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## **The Impact of Different Magnetic Resonance Imaging Equipment and Scanning Parameters on Signal Intensity Ratio Measurements in Phantoms and Healthy Volunteers**

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**Title:** The impact of different MRI equipment and scanning parameters on signal intensity ratio measurements in phantoms and healthy volunteers – implications for interpreting Gadolinium signal changes within the brain

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**Abstract:**

**Objectives:** To examine the variation in Signal Intensity Ratio (SIR) values in Eurospin gel phantoms and healthy volunteer brain images in response to different MRI hardware and software settings.

**Materials and Methods:** Gel phantoms with T1 relaxation times similar to the dentate nucleus (DN), pons (P), globus pallidus (GP) and thalamus (Th) were scanned using a T1-weighted 2D spin-echo sequence on two MRI scanners (3.0T and 1.5T). Imaging was performed by sequentially altering selected MR parameters relative to a default pulse sequence, and the protocol was implemented repeatedly over three months. The experiment was also repeated on a cohort of fifteen young healthy volunteers. Calculations of DN/P and GP/Th SIR values were derived for the images of the gels ( $Gel_{DN/P}$ ,  $Gel_{GP/Th}$ ) and the healthy volunteers ( $HV_{DN/P}$ ,  $HV_{GP/Th}$ ).

**Results:** For the default sequence the mean SIR values of  $Gel_{DN/P}$  and  $Gel_{GP/Th}$  varied by  $\pm 2.20\%$  and  $\pm 0.75\%$  respectively, when measured over multiple imaging sessions (3.0T). Within a single imaging session these variations were smaller ( $\pm 0.17\%$  for  $Gel_{DN/P}$  and  $\pm 0.15\%$  for  $Gel_{GP/Th}$ ). At 1.5T the equivalent SIR variations for  $Gel_{DN/P}$  were  $\pm 1.41\%$  (multiple sessions),  $\pm 0.41\%$  (single session); and for  $Gel_{GP/Th}$   $\pm 0.47\%$  (multiple sessions),  $\pm 0.33\%$  (single session).

Sequential changes to the MR sequence parameters resulted in gel SIR variations as follows:  $14.07 \pm 2.43\%$  (with/without normalisation filters);  $-7.80 \pm 0.28\%$  (different echo times, TE); and  $-5.06 \pm 0.59\%$  (selective activation of RF coil elements). The largest variations were noted when the gels were positioned below the scanner iso-centre - where SIR measurements were different by 22%.

For the healthy volunteers, the SIR values were found to be consistently within 0.64% (single session) for the default sequence. Sequential changes to the MR sequence parameters resulted in SIR variations of  $-24.47 \pm 2.47\%$  (with/without normalisation filters);  $-15.32 \pm 7.71\%$  (different echo times, TE); and  $-2.90 \pm 0.78\%$  (selective activation of RF coil elements).

**Conclusions:** This study has demonstrated that SIR percentage changes from baseline of a similar magnitude to brain gadolinium contrast agent 'signal hyper-intensities' can be replicated in phantom models and healthy volunteers by altering common MR acquisition parameters and hardware.

**Keywords:** MRI; Gadolinium; Contrast; Brain; Hyper-Signal; Phantom; Volunteer

## **Introduction:**

Gadolinium-based contrast agents (GdCAs) have been widely used for clinical MRI investigations for over 25 years. The first agent was Gd-DTPA dimeglumine which gained approval from the US Food and Drug Administration in 1988<sup>1</sup>, and there are now at least nine different commercially available GdCAs which are widely used for imaging in oncology, neurology and cardiovascular MRI studies<sup>2-4</sup>.

The safety profile of these agents is considered to be very good, although minor adverse events such as nausea and dizziness are known to occur in a very small proportion of patients<sup>5,6</sup>. However recently, there have been two notable safety alerts associated with GdCAs and longer term adverse events. One of these has involved the development of Nephrogenic Systemic Fibrosis in patients with end-stage renal disease after receiving agents of a linear structure<sup>7,8</sup>, and the other has involved the gradual development of 'signal hyper-intensities' (SHIs) in the dentate nuclei and globus pallidus within the brain after multiple GdCA injections<sup>9</sup>.

