Feasibility of Multi-platform, Multi-site Clinical Trials of Proton MRS

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Background: Despite repeated publication of MR brain spectra which show pathological abnormalities indicative of several disease processes[1], recent EBM surveys[2] universally reject its clinical diagnostic utility. Among the several criticisms leading to these conclusions are 1) Lack of standard MRS acquisition techniques; 2) Absence of multi-site trials on significant numbers of patients. In addressing these concerns, it will be important to demonstrate MRS findings that are independent of the manufacturer. In the present study we report normative MRS data for adults in two commonly employed platforms: GE 1.5T where an automated MRS procedure, PROBE, has been in use world-wide for many years, and Toshiba 1.5T newly introduced to the clinical field.

Methods and Human Subjects: Closely similar, but not identical acquisition conditions (GE: PRESS TE 35ms; 144ms, single voxel MRS and TE 35ms PRESS multi-voxel CSI; Toshiba Spin-echo a.k.a. PRESS TE 25ms; 136ms, single voxel MRS and TE 136ms spin-echo multivoxel CSI) were chosen for the study, based upon the optima selected by each Manufacturer. Voxel dimensions (2x2x2cm), locations (posterior cingulate gyrus for grey matter GM and L lateral parietal lobe for white matter WM) and number of acquisitions, 128 were kept constant to ensure comparable SNR. Manufacturer's automated, observer independent data processing, was applied with peak areas determined automatically, and heights determined manually. An identical 'phantom' containing five cerebral metabolites at known concentrations ("braino") was examined five times in each MR scanner, employing each of the 3 MRS/CSI techniques described. 20 normal subjects and 20 patients with well defined MRI pathologies were examined in each MR scanner. 40 spectra from each platform were evaluated, each by three independent observers. Data were expressed as ratios to Cr peak height (or area) and statistics applied were paired or unpaired t-test to obtain mean +/- standard error of the mean (SEM).

Results: All spectra acquired from normal subjects were of acceptable technical quality. Normal variation (SEM) for the principal metabolite peak-ratios, NAA/Cr, Cho/Cr and mI/Cr (in TE 25 and 35ms) between 5 – 12%. Normal metabolite ratios were indistinguishable for NAA/Cr and Cho/Cr ($P > 0.1$) but mI/Cr was significantly higher in Toshiba than GE ($P < 0.001$) spectra. Pathological spectra (Fig 1) acquired with Toshiba: Vantage showed very comparable features to those previously identified with GE LX.

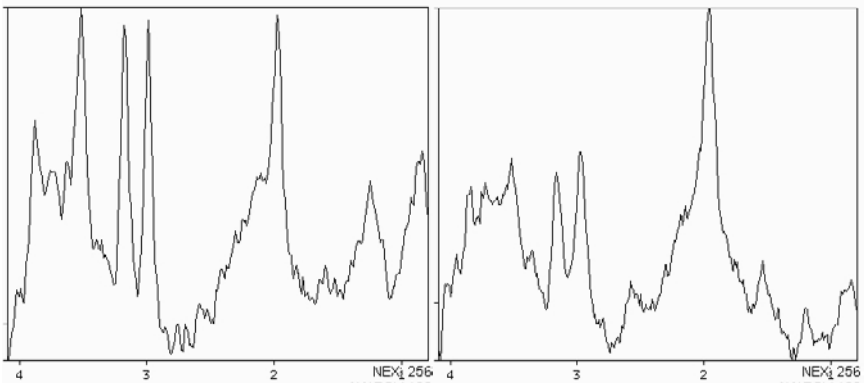

Fig 1: Representative pathological (left) and normal control (right) spectra from basal ganglia on Toshiba 1.5 T. MRI (not shown) was suggestive of low grade glioma or PML within right thalamus.

Discussion: None of the commonly feared pitfalls were identified in this cross-manufacturer MRS Trial. Using Manufacturers' optimized acquisition criteria, the two platforms generated identical MR spectra at short (TE 25 or 35ms) or long (TE 136 vs 144ms) echo times. Reproducibility was within 5 – 12% on each platforms, while reliability (failure rate negligible) was 100% in both. Diagnostic criteria for MRS were not part of the present evaluation; however, where pathology was identified (N= 10), MRS criteria were comparable across the two Manufacturers' platforms.

Conclusions: Simple criteria have been established which permit future clinical trials of MRS to employ more than a single Manufacturer. This greatly facilitates efforts to establish EBM criteria for MRS utility and reimbursement[3].

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3) Lin et al. *Impact of Evidence-based Medicine on MRS: Clinical Practice, Reimbursement, and Solutions*. NMR Biomed. In press

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