2}}{2\sigma_{e}^{2}}} - \frac{1}{\sqrt{2\pi}\sigma_{i}}e^{\frac{-x^{2}}{2\sigma_{i}^{2}}}$$
(49)

Writing $\sigma_e = \sigma$ and $\sigma_i = \sigma + d\sigma$

$$DoG(\sigma) = \frac{1}{\sqrt{2\pi}\sigma} e^{\frac{-x^2}{2\sigma^2}} - \frac{1}{\sqrt{2\pi}(\sigma + \delta\sigma)} e^{\frac{-x^2}{2(\sigma + \delta\sigma)^2}}$$
(50)

$$\approx \frac{1}{\sqrt{2\pi}} \delta \sigma \left(\frac{\partial}{\partial \sigma} \right) \left(\frac{1}{\sigma} e^{\frac{-\pi^2}{2\sigma^2}} \right)$$
(51)

$$\propto -\left(\frac{1}{\sigma^2} - \frac{x^2}{\sigma^4}\right)e^{\frac{-x^2}{2\sigma^4}}$$
(52)

which is equal to the LoG within a constant.

3.3.2.6 <u>Postprocessing of Edge Images.</u>

Ideally an edge detector should only yield points lying on image boundaries. In practise, the edge map seldom characterizes a boundary completely because of noise, blur and insufficient contrast at some parts of the boundary. False edge elements also arise because operators often produce a high response not only at the point located directly on a sharp boundary but in a whole neighbourhood of that point. Thus edge-detection algorithms are typically followed by linking and other boundary detection procedures designed to assemble edge pixels into a meaningful set of object boundaries.

Thresholding of Edge Images.

The output of most parallel edge detection methods is an edge image e(x) where each pixel has an associated magnitude and sometimes an associated orientation. One common method of detecting edges is to select a threshold h for extraction of edge elements by the condition e(x) > h. The threshold is usually selected so as to strike the right balance between omission of some edge pieces and detection of false edge elements, and is often selected interactively, although some authors select h automatically on the basis of the global properties of the image. For example Perkins [PERKINS80] chooses as a threshold the point of maximum curvature in the histogram of the edge image, and Rosenfeld [ROSENFELD81] uses clustering to define an edge cluster in the edge image. The thresholded image is then ready for further processing. If the operator produces false edge elements because of the high response near to the boundary it may be necessary to apply thinning. The simplest and most common method of thinning the edge operator response is based on suppression of non-maximal response values perpendicularly to the edge, where edge responses within a certain distance of a maximum edge response are zeroed ([JACOBUS81],[ROSENFELD71]).

Edge Linking.

Thresholding an edge map tends to produce streaking, the term used for incomplete boundaries. Several methods have been suggested for combining these streaks into complete and meaningful boundaries. Rosenfeld [ROSENFELD82] suggests that nonlinear curve detectors or techniques based on the Hough transform be used for edge linking. The Hough transform is commonly used as a shape detector, the linking of points is dependent on determining whether or not they lie on a curve of specific shape (for example an ellipse). Another approach is to examine the neighbourhoods of each point (typically 3x3 or 5x5) in, or close to, the direction along the edge (i.e. approximately perpendicular to the gradient direction). If other edge points are found in this direction on both sides, and if their slope does not differ too greatly from the slope of the given edge point, it is linked to them, otherwise it is deleted. i.e. the difference between the magnitudes of the gradient, and the differences between the orientations of the gradient, of neighbouring pixels must be less than some threshold.

Edge responses can also be improved by making use of both edge detection and thresholding (or more generally edge and spectral or spatial pixel classification). For example if an image is thresholded, edge pixels as defined by response to an edge detector, should lie close to the border determined by the threshold. Other positive responses to the edge detector can hence be rejected. One final method that can be used if spurious edge points can be removed, is elastic matching, where a contour is constructed by curve fitting to those edge pixels which are considered valid. This contour closely resembles the edge required. If edge elements in a part of the boundary where the curvature changes sharply are missing then the elastic matching will perform poorly here.

3.3.3.1 Edge Tracking.

Tracking methods can substantially reduce processing times, as a well tuned method will only track near to edge candidates, as opposed to most other methods where every image pixel is processed. The tracking method is defined by three rules, the choice of starting point, the rule for adding the next pixel to the contour, and the stopping rule [FU81]. The starting point may be determined by a high response of the edge operator. [MINSKII85, EHRICH81, KAZMIERCZAK77], by a specific brightness value between the brightness values of the objects or interactively. Tracking usually stops when the procedure does not find a new point which satisfies the adjoining condition. Tracking is a strictly sequential process, yet when taking a decision to adjoin the next edge pixel, it is possible to simultaneously consider various data - local, global and data accumulated in the process of edge construction. In this sense, the tracking process is similar to the sequential region growing process (as described in section 3.4).

Tracking is often based on an edge operator response, but in addition to the magnitude of the response to an edge detector, denoted by e(x), the orientation of the edge $\phi(x)$ can also be considered as Kazmierczak [KAZMIERCZAK77] has done. He specifies two thresholds h and h_{ϕ} . From the neighbourhood of the last adjoined element x, the procedure selects an element y such that e(y) > h and the direction from x to y, $\alpha(x,y)$ is maximally close to $\phi(x)$ with $|\phi(x) - \alpha(x,y)| \le h_{\phi}$. If no such element is found, the tracking of the given piece of boundary ends. It should be noted that in this method, the stopping criterion does not include closing.

3.3.3.2 <u>Surface Tracking.</u>

The extension of edge tracking into three dimensions is often termed surface tracking. One of the earliest three-dimensional boundary detection methods reported is due to Liu [LIU77]. His method is applicable to 2- and 3- dimensional images and utilises backtracking to correct for errors. A Roberts-like gradient is used in both the 2D and 3D cases to measure contrast level which the boundary follower attempts to maximise. Global information is limited to the monitoring of the mean gradient magnitude along the developing boundary and is primarily used to initiate backtracking. Herman and Liu [HERMAN78] have adapted Liu's earlier work to 4-dimensions, so time sequences of 3-D images can be examined. More recently, Cappalletti and

Rosenfeld have examined three-dimensional boundary following. They presented a graph search based method for boundary following with a cost function utilizing edge gradient magnitudes, edge circularity and comparison with neighbouring sections. They found that the use of 3-dimensional gradient operators greatly reduced search effort and gave slight improvements in edge localization.

3.4 <u>Region growing.</u>

Region growing is the process of joining neighbouring points or collections of points into larger regions subject to certain conditions, where a region is defined as an area in an image whose points have a common property. Zucker [ZUCKER76A] has written what is widely acknowledged to be an excellent survey on region extraction methods. Haralick [HARALICK86] has presented an in depth survey of region growing. A segmentation by region growing can be characterised by four conditions which must be met. These are -

(1) The final segmentation must be complete, so that each pixel is assigned to a region, even if one or more regions may later prove to be border regions.

(2) Pixels in a region must be connected. The particular definition of connectivity chosen may define the algorithmic structure in choosing the order of pixel processing.

(3) Some property must be chosen to determine the segmentation. This varies from grey level values to semantic interpretation.

(4) Adjacent regions must not be capable of being merged.

3.4.1 <u>Muerle and Allen's Approach.</u>

Muerle and Allen [MUERLE68] carried out some of the earliest work in the field. They chose to define a region as any portion of an image in which the statistical distribution of grey levels is reasonably uniform. Their method starts by segmenting the image into non-overlapping 'pattern cells' which are squares of 2x2, 4x4 or 8x8 pixels. For each cell a statistical measure is calculated, for example by estimating the probability distribution function of grey levels within a cell by fitting a Gaussian. A starting point is chosen and the statistics of neighbouring cells compared with this starting point. If the comparison proves successful then the cells are merged to form a fragment and the probability distribution of the fragment updated. Otherwise the

dissimilar cell is labelled as rejected. The fragment growing is continued until all neighbours have been examined, in which case the fragment is labelled as a completed region. The next uncompleted cell is then chosen as a new starting point and the above steps repeated until all pattern cells are labelled. This is illustrated by Figure 30. In this approach only grey level information is used, although the potential for using other criteria such as preferred shape or direction for growing the shape is apparent.

3.4.2 <u>Multi-regional Heuristics.</u>

Although the progress of the region growing process is based on decisions made with local information, the desired outcome is a satisfactory global segmentation. This lends credence to the argument that as much global information as possible should be made available to help make these local decisions. The first step towards a more global approach was to develop heuristics which evaluated parameters depending upon more than one region, an approach developed by Brice and Fennema [BRICE70]. Their process begins with lattice points between individual pixels being defined to provide space for boundary markers. The first stage produces atomic regions of constant grey level which obviously means a large number of starting regions. The vector boundary markers are then set between picture points of different intensity. Each elementary vector is assigned a strength proportional to the magnitude of the difference in the grey levels between it. The atomic regions are then combined by the successive application of two heuristics. The 'phagocyte' heuristic merges two adjacent regions if the boundary between them is weak, and the new region has a shorter length of weak boundary than the previous two. The 'weakness' heuristic merges two regions if the weak portion of their common boundary is some predetermined percentage of their total common boundary. This heuristic is applied to refine the results of the phagocyte heuristic.

3.4.3 <u>Functional Approximation and Merging.</u>

Pavlidis and his co-workers [PAVLIDIS72] have adopted functional approximation as a mathematical foundation for region growing. Loosely speaking, functional approximation is using one set of functions to approximate another set of functions which might be very complex or only known at discrete points. The functions can be quite general, the lowest order functions being constant values. This condition can be interpreted as average grey level over a region. In



Figure 30 - Muerle and Allen's Method of Region Growing.

principle the method followed is then similar to the previous techniques described but the approach is much more theoretically sound. A two-dimensional picture is first sliced into thin strips, then each strip partitioned into segments and these segments approximated by

polynomials. These approximated segments can then be merged into regions by comparing the polynomial coefficients of adjacent segments.

3.4.4 Issues Related to Region Growing.

There are two important issues integrally related to region growing. These are the threshold selection method, and for position-dependent threshold values, the order in which pixels are processed.

3.4.4.1 <u>Threshold Selection.</u>

The success of region growing systems is often linked to the selection of an appropriate threshold. The simplest technique is to select a constant threshold for the entire picture. For example if the difference between the growing region and a neighbouring point is less than a tolerance threshold, the predicate evaluates to true. A constant threshold could be evaluated on the basis of a priori assumptions about the class of images at hand. A more interesting idea is to allow the threshold to vary over the picture. What is learnt in the early sequential nature of the region growing algorithms might be used to influence the later stages. Harlow [HARLOW73] and his associates have developed a system for processing radiographic images. They use a highlevel scene description algorithm structured as a tree which serves as a model for program control. The root denotes an entire chest X-ray, with branches to the left lung, heart etc. Picture points are joined into regions if their grey levels are within some threshold of the average grey level of the growing region. The description tree directs the program to find regions that correspond to each of its nodes. The particular node in control dictates the threshold to be used and the picture area to be examined. If no suitable region can be found the program varies the threshold, using parameters attached to the node and another search is made. This illustrates the variety of possibilities for threshold selection.

3.4.4.2 <u>Order Dependence.</u>

The advantage of sequential region-growing algorithms is that information acquired in the earlier stages of processing can be used to influence the later stages. For example, the first picture points which are processed may affect the choice of which points are processed next. More importantly, the order in which picture points are processed may affect the final result. An algorithm is terminally order independent if the various derivational sequences obtained by different scannings produces the same final segmentation. The order is important, however, and may depend on the initial atoms too. The seed point choice can be determined by using features of the images to be examined, for example a hot spot in military Forward Looking Infra-Red imaging (FLIR) or the use of a histogram, clustering etc.

3.4.5 <u>Regional Interpretation</u>

The previous region growing approaches do not utilise any region interpretation. Other work has been carried out using information about the class of images being processed. Regions are interpreted as they are formed, and the interpretations influence the merging criteria. Gupta and Wintz [GUPTA74a and GUPTA74b] have carried out work on LANDSAT images. In their method, the image is first segmented into unit cells then neighbouring cells joined if their grey level distributions are statistically similar. This stage is followed by a minimum distance classifier which interprets each initial region as belonging to one of a small predetermined number of classes such as corn, soya bean, water or forest. As region growing does not produce a perfect segmentation, each physical region may correspond to several segmented regions. Neighbouring regions can then be merged on the basis of their class membership [see Figure 31].

3.4.6 <u>Region Splitting and Merging</u>

Region growing processes begin with small initial cells which are successively joined to create larger regions. The opposite approach is to start with the entire picture as a single region and successively divide into smaller regions. This process continues until each smaller region satisfies an appropriate uniformity criterion. This decreases the amount of overall processing in uninteresting background regions. Region split and merge is an approach closely linked to region growing. The 'split and merge' principle was developed by Horowitz and Pavlidis [HOROWITZ74]. The principle behind the method is to merge adjacent regions having similar pixel distributions and to split those regions that have different pixel distributions. The algorithms use a pyramidal data structure, a stack of pictures of the same image, of decreasing resolution, from the original image to a single pixel. The data structure consists of nonoverlapping squares of pixels in the image below. The pyramidal data structure can be represented concisely by a segmentation tree, where the leaves of the tree are individual pixels and the root is the entire image. Each block is characterised by the minimum and maximum



Figure 31 - Example of Gupta and Wintz's Method.

brightness values in the block. Unlike region growing the splitting methods mostly assess homogeneity by the integral properties of the segment e.g. the brightness variance in the segment does not exceed an admissible value [CHEN80] or the brightness in a segment is normally distributed [SAZON-YAROSHEVICH83]

The split method for image segmentation begins with the entire image as the initial segment. Then it successfully splits each current segment into quarters if the segment is not homogeneous enough. Homogeneity can be easily established by determining if the difference between the minimum and maximum grey levels is small enough. Other approaches use the sample variance instead. Algorithms of this type were first suggested by Robertson [ROBERTSON73] and Klinger [KLINGER73]. If only splitting were used, it is likely that the final partition would contain adjacent regions with identical properties so the splitting part of the algorithm is followed by merging. The grouping is a sideways merging of adjacent regions. Efficiency of the split and merge algorithm can be increased by arbitrarily partitioning the image into square regions of a user selected size, and then splitting these further if they are not homogeneous. It may be necessary to post-process the image to eliminate small regions. This is done simply by merging small regions with their most similar adjacent region. Split and link is a very similar method to split and merge that deserves to be mentioned. It uses a differential pyramid representation of the image, which is defined by 4x4 block averaging with 50% overlap in each direction.

3.4.7 Further Work.

The basic approaches discussed above have been used by many groups with slight adaptation. Miligram [MILIGRAM79] has proposed a method in which candidate object regions are extracted by thresholding the image in a region dependent way. Candidates are then accepted or rejected on the coincidence of an edge map with the region boundary. Regions that best match the edge map are used to describe the objects in the image. Obviously the method will be very dependent upon the edge detection method used. Gagalowicz and Monga's [GAGALOWICZ86] approach begins by obtaining an initial segmentation and constructing an adjacency graph of region pairs. A number of different statistical region-growing criteria are used to rank adjacent pairs of regions. An interactive choice and possibly a combination of criteria can then be made. This may lead to a more adaptive segmentation in some cases. Raafat and Wong [RAAFAT88] have worked on a texture based method which uses a texture information measure for the initiation of the texturally homogeneous core regions. The information measure is then used together with a texture distance measure to direct the growth of various homogeneous regions. Pavlidis [PAVLIDIS88] has investigated integrating region detection and edge detection. The method starts with an over-segmented image from a split and merge algorithm. Region boundaries are then eliminated or modified on the basis of criteria that integrate contrast with boundary smoothness, variation of image gradient along the boundary and a criteria that penalises for artifacts reflecting the quadtree data structure. This is because split and merge algorithms tend to output noticeably blocked regions, obviously made up of squares of pixels of differing sizes. As might be expected, region growing has also been extended to parallel implementations, for example by Gambotoo and Monga [GAMBOTTO85].

3.5 <u>Clustering.</u>

Clustering is the multidimensional extension of thresholding. It applies to images with more than one data value per pixel, for example the RGB components of colour photography, multispectral remote sensing images, the many parameters of MRI and even values calculated on the basis of local properties of the image such as texture, gradient etc. The concept of thresholding becomes one of finding clusters of points in n-dimensional space. Clustering generally gives better results than thresholding since it is based on several property results rather than one value. Automatic detection of clusters in multidimensional feature-space is much more complicated than thresholding since clusters can have complex shapes and can interact in many ways, for example one cluster surrounding another. Relatively globular clusters which do not overlap greatly can be segmented quite easily however. Clustering provides groupings of unlabelled data in terms of sets or clusters of data points. The clusters are assigned labels and the labels mapped back to the image to give a segmentation.

Rather than accomplish the clustering in the full measurement space, it is possible to work in multiple lower order projection spaces and then reflect the clusters back to the full measurement space. Suppose, for example, that the clustering is done using a 4-band image. If the clustering done in bands 1 and 2 yields clusters c_1 , c_2 , c_3 and the clustering done in bands 3 and 4 yields clusters c_4 and c_5 , then each possible 4-tuple from a pixel can be given a cluster label from the set { $(c_1,c_4), (c_1,c_5), (c_2,c_4), (c_2,c_5), (c_3,c_4), (c_3,c_5)$ }. A 4-tuple (x_1,x_2,x_3,x_4) gets the cluster label (c_2,c_4) if (x_1,x_2) is in cluster c_2 and (x_3,x_4) is in cluster c_4 . It should be noted that difficulties may arise if the clusters have complex geometries with respect to each other in feature space.

An important problem existing with most clustering algorithms is that the number of clusters in the data must be specified a priori before using the clustering algorithm. However in many applications it is desired to estimate this number directly from the observed data since a priori knowledge is generally not available. This is known as the cluster validation problem. Some approaches try to determine the number of clusters automatically, but their reliability can not be guaranteed.

Similarity is most commonly measured by a distance function in the feature space. It is generally desirable to make this function invariant to image variations that may be encountered such as translation, rotation and scaling. A criterion function is also used to measure the clustering quality of a particular partition of the image function value.

3.5.1 Methods of Clustering.

The basic operation of clustering is to examine each pixel individually and assign it to the cluster that best represents the value of its characteristic vector. This assignment is done according to the selected measure of similarity between data points and the criterion function measuring clustering quality. This process is repeated if necessary until some condition is satisfied by the grouping of data points. For example if similarity between pixels is measured in terms of the distance between the value of their characteristic vectors, then the sum of the squared distance from the cluster centres can be used as a criterion function; the aim is then to seek the grouping that minimises this function. For 2-clusters a commonly used algorithm is -

(1) Initialise cluster centres. The cluster centres are assigned the initial values $M_1 = M$ -S and $M_2 = M$ +S, where M is the mean image feature vector and S the mean standard deviation.

(2) Assign feature vectors to closest cluster centres.

(3) Compute new cluster centres by calculating the centre of gravity of the clusters.

(4) Compare new and old cluster centres. If they are close enough, the algorithm terminates; otherwise the procedure is iterated from step (2).

The IZODATA procedure is a particularly popular method which partitions the image pixels into a given number of clusters, minimizing the sum of the mean square deviations of the pixels from the cluster centres. Thresholding is the most popular technique for clustering. The multidimensional feature space is transformed into a one-dimensional space of a generalised feature (e.g. [KOHLER81]) and thresholded using techniques similar to those described for thresholding. Interactive expert procedures are also very popular. The expert may directly identify clusters or assign a small group of pixels to particular clusters and the remaining points are classified automatically between the expert-designated clusters, which is known as classification with learning. This approach is applicable when relatively few large images are involved, but would not be appropriate for many smaller images, since the experts time could be better spent elsewhere.

3.5.2 Local Information for Improving Clustering.

Clustering methods used in segmentation often consider not only the global properties of the image, as reflected in the distribution of points in the feature space, but also local information about the location of image points. If the local information is ignored, the elements assigned to the cluster may represent an unconnected scatter of points. Schachter *et al.* [SHACHTER75, SCHACHTER77] used clustering to perform image segmentation on multispectral remote sensor imagery. In [SCHACHTER75] they used the grey level values of several channels as features in the feature space. In [SCHACHTER77] they tried instead to do clustering using just one monochromatic image and features such as mean grey level and median filtered minimum total variation, typically computed over a 3x3 local neighbourhood. They concluded that the results of using one monochromatic image with locally computed features were not as good as those obtained with grey level values of several channels as features, however. A number of other authors have used local information to provide an extra dimension for clustering in a variety of ways. These include

(1) The use of neighbourhood features directly to provide an extra dimension of data.

(2) The use of local image characteristics to form the clusters. Haralick *et al.*, for example, only allocated points to a cluster centre if at least one point in its neighbourhood has been previously assigned to that cluster. [HARALICK85]

(3) Correcting the clustering result in the image plane after each element has been assigned to a cluster and labelled. Lattuati *et al.*, for example, have eliminated specks of foreign labels by shrinking and expanding [LATTUATI82], whilst another common approach is iterative relabelling with the objective of maximising the segmentation performance.

(4) Conditional clustering, with each element characterised by the degree of membership in each

cluster. These quantities are then revised allowing for the characteristics of the neighbouring points (relaxation). The final label is assigned by the maximum degree of membership.(5) Incomplete clustering in the parameter space, which assigns to clusters (and labels) only those points that are close to cluster centres (the peaks of the histogram) : the remaining points are labelled by label propagation in the image plane. [LAI82]

Many authors have used relaxation methods to ensure compatibility of the results of analysis of the image points in the feature space with the conditions imposed by the relative location of these points in the image plane, for example [DAVIS83] and [EKLUDH80]. Practical applications that use clustering have included those reported by Underwood and Aggarwal [UNDERWOOD77] for the detection of insect infestation in citrus orchards, and Goldberg and Shlien [GOLDBERG78] who used clustering for the interpretation of landsat imagery.

Clustering is more immune to noise than for example edge detection methods. However since the approach is based on the assumption that different classes of an image are represented by distinct modes, the technique will fail if this assumption is not true. A second drawback is that because in general the number of segments is not known, unsupervised systems may not produce the correct number of segments.

3.6 <u>Multiresolution techniques.</u>

3.6.1 <u>Introduction.</u>

Multiresolution techniques attempt to gain a global view of an image by examining it at many different resolution levels. The lower resolutions provides a global view of the image, and the higher resolutions provide the details. There are two ways in which the term resolution is used in multiresolution segmentation. The first is used to describe the spatial resolution of an image (i.e. the size of the pixels). In this case a linked pyramid data structure is often used to describe the relationship between father and son pixels in a stack of images, each subsequent image being a reduced resolution version of the previous one. The production of lower resolution images leads to a rather crude blurring by averaging over local neighbourhoods of pixels, although the median or mode pixel value etc. could also be taken. Alternatively, the term can be used to describe a variable parameter which is used to characterise an operator applied to the image. For example a Gaussian kernel used to blur an image can be characterised by the Gaussian's standard deviation or variance. The word "resolution" will in general be used as an abbreviation for "scale resolution" in this thesis. This parameter of resolution has in the literature often been termed "the parameter of scale". Witkin [WITKIN83] adopted the expression "scale space" which is a description of what happens with a grey level image or an edge image when varying the operator-parameter continuously. Once an appropriate operator has been chosen, a family of images in scale-space is defined. If one aims to retain all available structure and yet also vary the resolution (for example in order to be able to identify global objects through blurring) then the image must be treated on all levels of resolution simultaneously. In both cases there is an aggregation of information from neighbouring points, but this is much cruder in the case of the pyramid. It should be noted that parts of both Marr and Hildreth [MARR80] and Canny's [CANNY86] work can be considered as multiresolution techniques, but these have been included under edge detection (sections 3.3.2.4 and 3.3.2.5) because it is for this that their work has achieved the most attention and success.

3.6.2 <u>The Pyramid.</u>

Burt and Hong [BURT81, HONG82] carried out some of the earlier work in multiresolution segmentation. They proposed a pyramid of a layered arrangement of square arrays in which each array is half as long and wide as the next layer with the bottom level corresponding to the whole image. A son-father relationship is defined between nodes in adjacent layers, but unlike other pyramids, this relationship is not fixed and may be redefined at each iteration of their algorithm. A son is linked with the best fitting father within a 2x2 matrix just above this son. Following linking, each father will have between 0 and 16 "legitimate" sons. The son-father links then define windows in the image, and ultimately the image segments. A variable quantity is associated with each node of the pyramid representing the image property computed within the nodes's window. The value of the node is typically just the average of its' sons values. Thus the task of computing image properties is implemented as an averaging process between pyramidal levels. Image segmentation is implemented as the process which selects a legitimate father for each node from that node's four candidate fathers. The legitimate father is the candidate with a value most like that of the node itself. Due to this linking the selection of a node, and hence all nodes below it tend to correspond to homogeneous regions. This process is repeated iteratively.

3.6.3 The Stack Approach.

The stack approach was initially proposed by Koenderink [KOENDERINK84] and is a multiresolution image description and segmentation scheme. Koenderink believes that an image description should be stable against small perturbations of the grey level and the dimensions. A description should also be natural in that partial descriptions, for example truncations, should be simpler than the original description. Finally local deletion of detail should not affect global description. The image description is a method of decomposing the image into light and dark spots. The often quoted example is of a face described as a light spot containing three dark spots (the mouth and the two eye regions) and a light spot (reflection from the forehead). In turn the eye regions would be described as containing a dark spot (the eyebrow), a light spot (the eyelid) and a dark spot (the eye). These light and dark spots are termed extremal regions, since they each include a local intensity maximum or minimum.

The most important point to consider when choosing an appropriate convolution kernel for blurring is causality - extremum should not be created by blurring. Koenderink derives the following necessary and sufficient relationship at the locations of extrema

$$I_{xx}(x,y,s) + I_{yy}(x,y,s) = \alpha^2 I_{x}(x,y,s)$$
(53)

where I(x,y,s) is intensity, s is scale or resolution and a subscript denotes a partial derivative. This is the heat or diffusion equation. Koenderink has shown that convolution with a Gaussian kernel can be considered to be an appropriate solution to the diffusion equation for an insulated bounded image with zero intensity along it's boundary.

The image description in terms of extremal regions is produced by following the paths of extrema in a stack of images in which each higher image is a slightly blurred version of the previous one. Successive blurring causes each extremum to move continuously and eventually to annihilate as it blurs into the background. This movement is illustrated by Figure 32. Each path point has an associated iso-intensity contour, as illustrated by Figure 33. This contour has the same intensity as the path point and surrounds the extremum in the original image. It has been shown that all extremal paths must start in the original image if Gaussian blurring is used. The intensity of the topmost point on an extremal path is its annihilation intensity. This is the intensity of the iso-intensity contour that forms the boundary of the associated extremal region. When an extremum annihilates at some annihilation intensity, another region's isointensity contour at that intensity encloses the region associated with the annihilating extremum. The two extrema are only related, however, when the non-extremum path representing the annihilated extrema joins up with the other extremal path. Extremal paths are represented by solid lines, and non-extremal paths represented by dotted lines in Figure 33. A tree is a natural way to describe this relationship.



Figure 32 - Extremal paths through the stack.

The theory upon which the stack algorithm is based applies to continuous images embedded continuously in resolution space. A digital computer deals with discrete images which produces problems which must be resolved in any practical implementation of the method. Pizer and Lifshitz have carried out work to develop a working system [PIZER85, LIFSHITZ90]. The program has been used and updated by this author, as described in Chapter 8. By picking appropriate subtrees from the tree description, a segmentation can be made. Lifshitz notes two difficulties with the stack algorithm. Firstly, a region of interest might not be precisely represented by an extremal region. For example in an abdominal CT scan, an extremal region which includes the liver might also include part of the chest wall near the liver. The second problem is that a region of interest does not always show up as one explicit subtree in the tree structure. It may be two subtrees with no common root except the last extremum. For example the two parts of the kidney may be represented by two extremal regions, both of which link to the liver so that no single subtree will display the kidney alone. Lifshitz suggests the use of pixel and tree editing respectively to overcome these problems.


Figure 33 - Extremum paths and associated isointensity contours. Extremum paths are represented by solid lines and non-extremum paths by dotted lines.

3.6.4 The DOLP Transform.

Crowley [CROWLEY84a, CROWLEY84b] has examined the use of the Difference of Low-Pass Transform for image description and segmentation. This representation is based on a reversible transform that converts an image into a set of bandpass images. Each bandpass image is equivalent to a convolution of the original image with a bandpass filter b_k . Each bandpass filter is formed by the difference of two size-scaled copies of a low pass filter g_{k-1} and g_k .

$$b_{k} - g_{k-1} - g_{k} \tag{54}$$

Each low pass-filter g_k is a copy of the low-pass filter g_{k-1} scaled larger in size. There is experimental evidence to suggest that the visual systems of humans and other mammals separate images into a set of "spatial frequency" channels as a first encoding of visual information. This "multichannel theory" is based on measurements of the threshold sensitivity to vertical sinusoidal functions of various frequencies. This suggests that mammalian visual systems employ a set of bandpass channels with a width of about one octave. Such a set of channels would carry information from different resolutions in the images. These studies and physiological experiments supporting the concept of parallel spatial frequency analysis are reviewed by Campbell *et al.* [CAMPBELL74] and provide a theoretical impetus to the development of such a method for segmentation. Peaks and ridges in a DOLP transform provide a structural description of the greyscale shapes in an image. The patterns which are described by this representation are "grey-scale shapes" or "forms". A form is described by a tree of symbols which represent the structure of the form at every resolution. There are four types of symbols which mark locations (x,y,k) in the DOLP three-space where a band pass filter of radius R_k is a local "best-fit" to the form. The symbols represent 1D extrema in bandpass images, 1D extrema in the resolution direction (ie k), 2D extrema in bandpass images and 3D extrema in DOLP space. The segmentation and problems associated with the method are very similar to those already discussed in relation to the stack approach.

3.6.5 Edge Focusing.

Edge detection in a grey-scale image at a fine resolution often yields noise and unnecessary detail, whereas edge detection at a coarse resolution distorts edge contours. Several authors have investigated "edge focusing" - a coarse-to-fine tracking in a continuous manner combining high positional accuracy with good noise reduction. Accurate edge detection often requires that irrelevant details and noise be suppressed. This is in principle achieved by some sort of local averaging or smoothing, resulting in the loss of positional accuracy. The combined use of several processes using different degrees of smoothing has been proposed as a solution to this problem. Bergholm [BERGHOLM85, BERGHOLM87] proposes a way to achieve these goals which other authors have examined [BEAULIEU89, LU89, TANIMOTO89]. Firstly the significant edges should be detected using a high degree of smoothing at a coarse level. Then the edge's precise location is determined by tracking them over decreasing scale. This focusing process uses responses from one level to predict the occurrence of edges at the next, finer, level. The edges that can be determined at the coarsest level will be determined with high positional accuracy, including cases where several edges cause a single response at the coarsest level. These will then split up during the focusing procedure. The procedure for determining the intensity discontinuities is in principle independent of the focusing process. Bergholm smooths by a Gaussian and defines edges as maxima along the gradients of the smoothed image as done by Canny [CANNY81, CANNY86] because of the good theoretical foundation of this method. (See section 3.3.2.4) One approach to multiresolution edge detection is to compare a few edge images at different levels of resolution and try to match edge segments. The results of Marr and Hildreth [MARR81] and Lowe [LOWE85] have not been completely successful in this respect. Intuitively a continuous approach ought to be more robust, since one obtains a trivial matching problem if one moves in scale space with sufficiently small steps. Here the general philosophy is to use so

short a step length in scale space that edge elements do not jump further away than one pixel between successive steps. Edge detection is carried out with a small change in blurring parameter in a thin region close to the old edges. The old edge points are discarded and the new ones accepted. Subsequent edge focusing steps are performed analogously. Hence the coarse to fine tracking is carried out with a high degree of spatial accuracy. By restricting the edge detection to points close to the old edges, processing times are shorter than if more points were processed.

CHAPTER 4

REVIEW OF MAGNETIC RESONANCE IMAGING SEGMENTATION.

4.1 Introduction

A plethora of papers exist in the literature which have used MRI images for segmentation. Many of these appear in conference proceedings, where the data has been used to demonstrate the effects of an algorithm developed by a computer scientist. Often the applicability, quality and very nature of the data has been ignored. Following an extensive literature survey, the author has therefore only reviewed papers from peer reviewed journals or full length peer reviewed conference papers in this chapter, which has been broken down into the same categories as in Chapter 3 for convenience. Clinical papers using the methods described in this chapter are reviewed in section 9.2. Papers primarily concerned with shaded surface graphics which provide very little detail of segmentation, or merely repeat the methodology described in other papers by the same authors, have not been included.

4.2 <u>Thresholding.</u>

Badran *et al.* [BADRAN90] use segmentation of key features in the head such as the brain, corpus callosum and cerebellum, for patient realignment in MRI. These features are chosen because they are consistently stable in position over a long period. T_1 weighted scans are used, these being the fastest sequences available on the imager used by Badran. Such scans are difficult to segment using conventional thresholding or edge based techniques, as poor SNR gives them a grainy appearance. The need for speed also limits the complexity of processing algorithms. The authors select a region containing the corpus callosum or the cerebellum interactively which is thresholded at the region's grey level mode. Interactive processing of the thresholded binary image allows parts of the object lost in the binary image to be manually restored. Mathematical morphology operators are used to eliminate irregular boundaries, remove concave and convex defects, and clean the noisy background. They state that the

"technique can be applied universally if the windowing can be automated." Currently the method is highly interactive and their statement optimistic, particularly as they suggest no avenues for improvements.

Lang *et al.* [LANG88] start their method by correcting MR images for non-uniformities by lowpass filtering the image to reduce noise, applying extreme blurring to suppress details and dividing the original image by the blurred image. The corrected image is then thresholded on the grounds of both signal intensity and 2-D image homogeneity computed on a slice by slice basis for 3x3 pixel neighbourhoods. No further details are given. Drawbacks to such a method of uniformity correction are discussed in section 5.14.

Lim *et al.* [LIM89] use a cardiac gated dual-echo sequence to provide both PD and T_2 -weighted images. They first outline the brain by identifying and stripping away pixels representing the skull and scalp on the T_2 -weighted image. Edges are determined by identifying sharp drops in intensity along radii emanating from the centre of the image, a method which works best for roughly circular cross-sections. Interactive review and correction, if necessary, then take place. Image non-uniformity is corrected by a slightly modified form of division by a blurred version of the image discussed in more detail in section 5.14. Two new images are then created from the original images; the PD and T_2 -weighted images are added to enhance grey/white tissue contrast, and the T_2 -weighted image subtracted from the PD-weighted image to enhance the CSF/tissue contrast. Interactive thresholding is used to segment these new images in two stages. The first stage separates CSF from tissue by thresholding the early minus late echo combination image. These CSF pixels are then masked out on the early plus late echo image, and thresholding is used on the latter to separate grey and white matter. Postprocessing consists of identifying ambiguous pixels and determining their status based on surrounding pixels. The results seem encouraging as a semi-automatic method, but only work for relatively circular brain cross-sections.

Jernigan *et al.* [JERNIGAN90] use a method of segmentation similar in some ways to that of Lim *et al.* [LIM90]. Again a dual echo dataset is used which provides both PD weighted and T_2 -weighted images. The brain and CSF is initially isolated from the image using connectivity and a dual threshold after a pixel within each brain region (ie one pixel within each of possibly several brain lobes) has been interactively selected. Linear combinations of images are used to create two new images with enhanced CSF/tissue and enhanced grey matter/white matter contrast. Regions of grey and white matter are manually sampled and a threshold to separate the two tissues calculated from the two distributions. A similar method is used for segmenting CSF from brain parenchyma.

Pannizzo *et al.* [PANNIZZO92] use thresholding techniques for segmentation of MR images of advanced chronic MS patients, which are characterised by extensive multiple lesions. They aim to remove signal from the fat and scalp and to separate the cerebrum into white/grey matter and plaques and edema. The work is carried out using three slices per T_2 -weighted dataset. An area of brain parenchyma is manually selected to produce a reference intensity and a row by row search for pixels less than 25% of the reference intensity carried out starting at the centre of the image. These are then classified as border pixels. The method will not work for all slices containing the brain. Histogram analysis is then used to segment the lesions. This author does not believe that processing three slices from a dataset is sufficient to measure total lesion volume reliably.

Wicks *et al.* [WICKS92A] have developed a semi-automated thresholding approach to segmenting MS lesions using T_2 -weighted images. Image non-uniformity correction [WICKS92B], as discussed in section 5.2, is applied to all images. Two thresholds are selected manually - the first to separate brain from surrounding tissues and the second to isolate lesions. The same thresholds may be applied to all scans in a serial study of a patient provided image gains are standardised. The threshold for the brain is applied to the whole image, detecting most

tissues, but often failing to remove eyes, nose and facial tissues in inferior slices. By carrying out segmentation slice by slice in a superior to inferior direction it is possible to use 3-D connectivity to reject regions of similar area and intensity to the desired structures. Once the brain is identified, the lesion intensity threshold is applied and high intensity regions greater than 4 pixels in size labelled as lesion. Mis-labelled areas are rejected by manual interaction. The basis of this approach is sound, but superior results may well be achievable using a multi-echo approach because of the availability of more (relevant) information.

Brummer *et al.* [BRUMMER91] present an algorithm for detection of brain contours in single echo multi-slice coronal datasets consisting of two major steps - head contour detection and brain contour detection. The head contour is approximately identified by estimating the background noise level from an image histogram and thresholding the image above a fit to a Rayleigh noise distribution. Subtracting the noise peak from the image histogram and restricting processing to the superior half of the dataset allows the brain contour to be approximately identified by thresholding. Mathematical morphology operations such as erosion and dilation, along with "salt and pepper" noise removal steps and comparison of masks are used to generate improved head and brain masks. This produces approximate masks for the brain and head. The authors suggest that an interactive editing tool would be useful for correcting segmentation errors, for example in slices near the end of the datasets, in regions of severe partial volume effect and in regions of phase encoding artifacts caused by eye motion.

Many authors have claimed that image non-uniformity precludes the application of simple thresholding techniques for segmentation of MR images (eg [KOHN91]). Whilst image non-uniformity is particularly marked for images acquired using surface coils and some head and body coil designs such as the saddle coil, the use of more homogeneous coil designs such as the birdcage coil [HAYES85] produces better results. Indeed images from such birdcage coils suffer from only a small amount of non-uniformity in the axial plane (the source of over 95% of our head data) although there is a drop off of sensitivity along the long axis of the coil. This is discussed in chapter 5. Even using a single slice from the highly homogeneous centre of the birdcage coil, thresholding may not produce satisfactory results. Unlike authors such as Kohn *et al.* [[KOHN91], Cline *et al.* [CLINE90, CLINE91] correctly note that thresholding does not generally work as a segmentation method in the head because different tissues have inherently overlapping intensity ranges. Several of the authors of these thresholding papers have used uniformity correction methods, with that of Wicks *et al.* standing out as being simple, 3-D, fully

automatic and accurate. Work by this author investigating image non-uniformity at 1.5 T is described in chapter 5. Others have isolated regions of the neuroanatomy prior to thresholding because of overlapping tissue intensities. This author has used such an approach applied to thresholding and clustering as discussed in chapters 6 and 7.

4.3 Edge Detection

Levin *et al.* [LEVIN89] segment the surface of the brain for display purposes using T_1 weighted SE or gradient-echo data. Their volume rendering method allows for partial volume voxels and does not require a contour that precisely follows the brain surface. A seed point is chosen within the skull boundary and a contour tracked using a user-selected threshold value for each slice. Manual editing is used to correct for occasional gaps in the contours. This is a highly interactive method and uses only simple edge detection methods which could be greatly improved.

Kennedy *et al.* [KENNEDY89] use several edge-based approaches to segmentation of MR images. The use of intensity contours is proposed, as is the use of differential contours. Differential contours are created relative to a 'difference image' in which a pixel's intensity is given 'relative' to a reference pixel manually identified within the region of interest. Sobel edge images (as discussed in section 3.3.2.3) are also considered. The first two techniques are used to produce approximate candidate edges, and the Sobel edge image calculated in the vicinity of these candidate edges to improve precision. Each slice is then manually reviewed and correction made as necessary. The results for high contrast coronal images are encouraging.

Yla-Jaaski *et al.* [YLA-JAASKI91] use 3-D edge detection for visualisation of volume data. A 3-D difference of Gaussian's operator (DoG), as described in section 3.3.2.5, is used. A 20 pixel convolution in all three directions with a 256³ dataset may be achieved in less than 4 minutes using a vector processor. This requires pre-interpolation of non-isotropic data. Instead of detecting edges, the authors threshold the DoG dataset to zero to produce a binary image. The correspondence of the edges of the binary image to anatomical regions is very poor, but morphological erosion and dilation is used to refine these results. This produces a very rough approximation to edges of the brain, which can be enhanced by appropriate 3-D graphics visualisation techniques. 2-D connected components comprising the brain are manually identified in 4 slices and connectivity used to classify the other slices. This allows an approximation to the

surface of the brain to be found.

Bomans *et al.* [BOMANS90] use essentially the same approach as Yla-Jaaski *et al.* [YLA-JAASKI91] with a 3-D difference of Gaussian's operator and morphological dilation for T_1 -weighted gradient echo volume data. Typically 10% of slices require correction, and in each slice contours corresponding to skin, bone, brain and the ventricular surface are manually identified. The surface of the brain is also segmented very roughly indeed. These problems can be circumvented for visualisation purposes with appropriate shading methods.

Raman *et al.* [RAMAN91] use a variation of edge focusing, as discussed in section 3.6.5, to identify edges. Instead of tracking individual pixels, whole contours are instead tracked. The authors use edge-focusing in a similar way to Bergholm [BERGHOLM87] to reduce the effects of noise. Although Raman's approach seems to be a good one, no attempt at identifying any of the numerous contours which remain (including some due to noise in the background) is made. It would be interesting to see the work extended in this respect. Work carried out by this author using edge-focusing is discussed in section 6.6.3.

Edge detection methods are appropriate for situations where there are strong borders between regions and have been commonly used to identify the strong border of the brain. Many authors have used edge detection as a pre-processing step prior to visualisation. The approach of both [YLA-JAASKI91] and [BOMANS90] seems to be appropriate for such visualisation, although the method of [YLA-JAASKI91] has advantages in terms of speed and the degree of automation. As methods of compensating for segmentation imperfections are available when using 3-D display techniques, accuracy is not as important as when using segmentation for volume measurement. The edge detection reported for visualisation has thus often been approximate. Such methods have tended to use gradient-echo pulse sequences to acquire near isotropic data in acceptable imaging times. This is because gradient echo imaging tends to be considerably faster than spin echo imaging. Authors of such papers invariably neglect to mention that the contrast and image quality required of clinical data may not be available using gradient echo techniques. It is for this reason that spin echo and inversion recovery data is still used routinely for most brain imaging.