This latter safety alert has gained much recent attention as researchers have sought to quantify the association between GdCA accumulation and the appearance of SHIs<sup>10-16</sup>. Current studies in the field are typically divided into three experimental phases, namely (i) identification of a study cohort (i.e. those patients who have received multiple GdCA injections); (ii) methods of image analysis to identify the SHI regions; and (iii) results and discussion. It has been demonstrated that SHI can be detected on MRI images following at least six separate doses of a GdCA<sup>10-12</sup>.

The image analysis phase consists of the placement of regions of interest (ROIs) over different brain anatomical areas – in locations such as the dentate nucleus (DN) and globus pallidus (GP). These signal intensities are then normalised to the signal intensities of unaffected brain regions, such as the pons (P) or thalamus (Th), giving a 'signal intensity ratio' (SIR) that is used to compare images and detect SHI. The scientific definition of a brain SHI is variable, but studies have described an increase in SIR (e.g. between a baseline image where no contrast has been previously administered and one following

multiple doses of a GdCA) of 4% as being scientifically significant<sup>17</sup>, and 12% as being clinically significant from the perspective of radiological interpretation<sup>18</sup>.

The interpretation of these data involves relatively small changes in signal intensity, and for this reason Ramalho et al. recommended that different MRI pulse sequences should not be used inter-changeably since different contrast mechanisms may confound results<sup>18</sup>. Further studies have discussed and attempted to account for SIR variations associated with different magnetic field strength, sequence type, acquisition parameters etc, but a more definitive study is lacking<sup>12</sup>. The aim of this work therefore was to examine in detail the various hardware and software variations that could potentially affect the SIR values derived from a simple spin-echo pulse sequence.

Specifically, the study was divided into three phases, where firstly we sought to use commercial gel phantoms with  $T_1$  relaxation times closely matched to DN, GP, P and Th in order to establish how variations in common spin-echo pulse sequence settings (such as TR, TE, normalisation filters etc) might affect the SIR of the gels. Secondly, we planned to extend the experiment to involve another scanner vendor in order to establish how variable the measurements were when different scanners were used. Finally, we proposed to repeat the experiment on a small cohort of healthy volunteers in order to examine the effect of the spin-echo pulse sequence variations on SIR measurements derived from normal human brain regions.

This research is considered important since, in practical terms, the time taken for an individual to undergo six MRI scans (and doses of GdCA) may take a number of years – i.e. a sufficiently long time for changes and upgrades to scanner hardware and software to become relevant.

## **Materials and Methods:**

### **Eurospin Gel Phantom Model**

Four different Eurospin 'TO5' commercial gel phantoms were used as the sources of signal intensity for this investigation. The four gels were placed within a phantom holder (figure 1) for each scan and then positioned centrally in an 18 channel head/neck RF coil (Siemens) or an 8 channel head coil (GE). Imaging was performed on a 3T PrismaFIT scanner (Siemens Healthineers, Erlangen, Germany), with a 1.5T Signa Excite HDi scanner (GE Medical Systems, Milwaukee, USA) used for inter-scanner comparison purposes.

The most suitable gels were considered to be those with the closest  $T_1$  values to the brain regions under investigation, namely DN, P, GP and Th. The estimated  $T_1$  values for each of these brain tissue regions at 3.0T are highlighted in table 1 - these data provided by Badve et al.<sup>19</sup> and Madler et al.<sup>20</sup>.

The Eurospin gel manual<sup>21</sup> provides  $T_1$  estimates for all of the 18 gels provided commercially. From table 1, the brain tissue  $T_1$ 's are estimated to fall within the range 900-1100ms, and the theoretical  $T_1$  values for gels 10, 11 and 13 at 3.0T (temperature 296K) were established to be 831ms, 1007ms and 1078ms respectively. These three gels provided the closest match and were therefore used to represent the brain tissues in our study (gel 10 representing GP, gel 11 representing DN, and gel 13 representing both P and Th).

### **Imaging of Phantom Model**

The gel phantom was placed in the centre of the coil and imaging was performed by sequentially altering MR parameters in turn relative to a default protocol (table 2). The default protocol used was a simple  $T_1$ -weighted 2D spin echo sequence, with TR/TE 700/12 ms, 5mm slice thickness, field of view 250x250 mm, matrix 256x256 pixels and bandwidth 130 Hz/pixel. No image filters or partial Fourier techniques were used.

