Proton magnetic resonance spectroscopic imaging (MRSI) in a clinical setting: a scheme to reduce chemical shift VOI misregistration-induced metabolite ratio bias in edge voxels

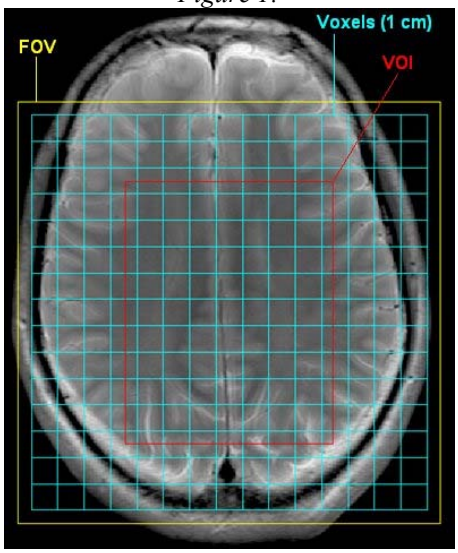
David J Manton[1], Lawrence Kenning[1], Ralph Noeske[2], Timo Schirmer[3], Gary P Liney[4], Martin Lowry[1], Martin D Pickles[1], Richard Bartlett[5], Christopher Rowland-Hill[5], and Lindsay W Turnbull[1]

[1]*YCR Centre for MR Investigations, The University of Hull, Hull, East Yorkshire, United Kingdom,* [2]*Applied Science Laboratory Europe, GE Healthcare, Berlin, Germany,* [3]*Applied Science Laboratory Europe, GE Healthcare, Muenchen, Germany,* [4]*Radiation Physics, Hull & East Yorkshire Hospitals NHS Trust, Cottingham, East Yorkshire, United Kingdom,* [5]*Radiology Department, Hull & East Yorkshire Hospitals NHS Trust, Hull, East Yorkshire, United Kingdom*

Introduction: Proton magnetic resonance spectroscopic imaging (MRSI) has shown clinical utility in defining optimal target volumes for radiotherapy treatment of brain tumours [1], but metabolite ratio bias arising from chemical shift-induced volume of interest (VOI) misregistration is a well-known an unwelcome confounding factor. This bias can be ameliorated using a range of techniques including buffer/dummy edge voxels, voxel over-sizing (whereby the VOI is enlarged by a given factor the trimmed back using saturation bands), and spectral-spatial or adiabatic pulses with increased excitation bandwidth. But where these facilities are not available (on clinical scanners, for example), or where their use is prohibited by the anatomy (tumours adjacent to the skull, for example, where out-of-volume lipid contamination of spectra is a concern), then some kind of calibration correction may be the only approach available. A robust phantom-based calibration protocol has, therefore, been developed for clinical use.

Methods: 2D MRSI was carried out in three normal, healthy volunteers and a spherical phantom test object filled with an aqueous model solution of brain metabolites (GE Healthcare, USA) using an MR750 3.0 Tesla clinical MRI scanner (GE Healthcare) and a PRESS pulse sequence (TR/TE = 1000/144 ms; pulse flip angles and bandwidths = 90°/137°/137° & 2367/1345/1345 Hz; default slice select centre frequency offset = –256 Hz; 16 cm field-of-view, FOV; 16×16 phase-encode grid; 1 cm slice thickness). VOIs measuring 7×9×1 cm were excited in all studies surrounded by a buffer zone of half-width voxels (see Fig. 1). The voxel over-sizing (overpress) factor was left at the default value of 1.0 for all studies, as higher values had previously been shown to give rise to increased out-of-volume lipid contamination in cases where tumours are near the skull.

Figure 1:



The frequency separation of water and choline was noted in volunteer (body temperature) and phantom (room temperature) studies, as the chemical shift of water is known to be temperature dependent, thus allowing the slice select centre frequency offset (SSCFO) to be changed in the final phantom studies so as to ensure that the offset geometry was the same for *in vivo* and calibration data. Choline:NAA concentration ratios (CNCRs) were measured using LCModel (s-provencher.com), and a calibration map was calculated from the phantom experiments by normalising the CNCRs to the mean CNCR in the central 3x3 voxels.

Figure 2:

Extra offset = -25 Hz (simulated body temp.)							3x3 median filtered centre-norm'd choline:NAA
121%	131%	143%	139%	145%	144%	166%	
88%	100%	101%	101%	108%	105%	120%	
83%	104%	101%	102%	104%	97%	110%	
85%	106%	107%	107%	102%	97%	109%	125%-135%
82%	97%	103%	104%	96%	97%	107%	115%-125%
79%	95%	99%	95%	89%	96%	108%	105%-115%
81%	101%	99%	96%	96%	97%	107%	95%-105%
82%	102%	99%	101%	106%	103%	112%	85%-95%
58%	71%	69%	72%	76%	75%	88%	75%-85%

							Centre row or column-referenced paired t tests
121%	131%	143%	139%	145%	144%	166%	
88%	100%	101%	101%	108%	105%	120%	
83%	104%	101%	102%	104%	97%	110%	
85%	106%	107%	107%	102%	97%	109%	
82%	97%	103%	104%	96%	97%	107%	
79%	95%	99%	95%	89%	96%	108%	
81%	101%	99%	96%	96%	97%	107%	P < 0.004
82%	102%	99%	101%	106%	103%	112%	p < 0.05
58%	71%	69%	72%	76%	75%	88%	p >= 0.05

Results: Comparison of *in vivo* and *in vitro* spectra showed the optimal room temperature SSCFO adjustment to be -25Hz. Fig. 2 gives the raw, centre-normalised CNCR ratios from a phantom experiment with optimal SSCFO adjustment, along with a colour map based on centre-normalised CNCR ratios after application of a 3×3 median smoothing filter. Data in the top and bottom rows, and the left- and right-most columns demonstrated statistically significant bias when compared to the central row or column using paired t-tests ($p < 0.004$, this being a Bonferroni corrected threshold of 0.05 divided by 14; the total number of columns and rows investigated), as also shown in Figure 2. The presence of significant bias *in vitro* demonstrated the need for calibration of *in vivo* studies, and the application of the calibration map to volunteer CNCR data allowed a more faithful representation of the metabolism of the normal brain to be calculated.

Conclusions: It has been shown that MRSI CNCRs obtained using a clinical scanner PRESS protocol (overpress = 1.0) can demonstrate appreciable bias (from 42% too low to 66% too high over a 7×9 cm VOI) in a homogenous phantom, even when using buffer voxels. Where these systematic errors are present, they can be corrected for by using a simple calibration map generated using phantom data. Failure to address and correct for metabolite ratio bias could lead to erroneous contours being used in radiotherapy treatment planning systems, thus leading to potentially sub-optimal effects upon clinical outcome.

[1] Functional MRI for radiotherapy of gliomas. (Review) Chang & Narayana. *Tech. Cancer. Res. Treat.* 9(4), 347-358 (2010).