4.4 <u>Region Growing</u>

Rusinek *et al.* [RUSINEK89] carry out simple segmentation of PD- and T_1 -weighted sagittal images of the brain as a pre-processing step for 3-D image display. A brain map is created by a simple region-growing algorithm which in essence consists of scanning the image radially from the centre until a signal corresponding to the extra-ventricular CSF is encountered. Such a method is very simple and appropriate in this case, although the accuracy of borders is not perfect.

Cline *et al.* [CLINE87] propose a method for visualisation of soft tissue anatomy using connectivity algorithms to follow the desired surface in three dimensions. The tissue of interest is defined by a surface value, selected by choosing a seed point inside the surface of interest in a similar way to Artzy [ARTZY81]. The connectivity method, using the surface value and seed point as input, locates the surface and marks those voxels that lie on it. This is done by initially thresholding the image into object and background using the surface value. A recursive procedure marks all voxels connected to the seed point and subsequently identifies all non-surface points. Regions of tissue connected to the brain, such as the optic nerve are eliminated by adding a more limited concept of connectivity that restricts paths forming small bridges. The method is also used to show the cerebral ventricular system and the skin of the patient. This work was reported using two datasets and must be extended to further subjects before comment can be made.

O'Donnell *et al.* [O'DONNELL86A, O'DONNELL86B] propose an IR self-normalising pulse sequence (that is, a sequence used to calculate T_1 and T_2 maps, which compensate for RF nonuniformity by dividing one image by another) which yields excellent tissue discrimination for T_1 maps, but is poor for T_2 maps. A hierarchical segmentation algorithm is applied to the data, using both T_1 and T_2 information. The basic algorithm is a histogram analysis method in which each image is recursively parsed into three new subregions. The same analysis is applied to each of the sub-images until one of a set of parsing rules is violated. The histogram of each subregion is fitted to a model of a double Gaussian distribution for simplicity. Using this model, one threshold is placed between the two peaks of the double Gaussian and a second threshold calculated at the 2σ point of the more probable distribution, on the opposite side to the first threshold. (The addition of a similar threshold for the less probable distribution did not affect the final segmentation.) Initial parsing is based on T_1 data and switches to T_2 data once one of the parsing rules is violated. This order of processing is chosen because the T_1 image SNR is much higher than the T_2 image SNR; it should be noted that the switch from T_1 to T_2 parsing will occur at different levels in different sub-images. This approach yields a variety of subimages, some of which correspond approximately to anatomical features. The authors believe that combining the various sub-images may prove a promising method of segmentation. Further work is needed towards such an approach, and so it is therefore difficult to comment at this stage in the work. The use of a single pulse sequence to produce the desired images for T_1 and T_2 calculations is an advantage over using several pulse sequences in terms of the problems of patient movement when appropriate movement-restraint techniques (eg [TOFTS90]) have not been used.

4.5 <u>Clustering</u>

The use of clustering for segmentation of MR images has mushroomed in the last few years, possibly because of the more widespread availability of 1.5 T scanners with a higher SNR than earlier machines. The use of multiple images, acquired using appropriate pulse sequences, provides more information to be used for segmentation. Two practical problems are the prolonged scanning time required for multiple sequences, scanning time normally being minimised on economic grounds and for patient comfort, and difficulty with image registration. These problems and some approaches to their solution are discussed in section 7.10.1.

Jungke *et al.* [JUNGKE88] use three SE sequences to calculate T_1 , T_2 and PD images. A training set is used to set up typical tissue clusters and a maximum likelihood classifier used to assign points in feature space to their nearest tissue type, although points far from any tissue type are considered as unclassifiable. Clusters are then projected into image space where they are accepted, rejected or marked as being of special interest by the user. A colour display allows easy identification of the spatial distribution of a cluster and the simultaneous display of the original image, (T_1 , T_2), (T_1 ,PD) and (T_2 ,PD) plots to allow visual confirmation of cluster. The results are far from perfect, part of the problem probably being the noisy data used.

Hyman *et al.* [HYMAN89] choose 13 regions of interest in MR images of the brain, dividing both the grey and white matter into several regions. An IR pulse sequence, three single echo SE sequences and a four echo SE sequence are used to estimate seven MRI parameters - three T_2 values, one T_1 value and three pseudo-PD values. Each value is calculated from between two and four of the images by a variety of methods. These calculated values are estimates of the true T_1s , T_2s and PDs. If the correlation between the various estimates is high, then there is little advantage in using more than one value. If the correlation is low, then the use of several values will provide more information to use in the clustering process. Discrimination is performed by a maximum likelihood classifier. They found their seven parameter classification system to be significantly more accurate than a three parameter system based on the most accurate values of T_1 , T_2 and PD; this result can be attributed to several factors. Firstly, discrimination accuracy generally increases with the number of classification parameters [LEVY85]. Secondly, the inclusion of two T_2 values determined from ratios of single-echo intensities may have more discriminating power than a single global T_2 value. Finally, one T_2 value is derived to take account of the non-exponential transverse magnetization decay components. The presence of at least two transverse magnetization decay components is shown in the paper. Again, a large number of pulse sequences have been used here, which may provide registration problems, unless movement restraint has been considered. Their use of 13 ROIs probably means that the large number of sequences is needed, however.

Vannier *et al.* [VANNIER85, VANNIER87, VANNIER89, VANNIER91] apply NASA supervised and unsupervised LANDSAT segmentation software to a set of three registered images - one IR and 2 SE images. Training regions are placed over known structures to teach the system and a number of images segmented. Vannier states that a training set for one slice may be used for the scans of a patient at different times, to other slices containing the same tissues and to other subjects. Image non-uniformity is approximated as a ramp function along z, with the ramp being subtracted from the data. This is an extremely crude approximation, however. The group attempt to segment muscle, bone, CSF and various regions of grey matter and white matter using a variety of statistical classifiers, and conclude that no technique is especially effective, with even the best having levels of correct identification that leave the majority of pixels incorrectly identified. This may reflect the medium field strength (0.5 T), the age of the equipment used, the fact that acquisition parameters were not specifically chosen so as to give appropriate contrast or that the authors may have tried to segment too many regions.

Gogahan *et al.* [GOGAHAN87] present preliminary results of multi-parametric analysis of MR breast images. The studies take nearly 2 hours to perform, and are used to produce T_2 calculated images as well as data for preliminary multi-spectral imaging. Noise reduction is carried out with a 7x7 median filter. Image non-uniformity correction is accomplished using scans of a uniform

glycol phantom. Scans of the phantom for each sequence are manually registered using glycol filled tubes attached permanently to the breast coil. Only scans of a standard orientation and thickness are used for this work. The preliminary work shows good potential for separation of abnormal tissues.

Brown *et al.* [BROWN92] use multi-parametric methods to produce classified colour display of the female pelvis. Fifteen spin echo and gradient echo images are obtained for each study using a body coil. A maximum likelihood algorithm is used to classify four of these images after a training set was used. The results can only be described as preliminary as the classification is often poor. The authors believe that magnetic field non-uniformities and patient motion may have contributed to this. The use of gradient echo images may have drawbacks in this respect, but the authors attempt to classify 12 tissues was probably a major cause. Attempting to optimise the approach for less tissue classes would probably have produced better results.

Taxt *et al.* [TAXT92] use multi-parametric MRI analysis to study uterine corpus tumours. Malignant tumours of the uterine corpus are studied because most of them are surgically removed, making pathological examination possible to both classify the tumours and determine their extent. All malignant test tumours are correctly or close to correctly classified as adenocarcinomas and sarcomas and their extent fairly well determined. Parts of normal endometrium and other mucosal linings are also classified as adenocarcinoma, however. In a few patients some of the malignant tissue is classified as normal endometrium. Four images with a variety of T_1 , T_2 and PD-weighting are used.

Cline *et al.* [CLINE90, CLINE92] report on a clustering-based method of segmentation using PD and T_2 -weighted images from a dual-echo sequence. The author's aim is to create a 3-D surface model for surgical planning. The initial phase is a training phase where the observer selects regions of tissues such as CSF, grey matter, white matter, lesion etc. which are used to define clusters in feature space. The whole dataset is then mapped to these clusters. Connectivity is used to aid the segmentation. The authors minimise partial volume effects by using 3 mm thick slices and compensated for the increased scanning time compared with the use of fewer thicker slices by using 1/2 NEX imaging. These images suffer from very poor SNR and would be unacceptable clinically in the Institute of Neurology NMR Research Group. In [CLINE91] angiography images are combined with segmented images of the brain to produce 3-D surface rendered images of the brain and its vasculature.

Kohn et al. [KOHN91] use clustering for estimation of brain parenchyma and CSF volumes. Kohn claims that image non-uniformities including RF and B₀ non-uniformity precludes the application of simple thresholding techniques despite recent software and hardware enhancements. While Kohn is correct that RF and B_0 non-uniformities affect images, the effect of the latter is small for the SE images he uses. He does not note the important point that there is often an intrinsic overlap in signal intensities of tissues, and that the partial volume effect plays a very major role. Kohn et al. claim that image non-uniformity distorts clusters by elongating them along a 'shading axis' parallel to a line extending from the centre of the cluster towards the origin of the coordinate system. Although image non-uniformity may well be the major source of this shading in the images used by Kohn, he neglects the fact that tissue heterogeneity will have exactly the same effect, due to the correlation between Proton Density and T_2 for each pixel, and partial volume effects. The description of the algorithm as one which will "automatically" segment brain and CSF is somewhat misleading. The operator must approximately identify the brain (to exclude skull fat) and CSF for each slice, and identify the brain and CSF clusters in feature space. The centre of the brain and CSF clusters is calculated using centre of gravity techniques and a line parallel to the principal axis of the brain cluster that passes through a point midway between the cluster centres used to segment CSF and brain.

Hillman *et al.* [HILLMAN91] propose a clustering method to determine CSF, grey matter and white matter volumes which is claimed to allow for the partial volume effect. A dual echo SE T_2 -weighted sequence and a T_1 -weighted IR sequence are used for six slices above the orbits. The intracranial region and approximate areas of white matter in the IR image and CSF in the T_2 -weighted image are identified by thresholding. The regions are skeletonised and acting on the assumption that the centremost pixels will be least affected by partial volume averaging with adjacent components, a distribution of pure tissue intensities identified from these skeletons. Each pixel is then scored as a mixture of two tissues according to its brightness and location. One improvement to the method would be to check that voxels adjacent in the third dimension also correspond to pure tissue. The authors do not account for non-uniformities of the image. It is rather worrying that the authors have carried out no validation except comparing their results to grey matter/white matter ratios obtained manually in other publications.

Choi *et al.* [CHOI91] use a statistical model based on Markov Random Field Theory for classifying partial volume voxels. They use limited anatomical knowledge to predict possible tissue combinations. The operator defines samples of pure tissue for input to the classifier, but

once again, no details of how the operator ensures that tissues are pure are given. Further phantom studies are needed to assess the accuracy of the method.

It is interesting to note that in a review of MR clustering papers, the most recent papers describing work done on new high field machines, produce significantly tighter clusters than earlier papers. The lack of detail in some papers is an obstacle to comment, but it may be that higher fields (and therefore, in general higher SNRs), better gradients and generally improved technology are the reason for this. As noted in section 3.5, clustering is the multi-dimensional extension of thresholding. The premise of the approach is that it may be possible to produce a superior segmentation using clustering to that obtained using thresholding on a single image. The problems with thresholding MR data are discussed in section 7.5.

Often T_1 , T_2 and PD weighted or calculated images are used to form a 3-D feature space which allows a clustering approach. In practise however, T_1 , T_2 and PD are often positively correlated in tissue. For example, an increase in water content will increase PD and will also lengthen the values of T_1 and T_2 . The mathematical constraints of producing T_1 , T_2 and PD maps may also give a positive correlation between the calculated values.

Although some papers propose using large numbers of images for clustering, this is normally an unrealistic approach because of the time necessary to acquire the images. MRI is an expensive modality and although T_1 -weighted images and a multi-echo sequence producing PD- and T_2 weighted images may be acquired, it is rare that additional time will be available. Indeed, often T_1 -weighted images are not acquired. The cost of MR means that T_1 -weighted scans are often acquired using a SE sequence rather than the slower IR sequence which can produce far superior grey/white matter contrast.

4.6 <u>Multiresolution techniques</u>

Ortendahl *et al.* [ORTENDAHL86] initially used a maximum likelihood method of clustering T_1 , T_2 and PD images but this showed variation between patients and gave serious problems with partial volume artifacts. They therefore use Burt and Kong's [BURT81] pyramid approach (as discussed in section 3.6.2) to create an initial over-segmented image from three images (PD, T_1 and T_2 -weighted). A region growing approach is used to merge similar segments whilst at the same time merging regions of four or less pixels with the surrounding segment.

Regions of low intensity, which usually correspond to partial volume averaging with bone or air, are also removed. Finally an operator can interactively merge segments on a colour display. As acknowledged by the authors the method shows a moderate degree of success, although the printing of colour images in black and white does not help others to analyze the accuracy of their results. De Graaf *et al.* [DE GRAAF86] have adapted Burt and Kong's [BURT81] pyramid method of segmentation to MR images to use PD, T_1 and T_2 images. Their results are not ideal and require further post-processing to correct edges and merge smaller regions. Neither of these methods produces particularly good results.

4.7 <u>Artificial Intelligence Approaches</u>

Artificial Intelligence (AI) is the emulation of mankind's intelligence using computer hardware and (often) specific AI computer languages. Some approaches to AI use three principal components to automatically resolve a problem. Firstly, a knowledge base (a set of rules extracted from experience), secondly a global data base of events, and thirdly a control system, often called an inference engine.

Lin *et al.* [LIN88] use a four component rule-based system applied to pairs of MRI and PET images. The feature computation subsystem extracts features of homogeneous regions segmented by the low-level image processing subsystem. The domain-independent subsystem employs knowledge to filter out "*obviously impossible*" regions, while the domain dependent subsystem uses domain-specific knowledge to improve results and recognise regions of interest. Perkins' edge segmentation method [PERKINS89] is used to provide an over-segmented image. The authors claim reasonable results but use a very simplified system operating on only three slices. The segmentation aims only to identify features corresponding to anatomy apparent in the PET images, thus greatly simplifying the problem. The accuracy of the boundaries is also questionable.

Menhardt and Schmidt [MENHARDT88] present an approach for automated interpretation of a single transverse slice which shows the ventricles fully. The head and intracranial region is identified by iteratively moving border points from the edge of the image towards the image's centre of gravity. CSF is identified by thresholding the intracranial region into fluid and brain regions. The ventricles are identified on the basis of position. The expert system also comprises a neurological inference engine to utilise knowledge of pathologies to restrict locations of lesions. After definition of the 'intracranial' part of the image the regions with high T_2 -values are labelled. A tumour is identified by an operator which detects large parameter homogeneous components. The examples given are simple and the tumour large and obvious, but the spirit of the segmentation scheme does seem to be quite reasonable. Extending the scheme to a multi-slice dataset would prove more difficult.

Dellepiane *et al.* [DELLEPIANE88, DELLEPIANE92] extended a 2-D knowledge-based system [VERNAZZA87] into a 3-D system applied to images of the head. The head is modelled by descriptions of each organ such as volume and average grey level and relationships between organs. To define the relational and intrinsic anatomical properties in a flexible way, the group uses fuzzy membership functions. The system uses an edge-preserving smoothing algorithm followed by 3-D region growing. Primitives of the region or volume type are extracted which are used for the symbolic interpretation process. Finally a group of regions is associated with an object, and each region assigned a fuzzy membership value related to its degree of reliability. By utilising previous results in a progressive way, the eyes, skull, grey matter and white matter, scalp fat, skin and CSF may be recognised although some of the segmentation results are only approximate. Their use of fuzzy knowledge is very interesting.

Suzuki and Toriwaki [SUZUKI91] propose a method of automatic segmentation of head MRI images by knowledge guided thresholding. Their statements are somewhat confusing at times. For example, they state that conventional imagers adjusts some parameters for each slice to maximise image contrast, and that intensity is normalised for each slice to fully utilise the dynamic range of the data. To the best of this author's knowledge both of these statements are incorrect. The procedure is controlled by a goodness measure, based on knowledge of the anatomic structure of the head, providing an index reflecting how well soft tissue is separated. They apply the method to the segmentation of subcutaneous fat, brain and the ventricles. Their results are quite poor as far as separation of tissues and accurate delineation is concerned.

Raya [RAYA90] uses an automatic rule-based low-level segmentation approach applicable to multi-slice MR brain images, justifying its use by stating that semi-automatic methods are often subject to inter- and intra-observer variability. Although Raya is correct when he states that an automatic system with consistent segmentation criteria will always provide the same results, these results are not, of course, necessarily more accurate than a semi-automated approach even

allowing for such variability. Raya's method is used to automatically extract brain parenchyma, CSF and high-intensity abnormalities such as MS plaques. He uses rules that work with partial voluming (fuzzy boundaries), uses connectivity extensively and concentrates on a simple and consistent decision making process in four steps. Firstly the brain parenchyma, CSF and abnormalities are separated from the background, then the brain and CSF separated. The high intensity abnormalities are separated and finally misclassified abnormalities identified and reclassified. It is difficult to assess the quality of the results due to the exceedingly small size of the illustrations.

Kapouleas [KAPOULEAS90] has developed a method for detecting white matter lesions in MR brain images using both axial and coronal PD and T_2 -weighted images and sagittal T_1 -weighted images. This large number of images allows many checks for consistency, but is not normally acquired clinically. The system begins by locating the brain in each slice and then locates landmarks and suspected lesions. The majority of false positives occur away from the white matter peri-ventricular area (where the majority of white matter lesions are found) and a model of this area is used to eliminate most false positives. The accuracy of the method can not be determined by this author as the illustrations have not been reproduced correctly (ie captions indicate feature identification, but there is no such indication in the images).

One major problem with many artificial intelligence approaches to MRI segmentation is the weakness of the initial segmentation. Such methods typically initially over-segment an image using a region-based method, and then demonstrate various artificial intelligence techniques on a limited sub-set of specially chosen key slices. As demonstrations of AI techniques, many are very interesting, but unfortunately their claims to be accurate segmentation methods are sometimes dubious. As stated in section 1.6.1, this author believes that a more appropriate approach would be to use AI to interactively drive the segmentation using an anatomical model, modality specific knowledge, information about the possible pathology, a task plan and performance data for various stages of the segmentation.

4.8 Discussion

Segmentation is not a trivial task. As this review shows, some segmentation methods have been developed for restricted clinical application, whilst others appear to be show-cases for various approaches to segmentation. Some authors have concentrated on data collection to the point of writing specific pulse sequences, whilst others appear to have chosen specific slices and concentrated on segmenting these. This author believes that better results can be obtained by combining both the concentration on data collection and the concentration on segmentation.

This author believes that AI approaches may be appropriate for driving a segmentation approach, but that current low-level procedures are often poor. Thus this thesis does not cover such AI techniques, but instead concentrates on low and medium level segmentation methods. Preliminary segmentation work by this author covered a wide variety of approaches. Initial work on region growing demonstrated that the final segmentation was critically dependent on the starting point, and often 'leakage' of the region occurred at a weak border between regions. Work with a split and merge algorithm led to a distinctly blocked effect and problems successfully merging regions. Edge detection is a promising method for segmentation of those regions characterised by large intensity changes at their border. This approach has therefore been followed up and is discussed in chapter 6.

An approach to segmentation using multiple images is attractive because MRI is intrinsically a multi-parametric imaging modality, and images acquired using a variety of appropriate pulse sequences will provide more information to aid the segmentation. The accuracy of clustering and thresholding approaches is critically dependent upon the non-uniformity of the images. The factors affecting image non-uniformity for our GE Signa are discussed in chapter 5 and methods for their correction used as a pre-processing step prior to segmentation. Other factors affecting the accuracy of clustering or thresholding are discussed in chapter 7. The use of the stack - a data-driven multi-resolution approach to segmentation claimed to be a totally general approach to segmentation - has also been investigated (see chapter 8).

CHAPTER 5

IMAGE NON-UNIFORMITY IN MRI.

5.1 <u>Introduction.</u>

Image non-uniformity correction has been used as the first pre-processing step in a multistage segmentation process. Anisotropic smoothing is used as a second pre-processing step and automatic edge detection methods used to identify the skin, eyes, ventricles and intracranial region. The intracranial region may be further divided into CSF, grey matter and white matter using semi-automatic contrast enhancement and clustering methods. In order to correct for image non-uniformity it is necessary to have a good understanding of the factors affecting image nonuniformity. This is the purpose of this chapter.

An MR image of a uniform sample will demonstrate areas of non-uniform image intensity. Such non-uniformity affects the visual appearance of images and may also affect diagnosis. Nonuniformity means that the underlying processes being measured in a sample (typically a combination of PD, T_1 and T_2) are not accurately represented in the resultant image. It also affects the accuracy of intensity-based segmentation methods for volume measurement such as dual-echo clustering [SIMMONS92] and thresholding [WICKS92A]. The aim of this work is to determine the dominant sources of image non-uniformity for a spin-echo sequence at 1.5 T and accurately correct for these where possible. Previously Wicks *et al.* [WICKS92B] have proposed an automatic, 3-D method of correcting for the dominant image non-uniformities at 0.5 T using measurements of uniform water phantoms, based upon the work of Condon *et al.* [CONDON87A]. Re-implementation of the method of Wicks *et al.* has shown that RF standing waves effects are an important consideration at 1.5 T. The characteristic stepping in intensity value in the slice direction noted but not explained by Wicks *et al.* and Johnson *et al.* [JOHNSON87] has been investigated, and the magnitude of several additional important sources of non-uniformity have been considered in depth. These investigations have been carried out on a 1.5 T GE Signa scanner, primarily using images of uniform oil and water phantoms and an array of small water bottles packed hexagonally. The images have been acquired with various parameters using standard head and body coils.

5.2 Literature

Several approaches to the correction of image non-uniformity have been considered by other authors. These include

- measuring image non-uniformity using scans of uniform phantoms
- approximating image non-uniformity by the variation in signal of pure white matter throughout the image

approximating image non-uniformity by a low pass filtered version of an image These approaches, their limitations and applicability will be considered in this section.

Condon *et al.* [CONDON87A] carried out what is probably the most thorough investigation of MRI non-uniformity to date. They discovered two major sources of image non-uniformity for head images acquired using their 0.15 T Picker scanner - RF receiver non-uniformity and the effects of receiver filters on bandwidth filtering the data. They used an approximation to low pass filtering and a curve fitted to the horizontal and vertical intensity profiles of the phantom for non-uniformity correction. This could be applied slice by slice in either the coronal, sagittal or transverse directions. Slice to slice variations were not studied.

Axel *et al.* [AXEL87] were interested in uniformity correction for surface coil imaging. They compared correction by phantom scans to division by a highly blurred version of the original image. Although the phantom scan approach was more accurate, they chose division by a blurred image for routine work because it did not require careful surface coil positioning. Such an approach is available as a standard image reconstruction option on the Signa scanner. Lim *et al.* [LIM89] attempted to correct for the non-uniformity of standard axial head images using low

pass filtering, as discussed in section 4.2. Following isolation of the brain, they 'feathered' out the images, by taking the average grey value of the 5 pixels on a radius from the image centre closest to the periphery of the brain, and replicating this value on a radius out to the edge of the image. The image was then filtered with a 33 x 33 point averaging filter and a 3 x 3 Gaussian filter. The original image was finally divided by this low pass image. The feathering step is necessary to prevent an artifactual rim around the edge of the brain. These methods of approximating non-uniformity by a highly blurred version of the image to be corrected are well suited for surface coil imaging when the coil position relevant to the patient is not known and there is a large variation of sensitivity within the field of view. The approximation breaks down, however, when the variation in sensitivity is not large.

Zijdenbos *et al.* [ZIJDENBOS91] developed a 2-D surface fitting approach to the correction of RF non-uniformities in which the authors assumed that white matter is a completely homogeneous tissue and choose a total of 10-20 points of white matter laying throughout the image. These points and their 4-connected neighbours (to counteract noise) are used to fit a surface, and then this surface used to correct the image for RF field non-uniformity. The coefficient of variation of white matter for images from their 1.5 T scanner drops from 8.7%, 8.4% and 7.9% for T_1 , T_2 and PD weighted images respectively, to 2.3%, 2.6% and 2.9%. Although the surface fitting approach could theoretically be extended to three dimensions, by fitting hypersurfaces to the data, the method as currently reported is still interactive, 2-dimensional, shows problems near the outer boundaries of objects and implicitly assumes white matter is homogeneous. The method is (as might be expected) sensitive to erroneous identification of grey matter pixels instead of white matter.

Wicks *et al.* measured non-uniformity at 0.5 T using three orthogonal datasets of a uniform water phantom and then used the data to significantly reduce RF non-uniformities in patient scans of any orientation via a fast, automatic, fully three-dimensional method [WICKS92]. Wicks *et al.* noted several possible sources of non-uniformity for MR head images taken using standard head coils:

- Main field (B_0) non-uniformity
- Bandwidth filtering of the data the time domain filter applied prior to digitisation and Fourier transformation in the frequency encoding direction.
- Transmitted RF field non-uniformity (determining flip angle)
- Received RF non-uniformity (determining sensitivity)

Non-uniformity due to gradient eddy-currents

These factors and a large number of others are considered for the GE Signa 1.5 T scanner in the following sections.

5.3 Sources of Image Non-Uniformity

5.3.1 Static Field Non-Uniformity

The use of a spin echo sequence compensates for the spin dephasing caused by B_0 nonuniformity which can therefore be ignored for standard imaging conditions. Such non-uniformity, however, is important for gradient echo images and phase maps, the latter of which may be corrected for by the use of field maps. Good shimming will generally minimise B_0 nonuniformity within a given region.

5.3.2 Bandwidth Filtering of the Data

Many MRI scanners utilise a time domain filter to reduce the incoming data to a bandwidth below the Nyquist frequency (ie half the digitising or sampling rate) and this filter can have a pronounced effect on image uniformity in the read direction where pixels near the edge of the image are attenuated in intensity. The effect of such a filter can be measured, by scanning air. The subsequent noise image will be weighted by the filter, which allows the form of the filter to be determined by fitting curves to the noisy data. The GE Signa utilises a digital filter instead of the physical (electronic) filter used on most scanners. This digital filter affects only the edge 2 or 3 pixels of the image and can therefore be ignored. Condon *et al.* [CONDON87A] have discussed methods for the correction of more severe effects.

5.3.3 **RF Penetration Effects.**

The conductivity of a phantom or patient may lead to an RF skin depth or penetration effect giving a sample dependent RF field distortion. The more conducting the phantom, the greater the effect, as the skin effect is caused by RF penetration being opposed by eddy-currents set up by the RF itself. The more conducting a phantom, the more easily eddy-currents can be created. The skin depth, δ , is given by

$$\delta = \sqrt{\frac{2}{\mu_r \mu_0 w\sigma}}$$
(55)

where σ is the sample's conductivity, $\mu_0 = 1.26 \times 10^{-6}$ H/m (the permeability of vacuum), μ_r is the relative permeability of the sample and w is the frequency of the applied electromagnetic wave. The skin depth of physiological saline ($\sigma = 1.00 \ \Omega m$ [CHEN89]) is 6.3 cm, whilst the skin depth of the manganese chloride solution used for the water based phantom is approximately a factor of 10,000 less (σ approximately $1 \times 10^4 \ \Omega m$) is 6.3 m.

Effects in biological tissue may be less than those predicted by models based on uniform conduction medium (eg [BOTTOMLEY78]) since there are insulating structures that prevent large diameter current loops from forming.

5.3.4 **<u>RF Transmission and Reception Non-Uniformity Considerations</u>**

If the amplitude of the excitation (transmission) field varies across the field of view, then spins will not be equally excited. For example, instead of all spins experiencing a 90° and 180° pulse, at some locations there may be under-flipping (eg 85°/170°), whereas at other locations, over-flipping may occur (eg 95°/190°). Both under- and over-flipping cause a reduction in the magnitude of the transverse magnetisation and a reduction in signal intensity, with image intensity being highest where excitation and refocusing pulses are closest to a 90° and 180° flip angle, respectively (provided TR >> T_1). It is therefore very important to have a highly uniform transmission field. In general, the uniformity of solenoidal coils is better than that of saddle shaped coils which are in turn better than surface coils [KEAN86]. Some coils are used for both RF transmission and reception, whilst others carry out a single function. For popular designs such as the saddle coil used in many machines, the small uniform region requires a transmit coil considerably larger than the sample. In the case of the saddle coil, major distortions are evident at distances greater than 0.7 times the radius from the coil centre.

It is crucially important to have a good receiver. A receive coil with the highest possible quality factor, Q (the ratio of reactance to resistance) is required, since in general this gives the best signal to noise ratio. For the same reason a small coil tightly coupled to the sample is preferred. This picks up signal efficiently and, since the resistance will depend upon the length of conductor making up the coil, will generate less thermal noise. It is not possible to increase the size of a receive coil to improve uniformity (as could be done with a transmit coil) because of this conflicting requirement of obtaining a high signal to noise ratio. Hence non-uniformity may be sacrificed somewhat for the sake of SNR.

In summary, the primary consideration for receiver coil design is for a high signal to noise ratio with secondary consideration given to response uniformity while for the transmit coil, RF uniformity is of prime importance.

An increasingly common coil design is the quadrature coil which uses two RF fields with a 90° phase shift between them. As the two received RF signals are correlated, but the noise is not, this allows an improvement in SNR. This is the case with the standard Signa head coil, a high-pass birdcage coil, and the Signa body coil, a low-pass birdcage coil. The birdcage coil is a design that produces a particularly uniform RF field as will be discussed in section 5.5.6. It is the RF uniformity of the head coil that is of particular interest for the work reported here, although some investigations were carried out in the body coil for reasons that will be described later.

5.4 The Signa Tuning Ring

The Signa head coil, a high pass birdcage coil, can be modelled well by a high Q resonance circuit, with Q approximately 250 for an unloaded coil. [Personal communication - Matthew Suminski, IGE, Milwaukee, USA]. The coil is tuned to approximately 250 kHz above the magnet's resonant frequency of 64 MHz. The presence of a patient's head within the coil leads to the Q dropping to 50-100 depending upon the size of the patient's head. Stray capacitance between the end ring and the patient's shoulders also leads to a drop in resonant frequency of the coil by 200-300 kHz leaving the coil tuned to within approximately 50 kHz of

the magnet's resonant frequency. Since the loaded bandwidth of this coil is 650-1300 kHz, patient to patient performance differences are minimal.

The Signa is provided with a tuning ring which is used for imaging objects such as head coil phantoms, small children and babies. The tuning ring introduces a frequency shift similar to that produced by a patient's shoulders, by introducing a small capacitance between small patches of copper on the tuning ring and the end ring of the coil. The tuning ring does not cause significant loading of the coil, however, unlike the patient's head. If the tuning ring were not used, the resonant frequency would remain offset by the initial 250 kHz, while the bandwidth may be as low as 300-400 kHz. As the bandwidth is about the same magnitude as the frequency offset, variations in system performance due to this offset will be apparent.

A hexagonal packed array of water bottles was scanned both with and without the presence of the GE tuning ring. The two images show distinct differences as illustrated by Figure 34 and Figure 35 respectively, which have both been thresholded to the same level. The image acquired using no tuning ring demonstrates a distinct asymmetry, which is assumed to be due to bandwidth limitations, whilst the image acquired using the ring demonstrates approximately circular symmetry as expected from the coil design. The magnitude of the asymmetry of the former image leads to a difference in approximately 9% in signal between bottles equidistant from the coil centre. This compares to less than a 1% difference for the latter case. The tuning ring was therefore used throughout this phantom work.



Figure 34 - Array of water and manganese chloride filled bottles scanned without the presence of the GE tuning ring.



Figure 35 - Array of water and manganese chloride filled bottles scanned with the presence of the GE tuning ring.

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5.5 **RF Standing Wave and Penetration Effects**

In order to reproduce the work of Wicks *et al.* [WICKS92B] for the Signa, a large phantom was obtained and filled with a non-loading solution consisting of a fraction of a gram of manganese chloride per litre of distilled water. The ratio of conductivities of this solution to saline is approximately 10^4 . There was no signal from the phantom when scanned in the head coil, possibly because of either the presence of an electric field close to the coil wires leading to subsequent electric losses, or de-tuning of the coil due to an object being placed too close to the wires comprising the coil. Both effects mean that not enough RF power was entering the phantom. Images obtained using the body coil were subject to severe non-uniformity as demonstrated by Figure 36 which illustrates a profile through an image. A possible explanation of this phenomena is the standing wave effect predicted by Bottomley *et al.* [BOTTOMLEY78]. (Penetration effects would lead to a dip in the centre of the profile.) Further experiments, as reported in section 5.5.1 - section 5.5.6 were carried out to determine if this was the major cause of the non-uniformity, and the possibility of RF penetration effects investigated. These effects were also investigated for a volunteer's head, as reported in section 5.5.7.



Figure 36 - Centre profile through glass phantom filled with water and manganese chloride.

5.5.1 Signa B1 Field Strength

The tip angle experienced by an isolated isochromat when subject to a RF pulse is given by

$$\theta = \gamma B_1 \tau \tag{56}$$

where B_1 is the magnitude of the applied RF field, τ is the pulse duration and γ is the gyromagnetic ratio. The pulse duration for a slice selective RF pulse is fixed and is typically approximately 5 ms for an MRI scanner. For a fixed τ , θ therefore only varies with B_1 , which is proportional to the voltage, V, applied for RF excitation.

The RF transmitter voltage of the Signa is characterised by the Signa's Transmitter Gain (TG), measured in tenths of a dB relative to the maximum output power which is defined as 20 dB or 200 TG units (a non-linear variation). The value of TG is set during an automatic pre-scan (APS) or manual pre-scan (MPS) procedure. The auto-prescan procedure on the Signa attempts to maximise signal over the volume of the centre slice. Now the dB scale is defined as

$$TG in \ dB - 10\log_{10}\left[\frac{PowerA}{PowerB}\right]$$
(57)

where A and B are two arbitrary values. As power is proportional to V^2 it follows that

$$TG in \ dB - 20\log_{10}\left[\frac{VoltageA}{VoltageB}\right]$$
(58)

From (58) it can be shown that the difference in transmitter gain between a 90° pulse and a 180° pulse (ie a doubling in voltage) is approximately 6 dB. From (58) it follows that

$$VoltageA - VoltageB \cdot 10^{\left(\frac{TGA - TGB}{200}\right)}$$
(59)

Now knowing that B_1 , and therefore θ , is proportional to voltage, it follows that the relationship between two different values of θ for the same isochromat is given by

$$\theta_{A} - \theta_{B} 10^{\left(\frac{TGA - TGB}{200}\right)}$$
(60)

According to Glover et al. [GLOVER85], the signal due to a SE sequence is given by

$$Signal - k \sin^3 \theta_A$$
 (61)

It is possible to scan a sample at a range of TGs and plot signal intensity against TG for a small volume approximating an isochromat. This has proved a useful tool for investigating image nonuniformity enabling the transmitted B₁ to be measured at a point independent of receive nonuniformity. The shape of the curve is the same for any small area approximating an isochromat, no matter what B₁ effects are present (eg standing waves, penetration effects etc.). It is only possible to determine the value of θ from such a plot for two situations - when $\theta = \pi/2$ which corresponds to a peak in a plot of TG against intensity, and when $\theta = \pi$ which corresponds to a null in a plot of TG against intensity. It is easier to identify a peak than a null for a sin³ θ variation, so only the position of $\theta = \pi/2$ in a TG plot will be considered further. The magnitude of the signal is measured, rather than its signed value. Thus, substituting for θ from (60) into (61) at $\theta = \pi/2$ gives

$$Signal - k \left| \sin^3 \left(\frac{\pi}{2} \, 10^{\left(\frac{TG - TG \pi/2}{200} \right)} \right) \right| \tag{62}$$

for a SE sequence. The signal predicted by this relationship has been compared to that measured for a small area approximating an isochromat. The value of TG and intensity corresponding to the first peak in the data have been used for the simulation, and the results are illustrated by Figure 37. The fit is very good for the first section of the curve up until the first null, which occurs for a 180° pulse. The fit for the third peak is a little less accurate, which may be due to amplifier non-linearities. It is of particular interest, however, that the magnitude of the second peak is significantly lower than that predicted. The author has no explanation for this phenomenon.

From (56) it follows that at the first peak, where $\theta = \pi/2$,

$$\frac{\pi}{2} - \gamma B_1 \tau_{\frac{\pi}{2}} \tag{63}$$

and therefore that

$$B_1 = \frac{\pi}{2\gamma\tau_{\pi}}$$
(64)

which allows the magnitude of B_1 to be determined if required.



Figure 37 - Comparison between observed and predicted variation of signal with transmitter gain for an isolated isochromat.

5.5.2 Variation of Non-Uniformity with Position in Body Coil

The high degree of non-uniformity of the water phantom images acquired in the body coil could either be due to a combination of RF transmit and receive non-uniformity or to sample dependent factors. If the main source of image non-uniformity were RF transmit and receive uniformity, then varying the position of the phantom within the body coil should map out this non-uniformity. If the uniformity were sample dependent, however, the non-uniformity should move with the sample.

To distinguish the effects the phantom was scanned at several positions within the body coil varying from the centre of the body coil to adjacent to the scanner bore. If there were large RF transmit and receive non-uniformities, then one might expect differences between the intensity of symmetric points about the centre of the phantom, and possibly differences in the value of TG for which the peaks and troughs in intensity occur for different points within the phantom. At each position, data were acquired for a range of TGs. All images were acquired with the same fixed field of view, whilst the phantom's position was varied within this field of view.

The signal intensity from images of the same phantom acquired in different positions within the fixed field of view may be compared in areas of overlap by dividing images. These comparisons clearly demonstrated a large variation of signal ratios for the area of overlap, and hence that RF transmit and receive uniformity was not the major cause of the non-uniformity. Plots of TG against intensity were used to investigate the non-uniformity in more detail. For each position of the phantom within the magnet bore, plots of TG versus intensity were constructed, one for the phantom's centre pixel, and one each for several pairs of positions along the centre x line of the phantom, symmetric with respect to the centre pixel, and along the centre y line of the phantom, symmetric with respect to the centre pixel. The position of the pixels near to the edge of the phantom were chosen so that any Gibbs artifact was negligible. All images are 256^2 in size and were acquired with a fixed 48 cm field of view centred in the magnet bore, which is just larger than 48 cm in diameter. The phantom is 27 cm, or 145 pixels in diameter. Figure 38 and Figure 39 are plots of the variation of intensity with TG for the phantom situated in the centre of the bore, and adjacent to the bore respectively. Both x, the position of a pixel with respect to the fixed field of view, and d, the position of a pixel with respect to the centre of the phantom, are indicated in these figures. Several points are of note

(1) That the peak intensity with respect to TG for each pixel decreases with increasing distance from the phantom centre (not the magnet/RF coil centre) for all phantom positions. The exception to this is the pixel nearest the side of the bore for each of the scans close to the side of the bore. This is due to body coil hot spots. If the dominant source of image non-uniformity was due to RF non-uniformity then the peak intensity should occur at the same TG for all pixels.

(2) That the difference in intensity at each value of TG for symmetric pairs of points is much greater for the phantom scans near the magnet bore than for the phantom scan centred in the magnet bore. This implies that there is some RF non-uniformity close to the magnet bore, as a standing wave effect alone would yield equal intensities for points equidistant from the phantom centre.

(3) That the greatest difference in intensity at each value of TG for any symmetric pair are those between the pixel position closest to the magnet bore and its symmetric pair. This implies an RF hot spot (or hot spots) close to the bore of the magnet.

(4) That the difference in TG for the first peak of the intensity versus TG curves for symmetric pairs is greatest for the pixel position closest to the magnet bore and its symmetric pair. Once again, this indicates RF non-uniformity close to the magnet bore.

If the main source of non-uniformity were RF transmit and receive non-uniformity, then one would expect large differences between the responses of points equidistant from the phantom surface when the phantom is near the bore. This is distinguished from sample dependent effects by comparison with curves due to the phantom centred in the bore. The drop off of peak intensity as pixel position increases from the phantom centre for all phantom positions indicates that there is a sample dependency, and the magnitude of the difference indicates that this is a major dependency. There is also a smaller RF transmit and receive effect.



Figure 38 - Variation of intensity with TG for phantom in the centre of the body coil. x is position with respect to a fixed 256^2 image, and d with respect to the centre of the phantom.



Figure 39 - Variation of intensity with TG for phantom situated adjacent to body coil bore. x is position with respect to a fixed 256^2 image, and d with respect to the phantom centre.

5.5.3 Comparing Images from Different Sized Phantoms

Bottomley and Andrew [BOTTOMLEY78] have shown that an RF wave incident on the side of a semi-infinite cylinder, will lead to RF standing waves in the sample. According to their theory, the wavelength of a standing wave is invariant with cylinder radius. Thus, for a perfect system, the response of a smaller cylinder will be identical to the response at the centre of a larger cylinder. Any penetration effect will vary with sample size, however. In order to further investigate the proposed standing wave effect, images of three cylindrical phantoms of diameter 27.7 cm, 24 cm and 14 cm filled with the same manganese chloride solution as discussed in section 5.5, were acquired in the body coil with each phantom accurately centred on the patient couch. The TG was set to the initial peak of the TG versus intensity curve for a small region surrounding the centre pixel of each phantom for each image. Thus the centre pixels of each phantom are all experiencing a 90° pulse which produces maximum signal intensity. Comparison of the three images was made using ratio images constructed by image division. Noise suppression was utilised in the division process so that small values of the divisor (noise) do not cause large peaks in the output image. In each comparison, the ratio image demonstrated that the non-uniformity was corrected for to first order. This is illustrated by Figure 40 showing a profile through the 24 cm phantom, and Figure 41 showing the noise suppressed division of the 24 cm phantom by the 27.7 cm phantom.



Figure 40 - Profile through 24 cm water phantom


Figure 41 - Profile through ratio image of 24 cm water phantom divided by 27.7 cm water phantom.

The presence of major RF penetration effects (a skin depth effect) may also be eliminated by these results. Such an effect would lead to a lower intensity signal in the middle of a larger phantom, giving a doming effect in the divided image as the result of dividing an image of a smaller bottle by that of a larger bottle, which is not apparent. This is to be expected because of the very large skin depth for the manganese chloride solution. The ratio images are not of constant signal in the areas of overlap, however, despite the correction to first order of image non-uniformity. This may be due to a number of factors which include

Slight mis-registration of phantom scans (which should manifest itself as an asymmetry)

Pronounced Gibbs artifact in the phase-encoding direction of the original data, due to sampling in the phase-encoding direction at only half the rate as in the frequency-encoding direction.