For the first scanning session (Siemens 3.0T scanner), twenty versions of the pulse sequence were applied - with variations as described in table 2. These variations included the sequential application of 'prescan normalise', 'normalise', distortion correction and B<sub>1</sub> filters, changes in TR and TE, and also selection of different subsets of RF channel combinations within the RF coil. The default protocol was performed on six occasions over the duration of the experiment to monitor SI consistency over time. The entire scanning session on the 3.0T machine was repeated a further nine times over the course of a three month period in order to examine the variations in SIR values over a longer timescale. The scanning session was performed three times on a GE 1.5T scanner using the sequential pulse sequence variations as described in table 2 (scans 21 – 35).

For the majority of the scanning, gels were placed within the central slots of the phantom holder. This configuration was considered a good approximation for a head of average size within the centre of the coil, since the four ROIs are located fairly centrally within the brain. However, to model cases where these scanning conditions may have not been met (e.g. a paediatric or infirm patient), the gels were scanned using the default protocol at a location offset from the centre of the field of view (figure 2).

### **Imaging of Healthy Volunteer Cohort**

In addition to the phantom scans, a cohort of fifteen fully consented healthy volunteers (HV) (Integrated Research Application System (IRAS) – ID 80626) was also scanned at 3.0T. The cohort comprised of 8 males and 7 females, mean age 30 years  $\pm$  6 years (range 25-46 years). Exclusion criteria included any individual with a history of gadolinium based contrast agent exposure, or MR specific exclusions such as claustrophobia; presence of metallic implants; devices or foreign bodies e.g. pacemakers, nerve stimulators; surgical clips or metal joints.

Imaging was performed sequentially, using scan numbers 4, 5, 10, 11, 13, 14, 16, 17 (from protocol in table 2) in addition to five further acquisitions using the default parameters. Axial images were



acquired (parallel to the AC-PC line) on each volunteer using the same 2D spin-echo sequence, with 15 slices within the slice block.

### **Image Analysis**

Image post-processing was performed using OsiriX Lite (Version 9.0, Pixemo, Bernex, Switzerland). On the phantom images, circular ROIs were placed over each gel phantom (incorporating approximately  $\frac{3}{4}$  of the total phantom area) and signal intensity values were recorded. On the healthy volunteer images, regions of interest were placed over the DN, P, GP and Th structures using methods as described elsewhere<sup>17</sup>. A single observer (LKY) undertook all measurements, and care was taken to avoid areas of 'partial volume' in order to ensure that the data were properly representative of the structures being measured. Typical ROIs are shown applied on a phantom image and example healthy volunteer images in figure 2.

The ROI data were recorded and converted to SIR for both the phantom ( $Gel_{DN/P}$  and  $Gel_{GP/Th}$ ) and the healthy volunteers ( $HV_{DN/P}$  and  $HV_{GP/Th}$ ). Percentage change in SIR from the nearest previous default scan was calculated and averaged over the repeat scans for each parameter change. Changes in SIR were compared alongside fluctuations associated with the default pulse sequence protocol, and also against definitions of both scientifically significant (4%) and clinically significant (12%) SHI.

## Results:

All phantom scans were performed successfully, and all healthy volunteer images were acquired as intended; no data were excluded from the final analysis.

### Phantom Model

Full details of the phantom default scans on the 3.0T machine are shown in figure 3 - illustrating the 'intra-session' and 'scan-to-scan' repeatability for measurements of the mean phantom DN/P ratio ( $Gel_{DN/P}$ ) and the mean phantom GP/Th ratio ( $Gel_{GP/Th}$ ). The mean  $Gel_{DN/P}$  derived from the default sequence across the ten imaging sessions (y-axis) was  $1.04 \pm 0.02$  ( $\pm 2.20\%$ ), and the mean  $Gel_{GP/Th}$  was  $1.21 \pm 0.01$  ( $\pm 0.75\%$ ). From figure 3, the mean 'intra-session' (x-axis) standard deviation was even lower ( $Gel_{DN/P}$ :  $\pm 0.002$  ( $\pm 0.17\%$ );  $Gel_{GP/Th}$ :  $\pm 0.002$  ( $\pm 0.15\%$ )). Similar data were obtained from the 1.5T machine, where the mean  $Gel_{DN/P}$  derived from the default sequence across the three imaging sessions was  $0.92 \pm 0.01$  ( $\pm 1.41\%$ ), and the mean  $Gel_{GP/Th}$  was  $1.07 \pm 0.01$  ( $\pm 0.47\%$ ). The mean 'intra-session' (x-axis) standard deviation was  $Gel_{DN/P}$ :  $\pm 0.004$  ( $\pm 0.41\%$ );  $Gel_{GP/Th}$ :  $\pm 0.004$  ( $\pm 0.33\%$ ).

