VIA MEDICA

Vol. 4, No. 1, pp. 43–45 Copyright © 2001 Via Medica ISSN 1506–9680

communication

# Brain studies — image co-registration and template creation

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# Abstract

Image co-registration requires special software, which is usually available for Unix workstations. This work presents two programs running under MS Windows, one for study co-registration and one for template creation. The co-registration can be done by minimising/maximising the count difference, squared difference, shape and mutual information. The quality of the fit can be estimated by evaluating the contours with different tools. The aligned images can be used for template creation. Both programs can be downloaded from http://www.homolka.cz/nm. Key words: registration, multimodal, mutual information, brain, PET

#### Introduction

In nuclear medicine there is often a need to compare two or more brain studies of the same patient or to compare a study with a "normal" template. This allows to compare the effect of a treatment (to distinguish tumour recurrence and necrotic tissue), to evaluate the cerebrovascular reserve (following from rest and stress scan), to find an epilectic focus (by subtraction of ictal and interictal scan) or to describe the influence of psychiatric disease on the metabolism and to express deviations from a normal study, etc. Therefore many departments and companies develop software which can co-register brain studies, normalise them, do some kind of further processing (finding differences, preparing statistics, ...) and graphically visual-

Correspondence to: Dr. Daniel Janeba Department of Nuclear Medicine — PET Centre Na Homolce Hospital Roentgenova 2, 150 30 Prague 5, Czech Republic Tel: (+420) 2 5727 2169, fax: (+420) 2 5727 2163 e-mail: Daniel.Janeba@homolka.cz ise the performed tasks [1]. The currently available software is usually implemented for Unix workstations. Today's situation in Central and Eastern Europe shows that access to PCs with MS Windows platforms is much easier. Therefore the authors have developed a free co-registration program with several applications running on MS Windows.

#### Method

The procedure of brain study comparison consists of several steps: first, studies have to be selected and scaled into the same space and coordinate system. Then, mutual reorientation follows, after which differences or any other statistics can be calculated and, finally, the output is displayed. When performing a reorientation, one has to keep in mind four important points. First, a class of transformation has to be chosen [2], second, a criterion (cost function) for evaluation of reorientation has to be selected [3–5]. The cost function is a similarity measure, which is maximal or minimal when both images are perfectly aligned. The third point is selection of a numerical algorithm used for searching for the minima/ maxima of the selected function. The last step is checking the coregistration. As the minimisation or maximisation is a non-linear task, one can expect local extremes of the function, which can be clinically incorrect. Therefore it is necessary to evaluate the result visually.

In this work the following cost functions were employed:

- count difference (CD)

$$CD = \sum_{i} (x_i - y_i)$$

where  $x_i$  is the number of counts in the i-th voxel of reference study and  $y_i$  is the number of counts in the i-th voxel of the study being co-registered;

— squared difference (SD)

$$SD = \sum_{i} (x_i - y_i)^2$$

with the same notation of variables; — shape (SH)

$$SH = \sum_{i} (B_i^r - B_i^c)$$

where  $B^{\rm r}$  and  $B^{\rm c}$  are the binary mask set on the reference and co-registered study;



Figure 1. Screenshot of the program Brien.



Figure 2. Tools for visual quality control: a) chess mode, b) contour mode, c) sliding window mode.

- mutual information (MI)

$$MI = \sum_{i,j} H_{i,j}^{rc} \log \frac{H_{i,j}^{rc}}{H_i^r H_j^r}$$

where  $H^r$  and  $H^c$  are the normalised histograms of reference and co-registered study and  $H^{rc}$  is the corresponding joint histogram.

The numerical algorithms used are Powell's method, downhill simplex and conjugate gradients [6].

### Results

The above-mentioned algorithms and cost functions have been implemented into the program Brien running on MS Windows. The program was written in Microsoft Visual C++ 6.0 using MFC libraries 4.2. This program was designed for PET and SPECT studies in the file format Interfile 3.3 [7] but in general MRI studies can also be imported. A screenshot of the program is shown in Figure 1. The program enables basic work with the files when assigning the reference and resliced study designed for co-registration, their display, thresholding, colour table choice, etc. Visualised images can be saved as png files. The co-registration of two PET brain studies (matrix size  $128 \times 128 \times 47$ ) takes about 10–30 minutes when using a standard PC (Celeron 366 MHz, 128 MB RAM).

Special attention was paid to the visual inspection of the coregistration results. The following tools were implemented to give users a way of evaluation of alignment quality. Chess mode (Fig. 2a) splits both studies into squared fields and shows the combined images. If the brains are co-registered properly, one gets a continuous contour of the head. Contour mode (Fig. 2b) shows the contours on a selected level of both images. The better the fit





Figure 3. Joint histogram for perfectly aligned studies and studies shifted by 1 cm.

of the contours, the better the co-registration. Sliding window (Fig 2c) shows a part of the second study in a moving window. A joint histogram used for mutual information calculation can also indicate the quality of co-registration (Fig. 3). During the minimisation process the value of the cost function can be seen on a graph.

Often it is necessary to express mathematically differences between two studies. The mode "differences" can be used for this purpose. It is possible to extract the differences of both studies on a certain level (e.g. 5%, 10% etc.) or to use a template with a standard deviations file as reference study and see the differences of the resliced study in comparison with the created template.

The template can be created in the program Tepito, which also reads Interfile 3.3 files. The program assumes that the inputs are already co-registered and can normalise the studies to total counts, maximum, median or any quantile of the histogram for a whole study or for a selected region. The template file and the standard deviation file are saved also as Interfile 3.3 and can be used in Brien or can be imported to different software.

#### Conclusions

Programs for brain co-registration (Brien) and for template creation (Tepito) running under MS Windows were developed. The co-registration can be done by minimising or maximising count difference, squared difference, shape difference or mutual information and there are several tools to evaluate the co-registration quality (chess mode, contour mode, sliding window and joint histogram). Differences between the two studies or between a study and a template can be shown. The template can be created as a mean value and standard deviations from studies, previously normalised to total counts, maximum or quantile from the histogram. The developed software for brain co-registration (Brien) and template creation (Tepito) is free and can be downloaded from http://www.homolka.cz/nm.

# Acknowledgements

The work was supported by the projects NC 5975-3 (Role of positron emission tomography for the diagnostics of recurrent brain tumour) and LN00B122 (Centre of Neuropsychiatric Studies).

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