• Smaller scale RF transmit/receive non-uniformity differences due to the fact that the bottles were actually scanned with their centres in slightly different positions within the body coil.

• The fact that the phantoms are not semi-infinite cylinders as assumed in the model but of finite length with non-square ends.

5.5.4 Comparing Images from Oil and Water Phantoms.

The magnitude of RF standing wave effects is dependent upon ε_r , the relative permittivity of the sample. The wavelength of electromagnetic waves within an infinite cylinder is given by

$$\lambda - \frac{2\pi}{w\left(\frac{1}{2}\varepsilon\mu\left\{\left[1+\frac{1}{\rho^{2}\varepsilon^{2}w^{2}}\right]^{1/2}+1\right\}\right)^{1/2}}$$
(65)

according to Bottomley and Andrew's model. At 1.5 T,

$$\frac{1}{\rho^2 \varepsilon^2 w^2} << 1 \tag{66}$$

for both the manganese chloride solution and oil. Thus

$$\lambda = \frac{2\pi}{w\sqrt{\varepsilon\mu}} \tag{67}$$

The standing wave shape scales as radius / λ and tends to zero as radius tends to +/- λ /4. The relative permittivity of water is 80, whilst that of oil is approximately 5. This leads to severe standing wave effects in water, but virtually none in oil, as demonstrated by comparing profiles through scans of the same phantom filled with water and oil respectively and scanned in the same position in the body coil (Figure 42 and Figure 43). Both images were acquired with their respective auto-prescan TGs.

It is of interest to compare the predicted magnitude of the standing wave effect for water with that measured. Using the $\sin^3\theta$ signal variation according to Glover *et al.* [GLOVER85] as discussed in section 5.5.1 and the theory of Bottomley and Andrew, the predicted profile through a 27 cm diameter water phantom has been compare to a measured profile normalised to the intensity at the centre of the phantom. The match between data and theory is very good, as indicated by Figure 45. The small differences between the theory and data may be ascribed to the Gibbs effect, RF non-uniformity and the fact that the phantom is not an infinite cylinder. The magnitude of the standing wave effect for oil leads to a drop in intensity of approximately 3% across the width of the cylinder. This is considered to be small enough to neglect.



Figure 42 - Profile through uniform water phantom in the Signa body coil.

It is interesting to compare a profile through a uniform phantom from the NMR Research Group's 0.5 T Picker scanner which used a body coil for transmission and a saddle head coil for reception (Figure 44). The profile is in the read direction and thus is affected by bandwidth filtering of the data as discussed in section 5.3.2. It is obvious that for the slice considered, the birdcage coil is much more uniform than the saddle coil. It should be noted that Figure 42 and Figure 43 correspond to a 48 cm field of view whilst Figure 44 corresponds to a 30 cm field of view.



Figure 43 - Profile through uniform oil phantom in the Signa body coil.



Figure 44 - Profile through uniform phantom scanned in the Picker head coil.



Figure 45 - Comparison of predicted intensity variation with measured data for RF standing wave effects in a 27 cm diameter uniform water phantom.

5.5.5 Comparing Bottle Array with Uniform Oil Phantom

The magnitude of the standing wave effect is dependent upon the size of the sample. To investigate whether standing wave effects occur in large oil phantoms, the response of an array of small water bottles was compared to that of a large oil phantom. The small size of the bottles means that any standing wave effects will be negligible, so the response of an array of bottles should map out the RF non-uniformity closely. The size of the bottles relative to the field of view requires that 512 x 512 images are used for these investigations in order to minimise the magnitude of the Gibbs artifact. The bottle array was scanned in the centre of the head coil using a large spread of values of TG, as well as a more finely sampled range of values centred on the auto pre-scan value of TG in order to investigate the variation of non-uniformity with TG. The uniformity does vary somewhat over the gross range of TG from 0-72. There is, however, little difference in the finely sampled range of TG from 36-42 close to the Auto Pre-Scan TG. Even examining difference images (the result of subtracting one image from a second image acquired using a different TG) shows little difference. It is noticeable, however, that several of the outermost bottles vary greatly in intensity between scans which may well be because these bottles are particularly close to coil elements, leading to hot spots. The fact that there is little difference in non-uniformity over the finely sampled range is important, as the value of TG calculated during the Signa's auto pre-scan procedure is liable to vary by up to 1 or 2 units for the same sample.

A series of multi-slice images of both the bottle array and oil phantom were acquired using the GE tuning ring, at a range of distances from the centre of the coil in order to map out RF nonuniformity. The results from the bottle array and oil phantom were compared by examining ratio images of one image divided by the other using noise suppression. A profile through a water bottle array scan and a second through a ratio of a water bottle scan and a scan of a uniform oil phantom are illustrated by Figure 46 and Figure 47. Image non-uniformity worsens considerably at distances greater than approximately 5 - 7.5 cm from the coil centre along the coil's major axis.



Figure 46 - Profile through bottle array



Figure 47 - Profile through ratio of bottle array to uniform oil phantom

5.5.6 Comparison with Predicted Birdcage Non-Uniformity

The RF non-uniformity measured using oil phantoms has been compared to theoretical calculations of the uniformity of the head coil presented by Hayes *et al.* [HAYES85]. High resolution 512 x 512 transverse images of uniform oil phantoms were acquired with a long TR and 16 NEX. These were then median filtered and the resolution reduced by pixel averaging to further reduce the effects of noise. The theoretical axial plot of Hayes (Figure 50) may be compared to the measured RF uniformity (Figure 49) using an approximately cylindrical phantom of diameter 27 cm and length 35 cm oriented with its length along the bore of the magnet (ie along z). A plot of the measured sagittal RF non-uniformity is also included (Figure 48) but there is no equivalent sagittal plot due to Hayes *et al.*. The sagittal plot is oriented with z vertical and y horizontal, where z lies along the magnet bore and y horizontally in the bore. Each contour line represents a 10% variation in signal intensity. It is obvious from the comparison that the coil uniformity is not perfect, perhaps due to tuning or manufacturing tolerances, but the general agreement is very good.



Figure 48 - Measured sagittal RF uniformity plot. Each contour corresponds to 10% of the maximum signal within the image.



Figure 49 - Measured axial RF uniformity plot - each contour corresponds to 10% of the maximum intensity within the image.



Figure 50 - Theoretical RF uniformity due to Hayes et al. reprinted by permission of Academic Press Inc, Florida, Fl 32887. Each contour corresponds to 10% of the maximum intensity within the image.

As may be appreciated from Figure 48 and Figure 49, the uniformity of the centre axial slice is good, but sensitivity drops off along the major axis of the coil. The uniformity of axial slices becomes worse with increasing distance from the centre of the coil. A variation in intensity of 25-30% occurs for a uniform oil phantom within the area normally occupied by the human head.

It is important to determine whether RF standing waves occur in the human head, and if they do, with what magnitude. The RF non-uniformity apparent within a volunteer's head has been investigated using plots of TG against intensity, as described in section 5.5.1, for a number of regions of pure white matter spaced throughout the head. The magnitude of the standing wave effect for an oil-filled phantom as large as the Signa head coil is insignificant, whereas the standing wave effect for the same-sized water-filled phantom is very significant. Although composed largely of water, the human head is not a homogeneous medium but rather a heterogeneous collection of bone, tissues and fluid, containing many membranes, and within the brain itself, many insulating cells. It is hence unlikely that exactly the same RF standing wave effect will be discernible within the human head as was apparent within the uniform water phantom, and visual observations seem to confirm this hypothesis. Further investigations have been carried out to confirm this. This has been done using scans of a volunteer's head acquired with a range of TGs surrounding the auto-prescan TG for the head using a dual echo sequence with a long repetition time (SE/4000/30,80) in order to allow tissues to fully relax. Small regions of white matter were identified in the late echo image where grey matter and CSF partial volume pixels could be more easily identified due to the superior grey matter/CSF contrast at this echo time. These regions were also checked using the early echo images to ensure that there were no grey matter and white matter partial volume pixels. To ensure that there were no in-slice partial volume effects, regions of white matter were only chosen if the same region in adjacent slices also contained only white matter. These checks were made for each scan in the sequence. For each region plots of TG versus intensity were constructed. As discussed in section 5.5.1, the TG at which intensity first peaks is a measure of the transmit B_1 necessary to give a 90° tip angle. The plots for each of the regions peak within a very small range of TGs as illustrated by Figure 51 and Figure 52 (80-81 for the early echo and 79-80 for the late echo) which demonstrates the absence of any RF standing wave or penetration effect in the volunteer's head. This is important because the presence of such sample dependent effects would lead to different effects for different sizes and shapes of head. This would make any correction for nonuniformity more difficult and also less accurate.



Figure 51 - Variation of intensity with TG for white matter regions from early-echo images of a volunteer's head.



Figure 52 - Variation of intensity with TG for white matter regions from late-echo images of volunteer's head.

5.5.8 Summary

The major source of non-uniformity within large uniform water phantoms at 1.5 T has been demonstrated to be due to RF standing wave effects by a variety of methods. The nonuniformity of oil and water phantom images have been compared, water phantom images acquired at various positions within the body coil compared and the magnitude of water nonuniformity compared to the predicted magnitude of standing wave effects. Images of different sized water phantoms have been compared, the non-uniformity of a uniform bottle array has been compared to that of a large uniform oil phantom, and the measured RF non-uniformity for a birdcage coil compared to the predicted non-uniformity. The non-uniformity of oil phantoms has been shown to reflect the RF non-uniformity of the head coil. RF standing waves have been shown not to play a dominant role within the human head for the Signa head coil at 1.5 T.

5.6 The Effect of Crosstalk on Contiguous Slice Datasets

It has been observed in previous papers reporting work on a 1.5 T GE Signa scanner and a 0.5 T Picker scanner that the drop off in intensity of a uniform phantom along z (ie along the scanner bore), does not occur smoothly for axial scans, but in an alternating stepping manner [JOHNSON87, WICKS91, OWEN90]. Johnson et al. noted non-uniformities in multi-slice axial datasets with interleaved slice acquisition and claimed that this effect was due to uncorrected eddy currents distorting the gradient field and introducing non uniformities from one slice to the next and also within a single slice. They postulated that slice to slice non-uniformity occurred because eddy currents built up during the multi-slice sequence and progressively altered slice width. Wicks et al. [WICKS91] have also investigated non-uniformity on the same 0.5 T scanner as Johnson et al. [JOHNSON87], after some hardware and software enhancements had been made. Again, they noted a significant odd-even slice-to-slice non-uniformity which they attributed to gradient eddy currents. Although gradient eddy-currents may have contributed to the stepping observed by Johnson *et al.* and Wicks *et al.*, it is likely that the major source of the stepping was due to crosstalk in the contiguous slice datasets they used. The proximity of these slices results in crosstalk for standard shaped RF pulses even for interleaved slice acquisition. The time between excitation of adjacent slices for interleaved acquisition is approximately TR/2. Hence the magnitude of such crosstalk effects will depend upon T1/(TR/2) - the relaxation of a slice between excitation by crosstalk and deliberate excitation. This leads to a characteristic

stepping of intensity values in the slice direction for an even number of slices as explained later in this section, but not for an odd number. If data are acquired in a contiguous manner, then the accuracy of the uniformity correction may be limited, in addition to patient image contrast being compromised.

The characteristic stepping of the z-profile may be explained by considering a simple model of a ten slice contiguous data acquisition with the slices acquired in an interleaved manner (ie 1,3,5,7,9,2,4,6,8,10) as illustrated by Figure 19. The Signa will excite each slice at intervals of 100 ms for a TR of 1000 ms (ie slice 1 at 0 ms, slice 2 at 500 ms, slice 3 at 100 ms etc.) The crosstalk that occurs with typical Gaussian or sinc shaped RF pulses leads to adjacent slices being partially excited in addition to the slice of interest. Thus, for example, the RF pulse applied to excite slice 4 will also partially excite some of the spins in slice 3 and 5. With an even number of slices in a contiguous block, even and odd numbered slices will have different times in which to relax after being partially excited by neighbouring slice RF pulses. As an example, consider slice 6 at the time of its slice acquisition. The last time that it was partially excited, by the acquisition of slice 7, was 400 ms ago, and by the acquisition of slice 4, 600 ms ago.

1	2	3	4	5	6	7	8	9	10	
0 ms	500 ms	100 ms	600 ms	200 ms	700 ms	300 ms	800 ms	400 ms	900 ms	

Figure 53 - Model of interleaved slice acquisition of 10 slice contiguous slice dataset.

Consider a similar situation for the acquisition of 9 slices as illustrated by Figure 54, with a repetition time of 900 ms and an interval of 100 ms between each interleaved slice excitation. For an odd number of slices, there is no stepping effect. As an example, consider slice 6 at the time of its slice acquisition. The last time that it was partially excited, by the acquisition of slice 7 was 400 ms ago, and by the acquisition of slice 6, 500 ms ago. This is the same for the case of slice 5, where the last time that it was partially excited, by the acquisition of slice 6, was 400 ms ago, and by the acquisition of slice 4, 500 ms ago.

Each of the end slices is adjacent to only one other slice, and thus experiences less partial excitation than the other slices. The intensity of the end slices is therefore expected to be higher than the other slices. It should also be noted that the magnitude of the partial excitation will decrease with increasing slice skip. It is therefore expected that image intensity will increase with increasing slice skip. Such stepping effects for even numbered slices, the absence of effects for odd numbers of slices and the presence of end effects have been confirmed both by experimentation with uniform phantoms, and have also been experienced clinically.

1	2	3	4	5	6	7	8	9
0 ms	500 ms	100 ms	600 ms	200 ms	700 ms	300 ms	800 ms	400 ms

Figure 54 - Model of interleaved slice acquisition of 9 slice contiguous slice block of data.

The phantom scans utilised the large oil phantom and were acquired using a spin echo sequence with 5 mm thick slices, a TE of 20 ms and a TR of 300 ms. The use of a short TR was necessary because of the short T_1 of oil (approximately 300 ms). The variation of intensity with the number of slices has been investigated by plotting the mean intensity of a small region at the centre of a slice against slice number for various contiguous slice datasets of 3-8 slices as illustrated by Figure 55. The distinct stepping is clear for an even number of slices and contrasts with the small difference for odd numbers of slices. End effects are noticeable for this data, as expected.

The stepping is greatly reduced for non-contiguous slices, as illustrated by Figure 56 which shows the variation of intensity for 7 and 8 slice datasets acquired both contiguously and with 2.5 mm and 5 mm slice skips. As predicted, image intensity increases with slice skip. It should be noted that there are small ripples for the 7 slice VEMP datasets acquired with 5 mm slice thickness and 2.5 mm slice skip. The model does not explain these findings.



Figure 55 - Variation of crosstalk with number of slices for contiguous slice VEMP datasets

The use of VEMP and CSMEMP pulse sequences has also been compared, the latter being distinguished from the former by slice profiles which are claimed by GE to be much squarer than those in standard use. This should make such pulses more suitable for contiguous slice acquisition as crosstalk should be reduced. Figure 57 demonstrates the difference between VEMP and CSMEMP for contiguous data and for 5 mm slice skip data using both 7 and 8 slice datasets. Although the variation of intensity with slice number for contiguous datasets is less for the CSMEMP sequence, a variation is still apparent. For datasets with a 5 mm slice skip, the use of CSMEMP does appear to give perfect results, the drop off in intensity from the centre being due to RF non-uniformity. The CSMEMP 7 slice dataset acquired with 0 mm slice skip again demonstrates small ripples not explained by the model.



Figure 56 - Variation of crosstalk with slice skip for 7 and 8 slice VEMP datasets

The magnitude of crosstalk effects is critically dependent upon TR and the T_1 s of the tissues under study, as previously discussed. The effects can be avoided or substantially reduced by the use of non-contiguous acquisition techniques, which typically require gaps between slices of at least half the slice width, or of better shaped RF pulses. One effective technique to avoid the problem and yet still acquire contiguous data is to force two data acquisitions where firstly all of the even numbered slices are completely acquired in one acquisition, and then secondly all of the odd numbered slices are completely acquired in a second acquisition. Within each acquisition, data is acquired in an interleaved fashion. The applicability of this approach depends upon the TR, the number of slices required and the flexibility of the acquisition software. Such an approach is possible on the Signa.



Figure 57 - Variation of crosstalk with slice skip for VEMP and CSMEMP pulse sequences and 7 and 8 slice datasets

5.7 Gradient Eddy-Current Effects

Johnson *et al.* [JOHNSON87] and Wicks *et al.* [WICKS92] reported work on the NMR Research Group's previous scanner, a 0.5 T Picker scanner and postulated that uncompensated gradient eddy-currents may cause non-uniformities in either of two ways. Firstly, unwanted gradients present during selective pulses may select a slice of a different thickness or in a different position to that required. Secondly unwanted time-varying gradients present during the spin-echo sequence may cause de-phasing, which is not re-focused by the 180^o pulse and therefore results in signal loss. In order to investigate the magnitude of any gradient eddy-current effects on the Signa, which has a shielded gradient system, a number of single slice scans were acquired with a fixed TE of 40 ms, and with TRs varying from 3000 ms down to the scanner minimum for a spin-echo of approximately 60 ms in the Signa head coil. Ratio images were used to compare the non-uniformity at different TRs. For long TRs (greater than 500 ms), there were no variations in non-uniformity. Figure 58 demonstrates a profile through a ratio image of a SE/3000/40 image divided by a SE/500/40 image. Figure 59 demonstrates a profile through a ratio image of a SE/3000/40 image divided by a SE/60/40 image.



Figure 58 - Profile through ratio image of an SE/3000/40 image divided by a SE/500/40 image. Fifty lines have been averaged to improve SNR.



Figure 59 - Profile through ratio image of a SE/3000/40 image divided by a SE/60/40 image. Fifty lines have been averaged to improve SNR.

Comparison of long TR images with progressively shorter and shorter TR images, however, demonstrated increasing differences between the non-uniformity of the scans, with small variations first apparent at a TR of 500 ms.

In order to isolate the effect of the RF transmit and receive non-uniformity from any gradient eddy-current effects, a second set of images were acquired using the same parameters as before but acquiring images in the body coil. Although a small proportion of the non-uniformity differences could be attributed to differences in coil homogeneity, the major distortions apparent for shorter TRs were still apparent with the body coil scans. The fact that no long TR differences exist between images and that distortions increase progressively for diminishing TR strongly suggests the presence of gradient eddy-current effects with a short characteristic time constant.

In addition to the experiments above, further scans of multi-slice datasets were acquired at TRs greater than 500 ms, to investigate whether multi-slice acquisition, which works the gradients harder than single slice acquisition, might induce gradient eddy-currents at these longer TRs. No evidence of any gradient eddy-currents was apparent. It is therefore concluded that nonuniformity depends on TR below 1000 ms.

5.8 Variation of Non-Uniformity with TE

The possibility of a variation of non-uniformity with echo time was investigated at a long repetition time with a single echo sequence for a range of echo times from 20 to 160 ms. Dividing early echo images by late echo images shows drop off of the ratio image in the poor homogeneity sections of the head coil. For small differences in echo time, the drop off is not large, but increases for larger differences in echo time. The signal to noise ratio of the later echo images makes accurate comparison very difficult for such images. This work was again repeated in the body coil, where virtually no non-uniformity was apparent in the ratio image, suggesting that the effects in the head coil are due to inaccuracies in the 180° pulses leading to poor refocusing because of the RF non-uniformity of the head coil. Figure 60 illustrates a profile through a SE/3000/20 image divided by a SE/3000/80 image for a head coil, whilst Figure 61 shows the equivalent ratio image for a body coil. Wicks *et al.* may not have experienced this effect as they transmitted with the body coil and received with a head coil, whilst the Signa both transmits and receives with the head coil.



Figure 60 - Profile through the ratio of a SE/3000/20 image divided by a SE/3000/80 image for a head coil. Profile is along the centre of the major axis of the head coil.



Figure 61 - Profile through the ratio of a SE/3000/20 image divided by a SE/3000/80 image for a body coil. Profile is along the centre of the major axis of the body coil.

5.9 Variation of Non uniformity with Receive Bandwidth

Typically, dual-echo clinical scans are acquired with widely varying echo times and a smaller bandwidth of the later echo image. Decreasing the receive bandwidth of the late echo image gives better signal to noise ratio on the image, but the non-uniformity for a wide range of different bandwidth late-echo images appears to be the same - the only difference being the signal to noise ratio. For the Signa, with variable bandwidth activated, the lowest possible bandwidth is selected as default.

5.10 Variation of Non-Uniformity with Number of Echoes.

As a dual-echo sequence is used clinically, any variation of non-uniformity with the number of echoes per sequence is of importance. Several four-echo datasets were acquired with a given echo time varying in position in the echo train between datasets. For example, a 40 ms echo might be acquired as the first echo in a 40/80/120/160 ms echo train, but the second echo in a 20/40/60/80 ms echo train. This allowed comparison of the effect of position within the echo train without variation with echo time biasing results. There are relatively large differences between the first and subsequent echoes in a train with subsequent echoes suffering more, as slight inaccuracies in the 180° pulse lead to increasingly poor refocusing. This is illustrated by Figure 62, which shows a profile through the result of dividing a SE/3000/80 image by the fourth echo of a SE/3000/20,40,60,80 image. The differences are more apparent in parts of the image further from the coil centre, where RF uniformity is inherently poor. Thus non-uniformity depends on the position of a given echo in the echo train of a multi-echo sequence.



Figure 62 - Profile through the ratio of a SE/3000/80 image divided by the fourth echo of a SE/3000/20,40,60,80 image. Profile is along the centre of the major axis of the head coil.

5.11 Difference in Non-Uniformity between Transverse and Sagittal/Coronal Scans.

Comparisons of the variation of intensity of scans of different orientations have shown that there are differences between the non-uniformity of transverse and sagittal/coronal scans. No difference was apparent between sagittal and coronal scans. Data acquired at the maximum recommended distance from the head coil centre with a coronal/sagittal scan has a 20-25% greater intensity than equivalent data from axial scans. This difference drops to less than a 1% difference (due to noise) when GRADWARP, GE's proprietary method of correcting for gradient non-linearities (as discussed in section 9.3.2.1) is switched off. This implies that there are differences in GE's method of correction between axial and sagittal/coronal scans.

5.12 <u>Non-Uniformity of the Size and Shape of Image Planes</u>

The size and shape of image planes, geometric distortion and slice warp is discussed in section 9.5

5.13 Temporal Stability of RF Non-Uniformity Measurements

The large oil phantom was scanned once a month following the manufacturer's service day on the Signa for 6 months. The bottle was carefully positioned and exactly the same protocol used each month. Each dataset was median filtered to reduce noise, and five ratio images created using the most recent image as the reference. Each ratio image was analyzed slice by slice using image profiles and small (100 pixel) regions throughout the area that the head occupies within the coil.

Absolute mean intensities of the ratio images varied by up to 15% throughout the six month period. Within the area occupied by the head, up to 4% variations in signal ratio could be identified. There was no observable drift with time of the maximum variation in signal ratio. Close to the coil wires and at the end of the coil furthest from the patient, variations in signal ratio could be larger however. A maximum 4% variation over a 6 month period is very encouraging.

5.14 Correction of RF Non-Uniformity

At the time of writing, the method of RF non-uniformity correction used by Wicks *et al.* [WICKS92B] for data from the Picker scanner had not been adapted to use Signa data. Until this is done, uniformity correction must be achieved by scan repetition. This involves acquiring a patient scan and a scan of a uniform oil phantom large enough to cover the area of interest, using the GE tuning ring. The phantom scan is median filtered in order to suppress noise whilst still retaining the underlying pattern of RF non-uniformity. A number of sizes of median filtered images have been investigated and the standard deviation of small square regions of interest measured. Plotting standard deviation against filter size for this data, as illustrated by Figure 63, demonstrates the magnitude of noise reduction achieved for a given filter size. The effect of the median filter on the standard deviation of a small region is similar to a plot of 1/(filter dimension), as illustrated by such a plot normalised to the first data point. A 9 x 9 pixel median filter gives a good compromise between accuracy and processing time. Using a median filter of larger width will not significantly increase the smoothness of the image but will significantly increase the processing time. Uniformity correction is achieved by dividing the patient data by the median filtered phantom data, using a simple method of noise suppression for pixels outside



Figure 63 - Variation of standard deviation of region of uniform oil phantom with size of median filter compared to a 1/dimension curve.

This method of non-uniformity correction has been compared to that reported by Lim *et al.* [LIM89] who also acquired data using a GE 1.5 T Signa. The method of Lim *et al.* is discussed in section 4.2 and is based upon using a low pass filtered version of an image to estimate image non-uniformity. With regards to RF non-uniformity, Lim *et al.* state that

"Radio frequency inhomogeneity is relatively low in spatial frequency compared with the anatomical information of interest, and one can use two dimensional digital filtering to remove this artifact."

This approach has been reproduced for the sake of comparison. The skull stripped and feathered images are illustrated by Figure 64 and Figure 65, whilst the low-pass image and the actual RF map corresponding to the position of the image slice are illustrated by Figure 66 and Figure 67. The low intensity regions to the left and right of the RF map are due to wraparound of data, which is in a region not occupied by the head and thus unimportant. The difference between the 'low pass' version of the feathered image and the actual RF map may best be illustrated by x and y profiles through the two images as shown by Figure 68 - Figure 71. These profiles clearly demonstrate that this approach is not particularly accurate for SE/3000/30 data using the current Signa RF coil for this slice position. Using SE/2000/30 data gives even worse results, as does the use of slices where the RF non-uniformity is worse. It can therefore be concluded that there are several disadvantages with the approach of Lim *et al.*

■ the approach is two dimensional, as opposed to the RF map illustrated by Figure 67 which is part of a 3-D dataset

■ the approach relies on the accuracy of skull stripping, and is therefore not a generally applicable method that could be used for data acquired at an arbitrary angle, as the skull stripping only works for near axial slices.

• the use of a low pass version of the image for correction is appropriate for surface coil imaging where the coil position relative to the patient is not known and there is a large variation of sensitivity within the field of view. Where positioning of the coil relative to the patient is known, and variation in sensitivity is not extreme, using highly blurred versions of images is not a generally applicable method of non-uniformity correction.

■ the method does not yield an image accurately reflecting the RF non-uniformity, so the absolute intensity of corrected image pixel values is not meaningful and can not be used for further intensity based processing such as thresholding or clustering.

The use of scans of uniform oil phantoms to correct for image non-uniformities therefore has a number of advantages over the method of *Lim et al.*, providing, as it does, an accurate, fully automatic, three dimensional approach suitable for images acquired at an arbitrary angle.



Figure 64 - Skull stripped image.



Figure 65 - Feathered image



Figure 66 - 'Low pass' version of feathered image



Figure 67 - Corresponding image of a uniform oil phantom.





Figure 68 - Horizontal profile through RF map.

Figure 69 - Horizontal profile through 'low pass' version of feathered image.



Figure 70 - Vertical profile through RF map



Figure 71 - Vertical profile through 'low pass' version of feathered image.

5.15 <u>Summary</u>

RF standing wave effects [BOTTOMLEY78] occur in water phantoms at 1.5 T with their wavelength dependent upon the permittivity of the sample. Some authors [UK90, LERSKI92] have failed to distinguish these effects from other sources of non-uniformity when using water phantoms at 1.5 T. The standing wave effects can be separated from others by comparing the response of a water and an oil filled phantom, since the permittivities of oil and water differ significantly, with negligible standing wave effects apparent in oil for the size of phantoms used. Oil phantoms have therefore been used for the majority of this work. The possibility of both RF standing waves and RF penetration effects has been investigated using plots of transmitter gain (ie tip angle) against amplitude for both uniform phantoms containing either water or oil, and a human volunteer. No evidence of RF penetration effects or RF standing waves was found for the oil phantom or the human volunteer. The use of a phantom requires that a tuning ring is used to ensure that the magnet and head coil frequencies are matched. The temporal stability of uniform oil phantom images is very good.

Wicks *et al.* believed that one set of scans for a given pulse sequence could be used to correct for the major image non-uniformities caused by RF transmit and receive non-uniformities for a head coil. It has been demonstrated that this is not the case for our 1.5 T scanner. Multiecho non-contiguous spin-echo data may be accurately corrected for non-uniformity at repetition times greater than approximately 1000 ms using multi-echo scans of oil phantoms acquired with a TR greater than or equal to 1000 ms and approximately the same TEs. There are additional small effects due to the variation of image non-uniformity with position in a multi-echo train and the nature of GRADWARP, however. Deviations from these requirements, especially the use of water phantoms, low TRs and contiguous datasets are likely to limit the accuracy of uniformity correction.

CHAPTER 6

EDGE-BASED SEGMENTATION.

6.1 Introduction

Edge based methods of segmentation are appropriate for segmenting regions that are characterised by a strong border. Such regions include the intracranial region, ventricles, eyes and skin for neurological images acquired with appropriate parameters. Different approaches to edge detection are proposed for each of the above regions, and the reasons behind the choice of approaches discussed. The intracranial region is identified by tracking strong edges through scale space, the ventricles by a dual thresholding of edge strength information, the eyes by a shape matcher known as the Hough transform and the skin by tracking edges in a binary localised edge image. Both 2-D and 3-D edge detection have been investigated.

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6.2 Edge Operators

6.2.1 Small Support Convolution Operators

A number of basic edge operators were investigated in the early stages of this work, including the two-dimensional Roberts [ROBERTS65] and Sobel operators and the threedimensional Zucker-Hummel operator [ZUCKER81], a 3-D generalisation of the Sobel operator. Canny [CANNY86] pointed out three criteria that a good edge operator should satisfy as discussed in section 3.3.2.4. The Roberts, Sobel and Zucker-Hummel operators tend to perform rather poorly on neurological MR images, the main problem being multiple responses to a single edge, which is not surprising for edge detectors of such small support.

6.2.2 <u>The Marr-Hildreth and Canny Edge Detectors.</u>

The Marr-Hildreth and Canny edge operators (sections 3.3.2.5 and 3.3.2.4) are both very popular in the literature because of their effectiveness and their firm theoretical basis, and have been used as the basis for this work. The Marr-Hildreth operator [MARR80] localises edges at zero-crossings in the second derivative of a Gaussian smoothed image, whilst Canny's operator smooths the image by a Gaussian and defines edges as maxima along the gradients of the smoothed image. The operators are characterised by the standard deviation of the blurring Gaussian measured in pixels. The two methods are similar, Canny's method being theoretically superior but computationally more intensive. Both can be implemented in the spatial or Fourier domains. The author's implementations are in the Fourier domain as the speed of processing is independent of kernel size, as opposed to a spatial implementation where speed is dependent upon the kernel size. This is important for flexibility in a research environment when large standard deviations of the blurring Gaussian are used.

Marr and Hildreth suggest that four filter widths are particularly appropriate to use for their filter, based upon physiological experiments of the eye. The channels, defined by standard deviations measured in minutes of an arc, and the corresponding details of contours to which they are supposed to match are

- 4.5 fine details.
- 9 medium details, usually the most useful for simple filtering.
- 17 gross outlines of objects present.
- 30 general lighting contours of highly blurred images.

They suggest that information should be combined from these four channels. Combining typical responses from two or more such images (using a logical and) gives very little useful information for any one of a wide range of MRI images, however. Edge-focusing and the concept of an edge-based stack, as discussed in sections 6.6.3 and 10.2.2.3, are both methods of using information from more than one scale.

There are two ways of calculating the position of edges using the Canny edge operator. Edge positions may be determined from first derivatives by calculating the first directional derivatives $I_x(i,j)$ and $I_y(i,j)$ of an image I(i,j). The direction of the edge is the direction of the tangent along the contour in the image plane, which can be trivially computed from the first directional derivatives. The gradient magnitude image is then thresholded with hysteresis (as discussed in section 6.2.3). Alternatively, one can locate edges using zero-crossings in the second derivative in the edge direction. These correspond to maxima of the first derivatives. The use of zero-crossings gives cleaner edges and has therefore been adopted as the method of choice.

6.2.3 <u>Hysteresis Thresholding</u>

The production of either magnitude edge images or localised zero-crossing edge-maps with an associated magnitude still leaves the task of isolating the edges of interest. One problem that is often encountered with a single edge strength threshold is streaking, where a single contour is separated into several elements as the edge strength dips (perhaps only marginally) below the threshold. Hysteresis thresholding is a dual thresholding method introduced by Canny [CANNY86] in which part of a contour above the higher threshold is output as well as the connected segment of contour which lies above the lower threshold. Examples of such an approach are illustrated by Figure 72 - Figure 75 and discussed in section 6.6.1.



Figure 72 - Original late echo image



Figure 73 - Canny edge image thresholded at 80% of maximum edge strength.



Figure 74 - Canny edge image thresholded at 20% of maximum edge strength.



Figure 75 - Canny edge image hysteresis thresholded at 20% and 80% of the maximum edge strength.

6.3 <u>Comparison of Two and Three Dimensional Edge Detection</u>

The results of the three-dimensional Zucker-Hummel edge detector show distinct improvement over that of its two dimensional equivalent, the Sobel operator, but as discussed already, there are major problems with multiple responses to single edges with operators of small support. Hence, the use of such operators has been discarded. The effect of both a 2-D and 3-D Marr-Hildreth operator has also been investigated and their performance compared. One would expect similar, if slightly better results, when comparing a 2-D and 3-D Canny operator.

The implementation of a three dimensional Marr-Hildreth operator has very important considerations for the method's speed. One approach is to carry out the blurring and Laplacian operations associated with the Marr-Hildreth operator in Fourier space. For flexibility in a research environment where a large range of standard deviations are being investigated, such a method is more appropriate than a spatial one. This is because blurring in the Fourier plane by point wise multiplication is more accurate than convolution in the spatial domain and faster for larger standard deviations. Processing very large data sets whilst keeping all data in memory is not practical using this method and Unix workstations with standard memory sizes, as the Fourier transform requires near-random access to the complete data set, leading to data constantly swapping from disk to memory and a disc-bound, rather than cpu bound process. The speed of operation is independent of the standard deviation of the blurring Gaussian, however.

A second approach is to use a Difference of Gaussians (DoG) operator (section 3.3.2.5), an approximation of the Marr-Hildreth operator, in the spatial domain. The processing time is proportional to the standard deviation of the blurring gaussian in contrast to a spatial method employing a 3-D kernel where speed is proportional to the cube of the kernel dimension. Thirdly, a 3-D version of Deriche's recursively implemented 2-D edge detector may be used [MONGA91] where processing takes place in the spatial domain, yet processing time is independent of the standard deviation of the blurring Gaussian. A 3-D recursive edge detector which could utilise dual-echo data, such as the multi-spectral edge detector suggested by Cumani [CUMANI91] might improve results.

Both volume gradient-echo data and multi-slice spin-echo data have been processed using both a spatial DoG and a Fourier transform Marr-Hildreth algorithm. The speed of the two implementations is critically dependent upon the size of the dataset, and, in the case of the DoG algorithm, upon the standard deviation of the blurring gaussian. For example, processing a 256x256x256 image with a standard deviation of 3 pixels takes 1 hour and 20 minutes on a Sun SparcStation 1+ workstation, with a cpu utilisation of 30% for the DoG algorithm. This could be vastly improved with more memory. For comparison, the same job took approximately 3 weeks for the Fourier transform algorithm due to the vast amount of swapping which takes place. This gave a utilisation of cpu of a small fraction of a percent. An increase in memory would again, dramatically increase the speed of such an approach. A comparison of the two methods shows differences in the positions of only a few edge pixels in the output images.

The gradient-echo data can be acquired as isotropic data, but the spin-echo data is acquired with a slice thickness approximately 3-5 times the in-plane voxel dimension. Spin-echo data is preprocessed by interpolating the data to produce isotropic voxels. Edges identified using the 3-D operator are better defined and the edges are contiguous in neighbouring slices. The finer sampling of the gradient echo data gave good results generally, but problems were apparent in places with spin-echo data, where the interpolation blurred edges and reduced edge strengths. Gradient echo data does not in general, however, give the same range of contrast as spin-echo data. It can not, therefore, be considered as a direct substitute for spin echo data.

6.4 <u>Skin Definition</u>

The early-echo images are used for skin definition because of the superior contrast between skin and background in these images. Edge-detection methods utilising contour following, thresholding of edge magnitude images, or hysteresis thresholding for various edgedetectors did not prove robust enough when a multi-slice data set was considered, although they could be fast and effective in limited situations. Such approaches failed due to the low intensity signal in the middle ear and nasal region producing poor contrast with the background and hence very weak edges. None of the techniques mentioned above performs well with weak edges.

The skin is currently defined using a simple edge-tracking process on a Canny edge image. A thinning operation (ie an operation which produces single thickness contours from thicker contours) is first applied to the Canny edge image to remove any double thickness lines, and a low threshold applied to remove the weak edges due to noise in the background. A starting point
for the tracking can be robustly identified by choosing the nearest edge-pixel to the posterior border of the image from a medium thresholded Canny edge image. A simple edge tracker is then initiated at this starting point on the **unthresholded Canny edge image**. This has the advantage of providing a stable starting point, whilst tracking on an image where edge sections have not been lost due to very weak edges such as those in the middle ear and the nasal region.

The tracker follows binary edges in an edge image in a clockwise manner, always attempting to turn anticlockwise to stay on the outer contour, and so avoid the need to make decisions at T-junctions. Occasionally data may be acquired with a slightly misplaced field of view so that the tip of the nose is missing in several slices. The tracker is therefore designed to handle simple dead-ends by reversing direction. The tracker then follows the outer contour in an anticlockwise direction, always attempting to turn clockwise first. This can be represented in pseudocode as

start

thin_Canny_edge_image
start_pixel = nearest edge pixel to posterior border of medium thresholded Canny edge
image
old_direction = direction closest to clockwise
loop until (current_pixel == start_pixel)
if (found_end)
new_direction = next_pixel_clockwise(8 neighbours in anticlockwise
order from old_direction)
else
new_direction = next_pixel_anticlockwise(8 neighbours in clockwise
order from old_direction)
if (new_direction = opposite(old_direction))
found_end = TRUE
end_loop

end

The results of this approach are illustrated by Figure 76 - Figure 79. Undoubtedly more complex tracking procedures could be used, but this approach has proved adequate and may possibly be faster than more complex methods. It has been found that strong contours in the nasal region often do not correspond to anatomical contours for the Canny and Marr-Hildreth operators used.

It will therefore be necessary to investigate morphological postprocessing (as discussed in section 6.6.3.2) or possibly a different edge detector for this region.



Figure 76 - Canny edge image at level of the ears thresholded above 20% of the maximum edge strength.



Figure 77 - Skin contour corresponding to thresholded Canny edge image at the level of the ears.



Figure 78 - Canny edge image superior to eyes thresholded above 20% of the maximum edge strength.



Figure 79 - Skin contour corresponding to thresholded Canny edge image at a level superior to the eyes.

6.5 Identification of the Eyes

The Hough transform is a popular means of matching a template to an image which works by accumulating estimates of parameters of a given shape. It has been used to identify the eyes because of their well defined shape. Late-echo images in which the high signal of the globe of the eyes provides better contrast with the ocular fat have been utilised here. Four binary edge images were tested as input to the Hough transform - a Roberts image (as discussed in section 3.3.2.2), a Canny edge image, a low-thresholded Canny edge image, and an edge-focused Canny edge image (see section 6.6.3). The results corresponding to each image are illustrated by Figure 80 - Figure 83. The Roberts operator fails to pick out the diffuse eye border in the original image, caused by the high partial volume effect due to the small size and high curvature of the eye relative to the slice thickness, and gives poor results. The standard Canny edge image performed poorly due to coincidental circular patterns amongst the edges due to background noise being identified in preference to the eyes. Edge focusing at the level of the eyes may on occasions miss short contour sections and again may not always give good performance, so a thresholded Canny edge image was chosen as the best image for eye detection. Using approximate anatomical knowledge of where the eyes should lie (in the anterior inferior section of the multi-slice dataset) allows the processing time to be cut down considerably over that needed to process the entire dataset.



Figure 80 - Strongest circle candidates in Roberts image overlaid upon original late-echo image



Figure 81 - Strongest circle candidates marked in a Canny edge image



Figure 82 - Strongest circle candidates marked in a Canny edge image thresholded at 20% of the maximum edge strength



Figure 83 - Strongest circle candidates marked in an edge-focused Canny edge image

6.6 <u>Intracranial Region Identification</u>

6.6.1 <u>Hysteresis Thresholding</u>

For late echo images and superior slices, Canny hysteresis thresholding applied to late echo images is a fast method of picking out the contour surrounding the intracranial region, as illustrated by Figure 72 - Figure 75. It is not a reliable technique for processing of the lower slices, however, because of the presence of other strong contours in addition to that surrounding the intracranial region.

6.6.2 Fast Radial CSF Identification

A fast method of intracranial region identification has been developed which relies on a sharp intensity change at the border between CSF and the skull. The long TR long TE spin echo images used for this work demonstrate such contrast (see Figure 84 and Figure 86). Edge pixels are identified as those pixels on a radius from the centre of gravity of the image at which the presence of a sharp drop from a running average of the last few pixels is identified. The presence of regions of CSF within the brain (such as the ventricles and sulci), means that other sharp transitions exist. These are avoided by two mechanisms. Firstly a 90° "warm-up" period is allowed during which border pixels are not marked in the output image. Secondly, the search for border pixels only starts at a radial position close to that at which the last border pixel was identified. Each border pixel is joined up using the Bresenham line drawing algorithm [FOLEY90] and the region filled to create a brain mask (Figure 85).

Using SE/3000/80 data at 1.5 T with its high CSF signal, the fast radial CSF approach generally works well on most slices. It does give a somewhat rough border for the most superior slices, however, because of heavy partial volume effects due to slice thickness. In one or two slices, just superior to the eyes, a small amount of partial volume leakage may occur at indistinct boundaries, typically characterised by extended protrusions at the position of ocular fat superior to the eyes (see Figure 87). Manual editing to correct for this is typically very fast and easily achieved. There may be problems for a number of lower slices at positions where the radius of the border changes sharply which may be overcome by combining images processed in both anticlockwise and clockwise manners with a logical or. The accuracy of this method is discussed



Figure 84 - High slice late-echo SE image (SE/3000/80)



Figure 85 - Intracranial region corresponding to high slice late-echo image identified by fast radial approach.



Figure 86 - Late-echo SE image just superior to eyes (SE/3000/80)



Figure 87 - Intracranial region corresponding to late-echo image just superior to eyes identified by fast radial approach.