From table 3, the default scanning conditions (scans 2, 9, 12, 16, 19, 22, 29, 32, and 35) resulted in very stable SIR values for both gel ratios when measured over successive scans within a session. The percentage SIR changes from the baseline default scan were found to be consistently within 0.47% - irrespective of whether the measurements were made at 3.0T or 1.5T (including the use of different vendor hardware and software). These data suggest that if the MR protocol is kept identical over time then SIR values do remain stable.

Small variations to the MR pulse sequence parameters resulted in changes of greater than 2.20% in a number of situations for the gels. The use of normalisation filters and signal intensity filters on both vendor machines resulted in changes to the measured SIR for each gel. The largest SIR change was measured for  $Gel_{DN/P}$  in the presence of the surface coil intensity correction (SCIC) filter, which resulted in a SIR change of  $14.07 \pm 2.43\%$  relative to the baseline value in the default protocol (no filters

applied). Of the other pulse sequence parameters examined, changes to the TR and TE also resulted in SIR changes of greater than 2.20%. The largest SIR change was measured for  $Gel_{DN/P}$  ( $-7.80 \pm 0.28\%$ ) at 1.5T when the TE was set to 36ms, relative to the baseline value (12ms) in the default protocol.

The use of selected RF coil receiver elements also had a clear effect on the measured SIR for both gels. The largest change was identified when elements H3+4 were selectively activated and the SIR value of  $Gel_{GP/Th}$  changed by  $-5.06 \pm 0.59\%$  relative to the default protocol condition.

The largest gel SIR variations however were noted when the phantoms were positioned slightly below iso-centre (figure 2) on the 3.0T machine. The SIR measurements at this 'off-axis' position were different by approximately 22% ( $-21.45 \pm 0.73\%$  for  $Gel_{DN/P}$  and  $-23.67 \pm 0.16\%$  for  $Gel_{GP/Th}$ ) relative to the default sequence performed with the gels positioned at iso-centre. These data suggest that measurements of SIR values are highly dependent upon the precise position of each ROI within the RF coil architecture.

### **Healthy Volunteer Data**

For the healthy volunteers, the mean DN/P ratio ( $HV_{DN/P}$ ) over 15 scan sessions was  $1.35 \pm 0.06$  and the mean GP/Th ratio ( $HV_{GP/Th}$ ) was  $1.09 \pm 0.04$ . The default scanning conditions within a session (scans 9, 12, 16, and 19) resulted in very stable SIR values when measured on the 3.0T machine. The percentage SIR changes from the baseline scan were found to be consistently within 0.64% - again suggesting that if the MR protocol is kept identical over time then SIR values do remain stable.

Small variations to the HV SIR measurements were again noted in response to small changes made to the MR pulse sequence parameters. Images acquired with the use of normalisation filters resulted in a 'worst case' mean SIR change of  $-24.47 \pm 2.47\%$  (for  $HV_{DN/P}$ ) relative to the baseline value in the default protocol (no filters applied) (figure 4). Variations in the TE also resulted in notable SIR changes, the largest of which was a mean HV SIR change of  $-15.32 \pm 7.71\%$  (for  $HV_{GP/Th}$ ) when a TE of 36ms was used, relative to the baseline value (12ms) in the default protocol (figure 4).

Finally, the use of selected RF coil receiver elements also had a small effect on the measured SIR values. The largest change was identified when RF coil elements H1-4 were selectively activated and the SIR value of  $HV_{DN/P}$  changed by  $-2.90 \pm 0.78\%$  relative to the default protocol condition.

## **Discussion:**

In this MRI study, a 'Eurospin' gel phantom and a cohort of healthy volunteers have been scanned in order to establish the effects of sequential hardware, software and positional variations on repeated signal intensity measurements. The results have established that repeated measurements over time using identical scan parameters do result in consistent SIR values. However the on/off activation of pulse sequence normalisation or signal intensity filters; small changes to the pulse sequence TR or TE; the selection of different combinations of RF coil elements; and the geometrical position of the object within the RF coil can all cause variations to the measurement of SIR values – sometimes by as much as 24%. These findings may have implications for the correct interpretation of GdCA 'signal hyper-intensities' in patient studies, where images from typically six successive contrast-enhanced clinical scans are compared over varying periods of time. For an individual patient, it is most unlikely that the hardware, software and positional settings will remain consistent over time – and for this reason the interpretation of GdCA signal hyper-intensity measurements should be interpreted and reported with these potential sources of error in mind.

The measurement of SIR was undertaken in order to mimic the approaches of previous studies in the field<sup>9-11,14,15,17</sup>. The original work by Kanda et al<sup>9</sup> identified increases in SI within the deep brain nuclei of the DN and the GP, and these regions are found anatomically within the same axial field-of-view as the P and Th respectively - which both remain unenhanced. The P and Th can therefore be used as anatomical controls for DN and GP within the same imaging slice. By using SIR calculations (DN/P and GP/Th), scanner performance variations associated with SI subtraction or difference techniques can be overcome. The SI changes at the P and DN are therefore normalised across the same imaging slice which should make the measurements more comparable across different scanners and imaging centres.

Previously published studies have discussed the concept of GdCA 'signal hyper-intensity' measurements and to what extent the changes in measured SIR values may prove to be scientifically

and/or clinically relevant. Previous studies suggest that clinically relevant changes are likely to be of the order of 12%, and scientifically relevant changes are likely to be of the order of 4%<sup>17,18</sup>. In this investigation, we considered all SIR changes – whether it be a negative or positive value. This approach differs from the clinical scenario in which GdCA ‘signal hyper-intensities’ are associated with increased SIR values, but the magnitude of SIR change was the main interest in this study. These are considered relevant since the reported ‘negative’ changes may also occur in the clinical situation if the pulse sequence parameters, hardware or patient positioning vary over time.

Changes associated with pulse sequence normalisation or signal intensity filters had a great impact on the measured SIR values. Receiver coils have the highest sensitivity closest to the surface of the object which can result in signal ‘flare’ at the periphery of the images if normalisation or intensity correction filters are not applied. The results presented here reflect the fact that if different sets of clinical images are being compared and the filter settings are not consistent between scans then SIR variations of up to 25% may be present. It is also clear that while machine vendors offer equivalent intensity correction filters, they can impact images differently. Algorithms used for intensity correction are known to vary in performance<sup>22</sup>. For the healthy volunteers, the average change in DN/P following the application of the normalise filter was much greater than was observed in the phantom model (24.47% vs -2.81%). This may indicate that the anatomical location of the DN and/or P is physically lower within the RF coil than was assumed in the centrally configured phantom – i.e. the healthy volunteer data may therefore be more susceptible to signal changes due to surface coil flare when filters are not applied.

The phantom used for this study was chosen carefully in order to best represent the brain regions of interest that have been associated with GdCA accumulation. A compromise was reached, where the gel T<sub>1</sub> values were closely matched to those of the brain regions of interest, and the measured SIR values were similar to those reported in the literature<sup>9</sup>.

The default SIR values for the gels were very consistent within the course of a specific scanning session, and a little less consistent when measured on a scan-to-scan basis (ten sessions over a three-month

duration). The minor drop in consistency was thought to be related to variations in ambient conditions within the scanner room (principally temperature) as these were not controlled within the study. However this variation represents the 'real world' situation where clinical scans are undertaken without routine scanner room temperature monitoring. The 'scan to scan' consistency of measurements derived from the default protocol was therefore deemed to represent the more realistic measure of SIR measurement stability.

In all experimental scenarios, increasing the TE resulted in changes to measured SIR values - of comparable magnitudes to 'signal hyper-intensities' (4%) and in some cases simulating clinical relevance (12%). In this study the gel  $T_2$  values were largely disregarded, although it is accepted that the signal from the gels and the HV tissues will have an influential component of  $T_2$  relaxation. Whilst the  $T_1$  values of the DN and P (and gel equivalents) are fairly similar, the  $T_2$  values of the gel equivalents are markedly different (139ms and 223ms at 1.5T and 292K<sup>21</sup>) and changes in SIR are observed as a result of  $T_2$  decay variations between the gels. This is also similar for the GP and Th gel equivalents, but the  $T_2$  values are a little closer (160 and 223ms at 1.5T and 292K<sup>21</sup>) – resulting in a slightly smaller change in SIR. Typically in the literature, the longest TE reported for  $T_1$ -weighted spin-echo sequences is approximately 20ms<sup>12</sup>. In the present study it may be argued that a TE of 36ms is too long. However the results remain demonstrative of the fact that potential changes in SIR may be achieved via alterations to the TE.