6.6.3 <u>Edge-Focusing.</u>

In edge detection schema incorporating a blurring step, detection at a fine resolution often yields noise and unnecessary detail, whereas edge detection at a coarse resolution distorts edge contours. Bergholm [BERGHOLM87] has investigated "edge focusing" - a coarse-to-fine tracking in a continuous manner combining high positional accuracy of edges with good noise reduction. Firstly the significant edges are detected using a high degree of smoothing at a coarse level. Then the precise location of each edge is determined by tracking it over decreasing scale. This focusing process uses responses from one level to predict the occurrence of edges at the next, finer, level. It is necessary to threshold only the initial (most blurred) edge image. A practical implementation uses a step length in scale space short enough that edge elements do not jump further away than one pixel between successive steps. Edge detection is carried out with a small change in blurring parameter in a thin region close to the old edges. The old edge points are discarded and the new ones accepted. Subsequent edge focusing steps are performed iteratively. If the edge detection is restricted to points close to the old edges, processing times will be shorter than if all points were processed. The basic scheme adopted by this author consists of

- Calculating an initial forward FT
- Calculating the spatial Canny image
- Finding the thresholded zero-crossing image
- Calculating an initial mask within a distance of one pixel of each zero-crossing pixel
- Calculating the new spatial Canny image using a smaller standard deviation of gaussian
- Finding the non-thresholded zero-crossing image
- Masking out the zero-crossing pixels <u>not</u> within the previous mask
- Creating a new mask from the remaining zero-crossing pixels

A Fourier Transform approach has been adopted because of the large standard deviations of the blurring Gaussian used. Such an approach does not allow restriction of edge detection to points close to the old edges, however. Preliminary work with the method of Monga *et al.* [MONGA91] (see section 6.3) indicates that their approach will provide an excellent basis for spatial domain edge focusing in terms of both speed and accuracy [MIRANDA92]. In this work, significantly greater standard deviations of the initial blurring Gaussian than previous authors have been used, with the aim of extracting only the single most dominant contour, as compared

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6.6.3.1 Early-Echo Images

It was initially envisaged that the strong skin and brain edges of early-echo long TR SE images might be isolated using a Canny edge-focusing algorithm. This is not possible, however, due to a complex interaction between contours corresponding to the air/skin and skull fat/bone interfaces, that occurs when the two merge. This complex morphological transformation is illustrated by Figure 88 - Figure 91. Edge-focusing with anything but the very finest of scale-space steps will not accurately follow these edges. For example, although a scale-space step of 0.5 pixels per standard deviation may be appropriate for the vast majority of scale-space, there may be an area of, for example 1.0 pixels per standard deviation when even a scale-space step of 0.01 pixels per standard deviation will not accurately follow the edges. It would be possible to specify an extremely small scale-space step, but this would make the algorithm excessively slow. Alternatively, a method of adaptively varying the step-size might be developed, but this does seem an extremely complex task, if possible at all. A critique of pyramid segmentation algorithms (as reviewed in section 3.6.2) by Bister *et al.* [BISTER90] discusses why multi-resolution algorithms in general have a fundamental and inherent difficulty in analysing elongated objects such as the ring of skull fat. They phrase the problem as

"An elongated object is characterised by two different spatial frequency components, namely one associated with its width (higher frequency) and one with its length (lower frequency). Any kind of low-pass filtering or blurring algorithm (even the Gaussian blurring used in the scale-space) will cause these objects to disappear when their highest (transversal) frequency is higher than the cut-off frequency of the filter. But for multi-resolution analysis of such objects, their global features become local only when their local (longitudinal) frequency comes close to the cut-off frequency"

A recent idea due to Romney [ROMNEY91] suggests that higher order derivatives may be able to help with such a problem. It is possible to avoid this problem for neurological MRI by using images where the skull-fat is less prominent due to the MRI sequence used. This approach is the one adopted and is discussed in section 6.6.3.2.



Figure 88 - Edge-focused Canny edge image corresponding to early echo image at spatial standard deviation = 7 pixels.



Figure 90 - Edge-focused Canny edge image corresponding to early echo image at spatial standard deviation = 5 pixels.



Figure 89 - Edge-focused Canny edge image corresponding to early echo image at spatial standard deviation = 6 pixels.



Figure 91 - Edge-focused Canny edge image corresponding to early echo image at spatial standard deviation = 4 pixels.

Methods and Results

Late echo images at the long TRs used, show less prominent signal from fat and hence are more suitable for processing by edge-focusing. With such images, it is normally possible to obtain better (cleaner and more complete) contours with edge-focusing than with a simple or hysteresis threshold. Ideally an edge detector should only yield points lying on image boundaries. In practise, the edge map seldom characterizes a boundary completely because of noise, blur and insufficient contrast at some parts of the boundary. False edge elements also arise because operators often produce a high response not only at the point located directly on a sharp boundary but in a whole neighbourhood of that point. Thus edge-detection algorithms are typically followed by linking and other boundary detection procedures designed to assemble edge pixels into a meaningful set of object boundaries. If edge-focusing can produce a cleaner more isolated contour than simple thresholding, then this will obviously lower the amount of postprocessing to be done on the zero-crossing images.

The author proposes that axial multi-slice datasets can be approximately divided into four spatial groups, within which slices are fairly similar in content, whereas between which there are large differences. The groups are

- (1) The most superior slices where CSF is evident in sulci across the whole of the image.
- (2) Slices superior to the eyes where CSF is evident only near the brain surface and in the ventricles.
- (3) Slices at the level of the eyes.
- (4) Slices inferior to the eyes at the level of the cerebellum.

Using a general initial edge magnitude threshold and initial standard deviation of the blurring Gaussian, the edge-focusing process significantly simplifies the edge images for all slices except those of type 4, where other contours are also tracked. Using prior knowledge of the position of the brain relative to the posterior of the head, knowledge of edge-strengths and how edge images behave in scale-space, it is possible to automatically identify the contour(s) which represent the brain in an edge map corresponding to a highly blurred version of the image. The

dominant contour is picked out in the Canny edge magnitude image by the same approach used to identify the skin. Experiment has shown that it is this dominant contour and any contours surrounded by it which represent the brain. These are identified using a simple masking procedure. Such an approach allows all images of the dataset to be processed with the same set of parameters, yet still produce an extremely simplified edge image. The results from each group using this improved method are shown in Figure 92 - Figure 99. It should be noted that

- (1) Some upper slices contain blood vessels enhanced by venous blood flow which may produce a deformation of the contours in places.
- (2) The high slice contours are very good.
- (3) The slices at the level of the eyes include the eyes and some spurious contours in addition to the brain.
- (4) The slices inferior to the eyes show good results.

Mathematical Morphology Post-Processing

The result of edge-focusing does not provide complete closed contours at every level. The edgefocusing must be followed by post-processing. This involves discarding short line segments and utilising morphological dilation and erosion operations [HARALICK87] to join gaps in contours. Mathematical morphology provides an approach to the processing of digital images which is based on shape. Its' exponents claim that, as the identification of objects and object features correlate directly with shape, then mathematical morphology is the natural approach to such processing. Mathematical morphology uses set theory as its basis to represent shapes. Serra covers the use and theory of mathematical morphology very comprehensively in his book [SERRA82]. Morphology analysis uses a "structuring element" to manipulate the image. The structuring element is a small template image, for example a 3x3 square, which is successively superimposed on each point in the real image, and compared with each point in the neighbourhood. The comparison could look for local minima or maxima, do averaging or some other operation. The point in the real image is then modified according to the operation, and the process repeated on the next point. An example would be the use of a single line element which could be set up to produce a processed image in which only the features larger then that line element were recognised. Using more complex structuring elements, one could specify other characteristics to look for, for example orientation, shape etc. In this way, unwanted detail can be removed quickly and the desired objects remain, ready for the detection process. On a grey

scale image, the two main morphological operations are dilation and erosion. Dilation looks for the maximum brightness value covered by the structuring element and transfers that value to the point under examination. Erosion is similar but looks for the minimum brightness. These operators are applied in the detection step together as opening (erosion followed by dilation) and closing (dilation followed by erosion) which respectively remove small objects or join together close objects.

Further work is currently focusing on correcting for the contour deformation caused by blood vessels enhanced by contrast due to flow. Pre-saturation of blood may be used successfully to reduce the contrast due to flow for arterial blood, but such an approach is not applicable for the venous flow causing enhanced contrast in this case. This is because blood may be saturated in the neck prior to it entering the head, whilst venous blood will enter the venous network from the diffuse capillary bed within the head.



Figure 92 - Upper late-echo slice with CSF evident in the sulci across the whole brain



Figure 93 - Edge-focused contours corresponding to the upper late-echo slice



Figure 94 - High late-echo slice with CSF evident only at the brain surface and within the ventricles.



Figure 95 - Edge-focused contours corresponding to high late-echo slice.



Figure 96 - Late echo slice at the level of the eyes



Figure 97 - Edge-focused contours corresponding to late echo slice at the level of the eyes



Figure 98 - Late echo slice at the level of the cerebellum



Figure 99 - Edge contours corresponding to the late echo slices at the level of the cerebellum.

6.7 Extraction of Ventricles

The identification of a contour corresponding to the intracranial region enables the approximate position of the ventricles to be determined. Using this region of interest, further edge-based processing may be carried out. Edge focusing is not an appropriate approach because of border effects at larger standard deviations of the blurring gaussian. Canny hysteresis, however, can be used to pick out the contours corresponding to the ventricles fully (see Figure 100 and Figure 101). The partial volume effect means that Canny contours surrounding the ventricles may correspond to edges between brain and brain/CSF partial volume pixels. This makes a region-based approach in which the partial volume effect is taken into account more appropriate, because the Canny contours do not accurately represent the extent of the CSF. Such region-based approaches are discussed in chapter 7.



Figure 100 - Section of image containing ventricles.



Figure 101 - Hysteresis thresholding extraction of edges corresponding to ventricles.

6.8 <u>Summary</u>

This chapter reports work by the author using edge-based processing techniques to isolate the intracranial region, and to identify the eyes, skin and ventricles. These forms of processing rely on different approaches to edge detection. Simple convolution based edge-operators respond strongly to discontinuities, but edge-detection requires that such discontinuities are localised and then connected components identified by processes such as edge-linking and thresholding. Edges can be localised using the Marr-Hildreth and Canny operators by locating the zero-crossings of the edge operator image. Hence with these operators, localised edges with an associated strength are available which must then be further processed in order to identify the edges of particular interest. The skin has been identified by tracking edges in a binary localised edge image from a robustly identified starting point. The intracranial region, and the ventricles, are isolated by attempting to identify only the strongest contours using localised Canny magnitude images and the eyes are identified by using the thresholded localised binary edge image as input to the Hough transform, a shape matcher, relying on the eyes's circular shape.

CHAPTER 7

REGION BASED SEGMENTATION.

Region based processing in the form of thresholding, contrast-enhancement and clustering has been used to isolate the intracranial region, to segment CSF from brain parenchyma and, depending upon the details of the MR pulse sequence used, to also separate grey matter from white matter. Region based methods utilising dual-echo datasets are more appropriate for segmenting CSF, grey matter and white matter than edge-based methods, as the borders between these tissues are often highly convoluted, the strength of these borders varies considerably and regions may be very thin. Edge detection is often very difficult and delivers imprecise results under any one of the above mentioned situations. The use of two images for region-based approaches also provides extra information to be utilised. It is important that these images can be used both for clinical diagnosis and segmentation purposes. RF non-uniformity correction and anisotropic smoothing are presented as two extremely valuable steps prior to region-based processing.

7.1 <u>The Use of Multiple Images for Region-Based Segmentation</u>

Region-based segmentation methods can often take advantage of the intrinsically multiparametric nature of MRI by utilising several images of the same part of the neuroanatomy, suitably registered, to produce a segmentation that is superior to that possible using one image alone. This chapter concentrates on work using image pairs and in particular on dual-echo images as such data is often acquired clinically. Long repetition time dual-echo standard and fast spin echo images are of particular interest because these are acquired routinely on the Institute of Neurology NMR Research Group's Signa scanner. Short T_I Inversion Recovery (STIR) and fast gradient echo image pairs are also considered, however, in order to demonstrate what may be achieved using different pulse sequences. STIR images demonstrate excellent grey/white matter contrast and because of this may provide good results for grey matter/white matter segmentation. The short repetition times associated with fast gradient echo imaging typically do not produce such good grey and white matter contrast as spin echo or inversion recovery imaging, but can produce very distinct CSF/brain parenchyma contrast with bright CSF and so can be used for segmenting these regions.

7.2 Quality of Multi-echo Data

7.2.1 Picker Data

The individual echoes from multi-echo data on the NMR Research Group's 0.5 T Picker scanner are mis-registered and alternate echoes often flipped (ie mirrored about the phase encoding direction). As a pre-processing step before segmentation any flipping is automatically identified and corrected for, and the images registered (see section 7.2.2). The disappointing results of initial dual-echo clustering work demonstrated that the two echoes were still not well registered, however. The registration method was rechecked with a series of software phantoms which proved the accuracy of the registration program to be better than 0.2 pixels. The possibility of geometric distortions varying with echo time was therefore investigated by phantom studies. Six sets of scans of MRI phantoms were acquired with slice orientation in each of the three orthogonal directions and with the phase encoding direction both vertical and horizontal. Several duplicate scans were also acquired in order to ensure consistency. Detailed measurements on the scans demonstrated that in some cases there were differences in size between the image from the first echo and the image from the second echo. The results are summarised in the following table.

Slice Orientation	Phase encode direction	Direction of size change	Magnitude of size change (pixels)
Axial	Horizontal	X	2
Axial	Vertical	у	4
Coronal	Horizontal	x	2
Coronal	Vertical	*	*
Sagittal	Horizontal	у	2
Sagittal	Vertical	*	*

Table 1 - Variation of phantom size with phase-encoding direction for 0.5 T Picker scanner

* No size change could be measured. The smallest change that can be measured is 2 pixels.

These changes are thought to be due to problems with the scanner gradients. If this is the case then the z-gradient is particularly poor, but the x and y gradients are also bad. These problems mean that data from the Picker scanner can not be used for this work as the magnitude of the size difference is of the order of the size of typical threads of CSF in the sulci.

7.2.2 Picker Data Image Registration

The individual echoes from multi-echo data on the NMR Research Group's Picker scanner are mis-registered (see section 7.2.1). It is difficult to identify particular features to register on with multi-echo data because of the changes in the image that occurs with echo-time. Projections and edge detection were investigated, but the lack of stable features between echoes hampered work. Cross-correlation, which does not depend on any particular image features, proved to be a much more promising method, allowing adjacent echoes in a sequence to be registered. Sub-pixel registration was achieved by using parabolic interpolation. The cross-correlation data is independent in x and y and therefore the 1-D parabolic fits to the three pixels in x, and the three pixels in y surrounding the peak are sufficient. It is not necessary to fit a 2-D parabolic surface to the data near the peak. The accuracy of this method of registration has been investigated using noisy software phantoms. Pairs of mis-registered noisy software

phantoms were created from higher resolution images by averaging blocks of pixels, and simultaneously introducing arbitrary but known offsets in the x and y directions. The shifts necessary to register pairs of images could then be compared with the known offsets. For such phantoms, the method of registration is accurate to better than 0.2 pixels.

7.2.3 Signa Data

The data acquired using the Signa scanner are far superior to that acquired using the Picker scanner. Detailed measurements on phantoms (using the same approach as described in section 7.2.1) show the two Signa echoes to be registered and of the same size. The signal to noise ratio is also improved due to the combined effects of the higher field strength, quadrature RF reception and a well designed RF receiver chain.

7.3 The Use of Prior Information in the Visual Segmentation of MR Images

It is interesting to consider the use of prior information in the visual segmentation of MRI images (ie how a human observer identifies regions of the neuroanatomy), although modelling of visual segmentation is probably not a viable approach for computer-based segmentation of MR images. Such prior information may be acquired from experience with MRI, or from other sources, such as knowledge of anatomy and post mortem studies. This author believes that the facts which are most important to an observer when deciding which tissue a particular pixel in an MRI image belongs to are

- (a) Absolute intensity
- (b) Anatomical cues knowing the approximate position of tissues
- (c) Shape
- (d) Neighbouring pixels (a small local region)
- (e) Contrast with neighbouring tissues
- (f) Contralateral symmetry

(g) Knowing that the partial volume effect occurs at tissue borders

Out of these (a), (d) and, depending upon one's definition, (e) are not prior information. Contrast with neighbouring tissues may be simulated, as discussed in section 7.7. It is difficult to separate the effects of these visual cues. For example, how does one differentiate between intensity and contrast with neighbouring tissues? A clinician might also make use of history, signs and

symptoms, experience with animal models and other scans in a time sequence. In addition to this visual information the tissue contrast for a given field strength and spin sequence and the noise characteristics of the image are also known. Rosenfeld and Kak [ROSENFELD82] state that

"It should be pointed out that the Visual System is much less accurate at judging the magnitude of a single stimulus than it is at determining which of the two stimuli is greater in magnitude; there is much less accuracy for absolute judgements than for relative judgements"

and with respect to local background:

"Apparent brightness depends strongly on the local background intensity". (A pixel looks brighter on a dark background than on a lighter background.)

7.4 Image Pre-processing

Three methods of image pre-processing prior to further region-based segmentation are proposed. These are image non-uniformity correction, anisotropic smoothing and isolation of the intracranial region.

7.4.1 Uniformity Correction

Image non-uniformity correction is carried out for each dataset, utilising a second scan of a uniform oil phantom as described in chapter 5. This is because image non-uniformity adversely affects intensity based methods of segmentation by broadening the intensity range representing a given tissue. The method of Wick *et al.* [WICKS92B] is being re-implemented for the Signa, which will do away with the constant repetition of scans.

7.4.2 Anisotropic Smoothing

Blurring is a standard method of reducing the effect of noise within an image. An ideal method of blurring would reduce the standard deviation of the signal within homogeneous regions without moving region boundaries. As discussed in section 3.3.2.5, Marr [MARR82] selected the Gaussian distribution as an optimal blurring function on the grounds that it has the desirable characteristics of being smooth and well localised in both the spatial and frequency domains. It is the unique distribution which is optimally localised when considering both

domains simultaneously. This is desirable because a blurring function which is as smooth as possible, both spatially and in the frequency domain, is least likely to introduce any features that were not present in the original image.

Whilst blurring with an isotropic Gaussian distribution does reduce the effect of noise within an image, it also moves and distorts region boundaries. Anisotropic blurring methods have therefore been considered. The properties required of an appropriate filter are:

- (1) That it must smooth out the dissimilarities between pixels within the same object
- (2) That it must preserve the edge information, and
- (3) That it must not create artificial structures.

Imme [IMME91] has demonstrated that many well known edge-preserving smoothing methods do not satisfy these criteria.

Perona and Malik [PERONA88] have proposed a method of anisotropic blurring derived from the theoretical foundation of scale-space. Scale space as originally described by Koenderink [KOENDERINK84] and discussed in section 3.6.1 is a hierarchical description of an image's behaviour under a continuum of isotropic Gaussian blurring kernels. The extension to using anisotropic blurring was derived to overcome the distortion of region boundaries associated with Gaussian blurring. The excellent results and theoretical derivation make this scheme more attractive than other anisotropic blurring methods. Koenderink has pointed out that scale space may be viewed as the solution of the heat conduction or diffusion equation. The anisotropic diffusion equation is given by

$$I_{\sigma} - div(c(x,y,\sigma)\nabla I) - c(x,y,\sigma)\Delta I + \nabla c.\nabla I$$
(68)

where $I_{\sigma} = \partial I/\partial \sigma$, I(x,y,0) = I(x,y) is the original image, div the divergence operator, and ∇ and Δ the gradient and Laplacian operators with respect to the space variables. This reduces to the isotropic heat diffusion equation $I_{\sigma} = c.\Delta I$ if $c(x,y,\sigma)$, the diffusion coefficient for a pixel at a given scale σ , is a constant. In Perona and Malik's method, the diffusion coefficient is chosen to vary spatially so as to encourage intra-region smoothing in preference to inter-region smoothing. This is accomplished by making the diffusion coefficient a function of the magnitude of the gradient of the brightness function at that scale, ie

$$c(x,y,\sigma) - g(|\nabla I(x,y,\sigma)|)$$
(69)

This means that borders of regions remain sharp and well localised, whilst noise and spurious detail are reduced. The scheme is iterative, updating the diffusion coefficient for each point at every pass. The method is discussed in more detail in section 8.8. The effects of two iterations of Perona's method have been compared with that of Gaussian blurring. The width of the standard deviation of the blurring Gaussian was chosen so that the standard deviation of the signal within a number of small white matter regions was the same as that for equivalent regions in the image processed with Perona's method. Figure 102 illustrates the original image, and the results of processing the image with one iteration of Perona's method, two iterations of Perona's method and Gaussian blurring are shown by Figure 103 - Figure 105. Perona and Malik suggest two functions for the conduction coefficient, $g(\nabla I)$ at a point.

$$g(\nabla I) - \exp\left(-\left(\frac{|\nabla I|}{\kappa}\right)^2\right)$$
(70)

or

$$g(\nabla I) = \frac{1}{1 + \left(\frac{|\nabla I|}{\kappa}\right)^2}$$
(71)



Figure 102 - Unprocessed image



Figure 103 - Image processed with one iteration of Perona's method.



Figure 104 - Image processed with two iterations of Perona's method.



Figure 105 - Image processed with Gaussian blurring.

The value of kappa determines the rate of blurring and has been determined by using the noise estimator proposed by Canny [CANNY86]. The implementation is discussed in more detail in section 8.8. The effect of the two functions are different, the first function favouring high contrast edges over low contrast edges, whilst the second function favours wide regions over smaller ones. It is very important that the processing does not destroy small detail such as thin threads of CSF in the sulci, so the first function has been chosen as more appropriate for the purposes of noise reduction. A large number of images were processed and examined to determine the effect of the algorithm on small details within images. Two iterations of the algorithm are currently used as this retains detail whilst reducing noise. The effect of anisotropic blurring can be illustrated in more detail by comparing profiles through processed and unprocessed images. This is demonstrated by Figure 106 - Figure 113 which illustrate an unprocessed early and late echo image and a processed early and late echo, with corresponding profiles.

The current anisotropic smoothing scheme is two dimensional and operates on each echo independently. It could be extended in two ways. Firstly, information from more than one image could be utilised to define κ and secondly, information from the third dimension could also be considered. Currently, the use of 5 mm thick slices and a 2.5 mm slice gap, means that there is little to be gained from a three dimensional approach. There is an inherent information loss when sampling data using a slice skip, but the slice thickness needs to be reduced in addition to the slice skip being eliminated. The use of contiguous data with a slice thickness of 3 mm, for example, or 3-D gradient echo data would improve the situation to a point where 3-D operators should be considered. The contrast to noise limitations of gradient echo data, however (as discussed in section 7.10.2.2), must be considered in this context.

7.4.3 Intracranial Region Isolation

It is necessary to isolate the intracranial region from fat, bone and muscle either prior to, or following region-based segmentation of the CSF, brain parenchyma, grey and white matter. This is due to cluster and threshold overlap that occurs with fat, blood vessels whose signal is enhanced due to flow and other soft tissues in the head. This has been done using automatic methods prior to subsequent processing. The intracranial region is isolated either by edge-based processing as described in chapter 6 or by other region-based segmentation as described in sections 7.5 and 7.6.



Figure 106 - Unprocessed early echo image.



Figure 107 - Profile through unprocessed early echo image.



Figure 108 - Early echo image processed by two iterations of anisotropic blurring.



Figure 109 - Profile through early echo image processed by two iterations of anisotropic blurring.



Figure 110 - Unprocessed late echo image.



Figure 111 - Profile through unprocessed late echo image.



Figure 112 - Late echo image processed by two iterations of anisotropic blurring.



Figure 113 - Profile through late echo image processed by two iterations of anisotropic blurring.

7.5 Thresholding of Late-Echo Images Following Anisotropic Blurring.

Thresholding is not a technique commonly used on its own for MRI segmentation, due to the presence of RF non-uniformities, inherent variation of signal response from any tissue, signal overlap from other tissues, the partial volume effect and the effects of noise. Signals from the brain and CSF are significantly more intense than that from skull fat at late echo times and long repetition times, for example in a SE/3000/80 sequence. There is however, other high signal present in the dataset outside the intracranial region due to signal from blood vessels and other soft tissues in the head such as the soft palate and muscle. Applying a thresholding approach to unprocessed data would not be straight forward due to the reasons described above. By preprocessing the image with RF non-uniformity correction and anisotropic blurring, however, automatic thresholding becomes a viable option. More iterations of the anisotropic blurring algorithm are used under these circumstances than for the clustering or contrast enhancement methods described in sections 7.10 and 7.9. Typically 20 - 60 iterations would be used depending upon the exact pulse sequence acquisition parameters. A threshold value of half the maximum image intensity has been chosen as this is half way between the high intensity CSF and brain parenchyma and the essentially zero signal from the surrounding bone. Binary thresholding isolates the intracranial region, but also produces additional smaller binary regions corresponding to blood vessels and soft tissues other than the intracranial region. The binary regions corresponding to a thresholded version of Figure 114 are illustrated by Figure 115. Using connectivity criteria, each binary region may be identified and its area calculated. The intracranial region is identified as the single largest region in each slice for all slices other than those including the brain stem. The largest connected component from Figure 115 is illustrated by Figure 116. A three dimensional connectivity approach has also been implemented, but is unsuitable for the current 5 mm slice thickness data acquired with an inter-slice skip of 2.5 mm. With thinner slices and contiguous slice acquisition, the three dimensional approach should be quicker. If the brain stem is of interest then three dimensional connectivity can be used on a limited number of the lower slices to isolate this.



Figure 114 - Late echo image (SE/3000/80)



Figure 115 - Binary regions corresponding to thresholded late echo image processed with anisotropic blurring.



Figure 116 - Intracranial region corresponding to largest binary region from thresholded late echo image processed with anisotropic blurring.

7.6 Thresholding of Late Echo Images Normalised to Early Echo Signal.

A second threshold-based method of intracranial region isolation has been developed. This approach also relies on the high intensity of the intracranial region relative to fat and blood vessels enhanced due to flow in the late echo images and the use of connectivity. In order to isolate the intracranial region, it is necessary to threshold the image at a level between the intensity of the intracranial region and the surrounding bone and bone marrow. The best choice is an intensity halfway between the intracranial region and the surrounding tissue. The late echo images are more appropriate for thresholding because there is a greater fractional intensity difference between intracranial region and surrounding tissue than for the early echo images.

It is not possible to identify the intensity of a known tissue from the late echo image in a simple manner. The peak intensity in such images will normally correspond to partial volume voxels composed of CSF and grey/white matter. The peak intensity of the early echo image will correspond to grey matter, however, and this intensity can be related to the predicted white matter signal at the late echo time. This approach ensures the variation in signal from tissue between subjects due to transmit power variations does not affect the method. The appropriate late echo image threshold is a fraction of the maximum early echo intensity. This fraction may be calculated by considering the grey matter intensity for both echoes, assuming the bone/bone marrow signal to be almost zero for the late echo images, whilst allowing for noise and tissue heterogeneity. Intensities have been calculated using a simulation of SE signal intensity as discussed in section 7.7. This yields a threshold fraction of approximately one fifth.

Using this fraction for thresholding results in processed images containing regions corresponding to the intracranial region, to blood vessels enhanced by flow, isolated areas of fat surrounding the skull and other soft tissues within the head. Two dimensional connectivity is once again used to isolate the intracranial region as the largest region per slice. This region can then be used as a mask to extract the intracranial region from the original early and late echo images. As mentioned in section 7.5, the relatively large slice thickness and the presence of a large interslice skip, makes a three dimensional connectivity approach unsuitable with the current data.



Figure 117 - Original early echo image



Figure 118 - Isolated brain and CSF using dual-echo ratio method.

7.7 Simulation of Image Contrast

Tissue contrast is necessary for the visualisation of anatomy and pathology but must not be obtained at the expense of contrast to noise ratio. The mechanisms governing contrast for common sequences have been discussed in section 2.5. In order to choose appropriate parameters for contrast enhancement by image combination and dual-echo clustering studies, as described in sections 7.9 and 7.10, it is necessary to simulate image contrast. For a given pulse sequence and timing parameters, it is possible to predict a tissues's intensity using equations modelling the tissue's relaxation and knowing the tissue's T_1 , T_2 and PD. Spin echo, inversion recovery and fast gradient echo pulse sequences have all been modelled. It should be noted that gradient echo predictions are subject to some inaccuracies, however, unless the sequence is spoilt (ie unless transverse magnetisation is destroyed at the end of each TR period), due to steady state effects not predicted by the model used. The equation modelling tissue relaxation for a spin-echo, for example, is given by

Intensity - k.PD.
$$\left(1 - \exp\left(-\frac{T_R}{T_1}\right)\right) \cdot \exp\left(-\frac{T_E}{T_2}\right)$$
 (72)

where k is the intensity for PD = 1 (ie water) at zero echo time. This value will be dependent upon such factors as the system gain and RF reception efficiency. The simulation allows the production of one dimensional plots of the variation of intensity with one of the acquisition parameters (eg TR, TE, TI, θ) or the production of two-dimensional plots illustrating the variation of intensity with two acquisition parameters. The two dimensional plots are viewed using xdispunc. The one dimensional plots are viewed by directing the output of the simulation to the input of xvgr. This approach allows plots to be created quickly and flexibly without the need for any knowledge of graph drawing.

The data used for these simulations has been collected from a number of papers [JOHNSON87, LARSSON88, CONDON87B]. It should be noted that the grey matter T_2 at 1.5 T was unavailable, and was therefore approximated by the product of the grey matter T_2 at 0.5 T multiplied by the ratio of the white matter T_2 at 1.5 T to the white matter T_2 at 0.5 T.

Many simulations of tissue contrast in the literature neglect the effects of noise, perhaps because for a given field strength, noise still depends upon the characteristics of individual systems. Signal to noise ratio varies with the number of averages, receive bandwidth, slice thickness and field of view for a given system and these factors are all included in this simulation. The variation of SNR with these parameters is given by

$$SNR \propto \sqrt{NEX}$$
 (73)

$$\sim \sqrt{\frac{1}{bandwidth}}$$
 (74)

$$\propto$$
 pixel area [ie (field of view)²] (75)

$$\propto$$
 slice thickness (76)

[FIELD90] where NEX (Number of EXcitations) is the number of averages of data. Any of these parameters may be varied in the simulation. It is possible to measure the signal to noise ratio of an image and by appropriate comparison with the model, determine the noise level to be used for the model. For a magnitude image, the signal to noise ratio (SNR) [TOFTS86] is given by

$$SNR = \frac{Signal Mean}{1.51 \times Noise S.D.}$$
(77)

where the factor of 1.51 takes into account the fact that noise in a magnitude image is represented by a Rayleigh distribution rather than a Gaussian distribution. Signal to noise ratio is measured using a small area of pure tissue which in the field of neurological imaging is often white matter because of difficulties associated with finding large enough areas of pure grey matter or CSF. The possibility of partial volume effect due to slice thickness affecting the results can be eliminated by ensuring that the same region in adjacent slices also contains only white matter. The noise should be measured in an area of background unaffected by low intensity signal artifacts which are often present in the phase-encoding direction due to motion, whether of the patient, or blood or CSF flow. Edelstein et al. [EDELSTEIN83] suggest that the noise level should be calculated from the difference of two images acquired with identical parameters in order to eliminate tissue heterogeneity effects. Typically such effects are negligible for small (100 pixel) regions of tissue sampled as described above. The predicted signal to noise ratio for both 0.5 T and 1.5 T calculated from the first echo acquired with a \pm 16 kHz bandwidth was checked against the second echo acquired with $a \pm 8$ kHz bandwidth and proved to be in very good agreement. The magnitude of the noise may be illustrated by plotting error bars for each intensity point of the simulation.

It is interesting to compare the signal to noise ratio of the two systems. Theoretically the Signa has an implicit advantage in terms of SNR with gains of $\sqrt{2}$ for the quadrature RF detection and a second gain because of the higher field strength. The variation of SNR with field strength is of continuing debate in the literature with authors claiming SNR is proportional to B₀ or B₀^{7/4} under different circumstances [EDELSTEIN86]. This author notes that the two postulated field dependencies yield gains due to change in field strength and quadrature detection from 0.5 T to 1.5 T of either 4.2 or 9.6 respectively. In practise, the change in SNR between the two imagers was 4.96 which suggest that a B₀ dependence is more appropriate than a B₀^{7/4} dependence in this case. The difference between the measured change in SNR and the predicted value of 4.2 is probably due to differences in the design of the RF coil and receiver chain between the 0.5 T and 1.5 T systems.
7.8 Choice of Imaging Parameters

Although it is possible to simulate tissue contrast using equations describing tissue relaxation for any combination of repetition times and echo times, both these and other acquisition parameters are subject to a number of practical constraints. The major considerations for the normal case where images must be used for both clinical diagnosis and segmentation are as follows

■ Imaging time is perhaps the most important consideration affecting the choice of acquisition parameters. Patient comfort, the minimisation of the effect of involuntary motion on image quality and the economic considerations due to the relatively high cost of MR imaging all preclude extended imaging times.

Repetition time is influenced by its direct effect upon imaging time but may also be varied somewhat in order to acquire the desired number of slices, so long as this does not adversely affect image contrast.

• The minimum echo time, TE_{min} is set by hardware constraints such as gradient switching time and pulse lengths whilst the maximum echo time is limited by signal to noise considerations. For gradient echo images, longer echo times may lead to susceptibility and B_0 non-uniformity induced signal losses as discussed in section 9.4.

■ Slice thickness and its effect on partial volume is a critical consideration and is a factor limiting the accuracy of segmentation. Partial volume effects can be minimised by acquiring data with as small a slice width as possible. Although multi slice Signa data acquired with the Signa minimum slice thickness of 3 mm would be of diagnostic quality in terms of signal to noise ratio, there are several reasons why such data is not routinely acquired. These include the increased amount of time spent reviewing scans, the preference of clinicians for higher SNR data [OWEN90, JACK90] and the cost of archiving larger studies.

Inter-slice skip, as shown in section 5.6, may have important effects on image contrast. If contiguous slice data is required then this should be acquired using two data acquisitions or RF pulses optimised for very rectangular slice profiles.

It is possible to trade some of these requirements off against one another, for example, longer repetition times versus the possibility of slightly reduced SNR. Compare, for instance, the imaging time for TR = 2000 ms and 1 NEX, with that for TR = 3000 ms and 3/4 NEX. Both cases would be acquired with 196 phase-encoding steps.

Acquisition time 1 (TR = 2000 ms, 1 NEX) = 1 x 196 x 2 seconds = 6.5 minutes
Acquisition time 2 (TR = 3000 ms, 3/4 NEX) = 3/4 x 196 x 3 seconds = 7.4 minutes
The repetition time can be increased with only a small increase in scanning time and a small (affordable) reduction in image quality. This increase in repetition time gives superior grey matter/white matter contrast for early echo times and superior csf/brain parenchyma contrast for late echo times.

7.9 Contrast Enhancement by Image Combination.

The choice of MRI sequence for visualisation of anatomy or pathology is normally made with the aim of optimising the contrast-to-noise ratio between two tissues, subject to constraints such as scan time and artefact minimisation. The contrast-to-noise ratio between three given tissues may therefore not be ideal, so it may be advantageous to obtain contrast enhancement between two tissues by combination of images. Addition and subtraction of the early and late echo images has been chosen as a simple and fast method of image subtraction that allows an interactive approach to segmentation as discussed in section 7.9.2. Other means of image combination are also possible, but have not been considered because of the emphasis on speed. Image division has some attraction, for instance, because the intensity of a ratio image is only dependent upon T_2 , as the T_1 and PD dependence has been removed. This can be appreciated by the form of the equation describing spin echo intensity (equation (72)). An effective segmentation method using such an approach must include a noise suppression step.

7.9.1 Simulation of Contrast

The simulation of contrast for the linear combination of images is achieved by linear combination of contrast plots for the two individual images, whilst considering the effects of noise. In practise this work has concentrated exclusively on long repetition time dual-echo images. The data acquired for dual-echo clustering (see section 7.10) has proved acceptable.

7.9.2 Method and Results

Dual-echo spin echo data sets are corrected for RF non-uniformity and subjected to anisotropic smoothing. The intracranial region is isolated using edge-based or region-based methods as described in sections 6.6.3, 7.5 and 7.6. Pairs of images are subtracted to enhance contrast between brain parenchyma and CSF, and added in order to enhance contrast between grey matter and white matter. Further anisotropic smoothing of these combined images allows simple interactive thresholding of the new calculated images to segment the tissues.

The main drawback with contrast enhancement by linear combination of images is that for some slices a single threshold can not adequately separate tissues due to the magnitude of the partial volume effect that occurs with 5 mm thick slice data. This is amply demonstrated by Figure 119 - Figure 122 which illustrate early and late echo images superior in the brain and corresponding profiles, where CSF is evident in sulci throughout the image. The four major peaks of the profile through the late-echo image all correspond to areas of CSF which are subject to varying degrees of the partial volume effect, so choosing a threshold to separate CSF from brain parenchyma using a linear combination of images is not an easy task. It is also hard to assess the accuracy of such a segmentation and to decide whether overestimation in some areas is compensated for by underestimation in other areas. Such compensation might be advantageous for volume measurement but would not be appropriate if precise delineation of structures was required. In this situation an accurate realistic phantom of part of the head (see section 10.2.4) would be of great use.

Although CSF partial volume due to slice thickness is less for slices where CSF is restricted to the edge of the brain, there are still grey and white matter partial volume problems due to slice thickness and this approach is therefore likely to have some mis-assigned pixels. No postprocessing of images has been carried out for this method, but obviously this could be implemented if desired. Isolated pixels would be re-examined in the context of their local neighbourhood and pixels reassigned if necessary. The accuracy of this method is not considered in this thesis, as initial experience showed that users could obtain better reproducibility and accuracy using dual-echo clustering.



Figure 119 - Early echo image at top of brain



Figure 120 - Late echo image at top of brain



Figure 121 - Profile through early echo image at top of brain



Figure 122 - Profile through late echo image at top of brain

7.10.1 Introduction

A simple approximation in which MRI signal depends only upon T_1 , T_2 and PD, implies that ideally, clustering of MRI data would use three spatially registered datasets (typically T_1 , T_2 and Proton Density weighted images), to form a multi-dimensional feature space. In practise, although T₁, T₂ and Proton Density are often positively correlated in tissue (implying some data redundancy), better results may be obtained with more then three images due to other tissue and machine dependent factors. As discussed in section 4.5, Hyman et al. [HYMAN89], for example, have shown that using 7 calculated datasets can give significantly better results than 3 parameters. The clinical protocols for multiple sclerosis patients at the Institute of Neurology consist of acquisition of a multi-slice transverse oblique dual-echo spin echo dataset covering the whole brain. In addition, studies of the spinal cord, pre- and post- gadolinium scans and proton spectroscopy may also be utilised, depending on the particular protocol. This relatively long period of scanning, combined with the patients' reduced tolerance to periods of immobility precludes the acquisition of further brain datasets. In practise it is therefore necessary to work with dual-echo datasets for both clinical diagnosis and segmentation purposes at the Institute of Neurology as these scans can typically be acquired in the same time as an equivalent single echo dataset.

Techniques other than simple SE acquisitions can provide multiple data sets, and the use of inversion recovery and gradient echo images has been considered (as such images are more appropriate for certain clinical situations). The prospects for fast spin echo dual image clustering are also discussed. STIR images can provide excellent grey and white matter contrast; gradient echo imaging allows the acquisition of volume data in realistic imaging times and fast spin echo imaging shows promise for reducing scan times whilst still retaining the quality of segmentation. Some Signa gradient echo and fast spin echo techniques allow dual echo acquisition but this is not the case for the Signa inversion recovery pulse sequence and some Signa gradient echo and fast spin echo variants.

When dual echo acquisition is not possible it is necessary to acquire separate datasets. There may be some advantages to such an approach, as the variation of other acquisition parameters in addition to, or instead of, echo time may produce better contrast. There are, however, drawbacks; in particular time constraints and the problem of patient motion between or during scans. Such motion typically leads to poor results where CSF in one image overlaps with grey matter in the second image or grey matter in one overlaps with white matter in the other. Motion also degrades the quality of the dual echo images somewhat, but does not produce mis-registration.

Subject motion has been restricted during these studies by three mechanisms. The first is education - requesting the subject to stay still for two or more scans and informing them that motion will degrade the quality of the data. This author has noticed, however, that while subjects typically stay still during scans, they often stretch and move between scans. Secondly a movement restraint device termed the nasal orientation device (NOD) [TOFTS90] has been utilised. This consists of a ring of wire which is attached to the Signa head coil using a plastic clamp and positioned just anterior to the tip of a cooperative subject's nose. If the subject does move by a mm or two, they can feel the wire touching their nose and can move back to their original position. The third method is the use of foam wedges to the left and right of the subjects head to restrict left/right movement. These three mechanisms have greatly reduced the probability of motion between separately acquired datasets. The NOD does have one major drawback though; some subjects have reported a tickling sensation when the ring lightly brushed the nose which has caused involuntary motion, moving the NOD in the process. The use of multiple echo or an appropriately interleaved sequence guarantees image registration and is also applicable to other parts of the body where a NOD or similar device might not be appropriate.

7.10.2 Simulation of Contrast

Both cluster separation and size affect the accuracy of dual-image clustering, the two being related to a certain extent. The cluster separation depends upon both the size of the clusters and the tissue contrast for the two images. The cluster size depends upon image nonuniformity, noise and inherent tissue heterogeneity. Image non-uniformity correction and anisotropic smoothing are used to reduce the effects of the first two factors. It is important that there is adequate contrast between each of the tissues in the cluster image. Contrast simulations have been used to study the variation of cluster separation with the various acquisition parameters for a system with perfect pulses, slice profiles etc., and spin-echo, inversion recovery and fast gradient echo pulse sequences. Noise has been simulated. There are several clinical applications that are of particular relevance for dual-image clustering. The segmentation of brain parenchyma and CSF and the segmentation of grey matter and white matter are of interest for conditions such as schizophrenia, epilepsy, alcoholism and the early stages of HIV infection, where changes in the volume of the brain and grey and white matter are of great importance. The segmentation of lesions is a further important area, for which multiple sclerosis lesions have been chosen as a particular example. The segmentation of an image into CSF and brain parenchyma has also been considered separately from the segmentation of an image into grey matter, white matter and CSF as the two approaches may be applied to different disease states.

7.10.2.1 Grey Matter, White Matter and CSF Segmentation.

The segmentation of grey matter, white matter and CSF has been achieved using either dual echo spin echo data or two inversion recovery datasets. Although dual echo gradient echo images may exhibit some grey/white matter contrast, such contrast is typically significantly less than that of inversion recovery or spin echo images and this compromises the accuracy of the results.

Spin Echo Imaging

It is important for tissue clusters to be adequately separated in cluster space so simulations of image contrast have been considered in order to choose appropriate acquisition parameters. For SE datasets and at short repetition times (for example TR = 1000 ms) grey matter, white matter and CSF are isointense for later echo times, whilst at TR = 2000 ms there is poor grey matter/white matter contrast for all echo times. At repetition times of greater than 5000 ms, grey and white matter are fully relaxed, and the contrast between the two tissues has reached a maximum with respect to TR. Although with a spin-echo sequence, long repetition times give better separation, a compromise must be made with scanning time. Experience has shown that using repetition times much less than approximately 3000 ms does not allow accurate grey matter/white matter segmentation because of the added effect of natural tissue variability. Typically, repetition times of 3000-4000 ms have therefore been used. Echo times of 30 ms and 80-90 ms have been chosen. The former corresponds to the minimum echo time when using software flow compensation whilst the latter has been chosen as a compromise between contrast and SNR.

STIR Imaging

The achievable contrast to noise ratio between grey and white matter is greater for STIR images than for SE images because the PD- and T_1 - weighting combine with STIR images, but oppose with SE images. An inversion time of 175 ms and a repetition time of 2500 ms have been utilised in this work to provide compatibility with existing clinical parameters (which are intended to optimise fat suppression). An early echo time of 16 ms was chosen to give good contrast between both grey matter and CSF, and white matter and CSF. A late echo time of 60 ms was chosen as a compromise between grey matter and CSF contrast, and grey and white matter contrast. The relevant contrast curves are indicated by Figure 124. The excellent grey and white matter contrast has provided good results for dual echo clustering, but the scanning time is a significant drawback. It takes 8 minutes per echo time to acquire 10 slices using the imaging parameters detailed above, which gives a total imaging time of 48 minutes to acquire the standard 22-27 slices needed clinically. This is an unacceptably long time for these purposes, but such an approach might be more appropriate for situations requiring less slices.

Fast Spin Echo Imaging

The Signa FAST-SE (FSE) sequence is a variant of RARE [HENNIG86] which is notable for allowing the acquisition of SE images with long TRs in short acquisition times. In conventional spin echo imaging the phase encoding gradient is applied only once per TR, with each acquisition filling one line of k space (Fourier space). In fast spin echo imaging several echoes (typically from 2 to 16) are generated and each is acquired with a different value of the phaseencoding gradient. This allows one line of k-space to be filled for each echo and thus allows Fourier space to be filled more quickly than for conventional spin echo imaging. The number of echoes per TR is termed the Echo Train Length (ETL), and the time between each echo is known as the echo spacing. Each phase-encoded echo exhibits a different amount of T_2 decay so as all echoes contribute to the signal, the TE prescribed is an **effective TE**. The middle lines of k-space are associated with the highest signals and have the greatest impact on contrast while the outer lines in k-space have less influence on contrast.

There are several reasons why fast spin echo images may appear different from spin echo images acquired with equivalent parameters. Signal in long TE images can be increased due to contribution from phase encoded echoes occurring early in the T_2 decay. Similarly, signal in

short TE PD-weighted images can be increased due to contribution from phase encoded echoes occurring late in T_2 decay. Phase encoding across T_2 decay can also produce image blurring for the Signa FSE sequences. Edge enhancement is possible with other FSE variants, however. When viewing a FSE image acquired using parameters which would produce PD-weighting for spin echo imaging (eg TR=3000, TE=20), signal from CSF is rather bright, due to high CSF signal in the later echoes affecting image contrast. In addition, a FSE image acquired using parameters which would produce T_2 -weighting for spin echo imaging (eg TR = 3000, TE = 80) demonstrates rather bright fat signal. Recent evidence suggests that this is mainly due to Jcoupling and to a lesser extent to magnetization transfer effects [KENNAN92, HINKS92, RUTT92, LISTERUD92], the latter of which is discussed in more detail later in this section.

As total scan time is directly related to the number of echoes acquired, a dual echo acquisition requires twice as many echoes to complete phase-encoding for two images as it does for one. Consequently the total acquisition time doubles. There are several ways of acquiring dual echo images using the GE fast spin echo pulse sequences.

■ Fast Variable Echo (FVE) uses the entire selected echo train length to complete the effective TE1 image. Then it merely repeats the scan with the middle view re-centred to complete the effective TE2 scan, again by using all of the echo train length (typical parameters would be FVE, ETL=8, effective echo times of 17 and 102 ms, TR=4000 ms).

• Fast Spin Echo Two (FSE2) takes the same time as FVE but acquires the data for each effective TE in a different manner. Rather than using the entire echo train length to acquire effective TE1 and then repeating for effective TE2, the FSE2 technique uses the first half of the echo train length to complete effective TE1 and the second half of the echo train length to acquire effective TE2 (typical parameters would be FSE2, ETL=8, effective echo times of 17 and 102 ms, TR = 4000 ms).

• Finally a single echo approach may be used to optimise contrast and the amount of blurring for each echo. For example, the first scan might be chosen to optimise early echo contrast by using a shorter TR/ETL combination (eg FSE, ETL=4, effective echo time of 17 ms, TR=2500 ms). The second scan would be chosen to optimise the late echo contrast using a longer TR/ETL combination (eg FSE, ETL = 16, effective echo time of 102 ms, TR=6000 ms).

The scan times for the three protocols discussed above are all equal (3.2 minutes). The latter approach can suffer from motion between the two scans due to subject stretching etc. as

discussed in section 7.10.1 and has therefore not been considered further. Data from three volunteers was acquired using the first two protocols and four experienced observers were asked to compare the image quality of the scans whilst blind to the protocol being used. All four observers noted that

- the FSE2 data was generally more "crisp" with regards to fine detail such as blood vessels, thin threads of CSF in sulci etc.

- that FSE2 data suffered less from motion artifacts (there is currently no flow compensation options for the GE fast spin echo pulse sequences)

- that FSE2 demonstrates lower CSF signal for the early effective echo image (ie the FSE2 early effective echo image is less T_2 -weighted).

Each of these factors is considered as an advantage for the FSE2 protocol, which has therefore been adopted as the fast spin echo protocol of choice by the Institute of Neurology NMR Research Group. Theoretically the FSE2 late effective echo image should be slightly more T_2 -weighted than for FVE but this was not noted by any of the observers.

Melki *et al.* [MELKI92] have investigated magnetization transfer effects in multi-slice fast spin echo sequences. Magnetization transfer is an effect which occurs when two distinct pools of protons exist. Protons in tissue consist of those that are bound to large structures such as proteins which are not visible using standard NMR techniques and so called free protons attached to water and fat which are NMR visible. These two pools of protons interact via diploe-dipole interaction and chemical exchange. This is illustrated schematically be Figure 123. Bound protons, due to their short T_2 , have a broad resonant peak surrounding that of the narrow (long T_2) free proton resonant peak so it is possible to saturate the bound protons using a frequency that does not directly excite free protons. The interaction of the two pools of protons then leads to the partial saturation of the free protons in areas where both exist. Such effects occur in FSE to a much greater extent than in conventional SE imaging because of the rapid RF echo trains used in the former case. These magnetization transfer effects lead to both an overall drop in signal of brain tissue, and a change in contrast to noise ratio between grey matter and white matter as a function of the number of slices for FSE PD weighted images. This must be taken into account when choosing sequence parameters, but has not greatly affected clustering results.



Figure 123 - Schematic diagram of the magnetization transfer effect.

7.10.2.2 Brain Parenchyma and CSF Segmentation.

The segmentation of the intracranial region may be achieved using conventional spin echo, fast spin echo or inversion recovery sequences, using similar parameters to those discussed in section 7.10.2.1. Of the three, the fast spin echo sequence is preferable due to its time efficiency and the fact that magnetisation transfer effects increase brain parenchyma to CSF contrast. Gradient echo data has been used for segmentation of brain parenchyma and CSF, although the contrast to noise ratio between grey matter and white matter is generally not high enough for a grey/white matter clustering approach to be considered. Two advantages which gradient echo imaging may have over spin echo and inversion recovery sequences are its speed and the consequent high spatial resolution that may be achieved in reasonable acquisition times. Two approaches to acquiring dual image data have been considered for gradient echo imaging - the acquisition of a dual echo image and the acquisition of two separate images.

The dual-echo sequence that has been considered is a multi-planar gradient recalled (MPGR) sequence (MPGR, TE1 = 6, TE2 = 30, TR = 500, $\theta = 15^{\circ}$). The early echo produces a PD-weighted image and the late echo a T_2^* -weighted image. The high contrast between CSF, brain

parenchyma and the background in the late echo, and between the intracranial region and background in the early echo, makes reliable segmentation using dual-echo clustering possible. The use of a relatively long second echo time, leads to susceptibility induced signal losses for some slices, however, making the method unsuitable for covering the whole brain. Typically the method produces good results for the slices superior to the eyes.

The second approach uses two separate datasets - a spoiled GRASS sequence (SPGR TE=5, TR=150, θ =10°) providing PD-weighted data and a steady state free precession (SSFP TR=24, θ =30°) pulse sequence providing T₂-weighted data. (Spoiling is the term for destruction of the transverse magnetization at the end of a TR period in order to prevent steady state effects building up). The PD-weighted data is of good quality - the very short echo time means no susceptibility artifacts are present. The T₂-weighted SSFP data is susceptible to motion and flow as this disturbs the steady state, so it is particularly important that the subject does not move their eyes during the scan which takes only a few minutes. Blood flow artifacts in the phase-encoding direction cause large variations in signal in the brain parenchyma but as this data is not being used for grey and white matter segmentation this is typically not a problem because the variation of intensity is not enough for the brain parenchyma to be misclassified as either background or CSF. There is also some signal reduction in parts of the ventricles due to CSF motion, but again this is not large enough to affect classification.



Figure 124 - Variation of intensity with TE for an Inversion Recovery pulse sequence using a TR of 2500 ms and a TI of 175 ms at 1.5 T

For lesion segmentation, the only images considered have been dual echo SE images as these are the scans acquired clinically. The early echo contrast between brain parenchyma (ie grey and white matter) and lesion is poor at short repetition times such as 1500 ms and also poor for longer repetition times such as 4500 ms. Repetition times of 2000 ms and 3000 ms give poor contrast between lesion and CSF at later echo times with lesion brighter then CSF for the shorter repetition time and CSF brighter then lesion for the longer repetition time. This is illustrated by considering the variation of contrast at an early and late TE with TR as illustrated by Figure 125 and Figure 126. A TR of 3700 ms provides a good compromise between brain parenchyma/lesion contrast for the early echo, and lesion/CSF for the late echo (Figure 127). TEs of TEmin and 80-90 ms give the best contrast for such a TR, whilst considering the loss in SNR at late echo times and the clinician's wishes to still have brain parenchyma easily visible, as illustrated by Figure 127.

The lesion T_1 and T_2 relaxation times used for these simulations are averages calculated from the work of Larsson *et al.* [LARSSON88]. The distribution of the T_1 and T_2 of lesions illustrated by them demonstrates a broad central distribution and a few outliers, but no indication of any correlation between T_1 and T_2 is given. Larsson notes one plaque within which the T_2 of the pixels varies from approximately 200 to 300 ms. The effects of such wide variations of relaxation times upon the contrast between lesion and CSF or brain parenchyma have been investigated using the four combinations of relaxation times taken from the extremes of the central distributions. These are short T_1 and short T_2 , short T_1 and long T_2 , long T_1 and short T_2 and long T_1 , dual-echo clustering with the parameters discussed above, would perform badly due to poor contrast between lesion and either CSF or brain parenchyma. For the other combinations of the extremes, contrast would be reduced when compared to that obtained with the average T_1 and T_2 values used for the simulation.

The current clinical protocol (ie TR = 2000, TE1 = 30, TE2 = 80) would in general, however, perform worse than the protocol proposed above (ie TR = 3700, TE1 = 30, TE2 = 80) for each combination of the extremes of T_1 and T_2 . Data indicating the correlation between T_1 and T_2 , or its absence, would be very valuable for use in such simulations.



Figure 125 - Variation of intensity with TR for a SE pulse sequence using a TE of 30 ms at 1.5 T. Each triplet of lines represents the mean predicted intensity and +/- one standard deviation from the mean due to noise.



Figure 126 - Variation of intensity with TR for a SE pulse sequence using a TE of 80 ms at 1.5 T. Each triplet of lines represents the man predicted intensity and +/- one standard deviation from the mean due to noise.



Figure 127 - Variation of intensity with TE for SE pulse sequence using TR=3700 ms at 1.5 T. Each triplet of lines represents mean predicted intensity +/-1 sd from this mean due to noise.

7.10.3 Method and Results

Several factors affect cluster size - image non-uniformity, signal to noise ratio and inherent tissue heterogeneity. The aim of this work is to reduce the cluster size and hence improve definition by concentrating on these effects. The approach that has been adopted for spin echo images consists firstly of pre-processing the images by correcting for RF non-uniformity as described in chapter 5, and smoothing using anisotropic iterative blurring (section 7.4.2). This processing decreases tissue cluster size as shown by Figure 128, which illustrates clusters corresponding to areas of CSF, skull fat, grey and white matter with and without anisotropic blurring. The decrease in cluster size improves cluster separation and allows the use of shorter repetition times, for example, where previously cluster overlap led to poor results. The intracranial region is isolated from the image using edge- or region- based processing as described in sections 6.6.3, 7.5 and 7.6. The tissues of interest - CSF, white matter and grey matter, or lesion and brain parenchyma, are then interactively segmented in one of two ways.

Firstly, small regions of tissue can be identified from a single-slice, which are used to define cluster positions in feature space. A feature space map is produced by plotting pixel intensity in the early-echo against intensity in the late-echo for each image and selecting a region from this map. Each pixel in the dataset is then mapped automatically to the nearest cluster centre in feature space. Alternatively, an experienced operator, using knowledge of cluster positions in feature-space for a particular pulse sequence, can interactively select a region from a feature-space map, which is then mapped back into image space. Other authors have exclusively used training datasets in image space. This author believes that a feature-space approach can be much faster than using training approaches. Results for the segmentation of white matter, grey matter, some partial volume voxels and CSF are illustrated by Figure 129 - Figure 133. Although many voxels may suffer from the partial volume effect, it is difficult to identify them. Some partial volume voxels may be easily identified as they lie in a broad diffuse band, the position of which is indicated by Figure 129 and may be appreciated from Figure 136. These voxels lie at the interface between brain parenchyma/CSF and bone/bone marrow, or at the interface between CSF and brain parenchyma. Work on identifying partial volume voxels is discussed in section 9.6.

Figure 127 demonstrates that for the protocol adopted (SE/3700/30,80-90) lesions should appear brighter than CSF, grey matter and white matter for the early echo. At the later echo time, CSF should appear brighter than lesion which should in turn appear brighter than grey matter and white matter. The variation of lesion T_1 and T_2 noted by Larsson *et al.* will lead to a spread in intensity values, however. This spread will be heightened by the fact that voxels identified by a radiologist as corresponding to lesion often suffer from the partial volume effect. Figure 134 and Figure 135 illustrate an early and late echo image from a multiple sclerosis patient acquired using the protocol described above. A lesion is apparent close to the grey/white matter border in the right half of the brain. The lesion pixels are represented in the cluster image (Figure 136) by the diffuse streak of points approximately two thirds of the way down the right hand side of the image. The lesion pixels are interactively identified from the cluster plot and are illustrated by Figure 137. The position of the streak of points is typical, but the partial volume effect means that some voxels identified by a radiologist may overlap with CSF voxels.

7.11 <u>Summary</u>

The importance of acquiring data which does not show a variation of geometric distortion with echo time has been demonstrated. The use of pre-processing routines to correct for RF non-uniformity and to provide anisotropic image smoothing to reduce the effects of noise have been introduced and are shown to be valuable for region-based processing. Image thresholding is demonstrated to be an efficient method of estimating brain and CSF volume if anisotropic smoothing is used. Alternatively, normalising late echo signal intensity to early echo grey matter intensity allows a second thresholding approach for isolating the brain and CSF, suitable for long repetition time datasets. Contrast enhancement by image combination is shown to be a fast method of approximating CSF, grey matter and white matter volumes, but one that is hindered by the partial volume effect in superior slices. Dual-echo clustering is shown to be an effective method of segmenting CSF, grey matter and white matter. The technique shows promise as the initial step in a MS lesion segmentation scheme but is not a perfect MS lesion segmentation method on its own using the current acquisition protocol because of signal overlap with CSF. There are limitations in current imaging practise for the visualisation of MS lesions, however, and these are also pointed out. Several pieces of important further work are proposed in chapter 10.

Early echo intensity ->



Figure 128 - Normalised plots of late echo intensity against early echo intensity for regions of several tissues both prior to, and following, anisotropic blurring.

CSF

White matter

Late echo intensity

1

V

Grey

matter

Fat

Early echo intensity ->

Late echo intensity I



Figure 129 - Dual echo spinecho feature map illustrating (from darkest to lightest) white matter, grey matter, CSF and partial volume clusters.



Figure 130 - Segmented partial volume voxels



Figure 132 - Segmented grey matter voxels



Figure 131 - Segmented white matter voxels



Figure 133 - Segmented CSF voxels

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Figure 134 - Early echo image demonstrating lesion.



Figure 135 - Late echo image demonstrating lesion.



Figure 136 - Cluster map for lesion data.



Figure 137 - Area corresponding to lesion identified from cluster map.

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CHAPTER 8

THE STACK

The stack, as described in section 3.6.3, is a multi-resolution image description and segmentation scheme initially proposed by Koenderink [KOENDERINK84]. The method examines intensity extrema (minima and maxima) as they move and merge through a series of progressively blurred images known as scale space. Such a data driven approach is attractive because it is claimed to be a generally applicable and natural method of image segmentation. Initial work on the stack by this author took the form of investigations of extrema lifetime in scale space, false extrema and the concept of defining extrema with respect to a sparse grid. Later studies involved the investigation of the work described by Lifshitz [LIFSHITZ90], the design of a new stack algorithm, an evaluation of the stack for the segmentation of neurological MRI data, and the investigation of anisotropic blurring both as a pre-processing step and within the stack.

8.1 Local Extrema in Gaussian-Smoothed Images.

The variation of the number of local extrema (ie those defined on a 3x3 grid) with standard deviation of the blurring Gaussian is the basis of the stack approach. Theoretically the number of extrema in an image should not increase with decreasing resolution (ie with increasing standard deviation of the blurring Gaussian). The discrete nature of the image, however, means that extrema are sometimes temporarily created, possibly at several different points in scalespace. Working with floating point representations of integer images for accuracy, it is clear that the number of extrema in an image is highly dependent upon the tolerance used to define an extremum as illustrated by Table 2. (eg for a pixel to be defined as an extremum with a tolerance of 0.1%, the pixel must have an intensity that exceeds the intensity of each of its local neighbours by at least 0.1%). The corresponding un-blurred image is illustrated by Figure 138. A valid tolerance can only be determined with some idea of the errors associated with the method of Gaussian blurring. A comparison of Fourier transform and convolution methods of Gaussian blurring has been made (see section 8.2) and from this a tolerance of 1 in 10^7 has been determined to be suitable. Typical image intensity values range from 0 to 1000 for the data used.

Tolerance (%)	Number of maxima.	Number of minima.
1e ⁻⁵	26	17
1e ⁻⁴	22	2
1e ⁻³	10	5
1e ⁻²	3	2
0.1	0	0
0.99	0	0

Table 2 - Variation of number of extrema with tolerance for image blurred with a Gaussian of standard deviation = 7

The variation of the number of extrema with standard deviation of the blurring function for a fixed tolerance has been examined for several images. A representative result for one particular image with an intensity range of 0 to 527 and a tolerance of $1e^{-3}\%$ is illustrated by Table 4. The annihilation of various extrema has been carefully examined in an effort to determine the precise standard deviation at which particular extrema annihilate. A situation which demonstrates that new extrema may be created has been investigated for an image where initially only two maxima are present. Further Gaussian blurring leads to the appearance of two further maxima and the subsequent disappearance of three maxima. The course of events appears to be that the third and then the fourth maxima are created, the third maxima is destroyed followed by the second maxima and finally the fourth maxima. This is illustrated by Figure 139 - Figure 144 and

Table 3. Although it is hard to guarantee this scenario as extrema move continuously in scale space, the extrema coordinates strongly suggest this. There is currently no satisfactory explanation for such an observation.



Figure 138 - Example image used in stack investigations of extrema tolerance.

Standard deviation of blurring Gaussian	Number of extrema (maxima)	
18.65	2	
18.67	3	
18.70	4	
18.75	3	
18.80	2	
18.90	1	

Table 3 - Variation of number of false extremawith standard deviation of the blurring Gaussian



Figure 139 - Extrema for standard deviation of blurring Gaussian = 18.65



Figure 140 - Extrema for standard deviation of blurring Gaussian = 18.67



Figure 141 - Extrema for standard deviation of blurring Gaussian = 18.70



Figure 143 - Extrema for standard deviation of blurring Gaussian = 18.80



Figure 142 - Extrema for standard deviation of blurring Gaussian = 18.75



Figure 144 - Extrema for standard deviation of blurring Gaussian = 18.90

Standard deviation.	Number of maxima.	Number of minima.
1.0	1307	1193
2.0	359	304
4.0	36	25
6.0	10	5
9.0	1	1
12.0	1	1
14.0	2	0
18.0	0	0

Table 4 - Variation of number of extrema with standarddeviation of the blurring gaussian for a tolerance of 0.01

8.2 <u>Comparison of Methods of Gaussian Smoothing.</u>

A comparison of Fourier transform and convolution methods of Gaussian smoothing has been carried out using floating point image representations. Commonly, convolution involving the neighbours of pixels at the boundaries of images is accomplished using either wraparound or mirroring. Wraparound assumes pixel values at a given distance outside the border to be the same as those at the opposite side of the image, whereas mirroring assumes such pixel values to be the same as those of pixels at the same distance inside the border. Wraparound or mirroring are not appropriate methods to use when comparing the two methods of blurring, so it is necessary to set to zero all pixels within a border around the image. The truncation of the Gaussian convolution kernel was 3 standard deviations, or a 5% cutoff. A range of standard deviations was used for the comparisons, with the maximum difference in intensity between corresponding pixels in integer images processed using the two methods proving to be 1 for standard deviations up to 20. The requirement to zero pixels within a border of the image limits the range of standard deviations over which comparisons can be made. The intensity range in the original images was as described previously. Fourier transform methods are inherently more accurate than convolution methods because of the number of samples normally used, but for standard deviations less than 20, it appears that this difference in accuracy is not important.

The images produced by the Picker scanner have a circular field of view with zero signal outside the field of view. This zero signal region in Picker images, and a variety of phantom step edges, have been used to measure the "noise" produced by the Fourier transform Gaussian blurring. For a small standard deviation of the blurring Gaussian, the centre of regions of constant signal in an output image should still be approximately constant in the blurred output image. Instead, such regions demonstrate a level of noise. Some floating point pixel values appear repeatedly in these regions (ie the noise is quantised) as illustrated by Figure 145. There is currently no clear explanation of this effect, although it may be due to the Fourier transform algorithm. Scaling the image intensity does not directly scale a profile through a noisy part of the image, but does scale the 'average' profile amplitude. The noise level is approximately 0.00001% of the image mean, and this level is used as the tolerance for defining extrema, as previously stated.



Figure 145 - Fourier Transform quantisation of noise values.

8.3 Sparse Extrema.

One problem with using a 3x3 region to define extrema is that the identified extrema are strictly local - hence even noise produces them. The possibility of identifying extrema with respect to a wider 'sparse' filter - the width of which might be based on the standard deviation of the blurring Gaussian - was investigated. The variation of filter width with standard deviation of the Gaussian is important, because feature size should increase with increased blurring. This method is inherently a blob-detector, although it should be noted that the investigations carried out have used square filters, whereas extended blobs would be better detected with rectangular filters oriented in the same direction as the major axis of the blob. This would necessitate all directions being searched, however, which is a more complex procedure. The smallest sparse filter is illustrated by Figure 146, where the nature of the centre pixel (marked *) in the extrema image is determined by its relation to the outer pixels (marked +) in the input image.

+	+	+
+	*	+
+	+	+

Figure 146 - The smallest sparse filter.

8.3.1 <u>Method</u>

Defining extrema with respect to a 3x3 local region leads to the identification of isolated extremal points. The equivalent of this for the sparse grid is a group of points, which will be referred to as a sparse extrema group. It is possible to identify extrema groups with a sparse grid that are not apparent with detection based upon 3x3 local regions. It is trivial to show that the larger a sparse-grid, the larger the potential size of the group of points which represents a single extremum. For small standard deviations the sparse-extrema group area is often equal to the square of the sparse grid size. The reasons for this area equality and its breakdown at larger standard deviations of the blurring Gaussian are discussed in the next section.

The possibility of using sparse extrema groups to reject some locally defined extrema has been investigated. It is very difficult, in general, to identify false extrema because the continuous movement of extrema in scale-space makes manual tracking problematic. False extrema may, however, be detected using small incremental blurring steps at large standard deviations of the blurring Gaussian since there are then few extrema and tracking is an easier task. Unfortunately, false extrema tend to be relatively close to other extrema at such large standard deviations of the blurring Gaussian and this close proximity leads to problems with the detection of sparse extrema groups as discussed in the next section. Thus it is not practical to use sparse extrema groups to reject locally defined extrema.

8.3.2 Area of the sparse extrema group

A one dimensional sparse grid is composed of three points - the left, right and centre. For small standard deviations, half the sparse-size (ie the distance between the central and outer pixels) is less than the typical peak width. Consider an isolated peak in the 1-D continuous case, as illustrated by Figure 147, where the sparse extrema grid scans from left to right. The first position for which the central point has a value greater than all other points is when the central point and the right hand point are both at the same height (or rather just to the right of this). In a position further to the right, the value of the central point is still greater than that of the left and right points. Eventually, a position is reached where the left hand point and the central point are at the same height. This is the further limit of the distance moved by the central point, while remaining a maxima and is equal to the distance between the central and left hand points. Thus the line-integral scanned is simply the sparse-length.

Such a description may be extended to higher dimensions and to the discrete case. The equality breaks down, for the simple case of a peak on a uniform background, when the sparse-distance is greater than the maximum peak-width (ie full width at zero amplitude).

If two or more close peaks are considered which are close to each other relative to the size of the sparse grid, then each peak will influence the response of the other to the sparse-extrema grid. The centre of the sparse-extrema response will in general not correspond to the centre of the peak. This is the main drawback with the use of a sparse grid, and is a very significant one as the positions of two extrema will not be accurately identified close to the annihilation of the pair, or in any other case where extrema are in close proximity. If the extrema are maxima the



Figure 147 - Response of sparse-grid to isolated peak.

lower intensity one may not be identified; if they are minima then the higher intensity one may be lost. Because of this limitation, the sparse grid has not been used further, and despite its limitations, it appears that the use of a 3x3 local region is a better way to define extrema.

8.4 Implementation of the Stack

The University of North Carolina's /usr/image package includes the thesis work of Lifshitz [LIFSHITZ87]. Investigation of the code structure reveals that the program has been modified repeatedly and the original structure has been completely lost, making further modification extremely problematic. The program only works for one particular combination of the 30 or so program parameters and sometimes crashes even using these options. The image output from the program is invalid, although a valid tree description is produced. These problems prompted a top-down plan for a new implementation of the stack outlined in Appendix 1, but this has not been realised due to time constraints.

8.5 <u>Visualisation of the Stack Tree</u>

The tree description produced by the stack is a complex hierarchical description. To visualise the relationship between nodes in the tree and the corresponding regions of neuroanatomy, a well designed display program is necessary. 'Stackview' is a /usr/image X based program written by Eric Fredericksen of the Computer Science department, University of North Carolina for displaying the pixels corresponding to any node in a stack tree. In its simplest

form the display shows two versions of an image, the first a reference image and the second an image with a red overlay to indicate the pixels corresponding to a given node in the tree. When the program is initialised, the overlay covers the full image, representing the top node of the tree. The tree may be traversed by selecting to display the parent, child or sibling of the current node. Such an approach is useful but has a number of limitations, specifically

- the tree structure can not be appreciated easily
- there is no method of ignoring nodes representing only a small number of pixels

• there is no method of tree editing (eg for joining or separating parts of the tree) For these reasons, an undergraduate project was designed to allow the display of the tree and regions that correspond to a given node. The resulting program, 'treeview', written by D.Sagoo of the Computer Science department, UCL, overcomes several of these limitations. The initial display shows a tree like relationship between the various nodes comprising the tree. It is possible to prune the tree by ignoring those nodes which correspond to less than a user specified number of pixels. Simple editing in the form of cutting nodes from the tree is also possible. The pixels corresponding to any node may be displayed by selecting the node. Although treeview is an improvement over stackview in a number of respects, its speed and ease of use still needs to be improved to make it a practical tool.

8.6 The Stack and Neurological MRI Segmentation.

The stack, by its very nature, uses large amounts of memory and can be slow. This has restricted processing to two dimensions. The standard size for a MRI head slice tends to be 256x256, but only 128x128 or smaller images have been processed because of these limitations. Both reduced resolution versions of whole images and full resolution subsections of various parts of the neuroanatomy have been considered. A large number of images have been processed and the corresponding tree descriptions investigated using the stackview and treeview programs. This work aims firstly to determine if the stack really is a general segmentation method as claimed and to study the effect of the algorithm on neurological MR images with common content and contrast. In addition, the findings of Bister *et al.* [BISTER90] (as discussed in section 6.6.3.1) prompted an investigation of the possibility of shift-, rotation- and scale-variance of the stack. Finally the ability of the stack to handle elongated objects was determined.

Bister *et al.* [BISTER90] have demonstrated shift-, rotation- and scale- variance for pyramid segmentation, another multi-resolution method. A series of experiments was therefore carried out

to ascertain the performance of the stack in relation to image shifts, rotations and scalings. Several representative reduced resolution versions of whole images and full resolution subsections of various parts of the neuroanatomy were artificially created by various means such as shifting the image sideways whilst also wrapping around pixels, adding blocks of pixels to one side of an image whilst subtracting blocks of pixels from the other side etc. A range of image rotations from a few degrees up to 180 degrees were selected and a range of images subjected to these rotations. Image scaling was similarly accomplished by the use of interpolation routines to create images of differing sizes representing the same region of neuroanatomy.

The comparison of tree descriptions was made by displaying several different versions of the same original image simultaneously, using treeview or stackview. This allows all of the trees to be traversed simultaneously, although it was not feasible to compare every single node in the tree for every version of an image that was processed. Instead the nodes corresponding to large numbers of pixels were examined. These investigations did not demonstrate any evidence of shift-, rotation-, or scale- variance for the stack for any regions corresponding to sections of neuroanatomy. This is to be expected because, in this implementation of the stack, the image resolution (ie the size of the image in pixels) does not change and image blurring is achieved using an isotropic gaussian filter. Scale space methods should, in general, be invariant to scale. The automatic comparison of the complete tree structures to determine whether or not two images of random orientation and scale were similar would be a very challenging task.

The utility of the stack for processing elongated objects was primarily evaluated by examining regions corresponding to skull fat in a variety of early echo images. Skull fat is the major elongated region in the neurological MRI images processed, although other regions exist in images acquired using appropriate slice orientation, for example the optic nerve and the spinal cord. The stack does not handle such elongated objects well, typically associating them with a large number of small regions. The reasons why multi-resolution algorithms such as the stack have fundamental and inherent difficulties in analysing elongated objects has been discussed in section 6.6.3.1. The performance of the stack for more compact regions is good, with large regions of tissues often being represented by a single node in the tree if there is adequate contrast with neighbouring tissues. The images used by Lifshitz *et al.* [LIFSHITZ87] were reduced resolution CT images of the abdomen, which consist of a number of compact objects such as the kidneys, spinal column, liver, spleen etc., with good contrast between the various organs. Lifshitz *et al.* did not mention any problems with elongated objects.

The behaviour of the stack with respect to partial volume pixels is of great interest. Two neighbouring regions divided by a border of partial volume pixels will normally be represented by two regions at a given level in the tree. The partial volume pixels will normally be represented by a series of small (often single pixel) regions. Further blurring will initially lead to partial volume pixels being linked to one or other of these two regions and finally to the two regions joining together and being represented by a single node. An example of this occurs at the border between the eye and ocular muscle, as discussed later in section 8.7.

Typical results are illustrated by Figure 148 - Figure 150 which show regions corresponding to the brain, grey matter and CSF in different images displayed by stackview. These results are very pleasing. One drawback of the current implementation of the algorithm is that it terminates once only a single extremum is present. At this stage many extrema have annihilated, but are represented by nonextremum paths which have not yet joined up with other extremal paths. A full tree description can only be realised when all of these paths have correctly linked up. The single node is currently artificially created by linking up all nodes to the remaining single extremum. This has made a full evaluation of the utility of the stack for the segmentation of neurological MRI problematic.

In addition to the problems associated with defining extrema with respect to 3x3 local regions, as discussed in section 8.3, two other particularly important drawbacks of the stack have been identified as a result of these investigations.

■ The fundamental assumption made when utilising the stack is that longevity of a particular extremum in scale-space is a reflection of the importance of the region associated with that extremum. Careful examination of the stack trees of a wide range of images has demonstrated that local contrast and features critically determine the longevity of extrema so that, for example, areas of background noise may appear as important features. Lindeberg [LINDEBERG90] has recently suggested the use of a combination of longevity and the spatial extent of the region represented by a node at a given scale to overcome this. The incorporation of such an approach into the current code would require considerable modifications to be made.

■ Ideally, an appropriate blurring scheme would blur all pixels within an object together, before blurring the objects together. Gaussian blurring often results in objects merging before all of the pixels within an object have joined in one region, so a different method of blurring is of interest.

This author proposes preprocessing with an anisotropic blurring method, and the incorporation of this method into the stack as discussed in sections 8.7 and 8.8.

Despite the limitations of the stack, it still has great merit. This author suggests that the stack may be particularly applicable for segmenting compact regions of neuroanatomy, once a focus of attention for a given region has been established. There are a wide range of approaches to establishing such a focus of attention. The ventricles, for example, could be focused upon by choosing a rectangular region of interest within the brain once the latter has been isolated. The position of the eyes may be established using the Hough transform (as discussed in section 6.5), whilst high intensity lesions might be indicated by an initial thresholding or dual-echo clustering segmentation. The border between grey and white matter might be identified by its proximity to the surface of the brain.



Figure 148 - Second level node corresponding to brain in subsection of near transverse slice at the level of the eyes for SE/3000/30 image.



Figure 149 - Second level node corresponding to white matter in late-echo image at the level of the ventricles for SE/3000/80 image.



Figure 150 - Second level node for high level lateecho slice corresponding to several spatially unconnected regions of CSF for SE/3000/80 image.
8.7 Pre-Processing by Anisotropic Blurring.

There are situations where a compact region of neuroanatomy demonstrating good contrast with surrounding tissues is not represented by a single node within the stack tree. This is the case, for example, when considering late echo images of the eye where Gaussian blurring may join the eye and ocular muscle before the pixels of the eye are all represented by a single node. This is illustrated by Figure 152, which demonstrates the smallest region which includes the whole of the eye. As well as the eye, the region includes parts of the ocular muscle. Such situations may often be avoided by pre-processing by anisotropic blurring, which blurs the pixels within objects, whilst preserving the border between them. Thus a single node representing the whole eye may be created as illustrated by Figure 151. Such preprocessing is also valuable for many other regions of neuroanatomy which demonstrate good contrast with surrounding tissues, such as the ventricles, for example.



Figure 151 Node corresponding to the whole eye does not include pixels from the ocular muscle for an image pre-processed by anisotropic blurring.



Figure 152 - Node corresponding to the whole eye also includes pixels from the ocular muscle for an original image.

8.8 Anisotropic Blurring within the Stack

Perona and Malik have proposed a method of anisotropic blurring based upon an anisotropic scale-space, as described in section 7.4.2. The approach is designed to preserve the strongest edges in the images, and does this very effectively. Using integer or floating point representations of an image, edges are preserved for at least 20,000 iterations. As one iteration takes approximately 7 seconds for a 256 x 256 image on a Sun SparcStation 2, such an approach is obviously not appropriate for an anisotropic stack because of the processing time required. An appropriate anisotropic smoothing scheme for the stack should initially allow blurring across the weakest of edges (noise) and, as scale increases, across stronger and stronger boundaries so that tissue variation is reduced. Organs then start to merge until eventually a single blob like structure, with an associated single extremum, is present. Ideally the strength of edges to be blurred should increase continuously with scale. This presents the problem of somehow deciding when and at what rate to change the strength of boundaries to be preserved. Without significant a priori information (and noting that the method is presented as a natural approach to segmentation, which implies the absence of any such knowledge) some method of measuring or estimating the rate of blurring must be developed. Each iteration of Perona and Malik's algorithm calculates a new intensity value, $I_{i,i}^{t+1}$ for each pixel at position (i,j) from the previous

intensity value $I_{i,j}^{t}$ using the equation,

$$I_{i,j}^{t+1} = I_{i,j}^{t} + \lambda [c_{N} \nabla_{N} I + c_{S} \nabla_{S} I + c_{E} \nabla_{E} I + c_{W} \nabla_{W} I]_{i,j}^{t}$$
(78)

where $0 \le \lambda \le 1/4$ for the scheme to be numerically stable, and

$$\nabla_{N} I_{i,j} - I_{i-1,j} - I_{i,j}$$
(79)

$$\nabla_{s}I_{i,j} - I_{i+1,j} - I_{i,j}$$
(80)

$$\nabla_{E}I_{i,j} - I_{i,j+1} - I_{i,j}$$
(81)

$$\nabla_{\mathbf{W}} I_{i,j} - I_{i,j-1} - I_{i,j}$$
(82)

The conduction coefficients $c_{x(i,j)}^{t}$ are given by

$$c_{x_{i,j}}^{t} = g(|\nabla_{x}I_{i,j}^{t}|)$$
(83)

where $x = \{N,S,E,W\}$ and N,S,E and W represent the pixels North, South, East and West of the centre pixel. For the simple schema adopted by Perona and Malik, g is given by either

$$g(\nabla I) = \exp\left(-\frac{|\nabla I|}{\kappa}\right)^2$$
 (84)

or

$$g(\nabla I) = \frac{1}{1 + \left(\frac{|\nabla I|}{\kappa}\right)^2}$$
(85)

where ∇I is the gradient of a pixel. The effect of the two functions is different, the first function favouring high contrast edges over low contrast edges, whilst the second function favours large regions over smaller ones. In neurological MRI, it is very important that the processing does not prematurely destroy small detail such as thin threads of CSF within the sulci, for example, so the first function has been chosen as more appropriate for this work.

The value of κ determines the rate of blurring. This can be fixed either manually, or by using the noise estimator described by Canny [CANNY86]. For the sake of automation the latter has been chosen for this author's implementation. Canny's noise estimator calculates κ as the 90th percentile of the integral of a histogram of the absolute value of the gradient throughout the image (or a 0.9 fraction). The value of 90% is known as the gradient threshold and is an arbitrary value which has provided good results; too small a value (for example 80%) gives little blurring, whilst too large a value (for example 99%) may lead to parts of a strong border being smoothed whilst other parts of the same border are preserved. The rate of change of κ is an indication of the rate of change of gradients within the image and can be visualised by plotting κ against the number of iterations. A pseudo-exponential decay occurs, with the value of κ tending to an approximate asymptote as indicated by Figure 153. This occurs as the intensity differences between pixels of similar intensity are progressively smoothed out.



Figure 153 - Typical variation of κ with number of iterations

This pseudo-exponential decay curve is found for a wide range of values of the gradient threshold and for a wide variety of images. Once κ has reached a constant value, little change occurs to the image with further iterations. For a 90% gradient threshold this situation is typically reached in significantly less than 100 iterations at which point all of the strong edges are still present in the image. As κ must be increased in order for significant changes to take place in the image, this suggests that a method is required where the gradient threshold varies with the number of iterations (time). There are several possible approaches to varying the value of the gradient threshold

- (1) Vary the gradient threshold as a function of the number of iterations, for example
 - (a) Increment the gradient threshold continuously
 - (b) Vary the gradient threshold logarithmically

(2) Increment the gradient threshold when the value of κ falls below a fraction 1/e of its initial value. At the same time reset the initial value of κ . The value 1/e has been chosen to reflect the pseudo-exponential nature of the plot of κ against iterations.

The first method requires *a priori* information about blurring rates for particular images. For this reason, the latter method has been chosen as the more promising approach, because of its ability to react to image changes directly and the subsequent time saving that such an approach can yield. A plot of κ against iterations for such an approach demonstrates a series of pseudo-exponential decays following each gradient threshold increment. It is possible to increase the value of the gradient threshold above 1.0 by setting κ equal to the product of the gradient threshold and the maximum gradient in the image. For values of gradient threshold < 1.0, there is a pronounced upward jump in the value of as the gradient threshold is incremented. There is no such jump in the value of κ as the gradient drops dramatically above this point as blurring of all pixels within the image begins. Both the variation of κ with number of iterations and the corresponding variation of the maximum gradient are illustrated by Figure 154.



Figure 154 - Variation of κ and maximum gradient with iterations for scheme where gradient threshold is incremented when κ drops below a fraction 1/e of its initial value. The initial value of κ is then reset.

Figure 154 corresponds to a situation where the gradient threshold is incremented by a fraction equal to 0.01. Too small an increment leads to a situation where parts of a border are preserved whilst other parts of the same border are blurred. This is not a natural way to create a smooth scale-space.

Incorporating this method of non-isotropic blurring into the stack gives the same advantages as pre-processing by anisotropic blurring with respect to the preservation of borders surrounding compact regions of neuroanatomy demonstrating good contrast with surrounding tissue. Its utility is demonstrated by Figure 155 and Figure 156 which illustrate the major nodes corresponding to an image slice at the level of the eyes where three sections of the brain are apparent. Using the standard stack, part of the main section of the brain and one front lobe are represented by a single node while with anisotropic blurring within the stack, the whole of the main section of the brain is represented by a single node.



Figure 155 - Brain region for a slice at the level of the ears processed with the isotropic stack. No node corresponds only to the whole of the largest rear brain lobe.



Figure 156 - Brain region for a slice at the level of the ears processed with the anisotropic stack. A single node corresponds to the whole of the largest rear brain lobe.