Altering the pulse sequence TR appeared to only affect the Gel<sub>GP/Th</sub> SIR. Since the  $T_1$  values for the Gel<sub>GP</sub> and Gel<sub>Th</sub> are dissimilar, they recover at different rates and this is reflected in the SIR change. Conversely, the relaxation times of the Gel<sub>DN</sub> and Gel<sub>P</sub> are quite similar, so altering the TR had little impact on Gel<sub>DN/P</sub>. Interestingly, the dependency on TR was not observed in the HV measurements, indicating that the  $T_1$  values of the GP and Th at 3.0T may in reality be more alike. Again, previous studies have acquired images with large TR ranges (typically between 300 and 700ms<sup>23,24</sup>) so associated variations in SIR may be relevant.

There were a few specific observations of note that were encountered only within the HV cohort. As the internal carotid artery is anterior to the DN, flow artefacts were noted to run through the centre of the DN when phase encoding was set from anterior to posterior (A-P). As a result, after initial testing we acquired our images with the phase encoding direction set from left to right (L-R). Although not considered further in this study, an average change in DN/P SIR of approximately 3-4% may be observed when phase encoding directions differ between acquisitions. In published studies, where an ROI is affected by artefacts, the images are usually either excluded or partial ROIs are sampled<sup>23</sup>.

This study has a number of limitations. The major limitation is that, in practice, the pulse sequence acquisition parameters are often altered in multiple combinations to achieve the desired image quality. In this study, parameters were changed individually such that SIR changes could be attributed to specific variables – i.e. we could not account for multiple factors within a single experiment. Another limitation was that the gel  $T_2$  values were not matched to the anatomical areas that they represented. However we still consider the ‘proof of concept’ that TR and TE changes can alter the measured SIR values to be valid. Thirdly, not all pulse sequence variables were tested fully.

In future work it would be useful to explore in more detail whether the phase encoding direction has a consistent effect on measured SIR differences. Similarly, it would be useful to examine other pulse sequence parameters such as the sequence bandwidth, image resolution, RF pulse types etc in order to see what other factors might affect the SIR measurements. Finally, it is acknowledged that in some previous patient studies involving GdCA ‘signal hyper-intensities’, comparator cohorts of images from patients who have undergone non-contrast MR imaging have been used to gather control SIR data<sup>9</sup>. It is possible therefore that if the non-contrast images were also acquired under a variety of acquisition parameters, that they may exhibit equivalent SIR fluctuations to the images from contrast exposed populations – i.e. the ‘non contrast’ group could by definition control for the type of changes that we report within this study. However in many situations ‘non contrast’ control populations are not reported – in which case the results of this study then become relevant.



In conclusion, this study has demonstrated that SIR percentage changes from baseline of a similar magnitude to those quoted as GdCA 'signal hyper-intensities' can be replicated in both phantom models and healthy volunteers by altering common MR acquisition parameters and hardware. It is therefore recommended that for future brain MR studies involving GdCAs that the effects of different MR hardware, pulse sequence parameters and positional variations are carefully considered when drawing conclusions about the significance of signal hyper-intensities.

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## Figure Legends:

Figure 1: Gel phantoms positioned centrally within a Siemens 18 channel head/neck RF coil.

Figure 2: Example phantom and healthy volunteer images, with schematic ROI positioning used during the post-processing analysis – to derive the DN/P and GP/Th ratios. Gels were placed within the centre of the phantom to represent the normal anatomy as closely as possible. Gels were also placed posteriorly away from iso-centre; a displacement of 4cm.

Figure 3: Mean  $Gel_{DN/P}$  (a) and  $Gel_{GP/Th}$  (b) acquired from the 3.0T phantom images. The individual data points (1-10) highlight mean (+/- SD) SIR values for all default sequences that were acquired during ten individual scanning sessions – i.e. these represent ‘within session’ SIR variations. The dotted lines represent the upper and lower SD of data acquired across ten scanning sessions – i.e. this represents the ‘scan-to-scan’ SIR variation.

Figure 4: Example images acquired from one healthy volunteer. (a) is the default sequence at the slice of the DN and P, (b) is the same slice but with the normalisation filter applied (change in  $HV_{DN/P}$  - 22.52%), (c) is the default sequence at the slice of the GP and Th, (d) is the same slice acquired with a TE of 36ms (change in  $HV_{GP/Th}$  -23.08%).

**Tables:**

Anatomical Region	T <sub>1</sub> (ms) at 3.0T		Average
	Right	Left	
Dentate Nucleus <sup>1</sup>	1012.5	1024.5	1018.5
Thalamus <sup>1</sup>	1072.5	1077.0	1074.8
Pons <sup>1</sup>	N/A	N/A	1054.1
Globus Pallidus <sup>2</sup>			951

Table 1

Table 1: Table of T<sub>1</sub> values (ms) at 3.0T. Single ROIs were used to measure the relaxation rates of the pons and globus pallidus. Data were provided by <sup>1</sup>Badve et al.<sup>19</sup> and <sup>2</sup>Madler et al.<sup>20</sup>.

Table 2

Scan No.	Field Strength	Position of Gels	TR (ms)	TE (ms)	RF Coil Elements	Filters
1	3.0T	Isocentre	700	12	H1-4, N1-2	None
2	3.0T	Isocentre	700	12	H1-4, N1-2	None
3	3.0T	Isocentre	700	12	H1-4, N1-2	Prescan Normalise
4	3.0T	Isocentre	700	12	H1-4, N1-2	Normalise
5	3.0T	Isocentre	700	12	H1-4, N1-2	B1 Filter Medium
6	3.0T	Isocentre	700	12	H1-4, N1-2	Distortion Correction
7	3.0T	Isocentre	700	12	H1-4, N1-2	Image Filter Medium
8	3.0T	Isocentre	700	12	H1-4, N1-2	Normalise + Distortion Correction
9	3.0T	Isocentre	700	12	H1-4, N1-2	None
10	3.0T	Isocentre	400	12	H1-4, N1-2	None
11	3.0T	Isocentre	1000	12	H1-4, N1-2	None
12	3.0T	Isocentre	700	12	H1-4, N1-2	None
13	3.0T	Isocentre	700	12	H1-4	None
14	3.0T	Isocentre	700	12	H3-4	None
15	3.0T	Isocentre	700	12	H1-2	None
16	3.0T	Isocentre	700	12	H1-4, N1-2	None
17	3.0T	Isocentre	700	24	H1-4, N1-2	None
18	3.0T	Isocentre	700	36	H1-4, N1-2	None
19	3.0T	Isocentre	700	12	H1-4, N1-2	None
20	3.0T	Off-isocentre	700	12	H1-4, N1-2	None
21	1.5T	Isocentre	700	12	8ch head	None
22	1.5T	Isocentre	700	12	8ch head	None
23	1.5T	Isocentre	700	12	8ch head	SCIC
24	1.5T	Isocentre	700	12	8ch head	Intensity Filter A
25	1.5T	Isocentre	700	12	8ch head	Intensity Filter A + SCIC
26	1.5T	Isocentre	700	12	8ch head	Extended Dynamic Range
27	1.5T	Isocentre	700	12	8ch head	PURE
28	1.5T	Isocentre	700	12	8ch head	Intensity Filter A + PURE
29	1.5T	Isocentre	700	12	8ch head	None
30	1.5T	Isocentre	400	12	8ch head	None
31	1.5T	Isocentre	1000	12	8ch head	None
32	1.5T	Isocentre	700	12	8ch head	None
33	1.5T	Isocentre	700	24	8ch head	None
34	1.5T	Isocentre	700	36	8ch head	None
35	1.5T	Isocentre	700	12	8ch head	None

Table 2: Details of sequence variations within the phantom scanning protocol. Only those parameters that were altered during the course of the protocol are shown, other variables remained constant as follows: slice thickness 5mm; field of view 250mm; pixel matrix 256x256; and bandwidth 130 Hz/pixel. Scan numbers 1, 2, 9, 12, 16 and 19 are the default

sequences acquired on the Siemens scanner. Scan numbers 21, 22, 29, 32 and 35 are the default sequences acquired on the GE scanner.