8.9 Summary

The presence of false extrema in scale-space has been demonstrated and methods of Gaussian smoothing compared. The limitations of extrema defined with respect to a 3×3 local region have been pointed out, the concept of the sparse extrema group introduced, and reasons for maintaining the original definition given. A critique of the stack has been presented and the inability of multi-resolution algorithms to successfully process elongated objects demonstrated. The stability of the stack as regards image shift, rotation and scaling has been illustrated. Pre-processing by anisotropic blurring has been introduced as a useful approach for reducing the probability of two regions separated by a high contrast border merging prematurely. The possibility of anisotropic blurring within the stack has been proposed using an approach where the strength of borders to be blurred varies with time. A split and merge approach for postprocessing the stack tree is presented in chapter 10.

CHAPTER 9

CONSIDERATIONS FOR VOLUME MEASUREMENT IN MRI

9.1 Introduction

This chapter considers the use of MRI for neurological volume measurement, arguably one of the most important applications for segmentation. Clinical applications of volume measurement in neurological MRI covering both the size of structures of the neuroanatomy and of lesions are reviewed. The sources of geometric distortion affecting MRI are considered, measurements of the magnitudes of such effects reported and methods for geometric distortion correction reviewed. Intensity variations due to spin dephasing are discussed and the accuracy of slice characteristics for our 1.5 T Signa are reported. The partial volume effect is discussed, as is the validation of volume measurement for the intracranial region, grey matter, white matter and CSF.

9.2 Clinical Applications of Volume Measurement in Neurological MRI

MRI is used for the visualisation of anatomy and pathology in many neurological conditions. It has a number of advantages over CT, its nearest rival in the field of neurological imaging as discussed in section 1.2. Pertinent to volume measurement is the fact that MRI does not suffer from the beam hardening found in CT, so regions of the brain abutting the skull are clearly demonstrated. Beam hardening has generally restricted the use of CT for CSF measurements to ventricular CSF. MRI's superior soft tissue contrast is also advantageous. There are, however, several sources of geometric distortion which may affect the accuracy of volume measurement under certain circumstances. These are discussed in section 9.3.

Conditions such as Alzheimer's disease, epilepsy, schizophrenia, AIDS, multiple sclerosis, Huntington's disease, senile dementia and hydrocephalus may all lead to changes in the size of neurological structures and/or the size and presence of lesions. The quantification of volumes of such structures and lesions may be valuable for diagnosis, for staging and following the natural history of disease and for following the patient's response to therapy. Volumes of intra- and extra- ventricular CSF, grey matter, white matter, total brain parenchyma, hippocampus, thalamus and temporal lobes are of particular importance. A review of the literature can not hope to cover every use of MRI for neurological volume measurement; instead this review focuses on the most common areas of application. Most papers in the literature have concentrated on the volume of neurological structures, although several papers have examined lesion volume. Total lesion volume can be used as a measure of disease load, to test the response to therapy.

Before MR imaging based volumetric measurements can be used to investigate volume changes due to disease, it is important to establish normal values using appropriately matched controls. Age is often an important consideration for such controls, and sex and handedness may also need to be considered. Numerous neuropathologic studies ([CRITCHLEY42, BRODY55] for example) have shown an age-related decrease in brain volume in non-demented subjects. These changes must be taken into account in any clinical studies. It may also be necessary to normalise volumes to take into account natural variations in total cranial size. This may be done with respect to height, weight or total intracranial volume or by adjusting volumes by an amount proportional to the difference between an individual's observed intracranial volume and the mean intracranial

volume for all subjects [JACK89].

The temporal lobe has received much attention in the literature because of its association with epilepsy, schizophrenia, Alzheimer's disease and amnesia and is discussed in section 9.2.1. Similarly, the measurement of CSF volume is of general interest, providing as it does, an index of brain atrophy (section 9.2.2). Aging is considered in section 9.2.3, followed by the main diseases considered in the literature - Alzheimer's disease, schizophrenia, epilepsy, multiple sclerosis - applications to paediatrics and neonatals, and a variety of other conditions.

9.2.1 <u>Temporal Lobe Measurements</u>

Increasingly, MR is replacing CT as the primary radiological modality in the evaluation of patients with suspected temporal lobe abnormalities, particularly those with temporal lobe epilepsy. In addition to identifying structural lesions, MR is often used to assess temporal lobe atrophy. The temporal lobe and its components are concerned with language production and memory and are of great interest in studies of epilepsy, Alzheimer's disease, amnesia and schizophrenia. The hippocampus is reported as being intimately involved with recent memory and with temporal lobe seizures [NAIDICH87].

Jack *et al.* have investigated the left-right asymmetry of the temporal lobe volume [JACK88] to assess whether or not asymmetry is common in normals. The authors found the median ratio of right to left temporal volume to be 1.16, with the non-dominant temporal lobe (ie the right hand lobe in left handed subjects and vice versa) significantly smaller then the dominant.

Jack *et al.* [JACK89] have measured the anterior lobes in hippocampal formations in young adults to provide normal values to be used in the evaluation of patients with a variety of disorders relating to the temporal lobes. A combination of thresholding and tracing was used to outline boundaries of the anterior temporal lobe on each image using ANALYZE. Normalisation was carried out by adjusting observed volumes by an amount proportional to the difference between an individual's observed intracranial volume and the mean intracranial volume for all subjects.

Bronen and Chenung have used MRI to determine normal variations of the temporal lobes [BRONEN91]. Their investigation focused on the symmetry of six anatomic regions - the temporal lobes, uncus, collateral white matter, choroidal fissure, temporal horn and Sylvian fissure. Visual assessment of the scans showed frequent asymmetry of the temporal horns, mild enlargement of the right temporal lobe and sometimes subtle asymmetry of the white matter between the hippocampus and the collateral sulcus.

9.2.2 <u>CSF Volumes</u>

Ventricular enlargement is found in patients suffering from schizophrenia, Alzheimer's disease, Huntington's chorea, Parkinson's disease, alcoholism, bipolar disorder, delusional depression and anorexia nervosa [PFEFFERBAUM88]. CSF volume measurement has wide neurological and neurosurgical applicability for differential diagnosis and as an objective monitor of therapy or progression in conditions such as hydrocephalus, atrophy and benign intracranial hypertension. Estimates of ventricular volume can be important in the diagnosis of hydrocephalus, for assessing the need for surgical intervention, and as an assessment of the efficacy of treatment. Estimates of extra-ventricular CSF may be useful as a means of differentiating between communicating and non-communicating hydrocephalus and as an index of cerebral atrophy in such conditions as senile dementia and alcoholism. In the latter case, where it has been reported that the condition is to some extent reversible, it may also be helpful in monitoring treatment. In cases of reduced CSF volumes due to brain swelling [for example benign intracranial hypertension], such measurement may also be helpful in the diagnosis, monitoring, and investigation of the aetiology and pathogenesis of the condition.

Cramer *et al.* [CRAMER90] have used manual segmentation to establish normal values for encephalic ventricular volumes. They found volumes ranging from 6 to 38 cm³ with a mean of 17 ± 8 cm³ for subjects from 5 to 60 years of age. A small but significant increase of ventricular volume with age was noted.

Condon *et al.* [CONDON86A, CONDON86B] have measured intracranial cerebrospinal fluid volume using MRI. According to Condon the use of X-Ray CT or radionuclide ventriculography for such measurements produces inaccuracies of 20-30%. An MR pulse sequence was therefore developed which produces a contrast of greater than 200 to 1 between a unit volume of CSF and a unit volume of combined grey and white matter. This is achieved using an inversion recovery sequence to 'null' the grey and white matter and a long echo time to reduce any remaining unwanted signal. Two sagittal images are used to determine the required volumes of CSF. The

first image is an 18 cm slice which contains all of the CSF within the head. A ROI is manually defined so as to exclude other sources of high intensity such as the eyes, sinuses and CSF in the spinal column. The signal within this ROI is directly proportional to the amount of intracranial CSF. A second sagittal slice of width just greater than the lateral ventricles is defined from a coronal pilot, so that there is no contribution to the signal from sulci in the region of the ventricles. It is then possible to manually delineate the region of the ventricles. A phial containing a known volume of distilled water at 37°C is used as a reference, having very similar relaxation times to CSF at body temperature. Condon *et al.* claim that there is a wide variation of "accepted" normal values of CSF in the literature. These are 7 to 57 ml for ventricular CSF and 10 to 100 ml for sulcal CSF. Whilst this method does appear to give good results, there are several drawbacks. The method requires a pulse sequence not widely available, the volume of brain parenchyma can not be determined and the spatial distribution of the CSF is unknown.

9.2.3 Aging

It is imperative to understand the effect of normal aging on MR images before abnormal findings are analyzed. The growing elderly fraction of the population and the fact that elderly people suffer a greater percentage of neurologic disease than young people both make such observations very important. Major changes that may occur in elderly individuals without neurological deficits include enlargement of the ventricles and cortical sulci and multi-focal areas of hyperintensity in the white matter and basal ganglia [DRAYER88A].

Jernigan *et al.* [JERNIGAN90A] have measured grey matter, white matter and CSF volumes using methods described in section 4.2. They showed significant increases in ventricular and extra-ventricular cranial CSF volumes with age, and decreases in brain volume and grey matter. A linear decrease over the age range is observed in the volume of the cerebrum. Linear increases are observed in measures of ventricular and sulcal fluid. A curvilinear decrease in cortical volume is found and may be demonstrated even in young adults.

Jernigan *et al.* [JERNIGAN90B] have also measured the volume of individual cerebral grey matter structures. These were separated from other grey matter areas either using manually-defined polygons to identify the regions or by manual tracing along complex borders between grey and white matter. They reported that there was no evidence for a reduction of overall white matter volume but that overall subcortical grey matter significantly declines with age. Results

suggest that between 30 and 79 years significant decreases occur in the volume of the caudate nucleus, the anterior diencephalic structures, and in the grey matter of most cortical regions. Studies of age-related changes in brain morphology seen on MR images have also been carried out, to measure individual cerebral grey matter structures and provide an index of white matter degeneration. Volumes of caudate, lentricular and diencephalic structures are estimated, as are grey matter volumes in eight separate cortical regions.

Gur *et al.* [GUR91B] used the method of Kohn *et al.* [KOHN91] as described in section 4.5 for measurement of brain and CSF volumes. They found a decrease in brain volume and an increase in CSF volume with age when corrected for cranial volume. There was no correlation of cranial volume with age. They found that there was a greater aging effect in men. There was a differential effect of age on sulcal compared to ventricular CSF with aging associated with more pronounced sulcal atrophy. Here again there was a greater gender difference: the differential effect was stronger in men. Average brain volume was 1090 ± 114 ml (range 822 - 1363 ml) and CSF volume was 127 ± 57 ml (range 34 - 297 ml). They found mean brain volume dropped by 2 ml per year from the age of 15 to 85 years (from 1190 to 1060 ml) and mean CSF volume increasing by 2 ml per year from 15 to 85 years of age (from 70 to 210 ml).

Agartz *et al.* [AGARTZ92] have demonstrated that age is the most significant parameter correlated with visual assessment of the size of cerebrospinal fluid spaces, that the lateral ventricles are larger in males than females and that body mass and other clinical parameters were not influential factors.

The most common pathologic conditions suffered by the elderly are dementia, movement disorders and focal neurologic deficit [DREAYER88B]. The most common cause of dementia is Alzheimer disease which is characterised by gyral atrophy and enlargement of the adjacent cortical sulci and leads to progressive memory loss. The total brain volume may decrease by 15-20% and the ventricles are generally enlarged. Generalised atrophy with enlarged cortical sulci and posterior fossa sub-arachnoid spaces is common in all Parkinsonian disorders.

9.2.4 Anatomical Template Creation

MRI may be used to provide high-resolution images of anatomy and pathology for use as references for lower resolution imaging modalities such as SPECT or PET, or indeed for mapping metabolites from localised NMR spectroscopy, chemical shift imaging or phosphorous MRI.

The limited spatial resolution of PET makes quantitative measurements of regional metabolism or neuroreceptor concentration susceptible to partial volume errors from averaging with CSF, bone and scalp. The problems are increased when cortical atrophy occurs, as is the case of patients suffering Alzheimer's disease. Meltzer *et al.* [MELTZER90] have segmented MR images slice by slice using ROIs in CSF and brain to produce a threshold between the two. These segmented images have been transformed to the resolution of the PET data, whilst keeping note of the constituents of partial volume voxels. This MRI data has then be used for correcting PET data for partial volume effects.

Tanna *et al.* [TANNA91] have used the method of Kohn *et al.* [KOHN91] (section 4.5) to compare the volumes of brain and cerebrospinal fluid of patients with Alzheimer's disease against healthy elderly controls. In both groups the atrophy measurement was used to correct metabolic values obtained with PET. Patients with Alzheimer disease had higher total CSF (mean 49%), extra-ventricular (mean 37%), total ventricular (mean 99%) and third ventricular CSF volumes (mean 74%) and lower brain volumes (mean 7%) than the control group. The patients also showed a more marked decline in brain volumes, a greater increase in CSF volumes with advancing age than the control group. They also had a larger increase in corrected whole brain metabolic rate.

9.2.5 <u>Alzheimer's Disease</u>

The most common cause of dementia in the elderly is Alzheimer's disease which accounts for at least half of all cases [JOLLES89]. MRI has shown ventricular and cortical sulcal enlargement in these patients to be more pronounced than those seen in normal aging. Focal temporal lobe atrophy with enlargement of the surrounding CSF has also been described. This is reported to be the only anatomic imaging finding to distinguish Alzheimer's disease patients from normally elderly subjects, with an 80-90% accuracy.

Kertesz *et al.* [KERTESZ90] have shown that language and some non-verbal cognitive deficits correlate with the extent of cortical and ventricular atrophy in Alzheimer's disease. The extent of atrophy was visually assessed.

Rusinek *et al.* [RUSINEK91] have examined the distributions of cerebral grey matter, white matter and intracranial CSF in Alzheimer's disease and normal controls. They used a method similar to that of Condon *et al.* [CONDON86] (as discussed in section 9.2.2) to measure CSF, and a thresholding method for measuring grey matter and white matter. They found the percentage of grey matter in the brains of Alzheimer's disease patients to be significantly less than that for normals. The largest reduction occurred in the temporal lobes but the reduction in frontal and occipital lobes was also significant.

Seab *et al.* have used MRI and manual tracing to measure hippocampal atrophy in Alzheimer's disease [SEAB88]. Using age matched controls the study shows that this atrophy can be used to distinguish Alzheimer's disease patients from normal age matched controls. Normalised hippocampal volumes were reduced by 40% in the Alzheimer's disease group compared to the controls, with no overlaps between the two groups. Hippocampal atrophy did not correlate with overall brain atrophy, but the degree of brain atrophy was correlated with dementia severity.

Jernigan *et al.* have used the methods described in [JERNIGAN90A] (see section 4.5) to investigate specific changes in Alzheimer's and Huntington's disease [JERNIGAN90C]. Groups of patients with each disease were compared with a large group of normal control subjects and measures of volume loss in various subcortical and cortical regions were obtained. Widespread cortical volume reductions were found in the Alzheimer's disease patients. These were especially severe in the mesial cortices, but comparable reductions were also present in subcortical structures, particularly the thalamus. In Huntington's disease, the greatest reductions were in striatal structures, but significant abnormalities were also detected in the thalamus and inferior cortical areas, especially in the mesial temporal lobe structures. Significant degeneration in white matter was present in both groups, but was greater in the Huntington's disease patients.

9.2.6 Schizophrenia

An interesting observation by several authors [JOLLES89, PFEFFERBAUM91] is that schizophrenia may be heterogeneous in its etiology and pathophysiology, which means that volume changes may only affect small sub-populations of patients. This may account in part for the conflicting and varying results of many studies of brain morphology and function [JOLLES89].

Pfefferbaum and Zipursky [PFEFFERBAUM91] have reviewed the literature on schizophrenia and MRI. Reduction in temporal lobe grey matter has been reported in schizophrenics. Smaller left than right temporal lobes have been reported in schizophrenia whereas in controls and manic depressive patients the left temporal lobe was greater in volume than the right.

Young *et al.* [YOUNG91] manually measured various neuroanatomical structures in a group of schizophrenics and a control group of age and sex matched controls. The temporal lobe was smaller than the right in both groups. In the schizophrenic group, ventricular enlargement and cerebral atrophy were significantly related to the severity of symptoms. There were no morphometric differences between patients with a short duration of the disease (two years or less) and those with chronic symptoms.

Gur *et al.* [GUR91A] used the method of Kohn *et al.* [KOHN91] (as discussed in section 4.5) for segmentation of the cranial volume into brain parenchyma, ventricular and extra-ventricular CSF. They compared these volumes for schizophrenic patients and a group of normal controls balanced for age and sociodemographic background. There was no significant difference in whole-brain volume between patients and controls, but the patients had higher whole brain CSF volume and higher ratios of ventricular and sulcal CSF to cranial volume. Considerable overlap in both CSF volumes and in CSF volume-cranium ratios were found with most patients within the normal range.

The findings of Schwarzkopf *et al.* [SCHWARZKOPF90] who used manual tracing for segmentation, indicate that a subgroup of schizophrenic patients may have etiologically relevant third and lateral ventricular enlargement. These findings also suggest that ventricular enlargement may be progressive in some patients. They showed that mild to moderate enlargement of the third and lateral ventricles was more characteristic in schizophrenic patients than lateral

ventricular enlargement in isolation.

Harvey *et al.* [HARVEY91] have shown that in schizophrenics the volume of the cerebral cortex is reduced and the sulcal volume increase when compared to healthy controls. Increased thickness of the corpus callosum has been found in right-handed female schizophrenics [RAINE90] using tracing and thresholding measurements.

9.2.7 Epilepsy

The epilepsies are a heterogeneous group of disorders. They are one of the more common serious neurological illnesses. Atrophy, determined by gross asymmetry, sulcal and temporal horn enlargement has been noted [JOLLES89]. MRI has replaced CT as the primary radiological modality in the evaluation of patients with suspected focal abnormalities, particularly in the temporal lobe. Focal atrophy is commonly found in the hippocampus; however even in severe hippocampal sclerosis there is only about 20% loss of volume [COOK92].

9.2.8 Multiple Sclerosis

Ormerod *et al.* [ORMEROD87] have reported in depth on the use of NMR imaging in the assessment of multiple sclerosis. The disease is characterised by the presence of periventricular lesions and isolated discrete white matter lesions. They discuss the distribution of lesions both in the peri-ventricular areas and those discrete from the ventricles and situated in the white matter.

Simon *et al.* [SIMON86] have shown that in patients with confirmed multiple sclerosis involvement of the corpus callosum is common. They noted diffuse moderate to severe atrophy of the corpus callosum in 40% of patients. 30% of patients had focal callosal lesions, whilst long inner callosal/sub-callosal lesions were found in 55% of patients, with signal characteristics similar to those of non-callosal peri-ventricular lesions. Determination of the normal anatomy of the corpus callosum on MR images was made by a detailed review of 60 control studies. Simon *et al.* determined atrophy of the corpus callosum visually based on the mid-sagittal section.

9.2.9 Paediatrics and Neonatals

McArdle *et al.* [McARDLE87A, McARDLE87B] have investigated the ventricular to brain ratios and extra-ventricular CSF spaces of neonates for single image slices, concluding that extra-ventricular spaces from 0 to 4 mm in diameter are normal as is a ventricular to brain (V/B) ratio of 0.26 to 0.34 at the level of the frontal horns and mid-body of the lateral ventricles. Neonates with greater V/B ratios typically suffer from cerebral atrophy or obstructive hydrocephalus and should be carefully monitored.

Hayakowa *et al.* [HAYAKOWA89] have used MR to investigate the development and aging of four mid line brain structures - the pituitary gland, pons, cerebellar vernis and corpus callosum. Measurements of distances and lengths were made manually. They have demonstrated that the pituitary gland shows linear growth except for growth spurts in the first year and in the 10-15 year age range. The pons, cerebellar vermis and corpus callosum all grow approximately exponentially. Such data are important for the evaluation of paediatric central nervous system diseases and the assessment of development in paediatrics.

9.2.10 Others

MRI can be very valuable for volume delineation of tumours and for use in radiotherapy planning [SHUMAN85, SHUMAN87, TOONKEL88, JUST91]. Precise delineation of tumours is critical, as this makes it possible to increase radiation doses to the tumour while minimising radiation to surrounding, dose-limiting normal tissues. Higher doses to the tumour can potentially improve survival rates and decrease the frequency of local re-occurrence. Although MRI generally provides excellent delineation of brain tumours [JOLLES89] when they are originally diagnosed, it is reported not to be able to distinguish recurrent tumour from radiation necrosis.

Schroth *et al.* [SCHROTH88] have measured the intracranial CSF volume in alcoholics before and after five weeks of confirmed abstinence. CSF was defined by locating rough regions for the extra-ventricular and ventricular spaces using manually drawn ROIs. Thresholding was then used inside these regions to give CSF volumes. The study showed a significant decrease in CSF volume for all patients studied. Chick *et al.* [CHICK89] have used simple 1-D manual measurements to examine atrophy in alcoholism. The most common finding in AIDS patients on MRI include cortical atrophy and white matter abnormalities which ranged from scattered peri-ventricular high-signal lesions to large complex lesions [DONOVAN POST88, HILTON89, KIEBURTZ90].

Huntington's disease is a lethal neurodegenerative disease characterised by progressive chorea and dementia. MRI has shown atrophy of the caudate nuclei and with progression of dementia and disease duration and also increasing generalised cerebral atrophy [JOLLES89].

Amongst several neurological symptoms of Parkinson's disease is moderate or marked cortical atrophy [JOLLES89]. Tomei *et al.* have also shown brain atrophy in hypothyroidism [TOMEI88].

9.3 <u>Geometric Distortion</u>

9.3.1 Sources of Geometric Distortion

9.3.1.1 Introduction

Geometric distortion is the deviation of image points from their position in a true representation of an object. The distortion is via a single valued mapping for MRI. The term has often been used rather loosely in the literature to describe one or more of the artifacts which may lead to image distortions in MRI. These artifacts may be sample dependent or sample independent and may cause both shifts in position and local intensity changes. Such artifacts may affect the accuracy of interactive, automatic or semi-automatic segmentation methods, and are an important consideration for stereotactic surgery, radiotherapy and interstitial therapy. Sample independent effects include gradient non-linearities and main field non-uniformities, the latter being compensated for, to a certain extent, by shimming. Similar effects may be caused by gradient eddy currents and temporal fluctuations in the gradient power supply [CHANG90B]. Sample dependent effects arise from changes in the local field experienced by the nucleus in addition to intrinsic (object independent) non-uniformities of the main field. These are due to the chemical shift effect and/or the tissue magnetisation that is induced by the applied field due to a property known as magnetic susceptibility. The magnitude of these effects vary both with field strength and the strength of the applied gradients. Although the magnitude of these effects can be reduced by using stronger gradients, this requires a larger bandwidth which decreases the signal to noise ratio of the acquired image. The effect of gradient non-linearities and main field non-uniformities may produce distortions in any direction, whilst chemical shift and susceptibility artifacts will cause distortions in the frequency-encoding and slice select directions. There is no effect in the phase-encoding direction for the latter two cases, as it is the application of a gradient that leads to the distortion. These sources of distortion and their dependencies are summarised in Table 5

Source of geometric distortion	Dependence on object	Directions affected by distortion	Dependence on B ₀	Dependence upon gradient strength
B ₀ non- uniformity	Object independent	Affects all directions	Independent	∝ 1/IGI
Gradient non- linearities	Object independent	Affects all directions	Independent	Independent
Susceptibility differences	Object dependent	Affects read and slice select directions	∝B₀	∝ 1/IGi
Chemical shift	Object dependent	Affects read and slice select directions	∝ B ₀	∝ 1/IGI

Table 5 - Characteristics of the four sources of geometric distortion.

9.3.1.2 Gradient Non-Linearities.

Spatial encoding is accomplished for 2D FT imaging by the use of field gradients, which are assumed to produce a linear variation of field with position, or a constant gradient. Deviations from such behaviour are commonly, if somewhat erroneously, termed gradient non-linearities. If B₀ non-uniformity, susceptibility and chemical shift are ignored then a linear relationship between position and frequency exists for linear gradients. The most stringent requirement that might need to be imposed on linearity is that the total distortion over the full dimensions of the object be less than one pixel width. Hence for a 256×256 image, a distortion less than 1/256 =0.39% would be required. In practice, gradients typically produce a linear variation of field within a few percent over 75% to 80% of their radius [MANSFIELD82] with linearity tending to decrease with distance from the gradient coil origin. This gives rise to spatial and intensity distortions close to the gradient coils if uncorrected for. Figure 157 demonstrates the spatial distortion that may occur when boundary point Xa is incorrectly mapped to appear at location Xa' due to gradient amplitude fall off towards the edges of the field of view. Most head images are currently acquired using whole body scanners for which the gradient coil is much larger than the head coil. For such small fields of view, or at the centre of larger fields of view, the image distortion due to non-linear gradients tends to be small. If head images are to be used for surgery or radiotherapy planning, however, even small distortions may be of great importance.

9.3.1.3 <u>Main Field Non-Uniformities</u>

The use of a spin-echo sequence corrects for spin dephasing and signal loss caused by B_0 nonuniformities, but does not correct for distorting effects, which are similar to that of gradient nonlinearities. This may lead to variations in pixel sizes within the image. Consider a non-uniformity in B_0 in the read direction leading to an additional gradient $\nabla_R B_0$

Total gradient =
$$\gamma(G_p + \nabla_p B_0) Hz/cm$$
 (86)

Now the total frequency range is the bandwidth, BW over N pixels.

Frequency range -
$$\frac{BW}{N}$$
 Hz/pixel (87)

Thus

Pixel size -
$$\frac{BW}{N\gamma(G_R + \nabla_R B_0)}$$
 cm/pixel (88)

Now

$$Bandwidth - \gamma (FOV \cdot G_p) Hz$$
(89)

where G_R is the gradient in the readout direction, and FOV the size of the field of view. Thus

Pixel size -
$$\frac{FOV \cdot G_R}{N(G_R + \nabla_R B_0)}$$
 (90)



Figure 157 - Effect of gradient non-linearity on spatial distortion. Boundary pixel Xa is incorrectly mapped to appear at location Xa'.

Susceptibility is a sample-dependent effect which causes a variation in local magnetic field. In general, there are both diamagnetic and paramagnetic contributions to tissue susceptibility. Diamagnetic susceptibility (negative in sign) affects all tissues, whilst paramagnetic susceptibility (positive in sign) is a rare special case in neurological MRI associated with blood and its breakdown products. (The introduction of ferromagnetic materials such as iron, metallic based mascara, ear rings etc., into the magnet will be ignored as a special case where signal intensity changes and border shifts may well be very severe). These magnetic field non-uniformities are caused by the magnetic properties of the sample - in this case, a human head. The susceptibility values for most tissues fall within a fairly narrow range, however the presence of air/tissue interfaces or the presence of ferromagnetic material leads to local variations in susceptibility which may affect both the position of borders, and give rise to local intensity variations. Susceptibility artefacts may cause both increases and decreases in signal intensity. In the head, such effects are particularly noticeable in the region of the sinuses and the nasopharynx. The effect of local susceptibility differences on geometric distortion will be dealt with here, whilst intensity changes due to spin dephasing in gradient echo images are discussed later in section 9.4.

Diamagnetic Susceptibility.

There are three definitions of diamagnetic susceptibility, these being the molar susceptibility, the specific or mass susceptibility and the volumetric susceptibility (a unitless quantity). This appears to have led to some confusion in the literature regarding susceptibility effects. According to classical electromagnetic theory, the relation between magnetic induction B (the magnetic field sensed by nuclei) and field strength H for cgs units is given by

$$B = H + 4\pi I \tag{91}$$

[CRC89] where I is the magnetisation or magnetic moment per unit volume. This may be written as

$$B - H + 4\pi K H - (1 + 4\pi K) H$$
(92)

where K is the volumetric diamagnetic susceptibility. Two tissues of susceptibility K_a and K_b will therefore have different values of B, leading to an intrinsic gradient G_i between them. Ignoring for the moment any paramagnetic materials, the largest local susceptibility differences in the head will be at an air tissue interface. The susceptibility of air is effectively zero and that of tissue approximately the same as pure water so the interface can be modelled as an air water boundary. At 20°c, the value of K for water is -0.719 x 10⁻⁶ so the magnitude of the change in local field at the interface will equal $4\pi K$, which is -9.04 ppm. This change in local field will give a corresponding change in resonant frequency and will affect the position to which local spins are mapped. For 2-D FT reconstruction, position and frequency are related by

$$x - \frac{w_0}{\gamma G} \tag{93}$$

where G is the applied gradient.

Now

$$\Delta x - \frac{\Delta w_0}{\gamma G} \tag{94}$$

and

$$\frac{\Delta w_0}{w_0} - \frac{\Delta B_0}{B_0} \tag{95}$$

from the Larmor equation. Thus

$$\Delta w_0 - \frac{w_0 \Delta B_0}{B_0} - 4\pi \kappa w_0 \tag{96}$$

and the gradient strength, G, is given by

$$G = \frac{BW}{\gamma.FOV}$$
(97)

substituting for Δw_0 and G from equations (96) and (97) gives

$$\Delta x - \frac{4\pi \kappa w_0 FOV}{BW}$$
(98)

For the Signa, a typical first echo RF receive bandwidth is 32 kHz and a typical field of view for the head is 24 cm. The RF receive bandwidth may be larger for subsequent echoes, however, the range of RF receive bandwidths being illustrated by Table 6. Hence Δx , the maximum possible shift for a first echo image due to local susceptibility differences at a water air interface is given by

$$\Delta x = \frac{9.04 \times 10^{-6} \cdot 6.4 \times 10^{7} \cdot 24}{32,000} = 0.43 \ cm \tag{99}$$

Thus for a typical field of view and early echo receive bandwidth, each ppm of non-uniformity translates into an absolute positioning error of 0.5 mm for the Signa. The actual magnitude of this effect for any given interface will be dependent upon the sharpness of the boundary and local geometry. It should be noted that the magnitude of the effect, for a fixed field of view, is both field and gradient dependent. The effect is worse for high fields and low gradient strengths.

Paramagnetic Susceptibility.

The order of magnitude calculation above is correct for diamagnetic materials, but the magnitude of the shift may be different if paramagnetic materials are also present. Young et al. [YOUNG87] have examined the clinical use of magnetic susceptibility mapping of the brain, being particular interested in the paramagnetic contribution that may be generated by various iron compounds associated with blood and its breakdown products. Using two partial saturation sequences employing gradient echoes with different echo times they produced two magnitude images and two phase images. The effect of susceptibility on the phase images varies with echo time. A third derived phase map displayed the difference between the two phase maps. A scan of a homogeneous water phantom was used to correct for B₀ variations. This method depends upon there being no large chemical shift effect differences in the brain, which will also cause local field variations. The two main chemical shifts are those of water and fat as discussed in section 9.3.1.5. It appears that there is generally negligible quantities of fat in the brain although at the time of writing, several groups are investigating the possibility of small quantities of lipid existing in the brain due to demyelinating diseases. Young et al. found susceptibility effects at the border of, or within some tumours and infarcts and some haematomas, but found no effect in MS plaques. Field variations of up to 0.5 ppm were observed which were attributed to field non-uniformities generated by the accumulation of paramagnetic species within specific pathological regions.

9.3.1.5 <u>Chemical shift effect</u>

The exact resonant frequency of a proton depends upon its chemical environment. The hydrogen attached to oxygen, as in water, experiences a magnetic field that is slightly different from that of hydrogen bonded to carbon in fat, for example. These two types of protons are the major constituents of 'NMR visible' protons within the human body. Although other protons exist, such as those comprising large proteins for example, they are not observable in conventional MRI experiments.

The resonance of the fat and water protons is separated by approximately 3 ppm, which corresponds to a difference of about 220 Hz in resonant frequency at 1.5 T. The bandwidth per pixel for a 256^2 imaging matrix and 32 kHz receiver bandwidth is 125 Hz (32000/256), so the frequency difference of 220 Hz translates into a pixel shift of 1.8 pixels in the read direction. The relevant shifts for other receiver bandwidths possible using the Signa are illustrated by Table 6.

Receiver bandwidth (kHz)	Image width (kHz)	Hz / pixel	Chemical shift (pixels)
± 16	32	125	1.8
± 13	26	94	2.2
± 8	16	62.5	3.3
±4	8	31	7.0
± 2	4	16	14.0

Table 6 - Variation of chemical shift with receiver bandwidth for 256x256 image

This pixel shift demonstrates itself as a misalignment, or shift, between signal due to fat and water. This may lead to an apparent increase or decrease in signal intensity on either side of a structure as illustrated by Figure 158.

Clinically, the chemical shift effect is a very relevant problem in terms of, for example, perinephretic fat being displace relative to kidneys and the apparent displacement of





intervertebral discs. In neurological MRI, the displacement of post-orbital fat relative to the optic nerve, and the shift of signal due to bone marrow and skull fat are of particular importance. Kaldoudi and Williams [KALDOUDI92] have recently reviewed fat and water differentiation in depth.

9.3.2 Correction of Geometric Distortion

9.3.2.1 Correction of Sample Independent Effects

O'Donnell *et al.* carried out what appears to be the first work on correction for magnetic field non-uniformities and gradient field non-linearities [O'DONNELL85]. They show that for field non-uniformities modelled as quadratics, the point spread function for spin warp reconstruction has the same form as the homogeneous case, but that coordinates in the readout direction are misplaced in proportion to the value of the local field relative to the gradient amplitude. The point spread function is independent of position for spin warp reconstruction and therefore it is possible to correct for non-uniformities both in terms of geometric distortion, and for slight intensity variations which occur due to variations in pixel size. The authors give simple equations for correction of both gradient non-linearities and B_0 non-uniformities that may be

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implemented via a lookup table. The Signa uses a method known as GRADWARP to retrospectively correct for the geometric distortions caused by non-linear gradients [GE90]. While the details of the correction are proprietary, it is believed to be similar to that described by O'Donnell *et al.*.

Various approaches using field mapping have been proposed for geometric distortion correction but none deal with susceptibility and chemical shift. Other techniques for the reduction of such distortions rely on the insensitivity of phase-encoding to field non-uniformity. These latter techniques require very long imaging times. Both approaches are reviewed in [CHANG90B].

9.3.2.2 Correction of Sample Dependent Effects

Chang *et al.* [CHANG90A, CHANG90B] have proposed a method of correcting for both intensity and positional changes due to main field non-uniformities and susceptibility effects, the two being difficult to separate. The approach consists of using a pair of images from the same object acquired using a set of gradients having a prescribed relationship and using a set of equations to relate the two images and thereby produce a distortion compensated image. The degree of accuracy required of volume measurement for a given application will determine whether or not sample dependent effects need to be corrected, and in addition to this, the number of additional scans, if any, that can be tolerated.

9.3.3 <u>Measurement of Geometric Distortion</u>

Distortions due to sample independent effects (ie gradient non-linearities and B_0 nonuniformities) can be measured using a phantom with a number of sharp clear lines, blocks with well defined lengths or an array of points. As will be shown in section 9.3.3.3, B_0 nonuniformity distortions are negligible for head images using the Signa. Work has been carried out using a point array phantom to investigate the magnitude of such effects with GRADWARP both on and off, to give some indication of the linearity of modern gradient coils, and the accuracy of the GRADWARP correction method. Measurements of sample dependent effects have been made to give an indication of possible worst case errors.

x

9.3.3.1 Previous Work

Schad *et al.* [SCHAD87] carried out pioneering work in accurate stereotaxy by MRI. They measured geometrical distortions within the imaging plane using a two-dimensional phantom consisting of a water-filled cylinder containing a rectangular grid of plastic rods spaced 2 cm apart and oriented perpendicular to the plane of interest. In addition to this a three dimensional phantom, similar in design to the Eurospin slice warp and offset phantom as described in section 9.5.2, was also used for the detection of displacement, warp and tilt of the image plane. Using Siemens Magnetom 0.5 and 1.5 T scanners they found two problems. Firstly axial MR images of the 2D phantom showed a pin-cushion like distortion pattern. Following correction for geometric distortion by a 2D polynomial, a second problem was apparent. This was a slant of the image plane, which was corrected by shimming in an iterative manner (i.e. shim, scan, analyze, shim, scan, analyze etc.) The authors claim an improvement of worst-case displacements in a typical sized head from 5 mm to 1-2 mm, the residual errors being due to the pixel size.

Clarysese *et al.* [CLARYSSE91] have considered geometric distortion for frameless stereotaxy using a GE MR Max 0.5 T scanner. They believe that non-linearity was satisfactorily rectified by means of "internal correction matrices registered in the scanner by the manufacturer", but that the electronic gains of the gradients, which determine the enlargement factors on the three axes, and the electronic offsets, which define the origin of the slices, may vary in time. They discarded the use of asymmetrical echo sequences (ie where the second echo time is not twice the first echo time) as they found size differences along the axis of the read gradient of up to 3 mm between the two echoes.

Just *et al.* [JUST91] have used MRI as their method of choice for radiotherapy planning of brain tumours because of the superior soft tissue contrast of MRI and the availability of sagittal scans. They require that the treatment volume should contain as little normal brain as possible, with the tumour safely encompassed within certain safety margins by the treatment volume. They determined geometric distortions to be less than 3% for their 0.28 T Bruker BMT 1100, and thus acceptable for their needs.

Valentino *et al.* [VALENTINO91] have considered the correction of geometric distortion, as a preprocessing step for volume rendering of MRI and PET images of the brain. Using scans from

a FONAR B-3000 and a GE Signa whole body scanner, they state that only the FONAR images suffered from geometric distortion. Using a three-dimensional phantom, the distortion for the FONAR was calculated on a pixel by pixel basis, and each pixel shifted to its correct position.

Lerski *et al.* have carried out a multi-centre trial for the assessment of MRI equipment [LERSKI88] which includes a study of object independent geometric distortions and report measuring errors of between 1 mm and 12 mm for a 140 mm object.

9.3.3.2 <u>Measurement of Sample Independent Effects</u>

The effect of sample independent distortions created by gradient non-linearities may be appreciated and quantified by using a phantom consisting of a regular pattern. An extremely simple form for such a phantom is that of a high or low intensity square, which is available as part of the Eurospin II set of Magnetic Resonance Quality Assessment test objects. These test objects are manufactured by Diagnostic Sonar Ltd. (Diagnostic Sonar Ltd., Kirkton Campus, Livingstone EH54 7BX) and are the second generation of European test objects as originally described by Lerski et al. [LERSKI88]. The use of such a simple phantom only provides information about geometric distortion over a limited portion of the typical field of view utilised when using a standard head coil. A custom phantom was designed and built at the Institute of Neurology, Queen Square, London, in order to more completely define the extent and magnitude of the geometric distortion. The body of the phantom was a solid block of perspex of circular cross-section with a 26 cm diameter and a depth of 8 cm. An array of holes on a square grid of diameter 1 mm, spaced 1 cm apart (a total of over 500 holes) was drilled to a depth of approximately 7 cm. A tightly fitting perspex lid is attached to the body of the phantom by six plastic screws. The design is illustrated by Figure 160, and a photograph of the phantom included in Figure 159.

The small diameter of each hole means that it is not possible to fill the holes by simply pouring water over the surface because of the effect of surface tension. Each hole was therefore filled by hand using water doped with a little Manganese Chloride solution (the same solution as described in section 5.3.3) using a six inch long lumber puncture needle.



Figure 159 - Photograph of gradient non-linearity phantom.

Measurements of the phantom were made both with and without the use of GRADWARP. The phantom was carefully positioned so as to lie in each of the sagittal, coronal and axial planes and scans were acquired at both the centre of the gradient coils and at a distance approximately 120-140 mm from their centre. The scans were analyzed in two ways, firstly to give a visual indication of the pattern and magnitude of any distortion, and secondly to quantify the magnitude of any such distortions. Measurements were primarily made of the extremes of the two central rectangular blocks of holes. Correction for distortions would require the use of more holes, however. The major axis of this rectangular block of holes measures 220 \pm 0.5 mm, whilst the minor axis measures 80 \pm 0.5 mm. Thus, for each scan, two sets of four measurements were taken (the two sets corresponding to orthogonal directions), each set consisting of an initial 80 mm length, two 220 mm lengths and a second 80 mm length. There are slight differences in the offset of the centre of the phantom relative to that of the centre of the gradients for each of the planes for which data was collected. The offsets were 140 mm for the axial scans, 123 mm for the sagittal scans and 133 mm for the coronal scans. The results of these measurements are indicated by Table 7, with the order of the measurements for each dataset indicated in the table being superior to inferior along z, left to right along x and anterior to posterior along y. The z coordinate lies along the bore of the magnet, the x coordinate is



Figure 160 - Cross-sectional views of gradient non-linearity phantom.

horizontal in the magnet bore and the y coordinate is vertical in the bore. The results indicate distortions of up to 12.5% in length for slices at the centre of the gradient coils and 18.9% for slices 120-140 mm from the centre of the gradient coils without the use of GRADWARP. The maximum distortions are reduced to 2.5% for both slices at the centre of the gradient coils and

for slices from the centre of the gradient coils using GRADWARP. This indicates that GRADWARP should be used for all imaging.

In addition to the measurements illustrated by Table 7, measurements of the area of the major rectangular blocks was also made as an indication of the magnitude of any errors in area measurements. The area was determined by joining the centre of each of the perimeter holes with a straight line and calculating the area of the resulting region. For the superior end of a coronal image the accuracy of the area measurement with GRADWARP was 0.5% and without GRADWARP was 8.9%, with reproducibility of the areas approximately \pm 0.1%. For the centre of the magnet the accuracy of area measurement with GRADWARP was 2.7% and without GRADWARP was 2.3%, with the reproducibility of the areas approximately 0.5%. The images corresponding to the superior end of coronal images are illustrated by Figure 161 and Figure 162.



Figure 161 - Coronal image with gradient non-linearity phantom at superior end of gradient coils with GRADWARP on.

Table 7 - Measurement of magnitude of gradient non-linearity distortions (mm). Nominaldistances are 80, 220, 220 and 80 mm within each cell.

	x at	x far	y at	y far	z at	z far
Image plane	centre	from	centre	from	centre	from
		centre		centre		centre
	(mm)	(mm)	(mm)	(mm)	(mm)	(mm)
	0.0	0.5	15	1.0		
Avial with	0.0	0.5	-1.0	-1.5	_	
	0.0	0.0	-1.0	-1.5	-	-
OKADWAR	1.0	0.0 -0.5	-2.0	-1.5		
	1.0	-0.5	-2.0	-0.5		
	1.0	-9.5	-1.5	-8.0		
Axial without	0.0	-21.0	0.0	-24.5	-	-
GRADWARP	1.0	-21.5	-1.0	-24.5		
	1.0	-9.0	-2.0	-9.0		
			-0.5	1.5	-2.0	-
Sagittal with	-	-	-0.5	-	-1.5	0.0
GRADWARP			1.0	-	-1.0	0.0
			-1.0	2.0	-2.0	-
			-1.0	2.0	-2.0	-
Sagittal	-	-	-1.0	-	-0.5	-33.0
without			1.0	-	-2.0	-6.0
GRADWARP			-1.0	0.5	-1.5	-
	-1.5	1.0			0.0	-
Coronal with	-2.5	-	-	-	-2.0	-0.5
GRADWARP	-2.0	-			-1.0	-1.5
	-2.0	1.0			-1.0	-1.0
	-10.0	3.0			-1.5	-
Coronal	-5.5	-	-	-	-1.0	-41.5
without	-1.5	-			-1.0	-10.5
GRADWARP	-6.5	3.0			-2.5	0.0



Figure 162 - Coronal image with gradient non-linearity phantom at superior end of gradient coils with GRADWARP off.

9.3.3.3 Measurement of Sample Dependent Effects

The magnitude of sample dependent geometric distortions has been investigated by using a dual echo spin echo sequence for which it is possible to reverse the direction of the readout gradient. Reversing the direction of the readout gradient will change the direction of chemical shift and susceptibility effects. By comparing pairs of images acquired with opposite readout gradient directions it is possible to identify regions of intensity change due to chemical shift and susceptibility effects. To minimise subject motion, the NOD was used for all such scans with padding also packed around the subject's head. To ensure that any differences between scans were not a result of a shift (eg a limited involuntary shift or the gradual compression of the headrest) seven sets of data were acquired with the direction of the readout gradient reversed for each scan. To ensure no movement had occurred within the dataset, the position of the head was compared between scans for the set of odd scans and the set of even scans by using difference images. Canny edge images were also compared by subtraction and the use of colour overlays, confirming the original conclusion. No significant difference was apparent between scans of each series.

Susceptibility and B. Non-Uniformity

As mentioned in section 9.3.1.4, local susceptibility differences in the brain will be greatest at fluid/air interfaces, one of the best examples of which is the head in the region of the frontal nasal sinuses. The volunteer chosen for this study had a heavy cold, with a lot of mucous in the sinuses. Under such circumstances, the mucosal cells are inflamed and contain a lot of water [GRAY88] giving a very good approximation to a fluid/air interface.

Both susceptibility and B_0 non-uniformity produce changes in local fields and it is not possible to design an experiment to distinguish between the effects of the two in the head, so any changes between pairs of images must be attributed to the combination of the two effects. The use of phase images of a uniform phantom to map out B_0 non-uniformity for the magnet would be highly desirable but it is not possible to produce phase maps using standard Signa software. Some indication of the uniformity of the Signa magnet is given by the fact that the field is specified as ± 0.25 ppm within a spherical volume of 20 cm diameter, which is approximately the size of the head. This corresponds to a ± 0.1 mm maximum distortion for typical imaging parameters.

Both Canny edge images and measurements on original images have been used to compare differences between given odd and even scans using subtraction images, the overlaying of images and measurements of the position of key anatomical structures. At the level of the sinuses there are severe distortions. Typically for the early echo images there is a 5 mm difference between identical points at the extremities of the sinuses for odd and even images (ie a 2.5 mm shift due to susceptibility and non-uniformity) For the late echo images there is typically a 10 mm difference (ie a 5 mm shift due to susceptibility and B_0 non-uniformity). This confirms that the magnitude of the shift is inversely proportional to receive bandwidth as discussed in section 9.3.1.4. The early echo image was acquired with a bandwidth of \pm 16 kHz and a late echo bandwidth of ± 8 kHz which implies that very large distortions would be seen if the use of ± 2 or ± 4 kHz bandwidth possible on the Signa were used. The TE and TR used for this study were not appropriate for using such bandwidths, however, and longer scan times would increase the risk of subject movement. A pair of late echo images is illustrated by Figure 163 and Figure 164. The mucosal cells correspond to the bright regions which are bottom left in the left sinus and bottom right in the right sinus. The level of the uppermost border of the mucosal cells in the left sinus is indicated by white lines in the two figures. The 2.5 mm shift
for a \pm 16 kHz image and a 24 cm FOV at 1.5 T is consistent with the predicted maximum shift of 4.4 mm, calculated in section 9.3.1.4.



Figure 163 - Late echo image at level of sinuses



Figure 164 - Late echo image at level of sinuses with direction of read gradient reversed.

According to Duck [DUCK90] the susceptibility of normal tissue is commonly considered to be the same as that of water. A number of investigations were carried out to ascertain whether or not the susceptibility of brain parenchyma is the same as that of CSF. At the border of the brain with extra-ventricular CSF, the large chemical shift due to bone marrow obscures detail and thus sulcal and ventricular boundaries must be considered instead. Measurements of various parts of the ventricles and sulci were made for difference images and from Canny edge images and original images themselves. These measurements show a shift of at least one pixel (approximately 1 mm) for the early echo and two pixels (approximately 2 mm) for the late echo images, with the accuracy of measurement being limited by the discrete nature of the image. This difference could be explained by local susceptibility differences between brain parenchyma and CSF.

Chemical Shift Effects

Chemical shift effects may be investigated by comparing the positions of fatty structures to those of watery structures within the head. Fat is typically found surrounding the skull and cheeks. The magnitude of this shift is calculated to be 1.8 pixels for $a \pm 16$ kHz early echo image and 3.5 pixels for $a \pm 8$ kHz image using a 256x256 image matrix, and measurements approximately confirm this. It is, however, difficult to compare images where the total signal is due to components of water signal and shifted fat signal (regions of fat give a signal due to OH protons and one due to CH₂/CH₃ protons). This chemical shift means that it is difficult to design experiments to precisely measure any susceptibility shift at the air/skin and exterior CSF/brain borders. If cephalometry, the study of measuring the dimensions and shape of the head, is of interest then fat suppression or elimination is desirable to avoid such problems.

9.3.3.4 <u>Summary</u>

The preceding sections have given an indication of the magnitude of possible geometric distortions. Distortions due to B_0 non-uniformities have been shown to be negligible for Signa head images. Gradient non-linearity distortions can yield errors in area measurements of approximately 2% despite the use of GRADWARP. Near air/tissue interfaces, susceptibility induced distortions can be large (up to 10 mm for the SE/3000/30,80 sequence used) with chemical shift effect distortions approximately 3 mm for the same sequence. Whether the

magnitude of these distortions is clinically acceptable or not depends upon the application. It may be that the magnitude of these effects makes a different modality, such as CT, more appropriate for measurements close to air/fluid interfaces such as the sinuses or nasopharynx, that methods of correction for sample independent and/or sample dependent effects might be employed or that different field strengths might be considered if available locally. The use of strong gradients (large bandwidths) might also be considered to minimise such effects.

If MRI is to be used for measurements in such regions of the neuroanatomy, then all subjects should be scanned with the same parameters and pulse sequence to ensure that the same strength of gradients, and the same phase-encoding and frequency-encoding directions are used for each subject. Comparisons between patients scanned using different imagers are difficult to make unless investigations such as those described in sections 9.3.3.2 and 9.3.3.3 have been made for each scanner. It is possible to reposition a patient to within 1 mm so for temporal studies of individual subjects there will be mainly constant systematic errors due to sample dependent shifts (assuming no variation of the air/tissue interface in the sinuses or nasopharynx). The possible variation of the magnitude of susceptibility effects due to the quality of the air/fluid interface in the sinuses is a point of interest, however. It may be that the presence and absence or severity of a cold will affect the magnitude of any susceptibility based shift.

9.4 Intensity Variations due to Spin Dephasing

Susceptibility differences may lead to intensity changes in addition to the possibility of a border shift at tissue interfaces. The use of a spin-echo ensures the refocusing of ΔB_0 so there is no change in signal due to spin dephasing for standard imaging conditions.

For a gradient echo, intensity variations due to spin dephasing may be severe and observable over a relatively large region. Haacke *et al.* [HAACKE89] and Wehrli [WEHRLI90] have noted variations over large regions near the pituitary gland in sagittal gradient echo images. This is due to spin dephasing close to tissue interfaces and may be understood by considering two neighbouring tissues with diamagnetic susceptibilities K_a K_b . At their interface, there is an intrinsic gradient G_i . Following excitation and generation of transverse magnetisation, the isochromats within a voxel experience a distribution of magnetic fields causing a dispersion of phases. At the echo time, this phase dispersion will cause a reduction in the transverse magnetisation. This is equivalent to an effective reduction in T_2^* . The phase dispersion $\Delta \phi$ increases with echo delay as

$$\Delta \phi = \gamma G_r \Delta r. TE \tag{100}$$

where Δr is the voxel size, the effect being more pronounced at longer echo times. This also implies that reducing the voxel size will reduce the effect, although in general this would lead to a loss in signal to noise ratio or increase in scan time for a fixed field of view.

9.5 Accuracy of Slice Characteristics

The accuracy of slice characteristics is a critical consideration for volume measurement. Slice width, slice warp (the distortion of an image slice in the slice select direction), slice offset (the distance between slice centres) and in plane distortions (the latter being discussed in section 9.3.3.2) all affect whether the pixel size and position prescribed by the operator is accurately reflected by the acquired data or not. This section considers the first three of these factors. The work has utilised the Eurospin II Magnetic Resonance Quality Assessment Test Objects.

9.5.1 Slice Width

Slice width has been measured using the test object TO2, as illustrated by the photograph in Figure 165. The test object contains a pair of 1 mm thick perspex sheets and a pair of ramps surrounded by a doped water solution. Both the sheets and ramps can be used for slice width measurements, but the method utilising ramps requires profile differentiation which makes very high SNR images necessary. Due to time constraints the use of the ramps is not considered further in this thesis. The sheets are inclined at an angle to the imaging plane and slope in opposite directions. A slice oriented parallel to the flat ends of the phantom and at the centre of the phantom is acquired using a spin echo with a TR of 500 ms, a TE of 20 ms and the desired slice thickness. A typical image is illustrated by Figure 166.



Figure 165 - Photograph of test object TO2



Figure 166 - Image from Eurospin slice width phantom test object TO2

A number of profiles taken through the sheets along the major axis of the sheets are averaged to create a less noisy average profile. The profile through the image yields a convolution of the slice profile with the sheet. A typical MEMP result is illustrated by Figure 167, and a typical CSMEMP result by Figure 168.



Figure 167 - Typical profile through test object TO2 for MEMP pulse sequence.



Figure 168 - Typical profile through test object TO2 for CSMEMP pulse sequence.

The slice width may be measured by calculating the Full Width at Half Maximum (FWHM) for each sheet. If the image slice passes through the centre of the phantom (so that both sheets intersect with the slice at the same angle), then the response from each of the sheets should give the same slice width profile at FWHM, w1 and w2

$$w1 - w2 - \frac{nw}{4} \tag{101}$$

where n is the FWHM of the image profile in pixels, w is the pixel size and the factor of 4 takes into account the angle that the slice makes with the sheets. If the test object is slightly misaligned then the values w1 and w2 are different. In this case the slice width profile FWHM is approximately the geometric mean of w1 and w2

$$w = \sqrt{wl.w2} \tag{102}$$

which is accurate to within 2% for w1/w2 < 1.7 where w1 is the greater value. This author has chosen that the measured slice width should be within 10% of the prescribed slice width on the grounds that an error of this magnitude will lead to little difference in partial volume and signal to noise ratio. Lerski *et al.* [LERSKI92] have also used this figure as their gold standard (or required standard).

According to Selikson *et al.* [SELIKSON88] the finite thickness of the sheet creates an error in the measurement of slice width for non-ideal slice profiles (ie non rectangular profiles). The image signal at any point is proportional to the integral of the slice profile over the finite thickness of the sheet. For an ideal (square) slice profile this integration distorts the shape of the image profile, but for a slice which is several times the sheet width, the FWHM of the image will be the same as the FWHM of the slice profile. If the slice profile is not square (eg rounded top with tails), the FWHM in the image will not be equal to the slice profile FWHM. Selikson *et al.* give an expression for the percentage error as a function of sheet width b, and FWHM, a, for this simple model is

Percentage Error - 100 x
$$\left(1 - \begin{cases} 2 + \frac{b\sqrt{2}}{a} - 2\sqrt{\frac{\sqrt{2}b}{a} - \frac{b^2}{2a^2}} : b > 0.565a \\ 1 + \frac{b}{2\sqrt{2}a} & : b < 0.565a \end{cases} \right)$$
(103)

There are several mistakes in the equations given by Selikson *et al.* which have been corrected. For a FWHM of 5 mm and a sheet width of 1 mm, as found in this phantom, this translates to a 7% error.

The calculated axial slice widths at a variety of positions along the magnet bore are illustrated by Table 8. There is no noticeable difference between the different slice profiles in the three principle planes. Each measurement falls within the 10% gold standard of the specified slice thickness, when the errors reported by Selikson *et al.* are considered.

Pulse sequence	Measured slice width (mm)	Offset from centre of scanner along magnet bore of axial plane (mm)
MEMP	5.25	-150
CSMEMP	5.58	-150
MEMP	5.36	0
CSMEMP	5.96	0
MEMP	5.28	+150
CSMEMP	5.73	+150

Table 8 - FWHM axial slice width measurements for MEMP and CSMEMP pulse sequences as a function of slice position for nominal 5 mm slice width.

9.5.2 Slice Warp

Both slice warp, the distortion of a slice along the slice select direction, and slice offset, the distance between slice centres, may be measured using the Eurospin II Test Object 3, which is comprised of a set of pairs of crossed perspex rods in a solution of doped water encased in a cylindrical perspex surround. By measuring the separation of each pair of rods within an image and examining the spatial variation of the separations it is possible to search for slice warp. The phantom and slice position is illustrated by Figure 169, a photograph included in Figure 170 and a typical slice through the phantom illustrated by Figure 172. Varying the position of the slice relative to the centre of the phantom leads to a variation in the distance between the pairs of rods in the resultant image (a vertical displacement in Figure 172). The lower left and upper right rod pairs in Figure 172 are sloped in the opposite direction to the other rod pairs in order to give information about which side of the phantom the image slice is positioned on.



Figure 169 - Eurospin II Test Object 3

Slice warp is the distortion of the imaging plane, for example by bending as illustrated by Figure 171. Slice warp has been investigated using multi-slice spin echo datasets acquired using a TR of 500 ms and a TE of 20 ms. Careful phantom positioning is essential for measurements of slice warp and slice offset and great care must be taken in aligning the phantom with the scanner alignment lights. This ensures that the imaging plane will be parallel to the flat ends of the phantom and hence correctly aligned with the perspex rods. The effects of slice warp can not be separated from those due to in-plane geometric distortion using this phantom, so tests of the accuracy of GRADWARP were needed before this study could be carried out. Datasets were acquired in axial, sagittal and coronal orientations both at the centre of the magnet and approximately 120-140 mm perpendicular to the imaging plane from the centre of the magnet. For each slice of each multi-slice dataset, the distance between each of the pairs of rods was measured. There was no significant deviation of any single measurement from the mean rod separation for a given slice and no spatial pattern to the small deviations from the mean. Typical results are given by Table 9. The range of separation for rod pairs gives an upper limit for slice warp of less then 1 mm, which includes the effects of manufacturing tolerance, noise and measurement accuracy. It is therefore concluded that there is no significant slice warp for neurological images acquired using our Signa scanner and the head coil.



Figure 170 - Photograph of Eurospin II Test Object 3



Figure 171 - Illustration of slice warp

Rod pair	Separation (mm)	Rod pair	Separation (mm)	
1	12.89	9	11.72	
2	13.36	10	11.48	
3	11.48 11		13.36	
4	13.13	12	12.66	
5	12.42	13	12.66	
6	12.42	14	13.13	
7	12.89 15		13.83	
8	12.89	16	12.19	
Range	11.48 - 13.36	Total (mean ± sd)	12.66 ± 0.66	

Table 9 - Typical separation of rod pairs for Eurospin slice warp and offset phantom TO3

9.5.3 Slice Offset

Slice offset, the distance between slice centres, may be investigated using the measurements reported in the previous section. A typical image is illustrated by Figure 172. The average separation of the rods is calculated for each slice, and can be related to the offset between slices if the angle of rods is known. According to Lerski [LERSKI92] the measured slice offset, taking into account both the manufacturing tolerances associated with the phantom's construction and the distance between slice centres should be within 1 mm of the specified slice offset. The average offset for groups of slices varied from 4.64 - 5.17 mm which is less than 0.5 mm from the specified offset of 5 mm and therefore acceptable. Similarly, the offset for non-contiguous datasets is also acceptable.



Figure 172 - Image of slice through slice warp and offset phantom

Slice offset and slice width both vary somewhat with distance from the centre of the gradient coils, both decreasing with increasing distance. For example, using the slice warp and slice width phantoms in a coronal orientation, aligned at the centre in x and z, but with the phantom position varying in y the results are as follows. The average slice offset for 6 slices centred on y = +24 mm is 5.17 mm whilst the uncorrected geometric mean of slice width = 5.55 mm for a 5 mm nominal slice thickness. The average slice offset for 6 slices centred on y = +1452 mm is 4.64 mm whilst the geometric mean of slice width = 5.19 mm. Similar results were obtained for the coronal and sagittal orientations. These measurements may be compared favourably to the gold standard of a maximum of 10% error.

The accuracy of alignment of the centre slice with the alignment lights may also be tested using these results. The centre slice of the phantom should be perfectly aligned with the centre of the crossed rods, so that there is no separation between the centre of the rods. The cylindrical surface of the Eurospin II test objects is opaque making the "white light" alignment lights on the Signa very difficult to use. In addition to this, the physical orientation of phantoms of a small depth, such as these, is very difficult and extremely time consuming. The phantoms may also move when the couch is advanced into the magnet but if the phantom is carefully positioned the accuracy of the alignment is better than 1 mm in all three major orthogonal planes.

The accuracy of the Signa couch positioning was measured using a metre rule aligned parallel

to the sagittal plane alignment light. The coronal plane alignment light was used to make measurements. Both 50 cm and 95 cm distances on the ruler were compared with the Signa's electronic couch positioning and the measurements were repeated 6 times. The distances indicated by the electronic positioning were 49.9 and 94.8 cm respectively with no variation for any of the measurements.

Slice offset for small distances may be measured by comparing different slices from the slice offset/warp phantom. Larger distances require a different approach. This may be achieved by positioning the centre of the slices offset/warp phantom at a known distance from the alignment beams. Data may then be acquired at an offset from the centre of the alignment beams. For 150 mm offset, the average error calculated from each of the pairs of rods was less than 0.5 mm, which is as good as the accuracy of the alignment itself.

9.6 Visualisation and Quantification of Partial Volume Effects

Partial volume effect is the term given to describe a voxel that contains two or more tissues, for example, grey matter and white matter or white matter and CSF. The observed signal is then a weighted average of the signal from the two constituent tissues. In multi-slice MRI (as opposed to volumetric MRI), such effects are sometimes attributed to the fact that slice thickness is typically 3-10 times the in-slice pixel size. This is indeed the major cause, but the partial volume effect still exists for isotropic volume data. If no efforts are made to account for the partial volume effect when carrying out volume measurement, the accuracy of results will be critically dependent upon both the ratio of slice thickness and in slice voxel dimension to the size of the region to be measured and to the three dimensional morphology of the region. For example, although 10 mm slices might yield a good estimate of the total volume of a smoothly varying organ such as the liver, they would be unlikely to yield reliable estimates for the volume of a highly curved structure such as the ventricles.

The accuracy required for volume measurement is application specific. To obtain the required accuracy, it may be necessary to use given clinical scans, it may be possible to adjust the acquisition of clinical scans somewhat, or it may be possible to specifically design the data acquisition. The magnitude of partial volume effects can be reduced by minimising the fraction of voxels affected. This can be achieved for multi-slice MRI (possibly at the expense of scan time or SNR) by minimising voxel dimensions, which amounts to achieving the minimum

possible slice thickness. It is also crucially important to align the voxels with the structure of interest by choosing an appropriate orientation of the image plane.

With 4 or 5 mm slice data as typically used clinically for neurological MRI imaging, partial volume effects between CSF and grey matter and grey and white matter may be severe for some slices. If the total volume of grey matter, CSF or brain parenchyma is of interest, then although the partial volume effect is severe for these slices, averaging over the whole dataset will reduce the magnitude of the effect on total volume measurement. Trying to segment a single slice for which partial volumes are severe will be extremely difficult, however.

If non-isotropic gradient echo volumetric data were acceptable clinically (in terms of achievable contrast), then such data would be preferable because of the reduced magnitude of the partial volume effect. The effects of B_0 non-uniformities and susceptibility may be a disadvantage however, and the contrast to noise ratio may not be ideal for semi-automatic clustering of some tissues (see section 7.10.2.1). Four methods of visualising and quantifying the extent of the partial volume effect are proposed - the use of grey level/edge clustering, long inversion time IR sequences, the comparison of predicted and observed signal intensities and the use of an anthropomorphic phantom.

9.6.1 <u>Use of Grey Level/Edge Clustering</u>

Partial volume voxels may be approximately divided into two groups based on whether or not such voxels are close to edges in the image. Voxels close to edges typically generate a high response to edge operators and this characteristic has been utilised for grey level/edge clustering in order to identify partial volume voxels. Edges may be defined using 2-D operators slice by slice, or by using 3-D operators. The 5 mm thick slice and 2.5 mm slice skip data used for this work is not suitable for a 3-D approach, however, so only 2-D techniques have been considered. This author has used a single input image (as opposed to the two images available form a dual-echo sequence, or possibly more images) for this work. The gradient of an image, as discussed in section 3.3.2.2, has been used as the edge operator because of its speed, simplicity and the fact that it produces an edge response for every pixel. In contrast to the requirements for edge detection as discussed in section 6.2.1, under these circumstances it is desired to differentiate between those voxels affected by the partial volume effect due to their proximity to an edge, and not to generate a single pixel width response. Thus, under these circumstances, a zero-crossing algorithm such as those due to Canny [CANNY86] or Marr and Hildreth [MARR80], as discussed in section 3.3, is inappropriate. The use of edge operators such as the Sobel operator might also be considered. The use of thinner slice contiguous data would also make the use of a three dimensional operator such as the Zucker-Hummel operator [ZUCKER81] more appropriate, but the 5 mm thick slices and 2.5 mm slice skip currently used renders such an approach inappropriate, as discussed in section 7.5.

The method is similar in some respects to that used for dual-echo clustering as described in section 7.10. Figure 173 and Figure 174 illustrate a late echo long TR spin echo image and its gradient image, whilst Figure 176 shows a gradient/grey level cluster image. This latter image clearly shows three separate clusters, the cluster top left corresponding to background noise and low intensity fat and bone marrow. The central cluster is largely composed of brain parenchyma whilst the high intensity top right cluster corresponds to the high intensity CSF, vitreous and aqueous humour (the fluid within the eyes) A histogram of those pixels corresponding to the head is illustrated by Figure 175. The background noise pixels have been removed from the histogram by image masking in order that the intensity distribution of the head can be visualised.

The cluster image can be used in two ways - either to identify partial volume voxels (ie those voxels not within the main clusters) or to use the main clusters for segmentation of the four main voxel classes. Manual delineation in cluster space has been used to identify regions of interest. This is illustrated by Figure 177 - Figure 180 which demonstrate those voxels belonging to the brain parenchyma cluster (which also comprises some voxels due to nasal tissues), the fluid cluster, the fat and background cluster and the partial volume voxels. It should be noted that the majority of voxels containing CSF appear to suffer from the partial volume effect.

After the identification of such partial volume voxels, further processing is required to quantify the extent of the partial volume effect for each voxel in order to produce accurate volume measurements. One such approach is discussed in section 10.2.2.7. A further approach is to predict tissue intensity for normal tissue and a given pulse sequence and use these values to help to define partial volume voxels. It should be noted that there will be a range of values of tissue intensity due to range of intensities of T_1s , T_2s and PDs of normal tissue. A clustering approach allows for better classification than a multi-thresholding approach as can be seen by considering the histogram of the image (Figure 175) and the gradient/grey level cluster image (Figure 176). The definition of the clusters is far clearer than the definition of histogram peaks because partial volume voxels are easily visualised using this approach.



Figure 173 - Late echo long TR spin echo image (SE/3000/80).



Figure 174 - Gradient image of late echo long TR spin echo image



Figure 175 - Histogram of late echo long TR spin echo image excluding background



Figure 176 - Gradient/grey level cluster image. Gradient is plotted from top to bottom and intensity from left to right, with the origin top left.



Figure 177 - Segmented brain parenchyma



Figure 178 - Segmented CSF and vitreous/aqueous humour



Figure 179 - Segmented fat/bone/flesh and background



Figure 180 - Partial volume voxels

9.6.2 <u>Visualisation of Partial Volume Voxels Using Long Inversion Time</u> <u>Inversion Recovery Images</u>

It is often very difficult to assess the magnitude of the partial volume effect for a given slice thickness and region of anatomy. To do so needs detailed knowledge of the exact size and shape of the anatomy and its relationship to a given (possibly oblique) image plane. This author has therefore developed a method for the visualisation of the magnitude of the partial volume effect. The approach takes advantage of the fact that inversion recovery data is inherently signed (ie can either be positive or negative in nature). Commonly inversion recovery images are reconstructed as magnitude images. This is the case with the Signa, where signed data is not available. For neurological imaging and relatively long inversion times (eg IR/2500/600/40) it is possible to produce a signed image where the magnitude of the signal of two given tissues is similar but the signs are different. This is demonstrated by Figure 182 which illustrates a simulation of the contrast for an IR/2500/600/40 image.

The creation of a magnitude image yields voxels of similar intensity for pure regions of tissues, but reduced intensity voxels where there are mixtures of the two tissues in the same voxel. Figure 183 demonstrates the effectiveness of this approach for the parameters used in the simulation depicted by Figure 182. The parameters were chosen for the visualisation of both grey matter/white matter and white matter/CSF partial volume voxels. Superior visualisation of the partial volume effect for a single tissue pair may be achieved by varying the echo time, repetition time or inversion time appropriately. As an example, a IR/3000/1000/75 pulse sequence is particularly good for visualising grey matter/CSF partial volume voxels. The intensity of pure white matter is approximately twice that of pure CSF or pure grey matter, which are approximately isointense. An example of such an image is illustrated by Figure 184.



Figure 182 - Variation of intensity with echo time for long inversion time IR image TI = 600 ms, TR = 2500 ms).



Figure 183 Inversion recovery imaging demonstrating partial volume effect between both grey matter and white matter, and white matter and CSF.



Figure 184 - Inversion recovery image demonstrating partial volume effect between white matter and CSF.

9.6.3 Assessment of Magnitude of Partial Volume Effect

Initial dual-echo clustering studies indicated a wide spread in intensity of voxels judged by observers to contain CSF. This is due to the partial volume effect between CSF and neighbouring tissues. The use of long inversion time IR sequences, such as those described in section 9.6.2, allows the visualisation of voxels affected by the partial volume effect but a method of quantifying the extent of the partial volume effect would also be very useful. Such quantification is of particular interest for measurement of CSF, grey matter and white matter volumes using typical non-isotropic SE or IR datasets. It should be emphasised that the work reported here is aimed at determining the magnitude of the partial volume effect within regions delineated by an observer. A general method of volume measurement which takes into account the partial volume effect would be very useful, but has not been considered in this thesis. Such a potential method is discussed in section 10.2.2.7. The volume of ventricular CSF for normal subjects will be considered here, but the extension of such work to grey matter and white matter volumes would also be of great interest. Two approaches to quantifying the volume of ventricular CSF have been adopted - the use of intensity information from a IR/3000/1000/75 pulse sequence, as detailed in section 9.6.2, and the method of Condon et al. [CONDON86A, CONDON86B] as discussed in section 9.2.2.

9.6.3.1 Use of Partial Volume Inversion Recovery Images

The ventricles appear dark using a IR/3000/1000/75 sequence (see Figure 184) due to the partial volume effect between CSF and surrounding tissue. The images considered for this work are magnitude images and it is not possible to tell the sign of the signal within the ventricles using intensity information alone. Thus, for a profile through a section of the ventricles as illustrated by Figure 185, it is not possible to tell whether the section in the centre of the ventricles bordered by the two local minima, was originally of the same sign as the surrounding data.

The border between CSF and the wall of the ventricles is a smooth one so it is not expected that there will be strong discontinuities apparent in a profile through the ventricles. The local minima bounding the central hump in the centre of the profile through the ventricles appear to be discontinuous in nature. By applying a local smoothness constraint, it is possible to reconstruct the sign of the data manually in the region of this central hump. The original magnitude data for Figure 185 and the reconstructed signed data is illustrated by Figure 186.



Figure 185 - Profile through section of the ventricles for IR/3000/1000/75 image.



Figure 186 - Illustration of sign reconstruction of magnitude data based upon border smoothness constraint.

Two registered datasets were considered for this work - the late echo images from a SE/3000/30,80 sequence and a IR/3000/1000/75 dataset. Motion restraint for the two scans was as described in section 7.10.1, and various post-acquisition checks were also carried out to ensure that registration was accurate. It is possible to consider each part of the ventricles as being composed of two regions, each initially of a different sign, by using a smoothness constraint. The first region corresponds to an observers opinion as to the position of the border between ventricles and tissue for a T_2 -weighted image from a standard dual echo SE pair (SE/3000/30,80). The border of the second region corresponds to the position of sign change for a registered IR/3000/1000/75 image. It is possible to measure the mean intensity for a region of pure white matter, and thus predict the intensity of pure CSF and grey matter for the dataset from a simulation of signal intensity as described in section 7.7. The mean intensity of each of the two regions and their area can therefore be used to evaluate the proportion of CSF within the area considered by the observer to contain the ventricles. This was carried out for one normal volunteer as a demonstration of the approach. The tissue surrounding the ventricles is mostly white matter but does include some deep grey matter. The calculations have been carried out assuming the surrounding tissue is purely white matter, which will lead to an overestimate of the amount of CSF within the ventricles, as white matter is brighter than grey matter for this sequence. The ventricular volume as defined by an expert observer was calculated to contain 53% CSF which, as mentioned already, is an overestimate of CSF content.

9.6.3.2 Condon's Method of CSF Volume Measurement

Condon *et al.* [CONDON86A, CONDON86B] have proposed a method for CSF measurement which relies on approximately nulling the grey matter and white matter tissue signal with a IR pulse sequence and using a long echo time to reduce the remaining tissue signal, as discussed in section 9.2.2. The method has been reproduced using a IR/5000/300/430 pulse sequence. It would not be possible to use such a method regularly within the NMR Research Group for volume measurement, because of time constraints and the fact that such an approach only gives CSF volumes. Again, the volume of CSF calculated using Condon's method has been compared to that calculated by an observer using manual delineation of the ventricles. The ventricular volume as defined by the expert observer was calculated to contain 40% CSF using Condon's method. Given that the 53% volume of CSF calculated from section 9.6.3.1 was an overestimate, the two methods are in broad agreement as to the magnitude of the partial volume effect for CSF within the ventricular volume defined by the expert observer.

9.6.4 <u>Assessment of Effect of Partial Volume Effect on Measurement of</u> <u>Anthropomorphic Brain Phantom</u>

The accuracy of volume measurement of the human brain using MRI has been investigated using an anthropomorphic phantom. This phantom is a wax replica of a human brain made from a cast of a fresh human cadaver by the Department of Physiology, UCL, and very closely resembles the shape of a human brain. Wax produces effectively zero NMR signal, so the phantom is immersed in oil in order that its shape can be visualised. Oil is used in order to avoid the large standing wave effects associated with water (section 5.5). The wax phantom floats in oil and therefore had to be weighted down slightly using a plastic container placed over the top of the phantom. The phantom was advanced into the scanner and left to settle for ten minutes to ensure no motion of the phantom during image acquisition. Two pilot scans were used to align the imaging plane in the same orientation as subjects are normally scanned (ie an oblique axial slice orientation). The whole phantom was scanned using a variety of slice configurations - contiguous 3 mm thick slices, contiguous 4 mm thick slices, contiguous 5 mm thick slices, 5 mm thick slices with a 2.5 mm slice skip and 5 mm slices with a 5 mm slice skip. Each dataset was automatically thresholded at a value halfway between the minimum and maximum voxel intensity for the dataset. The total number of voxels comprising the brain phantom was then evaluated for each scan and the voxel dimensions (and slice skip if appropriate) used to calculate the phantom volume as measured by MRI. The volumes calculated for each dataset are given in Table 10

Slice thickness and slice skip	Total volume (ml)
3 mm slice thickness contiguous data	1,182
4 mm slice thickness contiguous data	1,163
5 mm slice thickness contiguous data	1,164
5 mm slice thickness + 2.5 mm slice skip	1,171
5 mm slice thickness + 5 mm slice skip	1,151

Table 10 - Volume of wax phantom for various slice width and slice skip combinations

The actual volume of the wax brain has been calculated by measuring the volume of water displaced by immersing the phantom in water. Several methods of calculating the volume of the phantom using this approach were initially investigated. The final method utilises a plastic receptacle somewhat larger than the phantom and a catch tray in which the plastic receptacle was placed. The receptacle is filled with soapy water (having a reduced surface tension when compared to pure water) until almost overflowing. A little more water is slowly and carefully added until water flows over the sides of the receptacle. This overflow is captured by absorbent materials for up to five minutes when typically the overflow has finished or is proceeding at a negligible rate. The wax phantom is carefully immersed into the receptacle and completely submerged using two thin rods thus forcing water over the sides of the receptacle and into the catch tray. The phantom is kept submerged for five minutes in order to allow the overflow to finish or to slow to a negligible rate. The receptacle is removed from the catch tray and left to drip above it for up to five minutes in order to catch any liquid on the receptacle's surface. The volume of liquid caught in the tray is measured in a 2 litre measuring cylinder. This measurement has been repeated six times yielding volumes of 1159, 1166, 1164, 1160, 1154 and 1170 ml with an associated ± 2 ml uncertainty concerned with assessing the level of the bottom of the meniscus. The mean volume is 1162.2 ml with a standard deviation of 6.0 ml.

There are three sources of error or uncertainty associated with the measurement in addition to assessing the level of the bottom of the meniscus

- the excess water left in the catch tray or on the surface of the receptacle
- the uncertainty associated with the accuracy of the cylinder, and
- the reproducibility of the initial volume of water within the receptacle.

The excess water left in the tray after the water has been poured into the measuring cylinder has been measured by collecting as much of the water as possible using a syringe and similarly for the plastic receptacle. It was not possible to collect all of the water due to surface tension, so an overestimate of the maximum amount of water present in the catch tray and on the surface of the receptacle was also made which gives a systematic error of approximately 1-2 ml. The uncertainty associated with the accuracy of the cylinder is \pm 20 ml for the 2000 ml BDH cylinder used (BDH Laboratory Supplies Catalogue 1992, Merck 1992). The volume of water contained in the receptacle after water has ceased to flow has been evaluated by filling the receptacle to overfilling and then flattening the surface using a ruler. Water is then added until the meniscus just bursts and the volume of water added recorded. A variation of up to 10 ml has been determined which depends upon how steadily the water is poured.

One method of improving the accuracy of the measurement of the volume of the wax phantom would be to calibrate the cylinder by weighing approximately 1200 ml of water and calculating the actual volume of this water from its weight. High precision balances normally weigh only up to maximum of 160 g and the errors associated with either using a balance capable of weighing larger weights or measuring several volumes of less than 160 g would not give more accurate results than the known precision of the cylinder.

This work produces an estimate of the accuracy of MRI for volume measurement of the human brain. The accuracy will be dependent upon a number of factors including gradient non-linearity geometric distortions, susceptibility shifts at the oil/wax boundary and the partial volume effect. There is no trend to the volume measurements made with different slice thickness and slice skip combinations which implies that either this range of particular parameters do not affect the accuracy of volume measurement for this phantom, or that the errors associated with the reproducibility of the measurements have not been appreciated. The latter explanation may well be true, but there was no available scanning time to repeat the measurements. The measurements and errors associated with both the water displacement and MRI methods of volume measurement are illustrated by Table 11. Each of the MRI measurements is within the range of uncertainties associated with the water displacement measurements.

Method of measurement	Mcan volume (ml)	Standard deviation of volume (ml)	Range of volumes (ml)	Random error (ml)	Systematic error (ml)
Water displacement	1160	6	1152 - 1168	± 7	20
MRI measurement	1166	12	1151 - 1182	-	-

 Table 11 - Summary of measurements and errors associated with the water displacement and MRI methods of volume measurement for an anthropomorphic phantom.

9.7 Validation of Volume Measurement by Automatic and Semi-Automatic Methods

It is all well and good to develop methods of manual, semi-automatic and automatic segmentation for volume measurement, but it is also necessary to validate these measured volumes. To quote Gabor Herman [HERMAN89] on the output of volumetric calculations.

"To use these numbers without having performed careful validation studies ... is foolhardy. Alas, such studies are time consuming, and frankly, boring. There is a great temptation to simply accept the output of the computer; this temptation must be resisted."

There are several reasons why it is necessary to carry out validation procedures for volume measurement

• to investigate the effect of artifacts such as geometric distortions (both sample independent and sample dependent) and slice warp, and partial volume effects (due primarily to slice thickness but also to the finite in-slice voxel dimension).

• to determine the accuracy of automatic and semi-automatic methods of segmentation as compared to an expert observer

• to determine whether MRI visualises the anatomy and pathology as defined histologically. If this is not the case it is important to understand what MRI does visualise, whether this is itself useful for the problem being tackled and/or whether it can be related in some way to the required volume.

Several approaches to validation have been used to investigate these effects

[A] The use of phantoms to measure the magnitude of the individual artifacts, such as geometric distortions due to gradient non-linearities. This has been done using a specially constructed phantom as discussed in section 9.3.3.2.

[B] The use of human volunteers to measure the magnitude of sample dependent artifacts, such as susceptibility and the partial volume effect, as discussed in section 9.3.3.3.

[C] Anthropomorphic phantoms may be used to investigate the gross effect of geometric distortions, the partial volume effect and other artifacts on the accuracy of volume measurements. A wax cast of a human brain has been used in this work to investigate the magnitude of such inaccuracies for volume measurement of the human brain, as described in section 9.6.4. An accurate phantom simulating the brain or even simply a single slice of the brain would be extremely complex. The most sophisticated phantom

reported in the literature is due to Cline *et al.* [CLINE91] but even this has several drawbacks.

[D] The comparison of automatic and semi-automatic segmentation to the manual segmentation of an expert observer.

[E] The comparison of post mortem pathology (histology) with MRI scans. This has not been carried out as part of this thesis due to the rarity of post mortem specimens.

The work in this section concentrates on the validation of semi-automatic and automatic methods of volume calculation for the human brain, grey matter, white matter and CSF by comparison with one or more expert observers.

9.7.1 <u>Method of Manual Delineation of Neuroanatomy for Comparison of</u> Volumes With Semi-Automatic and Automatic Segmentation Methods.

The measurement of normal anatomical structures has been made from eight dual echo SE datasets (SE/3000/30,80) of healthy normal volunteers ranging in age from 24 to 53 years (mean = 30 years, standard deviation = 9 years). The data acquisition has already been discussed in chapter 1. Multi-slice SE data has been considered because of its prevalence. Although the near-isotropic nature of 3-D gradient echo data would be an advantage in terms of reduced partial volume effect, the contrast to noise ratio achievable in realistic imaging times does not match that of SE data. The volunteers were screened to ensure no past history of neurological disease, neurological or psychological symptoms, excessive alcohol intake and drug abuse. One additional volunteer was excluded from the study on the basis of alcohol intake. The measurement of abnormal structures (i.e. enlarged ventricles due to brain atrophy) has been made using datasets from patients scanned as part of standard research protocols. The validation of measurement of lesion volume was not possible due to clinical commitments of the neurologists and neuroradiologists from the Institute of Neurology NMR Research Group.

The method of manual volume measurement is the same for each structure measured. Xdispunc is used to display each dataset at full screen size on a Sun 4 workstation. Windowing is set by reducing the maximum window intensity, using a slice at the level of the ventricles, until the contrast between either grey and white matter for an early echo, or CSF and brain parenchyma for a late echo, is good. This setting is used for each measurement within the given dataset. The reproducibility of this window setting has been shown to be good both for the same observer

and between observers. The observer is asked to delineate the regions of interest for each slice along the border between the two regions using the Sun's mouse. Results are stored in xdispunc regions of interest files and areas calculated automatically. Volumes are calculated by multiplying the sum of the areas from each slice by the distance between slice centres.

Each measurement was repeated once, with the two measurements separated by a period of between 24 hours and one month, in order to give some indication of the reproducibility of such measurements. The time taken by the observer for each task was recorded.

9.7.2 Intracranial Volume

9.7.2.1 <u>Method</u>

The Proton Density weighted images (SE/3000/30) have been used to measure the intracranial volume manually. One observer only measured the datasets corresponding to subjects 3-8, whilst two additional observers (three total) also measured datasets 1 and 2, in order to give some idea of the intra-observer variability. The manual delineation of the intracranial region took from 55 minutes to 1 hour 50 minutes for each repetition of each dataset.

The intracranial volume has also been calculated automatically using the fast radial CSF identification method (see section 6.6.2), the normalised thresholding method (see section 7.6), thresholding following heavy Perona anisotropic blurring (see section 7.5) and semi-automatically using dual echo clustering (see section 7.10). The former three methods are totally automatic, requiring no manual interaction. The latter method requires the user to manually delineate the white matter, grey matter and CSF clusters from the fat/bone and background clusters. This takes an operator used to the operation of xdispunc approximately 30 seconds to carry out. Connectivity is then used to identify the intracranial region in a similar way to that described for the thresholding approach in section 7.5.

The current edge-focusing algorithm is a Fourier domain method which, by its very nature, must re-evaluate each image pixel for each iteration. This is not an efficient approach and thus renders the current algorithm unfeasible for practical use. It should be stressed that the method itself is practical - it is the implementation that causes problems. An M.Sc. project to implement a recursive spatial method [MONGA91] has been designed by the author and is currently underway. Preliminary results indicate that the approach of Monga *et al.* will be very fast for edge focusing.

9.7.2.2 <u>Results</u>

The mean total volume for each manual intracranial volume measurement is given by Table 12. The reproducibility of each observer is indicated by the percentage difference between the observer's two measurements. The ratio of partial volume voxels to region area is small for the intracranial region. Thus an expert observer should be able to produce a good estimate of intracranial volume by manual delineation. This is confirmed by a small inter-observer variability (maximum 4.0%) and a small intra-observer variability (maximum 1.6%) for the intracranial region delineation detailed in Table 12. Each of the automatic and semi-automatic methods has therefore been compared to the mean of the manual measurements for each of the 8 volunteer datasets. The percentage difference of the automatic/semi-automatic methods from the mean of each manual result, and the mean and standard deviation of these percentage differences are given in Table 13.