Table 3

Scan No.	Parameter changed	Mean Gel <sub>DN/P</sub> (% change from baseline)	Mean Gel <sub>GP/Th</sub> (% change from baseline)	Mean HV <sub>DN/P</sub> (% change from baseline)	Mean HV <sub>GP/Th</sub> (% change from baseline)
1	-	-	-	-	-
2	-	0.05 ± 0.11	0.04 ± 0.09	-	-
3	Prescan Normalise	-0.71 ± 1.23	-0.69 ± 0.04	-	-
4	Normalise	-2.81 ± 1.52	-1.34 ± 0.61	-24.47 ± 2.47	-4.17 ± 3.89
5	B1 Filter Medium	0.51 ± -3.48	2.14 ± -1.15	-15.93 ± 3.03	-0.95 ± 2.55
6	Distortion Correction	0.43 ± 0.29	0.38 ± 0.24	-	-
7	Image Filter Medium	0.22 ± 0.32	0.32 ± 0.29	-	-
8	Normalise + Distortion Correction	-2.80 ± 1.46	-1.21 ± 0.69	-	-
9	-	0.13 ± 0.35	0.09 ± 0.30	0.64 ± 1.70	-0.10 ± 0.94
10	TR = 400ms	0.07 ± 0.90	2.54 ± 1.04	0.34 ± 1.53	0.40 ± 1.37
11	TR = 1000ms	-0.59 ± 0.80	-3.22 ± 0.60	-0.82 ± 1.47	-0.68 ± 1.26
12	-	-0.13 ± 0.24	-0.03 ± 0.25	0.28 ± 1.29	-0.23 ± 1.32
13	H1-4	-3.05 ± 0.66	-1.76 ± 0.45	2.90 ± 0.78	0.03 ± 1.05
14	H3-4	-2.85 ± 1.49	-5.06 ± 0.59	2.39 ± 1.44	0.84 ± 3.89
15	H1-2	-0.56 ± 0.90	0.81 ± 0.47	-	-
16	-	0.03 ± 0.06	-0.14 ± 0.05	-0.38 ± 1.26	0.09 ± 0.75
17	TE = 24ms	-3.59 ± 0.62	-2.41 ± 0.52	-6.09 ± 10.59	-7.90 ± 4.26
18	TE = 36ms	-7.54 ± 0.72	-5.20 ± 0.64	-8.89 ± 4.34	-15.32 ± 7.71
19	-	0.05 ± 0.28	0.11 ± 0.21	0.15 ± 1.36	-0.03 ± 0.84
20	Off-isocentre	-21.45 ± 0.73	-23.67 ± 0.16	-	-
21	-	-	-	-	-
22	-	0.36 ± 0.11	-0.20 ± 0.21	-	-
23	SCIC	14.07 ± 2.43	12.31 ± 0.33	-	-
24	Intensity Filter A	0.43 ± 0.92	-0.23 ± 0.53	-	-
25	Intensity Filter A + SCIC	13.38 ± 2.72	12.19 ± 0.27	-	-
26	Extended Dynamic Range	-0.09 ± 0.68	-0.28 ± 0.63	-	-
27	PURE	9.42 ± 1.94	10.96 ± 0.24	-	-
28	Intensity Filter A + PURE	9.40 ± 2.53	10.71 ± 0.05	-	-
29	-	-0.24 ± 0.69	-0.47 ± 0.35	-	-
30	TR = 400ms	0.41 ± 0.52	2.71 ± 0.53	-	-
31	TR = 1000ms	-0.65 ± 0.66	-3.25 ± 0.15	-	-
32	-	-0.21 ± 0.54	-0.35 ± 0.20	-	-
33	TE = 24ms	-3.52 ± 0.37	-2.41 ± 0.05	-	-
34	TE = 36ms	-7.80 ± 0.28	-5.12 ± 0.29	-	-
35	-	0.45 ± 0.39	0.28 ± 0.13	-	-

Table 3: Average phantom SIR percentage changes from baseline for each parameter alteration made over successive scans. The highlighted cells indicate percentage changes that were greater than the largest mean scan-to-scan changes ( $\pm 2.20\%$ ) derived from repeated acquisitions using the default protocol. Further details of the scan parameters prescribed for each scan (1-35) are described in table 2.