The gold standard for intracranial volume measurement accuracy set by the clinicians in the Institute of Neurology NMR Research Group is within 5% of the range of manual results. Each method for each dataset is in fact within 5% of the mean of the manual results, which is better than required. The accuracy for the more inferior slices is generally worse than for the those slices superior to the eyes. The equivalent results for slices superior to the eyes are reported in Table 14. The accuracy for those slices superior to the eyes alone is considerably improved over those for the whole intracranial region. Each automatic measurement for each dataset is within 2% of the mean of the manual measurements. One semi-automatic measurement is -2.1% from the mean of the manual measurements. The accuracy of the most inferior slice and slice 15 the most superior slice. Figure 187 where slice 0 is the most inferior slice and slice 15 the most superior slice. Figure 187 demonstrates graphically that the accuracy of measurement of those slices superior to the eyes (slices 5-15) is greater than those inferior. This is primarily due to problems that arise using these methods with slices containing multiple isolated regions of the brain, and the severe partial volume effects for the lower slices.

Subject	Observer 1	Observer 2	Observer 3
	mean volume (mm ³)	mean volume (mm ³)	mean volume (mm ³)
	(% difference	(% difference	(% difference
	between repeat	between repeat	between repeat
	measurements)	measurements)	measurements)
1	1,555,000 (0.2%)	1,554,000 (0.1%)	1,514,900 (0.9%)
2	1,411,400 (1.0%)	1,396,500 (1.6%)	1,356,200 (0.1%)
3	1,535,300 (1.0%)	-	-
4	1,471,500 (0.2%)	-	-
5	1,450,100 (0.2%)	-	-
6	1,281,600 (0.6%)	-	-
7	1,204,000 (0.3%)	-	-
8	1,270,700 (0.4%)	-	-
Mean ± sd	0.5 ± 0.3		
(maximum) of	(1.0%)	-	-
% differences			
between repeat			
measurements			
Mean ± sd	1,397,500	-	-
of volumes	± 129,200		

 Table 12 - Total intracranial volume measured manually.

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Subject	Fast radial CSF	Normalised	Perona	Interactive
	identification	thresholding	threshold	dual-echo
	accuracy (%)	method	accuracy (%)	clustering
		accuracy (%)		accuracy-mean
				(%) (%
				difference
				between repeat
				measurements)
1	- 0.6	+ 0.8	- 0.8	- 1.8 (1.3)
2	+ 2.6	- 1.1	+ 3.1	- 0.3 (0.8)
3	- 2.1	- 3.0	- 3.0	- 4.0 (0.0)
4	+ 1.5	- 4.0	- 0.9	- 4.7 (0.4)
5	+ 1.0	+ 0.5	+ 0.7	- 3.2 (0.9)
6	+ 2.8	+ 3.3	+ 1.7	- 3.6 (0.1)
7	+ 4.2	- 2.3	- 4.3	- 4.1 (0.2)
8	+ 0.6	- 1.0	- 2.9	- 1.5 (0.4)
Mean ± sd				
(maximum)	-	-	-	0.5 ± 0.4
of differences				(1.3)
between repeat				
measurements				
Mean ± sd	+ 1.2 ± 1.9	- 0.9 ± 2.2	-0.8 ± 2.5	-2.7 ± 1.5
(maximum)	(4.2)	(-4.0)	(-4.3)	(-4.7)
of accuracy				

Table 13 - Difference of automatic and semi-automatic methods from mean of manualmeasurements for intracranial measurement of the whole dataset.

Subject	Fast radial CSF identification accuracy (%)	Normalised thresholding method accuracy (%)	Perona threshold accuracy (%)	Dual-echo clustering accuracy (%) (% difference between repeat measurements)
1	+ 0.6	+ 1.5	+ 0.2	- 0.3 (1.8)
2	- 0.4	+ 0.4	- 0.4	- 0.4 (1.4)
3	- 0.8	- 1.2	- 0.9	- 2.1 (0.0)
4	+ 1.1	- 0.4	+ 0.4	- 1.0 (1.8)
5	+ 0.1	+ 0.4	+ 0.5	- 1.9 (0.4)
6	+ 0.4	+ 2.0	+ 0.5	- 1.8 (0.3)
7	+ 1.5	+ 1.5	+ 1.5	- 1.1 (0.1)
8	+ 0.7	+ 0.9	+ 0.6	- 1.3 (0.3)
Mean ± sd (maximum) of differences between repeat measurements	-	-	-	0.7 ± 0.7 (1.8)
Mean ± sd (maximum) of accuracy	+ 0.4 ± 0.8 (+1.5)	+ 0.6 ± 1.1 (+2.0)	+ 0.3 ± 0.7 (+1.5)	- 1.2 ± 0.6 (-2.1)

Table 14 - Difference of automatic and semi-automatic methods from mean of manualmeasurements for intracranial measurement of slices superior to the eyes.



Figure 187 - Difference in area between automatic/semi-automatic methods of intracranial region segmentation and mean of the expert observer's measurements per slice for subject 2. Slice 0 is inferior and slice 15 superior.

9.7.3 Grey Matter and White Matter Volumes

9.7.3.1 <u>Method</u>

The Proton Density weighted images have been used for manual delineation of grey and white matter volumes because they demonstrate superior grey matter/white matter differentiation as compared to the T_2 -weighted images. Measurements of grey and white matter were made for several slices superior to the eyes. This region is normally used for manual grey matter/white matter volume measurement because the grey/white border is relatively clear at this level [LIM89]. This is not the case for inferior slices or the most superior slices where partial volume effects dominate. Measurements of white matter are reported below, to give an indication of the reproducibility and dual-echo clustering measurements. Grey matter could similarly be measured, but the observers were not confident that they could delineate the border of grey matter and CSF. It would therefore not be meaningful to compare the volume of grey matter measured manually with that measured from dual-echo clustering. It took between 35 minutes and 1 hour 10 minutes for each manual repetition of each dataset measurement. Manual measurements have been compared to the results of two semi-automatic clustering methods.

The k-means clustering algorithm is a popular clustering method. The algorithm takes as input several images, the number of clusters required and a mean intensity for each cluster in each image. In the author's implementation, four regions of approximately 10-20 voxels of each tissue are sampled, and the mean intensity calculated for each tissue. The first iteration of the algorithm consists of assigning each pixel to the nearest cluster centre (defined by the input tissue mean intensities) in cluster space. The centre of gravity of each cluster is then calculated. The second iteration of the algorithm maps all pixels to the nearest of the new cluster centres, and so on for subsequent iterations. Although it is not possible to prove mathematically that the algorithm will converge under all circumstances, the algorithm does stabilise, typically in 40-50 iterations. The way in which the algorithm works implicitly assumes the 'spread' of each cluster is similar. For Gaussian cluster distributions this is equivalent to assuming equivalent variances for each cluster. If this is not true, then it is not valid to assume that a voxel closest to the centre of one cluster should necessarily be associated with that cluster. The larger spread of grey matter values compared with white matter values, due to both the partial volume effect and to tissue
heterogeneity, leads to gross overestimates of white matter volumes using this approach. Typically, at least a 70% overestimate is made. Thus, a clustering approach using both the spread of tissue intensities as well as the mean of tissue intensities is required. Such a method has not been considered as part of this thesis, but would be an interesting piece of future work.

The second approach to semi-automatic dual-echo clustering is the interactive delineation of the white matter cluster from a cluster image in a similar way to that described for the total intracranial volume measurements in section 9.7.2. The position of the white matter cluster is illustrated by Figure 129 for a SE/3000/30,80 pulse sequence.

9.7.3.2 <u>Results</u>

Table 15 shows the results of the manual measurements and the latter semi-automatic method. Each of the measurements of white matter volume is within 10% of the range of manual measurements as required by the Institute of Neurology NMR Research Group clinicians. This figure has been chosen in order to take into account the large partial volume effect and the difficulties in manual delineation of the border between grey matter and white matter in cluster space. For two of the subjects datasets, it was difficult to identify an obvious delineation between grey and white matter. It was therefore necessary to estimate the position of the border in cluster space from knowledge of previous datasets, and use feedback from comparison of the resulting classification to the input images to modify the cluster delineation. Such a task would be made considerably easier by the availability of a graphical software tool designed specifically for the task.

9.7.4 Ventricular CSF Volumes Results

9.7.4.1 <u>Method</u>

The T_2 -weighted images (SE/3000/80) were used to measure CSF volumes because they demonstrate superior CSF/brain parenchyma contrast compared to the early echo images. The ventricular volume has been compared to the volume calculated using dual-echo clustering. This is because the observers felt more confident in delineating the ventricles rather than the extra-

Subject	Manual measurement mean (mm ³) (% difference between repeat measurements)	Cluster mean (mm ³) (% difference between repeat measurements)
1	256,263 (5.8%)	228,045 (2.8%)
2	186,910 (5.8%)	170,833 (4.7%)
3	166,548 (8.9%)	170,786 (7.0%)
4	141,499 (3.1%)	146,876 (7.4%)

Table 15 - Volume of white matter measured manually and calculated automatically using interactive delineation of the white matter cluster from a cluster map.

ventricular fluid spaces, due to the high degree of partial volume effect in the latter regions. As discussed in section 9.6.3, for normal sized ventricles and extra-ventricular spaces, many voxels containing CSF suffer heavily from the partial volume effect. This is confirmed by the large standard deviation of intensities within regions manually delineated by an operator, and a large spread of CSF intensity values in cluster space. Patients suffering from atrophy demonstrated larger CSF spaces. This leads to a reduction in the fraction of voxels that contain CSF which suffer heavily from the partial volume effect. Validation was carried out using two studies of patients and two studies of normals. Manual delineation took between 20 and 30 minutes for each repetition of each measurement on volunteer datasets and between 55 minutes and 1 hour 25 minutes for each repetition of each measurement on atrophied patient datasets. The difference in time for manual delineation between patients and volunteers is due to the difference in ventricular size between the two groups. Identification of CSF was carried out using semiautomatic dual-echo clustering. This required the operator to delineate a border between brain parenchyma and CSF clusters. The border was placed half way between the centres of the two clusters and parallel to the major axis of the brain parenchyma cluster, which takes the trained observer approximately 30 seconds. The position of the border is indicated by Figure 188. The ventricles may be separated from the extra-ventricular CSF by interactively identifying the regions representing the ventricles in each slice. This takes approximately 20 seconds per slice which translates to under 2 minutes for each dataset from normals and under 5 minutes for each dataset from atrophied patients. Alternatively, an automatic approach which identifies the largest connected component for a range of slices may be used. Such an approach will yield an approximate order of magnitude value for ventricular volume but is not expected to be accurate. A 3-D connectivity approach is not applicable for normal ventricles, because the various components are typically not connected in the 5 mm slice thickness and 2.5 mm slice skip data normally acquired.



Figure 188 - Border between brain parenchyma and CSF clusters for semi-automatic CSF identification in cluster space.

Measurements of total CSF give an indication of brain atrophy, assuming the intracranial region remains constant (ie the skull does not change size). This is the case for all of the neurological diseases discussed in this thesis. Equivalently, brain volume could be measured, but this does not give an indication of ventricular and extra-ventricular volume which is important information, for example for differential diagnosis as discussed in section 9.2.2.

9.7.4.2 <u>Results</u>

The ventricular volume is indicated by Table 16. The reproducibility of the measurements is indicated by the percentage difference between the repeat measurements. The repeat measurements made using the dual-echo clustering were worse for the volunteers than for the patients. This is because of the dominance of the partial volume effect in areas containing CSF which produces a spread of intensity values, instead of a cluster of CSF. Thus it is difficult to

accurately delineate between brain parenchyma and CSF. Work using an IR sequence to visualise partial volume effects and Condon's method of CSF measurement (see section 9.6.3) has indicated that only approximately 40-50% of the volume delineated by an expert observer corresponds to CSF for the normal volunteers in this study. This is in broad agreement with the difference between volumes from manual delineation of the ventricles and semi-automatic dualecho clustering as detailed in Table 16. The CSF volumes for normals is in agreement with those values given by Condon *et al.* in section 9.2.2.

Subject	Observer 1	Observer 2	Observer 1	Observer 1
	manual delineation (mm ³)	manual delineation (mm ³)	semi-automatic CSF identification	semi-automatic CSF identification
			manual ventricles identification (mm ³)	automatic ventricle identification (mm ³)
patient 1	84,780 (17.3%)	89,961 (6.0%)	73,439 (0.3%)	72,821 (4.1%)
patient 2	83,898 (11.1%)	88,191 (4.5%)	83,736 (0.2%)	64,188 (0.1%)
volunteer 1	11,948 (26.0%)	18,714 (0.3%)	8,045 (6.8%)	5,952 (6.2%)
volunteer 2	12,880 (4.4%)	15,741 (24%)	7,804 (20.0%)	7,550 (17.8%)

 Table 16 - Volume of ventricles - identification of ventricles from CSF image

9.8 Summary

The identification and quantification of volume changes of neurological structures has been investigated by many authors. To a large extent such work has been based on visual observation or interactive segmentation. The potential for semi-automated and automated approaches to neurological volume measurement is great for conditions such as aging, Alzheimer's disease, schizophrenia, epilepsy and multiple sclerosis. The major sources of geometric distortion - gradient non-linearities, main field non-uniformities, local susceptibility differences and the chemical shift effect have all been considered, their magnitudes for a 1.5 T GE Signa measured, and methods for their correction reviewed. Local susceptibility differences produce the largest distortion, which occurs at borders between air and tissue in regions such as the sinuses and nasopharynx. Unless techniques for the reduction or correction of these distortions are employed, it may be necessary to consider the use of another imaging modality such as CT to image such regions for volume measurement purposes. The slice characteristics of the Signa in terms of slice width, slice warp and slice offset have been studied within the head coil for the primary imaging planes. The performance of the Signa has been demonstrated to be acceptable for all such characteristics.

The magnitude of the partial volume effect is an important consideration for volume measurement. Grey level/edge clustering has been considered as one method for identification of partial volume voxels. The slice thickness of the data used makes such an approach twodimensional in nature. The accuracy of the approach could be improved with near isotropic data, as a three dimensional gradient operator could be used to identify edges in the third dimension. The visualisation of partial volume effects using IR data is proposed as an attractive alternative to grey level/edge clustering which inherently identifies partial volume voxels caused by slice thickness effects. The accuracy of measurement of an anthropomorphic phantom of the human brain as a function of slice thickness has been investigated. Finally, the accuracy of automatic and semi-automatic methods of segmentation proposed in this thesis is compared to that of expert observers. The intracranial volume may be estimated using these methods to within 5% of expert observers' measurements with the accuracy of those slices superior to the eyes within 2.1%. White matter volumes may be calculated to within 10%. The CSF volumes calculated are consistently less than those measured by expert observers due to the inability of the observers to take into account the partial volume effect.

CHAPTER 10

SUMMARY, FURTHER WORK AND CONCLUSIONS

The work reported in this thesis is summarised here, fruitful avenues for future work are suggested and conclusions are drawn.

10.1 Summary

This thesis surveys the image segmentation literature, both in the general case, and as specifically applied to MRI images. The sources of image non-uniformity for our 1.5 T Signa Advantage scanner and methods for their correction have been discussed. A variety of edge-based and region-based segmentation methods have been proposed, and their applicability and limitations discussed. These methods are primarily applicable to dual image pairs which are widely acquired clinically. Image non-uniformity correction and non-isotropic blurring have been proposed as two methods of pre-processing prior to region-based segmentation. The stack, a multi-resolution image segmentation method, has been evaluated and several approaches have been proposed for overcoming some of its drawbacks. The applicability of MRI for volume measurement has been discussed, the clinical literature on volume measurement reviewed and the slice characteristics and the magnitude of geometric distortions have been studied for our Signa scanner. Finally, methods of visualising and quantifying the magnitude of the partial volume effect have been proposed and the accuracy of the edge and region based segmentation methods proposed in this thesis have been evaluated.

10.1.1 Image Non-Uniformity

Image non-uniformity has been investigated for our 1.5 T GE Signa Advantage scanner. The presence of RF standing waves has been demonstrated in water based phantoms, the magnitude of which is dependent upon the permittivity of the sample and which is negligible for oil based phantoms. No evidence of RF standing wave effects has been found for a human subject. The use of digital filtering of data, rather than the more common digital receiver filtering, means that data filtering has a negligible effect on image uniformity apart from the edge 2 or 3 pixels in the frequency encoding direction. It has been demonstrated that RF crosstalk can have major effects on image uniformity and that the use of datasets containing odd and even numbers of image slices produces different characteristic effects. Gradient eddy-currents may also affect images at shorter TRs. There are smaller effects associated with echo time, position of an echo in a multi-echo train and the manufacturer's internal correction for gradient non-linearities. These results show that spin echo data may be accurately corrected for non-uniformity provided that a long TR is used, that non-contiguous data is acquired and that oil-based phantoms are used for correction.

10.1.2 Edge-based Processing

Two and three dimensional edge detection have been compared, demonstrating that for near-isotropic data, edges identified using 3-D operators are better defined and contiguous in neighbouring slices. Interpolating non-isotropic data, where the slice thickness is much greater than the in-slice voxel dimension, generally blurs edges and reduces edge strength, however, making 2-D detection the preferred option for such data. The skin may be defined using a simple edge-tracking procedure on Canny edge images. The eyes have been identified on the basis of their shape using the Hough transform and a low-thresholded Canny edge image. Several edgebased methods of identifying the intracranial region have been proposed including hysteresis thresholding, a fast radial border identification method, and edge focusing - a coarse to fine tracking of edges which provides high positional accuracy with good noise reduction. The ventricles may also be identified using hysteresis thresholding.

10.1.3 <u>Region-based Processing</u>

Image non-uniformity correction and non-isotropic blurring have been proposed as two appropriate methods of pre-processing data prior to region-based processing. It is argued that high quality multi-echo data provides more information to use in the segmentation process, but that care must be taken with data acquisition. If the scanner hardware and software do not produce precisely registered images of the same size then the data will not be suitable for multiimage segmentation. The Institute of Neurology NMR Research Group's previous Picker scanner produced unsuitable data (section 7.2.1) as do some modern scanners [CLARYSSE91]. Thresholding on its own is not commonly used for MRI segmentation because of the effect of RF non-uniformities, noise and inherent tissue heterogeneity. It has been demonstrated that image non-uniformity correction, the application of heavy anisotropic blurring and the use of connectivity allows thresholding to isolate the intracranial region. Normalising late echo image intensity to early echo grey matter intensity allows successful segmentation of the intracranial region in a similar manner. Contrast simulations incorporating the effects of noise have been carried out in order to determine appropriate parameters for dual image clustering and contrast enhancement by image combination. Spin echo, inversion recovery and gradient echo imaging approaches have all been proposed for effective dual-image clustering. The use of non-uniformity correction and anisotropic blurring has been demonstrated to significantly reduce cluster size. It is important that such work be applicable to those images acquired clinically as is the case here.

10.1.4 The Stack

The existence of false extrema in scale-space has been demonstrated and methods of Gaussian blurring compared. The definition of extrema with respect to a sparse grid has been shown to be problematic, indicating that extrema should be defined with respect to a 3x3 local grid. The inability of the stack to handle elongated objects has been demonstrated, and the effects of the stack investigated for neurological MRI images of common content and contrast. No indication of shift-, rotation- or scale- variance was apparent for this implementation of the stack. Pre-processing by anisotropic blurring has been proposed as an effective method for preventing premature joining of a compact region of the neuroanatomy with surrounding tissues, despite good contrast. A method of anisotropic blurring within the stack has been proposed

which can produce a more natural stack than Gaussian blurring. Finally, a split and merge approach for postprocessing the stack tree is proposed in section 10.2.3.

10.1.5 Volume Measurement in Neurological MRI

Clinical applications of volume measurement in neurological MRI have been reviewed, noting in particular that it is important to establish normal volumes using appropriately matched controls before investigations of volumes relating to disease can be made. Four major sources of geometric distortion - gradient non-linearities, main field non-uniformities, local susceptibility differences and the chemical shift effect have been noted; the former two are sample independent, whilst the latter two are sample dependent. The magnitude of these effects has been demonstrated for the 1.5 T GE Signa Advantage scanner used and the accuracy of slice width, slice warp and slice offset shown to be acceptable for the Signa. Several methods of visualising voxels affected by the partial volume effect have been proposed which include grey level/edge clustering, the use of long inversion time IR pulse sequences and dual image clustering. An anthropomorphic phantom of the human brain has been used to demonstrate that the volume calculated using MRI with typical slice thicknesses and slice skips is within the range of uncertainty associated with volume measurement by a water displacement method.

The automatic and semi-automatic methods of segmentation proposed in chapters 6 and 7 have been compared to manual segmentation by human experts. Intracranial volumes are within 5% of the expert observers' volumes (within 2.1% for those slices superior to the eyes) and within 10% for white matter volumes. The volumes of CSF are lower than the expert observers' volumes due to the inability of the observers to take into account the partial volume effect.

10.2 Further Work

There is a wealth of further work that has either been prompted by work described in this thesis, or would be of interest in different application areas. These include firstly data improvements, improvements to processing and comparisons of processing methods. The use of temporal data, information from other modalities and the validation of volume measurement is then considered. Finally other application areas of MRI segmentation, the utilisation of multiple detectors to decide anomalies and ways of increasing algorithm speed are described.

10.2.1 Data Improvements

The quality of data used for the work reported in this thesis has generally been high in terms of contrast to noise ratio and lack of artifacts. There are, however, several improvements to data acquisition that may be possible. The first of these is the use of flow compensation to prevent or reduce the flow artifacts that occur when using the GE fast spin echo sequence. The short time between echoes (typically of the order of 16-18 ms) makes such an addition technically difficult. The second possible improvement is the use of either an inversion recovery sequence, or an inversion pre-pulse prior to a fast spin echo pulse sequence to null the signal from CSF [WHITE92]. This should allow distinction between watery and non-watery lesions and has the added benefit that the difference in signal between CSF and non-watery lesions would be advantageous for a clustering approach to segmentation.

10.2.2 Processing Improvements and Comparisons

A variety of processing improvements and comparisons arise from the work described in this thesis, particularly as relates to dual-image clustering. Several of the most important improvements and comparisons are briefly considered below.

10.2.2.1 Pre-Processing by Non-Isotopic Blurring for Region-Based Segmentation

If appropriate data were available (ie the ratio of distance between slice centres to the in slice voxel dimension was considerably less than the current value of 8) then a 3-D multi-parametric non-isotropic blurring approach would be advantageous. Such data is not currently acquired by the Institute of Neurology NMR Research group, because of the clinician's preference for high SNR data, the increased clinical work load to review scans and the increased cost of storage media.

The possibility of an edge-focusing approach using many different resolution versions of an image (ie different matrix sizes) to increase speed is an interesting one. For example, a low resolution (small matrix size) image could be used for the edge-focusing steps with the largest standard deviation of the blurring gaussian, whilst a larger image could be used for those steps with the smallest standard deviation of the blurring gaussian. Such an approach requires a practical implementation of a multi-scale contour matching algorithm, however, which is non-trivial. The use of edge strength and edge orientation information would be an important part of such an approach.

10.2.2.3 An Edge-Based Stack

Edge-focusing tracks edges through scale-space, but does not use all the information available. The starting standard deviation of the blurring gaussian is the choice of a scale that is considered to be most important, based upon *a priori* information. A more complete approach, and one which requires no *a priori* information, is the concept of a zero-crossing scale-space. As the standard deviation of the blurring gaussian increases, edge maps simplify due to three processes. Firstly, some contours disappear because the edges which they once corresponded to have been smoothed out. Secondly, pairs of contours may merge and subsequently annihilate. Finally, the two ends of a horse shoe shaped contour may join and create two nested contours. The survival of edges in scale-space and their merging, splitting and annihilation is similar in some ways to that of the extrema-based stack. The use of edge orientation and strengths as well as position would be very important in such a scheme.

10.2.2.4 Feature Identification in Scale-Space

The identification of contours in scale space corresponding to the brain, as discussed in section 6.6.3.2, is a simple example of the definition of a region of the neuroanatomy utilising prior knowledge in scale-space. Knowledge of anatomy, edge strengths and how thresholded zero-crossing Canny edge images behave in scale-space have all been used. If an anatomical feature such as this can be identified, then perhaps it can be used to influence scale-space processing. For example, the identification of a contour corresponding to the brain, would allow extrema outside of the brain to be ignored for a stack based approach, which may reject some false or

insignificant extrema in the background.

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10.2.2.5 <u>Comparison of Clustering Methods</u>

It would be very interesting to compare the accuracy of dual-echo clustering and of clustering using PD-, T_1 - and T_2 - weighted images to that using PD, T_1 and T_2 maps. It is not possible to calculate accurate PD, T₁ and T₂ maps for all tissues from typical datasets such as a T₁ weighted spin echo (TR = 500, TE = 20 ms) and PD and T_2 weighted dual echo spin echo (TR = 3000 ms, TE1 = 30 ms, TE2 = 80-90 ms). To calculate T_1s and T_2s of CSF accurately requires one very long TR scan (eg TR1 = 6000, TR2 = 2000), whilst secondly, the calculation of grey matter and white matter T_1 s is not accurate with such a long TR for the T_1 weighted scan. In the latter case, a TR of 300 ms would be more appropriate. To measure the relaxation times accurately would require a number of additional images, which it is not practical to acquire under standard clinical conditions. The use of more than three images for clustering could also be considered if appropriate images could be acquired in a reasonable time. Possibly, some of the images might be obtained as a four echo dataset, for example. The use of non-interleaved image acquisition for clustering requires accurate image registration. As discussed in section 7.2.1, a misregistration of a few mm due to patient motion between scans often leads to CSF in one dataset being registered with grey matter or white matter in another dataset and a similar grey matter/white matter overlap problem. The implementation of an appropriately interleaved sequence yielding T₁-, T₂- and PD- weighted data would be a major advancement in this respect.

10.2.2.6 Adding a Spatial Measure to Clustering

One method of improving current clustering approaches would be to consider the use of a spatial measure in the clustering. This could be achieved by adding an extra dimension to the clustering using a measure of average intensity for a local region, or some form of texture measure etc. Such approaches are successful for other types of image and have been discussed in section 3.5.2

10.2.2.7 Fuzzy Set Partial Volume Voxel Classification

Currently, most clustering approaches, including those described in this thesis to a certain extent impose hard limits on cluster definitions so that each pixel is classified as, for example grey matter, white matter or CSF. This approach gives no capability for the treatment of partial volume voxels. A more flexible approach would consider the membership of cluster classes as being "fuzzy", so that each pixel would be assigned a probability of belonging to a given class. As clusters tend to be pseudo-gaussian in shape, one approach would be to classify pixels corresponding to the peak of the pseudo-gaussian as having 100% probability of belonging to the cluster whilst those out in the wings of the pseudo-gaussian would have a lower probability. The classification of partial volume effect due to slice thickness is of particular importance as it is this, as opposed to in-plane partial volume effects, which dominates partial volume inaccuracies.

10.2.3 A Split and Merge Approach for Postprocessing the Stack Tree

The stack tree description does not fully and accurately represent the natural regions within an image. It may be possible to perform postprocessing on the stack tree description in the form of a split and merge approach to improve the situation. Such an approach requires

- A set of starting regions
- A method of splitting, which should use both a uniformity and a connectivity criterion
- A method of merging using the same uniformity criterion as for splitting

A set of starting regions could be determined by either using all of the regions at the top of the tree, ignoring the small regions at the top of the tree, or pre-merging small regions at the top of the tree with larger regions.

The method of splitting would require some method of characterising the homogeneity of a region such as the region's standard deviation, minimum, maximum, mean or a range of intensities. If the homogeneity criterion is not satisfied for a given region then the region can be split by

- dropping down the tree by one level
- dropping down the tree until the region splits into more than one major region

some other approach for splitting an irregular region, perhaps using edge information

The method would also need a connectivity criterion because separate parts of the image may

be represented by a single node. There are situations when one node representing spatially unconnected regions is advantageous, such as 2-D image slices where two spatially separated parts of the ventricles are represented as one region. A decision would have to be made as to whether this was generally advantageous, however. If the connectivity criterion is not satisfied for a particular region, the region should be split into connected regions.

A large number of nodes at any one level in the tree only represent single pixels. This must be taken into account in a merging strategy which must merge neighbouring regions recursively, possibly pre-merging small regions to larger regions.

10.2.4 Validation of Volume Measurement Using Sophisticated Phantoms

The validation of segmentation is often difficult in neurological MRI because of the highly convoluted nature of many neurological structures, and the high degree of partial volume effect in the heavily anisotropic spin echo or fast spin echo data predominantly. Such images are normally preferred because of the speed advantages over inversion recovery data, and the contrast and image quality advantages over gradient echo data. The availability of a sophisticated, realistic phantom consisting of white matter, grey matter, CSF and lesion compartments would be a major advance in this respect. Such a phantom would mimic the shape of the brain and other tissue borders, would be of a similar size to the brain and have a variety of lesions embedded within it. The volume of each compartment would be known, with the phantom being composed of a variety of gel or fluid compartments with T_1s , T_2s and if required, PDs, similar to that of human tissue. It is important that the phantom be stable with temperature and over time, and that if results are to be compared between sites, that the field dependence of T_1 and T_2 of the gels is known. The gels necessary for such an approach have been described in the literature [KRAFT87, WALKER88, WALKER89, WAITER91, CLINE91]. The major impediments to acquiring such a phantom are cost and complexity; a built to order phantom would typically cost on the order of \pounds 7000, although price would vary with complexity. Several attempts at designing and evaluating such a phantom would probably be necessary.

10.2.5 Temporal Data and Information from Other Modalities

Temporal series of datasets are typically used to study the natural history of disease and response to therapy. It may be possible to use such temporal data to aid segmentation, although how and when such data is used would be application specific. For example, if data were corrected for imager gain, it might be possible to segment brain parenchyma and CSF from one dataset by dual echo clustering, and use the same delineation in cluster space for other datasets.

The use of information from other imaging modalities has great potential for aiding segmentation, provided that a method for accurate registration is available and the resolution of each modality is taken into account. For example, registered MRI and CT data would allow the segmentation of soft tissue, air and bone by thresholding CT data. This would provide valuable information about the localisation of the intracranial region, extra-cranial region and the nasal and orbital regions, for further processing of the MRI data.

10.2.6 Other Application Areas Of MRI Segmentation

There are many applications for the work described in this thesis. Volume measurement has been emphasised as of particular interest, but 3-D graphical display, radiotherapy and surgical planning, image compression, the provision of anatomical maps for correlation with lower resolution techniques, the use of segmentation for reconstruction of other imaging modalities based on a priori information and segmentation as a pre-processing step for image analysis are also of importance.

10.2.7 Utilisation of Multiple Detectors to Decide Anomalies

It has been shown that a range of approaches are necessary for the successful segmentation of a variety of regions of the neuroanatomy. Knowledge of the strengths and weaknesses of a variety of detectors as applied to MR datasets would allow comparison between them. For example, the fast radial CSF identifier works poorly in slices just superior to the eyes, as discussed in section 6.6.2, whilst edge-focusing works well in this area. Knowledge of the strengths and weaknesses of a battery of operators applied to MR datasets would allow the weaknesses of any single operator to be overcome by applying a different operator or operators

in regions of difficulty. Information from different operators could be combined using a nonstatic fuzzy set approach which would calculate probabilities of accurate segmentation as a function of position for a variety of operators.

10.2.8 Algorithm Speed

The speed of the algorithms reported in this thesis vary greatly. For example, the clustering, fast radial CSF identification and normalised thresholding methods are typically quite fast, as is the Hough transform identification of the eyes. Typically, the un-optimised algorithm speeds may be summarised as below in Table 17. Methods using Canny edge images are slower because the algorithm used for this work is FFT based. The current edge-focusing approach is prohibitively slow as FFTs are calculated for each iteration of the algorithm. The speed of these approaches will be improved from the current 23 s per slice by the availability of a recursive algorithm such as that described by Monga *et al.* [MONGA91]. In general algorithms have not been optimised, but if data is to be routinely processed clinically then speed will be important. There are many approaches to improving the speed of the algorithms reported in this thesis. These include

- optimization of algorithms
- array processing, if applicable to the method.
- the use of parallel methods if appropriate.
- multi-resolution processing

improvements in technology. The decreasing cost and increasing performance of new workstation technology has constantly produced faster and more powerful machines. The speed of workstations is currently approximately doubling each year.

■ use of specialised hardware for processing. For example, sub-second (1/20 s) implementations of the Canny edge detector already exist [EVANS90]

Having made such improvements, algorithms must also be tailored to the properties of the workstation on which they will be executed. Factors such as system memory, swap space and whether the disc to which data and temporary files are being written is local or accessed across a network, can have tremendous effects on algorithm speed. For machines with little memory, only small amounts of data should be accessed at any time and then written to disc. For larger memory sizes, such constant disc accessing would probably reduce performance. Writing to discs served by remote machines will be significantly slower than writing to discs on local machines.

Method	Speed
Fast radial CSF identifier	< 3 s
Dual ratio image	< 8 s
Hough transform	< 19 s
Edge-focusing	< 23 s
Basic dual image clustering	< 5 s
Thresholding following anisotropic blurring	< 4 mins 45 s

Table 17 - Comparison of algorithm speeds per image slice

Probably the most time efficient approach to segmentation would be to process different parts of the dataset with different algorithms. The faster methods could be used for those parts of the dataset which are simpler to process, and slower more accurate methods used for the more complex parts of the dataset where simpler methods may produce errors.

10.3 Conclusions

Image non-uniformity correction and non-isotropic smoothing have been shown to be valuable methods of pre-processing prior to intensity based segmentation methods. Image non-uniformity can be accurately corrected for at 1.5 T by the use of non-contiguous datasets of a uniform oil phantom acquired with repetition times not less than 1000 ms and similar echo times to the data. These requirements take into account the effects of standing waves, eddy-currents and cross-talk, but there are also a number of other more minor causes of image non-uniformity. Although axial plane uniformity is generally good for the Signa birdcage head coil, the sensitivity drops off along the major axis of the coil. RF non-uniformity is an even more important consideration for intensity based segmentation methods for those machines with less uniform head coils, such as a saddle coil.

A number of sources of geometric distortion affect neurological MRI. Susceptibility is

particularly important, as are gradient non-linearities. (The latter may be corrected for by a procedure such as GRADWARP, but most manufacturers do not currently use such an approach). B_0 non-uniformity has little affect on spin echo images for the 1.5 T GE Signa used for this work, whilst chemical shift may be important depending upon the application being considered.

The task of segmenting full multi-slice head datasets is arguably more difficult than demonstrating various image processing or artificial intelligence techniques on a limited subset of specially chosen key slices. A variety of edge-based and region-based segmentation techniques have been developed, as no single technique is suitable for all of the tasks. The methods vary in their accuracy, computing requirements, speed and the type of data to which they are applicable. There is often a necessary trade off between these requirements. By using dual-echo images more information is available, which can make the segmentation task easier, whilst taking no more time to acquire than the equivalent single-echo images. This author has successfully segmented the skin, eyes, ventricles, intracranial region, CSF, grey matter and white matter and has carried out some work towards MS lesion segmentation. Edge based techniques include the use of the Hough transform for identifying the eyes, edge-focusing to isolate the intracranial region, hysteresis thresholding to locate the ventricles, and edge tracking to define the skin. Two threshold based methods are also described to segment the intracranial region, whilst contrast enhancement by image combination and dual-image clustering are proposed for the segmentation of CSF, grey matter, white matter and MS lesions. Data driven segmentation algorithms such as the stack are attractive because they have been claimed to be totally general, but there are a number of practical difficulties associated with their use. This author has proposed several methods of improving the stack's performance including pre-processing by anisotropic blurring and the use of anisotropic blurring within the stack.

The methods described in this thesis are largely applicable to dual echo or dual image datasets. Dual echo data is widely acquired clinically so no extra data needs to be acquired. This is important if methods are to gain widespread acceptance. Other authors have often used multiple datasets and such approaches are generally not viable due to the time constraints associated with clinical imaging. Although 3-D methods may appear attractive because of the extra information from the third dimension, in practise clinical data is often not acquired with appropriate slice skip and slice thickness. Gradient echo data may be acquired with appropriate slice characteristics, but such data does not generally give the contrast or contrast to noise ratio required clinically, so SE and IR data are still the most commonly used sequences in

The automatic and semi-automatic methods of segmentation proposed in this thesis have been demonstrated to produce volumes within 5% of an observer's opinion for the intracranial region (within 2% for slices superior to the eyes). Grey matter volumes are within 10% and CSF volumes consistently lower than an expert observer's opinion because of the observer's inability to take the partial volume effect into account. These accuracies are all within the limits required by the Institute of Neurology NMR Research Group clinicians. The automatic and semi-automatic methods of segmentation reduce the human observer's interaction considerably compared with manual delineation. Several methods of visualising and quantifying the partial volume effect are proposed which provide valuable information about the position and extent of voxels suffering from the partial volume effect. The magnitude of the partial volume effect plays an important role in determining the accuracy of many approaches to volume measurement.

There are a number of pieces of further work which would be of great interest to follow up, the most important of which include the construction of sophisticated phantoms for the validation of volume measurement, the utilisation of multiple detectors to decide segmentation anomalies, development of a general partial volume classification algorithm and comparison of the accuracy of a variety of clustering methods.

APPENDIX 1 - STACK PROGRAM DESIGN.

The structure of the author's proposed stack program may be summarised as below. The two most important routines are summarised in pseudocode, and the other main subroutines laid out on the following pages.

Main Subroutine

if (preblur_flag) preblur

initialise_program_structures

extremes - sets current number of minima and maxima

Loop until one max left.

setblur - set standard deviation to blur with depending on number of extrema left.

level++

blurimage

extremes

create_links - create links for both extrema and normals

End loop

Create links Subroutine

Loop for each pixel

if pixel an extrema - link_extrema

End loop

Loop for each pixel

if pixel a normal - link_normal

End loop

permanent_links

print out extrema not linked

print out normals non_linked

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End loop

Create links Subroutine

Loop for each pixel				
if pixel an extrema	- link_extrema			
End loop				
Loop for each pixel				
if pixel a normal	- link_normal			
End loop				
permanent_links				
print out extrema not linked				
print out normals non_linked				

Link_extrema

i

Extremal paths can be characterised by the fact that their intensity should decrease if a maxima and increase if a minima with increasing blurring. This function tries to link an extremum pixel in the lower image to a similar type in the upper image. The general strategy is to search for a parent in the small neighbourhood surrounding the pixel directly above it in the upper image. The extrema in the upper image must be the same type as those in the lower image and their intensities must be correctly related. (eg the intensity of a maximum must decrease towards lower resolution.) There is a maximum intensity difference allowed between a pixel in the lower plane and its parent. If no pixel in the selected upper plane neighbourhood is close enough in intensity to the lower pixel, the neighbourhood is enlarged slightly and the search continues. If no viable candidate is found then maximum intensity difference is incremented and the neighbourhood search repeated. Extrema which do not end up linked to another extremum are passed to link_extrema_to_normal

Link extrema to normal

If the intensity of the extremum is an interpolant among the nonextremum pixels in the region, it is linked to one of them. Otherwise it is assumed that the nonextremum path that it would have become has itself already joined an extremal path. Therefore the extremum is linked to an extremum path, but not as the main path. This is not foolproof.

Link normal

Nonextremum paths can be characterised by two properties namely that their intensity should stay constant along the path and that a point should move along the isointensity path (in x,y,standard_deviation space) in a path of steepest ascent. To ensure that intensity does not drift, an original intensity field is maintained for each path, and this is always used when comparing non-extremum intensities. The 3x3 region above the pixel in the lower plane is tested to see if the pixel is neither a maximum or minimum when compared with these 9 intensity values. If not then it is possible to interpolate this pixel's value to the region. If the intensity of the nonextremum is above (below) the intensity of the current local neighbourhood, the steepest path up (down) hill is traversed. Hill walking is terminated when a region is reached in which the nonextremum path intensity is an interpolant, or when a local extremum is reached. A nonextremum link is not found if hillwalking results in a local extremum being reached without reaching a neighbourhood that has the original path intensity as an interpolant. If no

Link normal to extrema.

In link_normal, a nonextremum link is not found if hillwalking results in a local extremum being reached without reaching a neighbourhood that has the original path intensity as an interpolant. In such a case, link_normal_to_extrema is called and the possibility of linking to an extremum path is examined. There are 3 types of extremum path to check, regular extremum paths, paths which are annihilating at the present level and paths appearing at the present level. The local area is searched for extremum paths. If an extremum is found, and the normals original intensity is between the extremal paths intensity in the two images, the normal path is considered to have annihilated by connecting up with the extremum.

It is more difficult to recognise a near-extremum when the associated extremum itself annihilates between the higher and lower resolution images. This creates two problems. Firstly, how does one continue the extremum path (as a nonextremum path after the extrema annihilates) ? An educated guess must be made as to which nonextremum path it should join. Secondly, since the exact annihilation intensity of the extremum which the near-extrema are near is not known, there can be no accurate intensity range associated with the last link of the extremum path. Yet this range is precisely what near-extrema examine in order to make the decision for linkage to the extremum path. Incorrect links may result from an inaccurate intensity range assigned to the annihilating extremum path.

The link continuing an annihilating extremum is created by hill walking on the lower resolution image until reaching a region where the extremum intensity is an interpolant of the neighbourhood pixel intensities. A link is created to a nonextremum pixel in this neighbourhood. Near-extrema examine the intensity range between the extremum pixel's intensity and the intensity of the nonextremum pixel to which the extremum links. If the near-extremum has an intensity in this range, it is linked to the annihilating extremum. If a decision is made to link to an annihilating extremum path, the near extremum is linked in a manner which incorporates it into the extremul region of the annihilating extremum, and not into the larger region within which the extremum will be resting (the nonextremum path the extremum joins will be associated with this larger region).

PUBLICATIONS ARISING FROM THIS WORK

Simmons A, Arridge SR, Barker GJ, Tofts PS, 1992, Segmentation of Neuroanatomy in Magnetic Resonance Images, Proceedings SPIE Volume 1652, Newport Beach, California

Simmons A, Barker GJ, Tofts PS, Arridge SR, 1992, Improvements to Dual-Echo Clustering of Neuroanatomy in MRI, Abstract 4202, Proceedings of 11th Annual Conference of SMRM, Berlin, Germany

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