Manually Adjusted Versus Vendor-Preset Definition of Metabolite Boundaries:
Impact on Proton Metabolite Ratios[1]

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Rationale and Objectives. Metabolite peak boundary definition is an important postprocessing step in proton magnetic resonance spectroscopy (^{1}H-MRS). We compare metabolite ratios calculated using three different postprocessing strategies: software-rendered default peak boundaries, manually adjusted peak boundaries and a curve-fitting program. The first two of these methods are commercially available.

Materials and Methods. A total of 42 spectra acquired on a 1.5-T MR unit using two-dimensional chemical shift proton MR spectroscopy (TR/TE = 1500/144 ms) were analyzed. Choline (Cho), creatine (Cr), and *N*-acetylaspartate (NAA) relative concentrations were derived and the following metabolite ratios were calculated: Cho/Cr, Cho/NAA, and NAA/Cr. Metabolite concentrations/ratios were calculated using (a) default peak boundaries rendered by commercially available, postprocessing software (Functool 2000, version 2.6.0); (b) manually adjusted peak boundaries by an experienced spectroscopist, using an option offered by the same commercially available software; and (c) an offline in-house curve-fitting program. Measurements obtained with method (c) were considered as the "gold standard." Paired *t*-tests comparing default and adjusted metabolite ratios, as well as default and adjusted ratios with their respective curve-fit values were used for statistical analysis.

Results. Significant differences between default and manually adjusted values were found for Cho/Cr ratios <1.5 and for all Cho/NAA ratios. For Cho/Cr ratios <1.5, significant differences between default and curve-fit values were present; this was not the case when comparing manually adjusted and curve-fit values. Default and manually adjusted Cho/NAA ratios were significantly higher than corresponding curve-fit ratios. Manually adjusted values were, however, closer to the curve-fit values. No significant differences were noted between default and adjusted NAA/Cr values; default and manually adjusted ratios were significantly lower than curve-fit ratios.

Conclusion. There can be significant differences in metabolite ratios calculated using default and manually adjusted peak limits in proton MR spectroscopy. Furthermore, Cho/Cr and NAA/Cho adjusted metabolite ratios are closer to curve-fit values, which are considered the most accurate of the three.

Key Words. proton MR spectroscopy; post-processing; metabolite ratios.

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In vivo proton MR spectroscopy has become an important tool in the workup of focal brain lesions (1–3). Spectral interpretation involves visual analysis of metabolic peaks and metabolite ratio calculations for lesion characterization. Vendor-provided spectral analysis software is commonly used in clinical practice since it offers an efficient and standardized means for data reduction. These vendor-provided software packages may invoke preset boundaries for metabolite peak area integration. In our experience

with spectral postprocessing, we have often encountered a visually apparent misalignment of spectral locations using the preset vendor-provided limits relative to the "true" metabolite peaks. This misalignment can present either as a generalized trend or within a subset of voxels in a 2D CSI dataset and could lead to clinically significant alterations in metabolite ratio calculations.

One strategy to approach this apparent discrepancy between preset and "true" metabolite peak limits is to manually adjust the different peak boundaries for each dataset. A more elaborate way of addressing metabolite peak limits is by using a curve-fitting program that ameliorates quantification of partially overlapping peaks (4–6). A number of these curve-fitting programs are commercially available. The purpose of our study was to assess changes in calculated metabolite ratios when using preset vendor-provided metabolite peak limits as opposed to manually adjusted peak boundaries and curve-fitting methods.

MATERIALS AND METHODS

A total of 42 spectra spanning a range of normal and abnormal spectroscopic features and qualities were included in the study. The 42 spectra were derived from seven subjects, including three healthy adults with unremarkable brain MR examinations (one man and two women, age range 48−52 years, mean age 51 years) and four patients with a brain tumor (four men, age range 7−53 years, mean age 34 years). Institutional board review approval was obtained for the study.

Spectra were acquired using two-dimensional chemical shift proton MR spectroscopy. The following parameters were used: 1.5-T MR unit; quadrature birdcage head coil; a point-resolved spectroscopy sequence (PRESS); TR/TE 1500/144, field of view 16 cm; matrix 16 × 16; slice thickness 10 mm; acquisition 1 average; scanning time 5 minutes. Automatic shimming/prescanning was performed at least twice, to achieve adequate water suppression and acceptable full-width half-maximum values. No manual shimming was done.

The CSI data were analyzed on a clinical workstation (GE Advantage Workstation, version 4.1) using commercially available software (Functool 2000, version 2.6.0) to calculate metabolite ratios. A total of seven slabs (one slab per patient) were used. 42 spectra were derived by placing 1 × 1 × 1−cm regions of interest within the individual slabs; six such regions of interest were placed

per patient. Metabolite concentrations used to calculate metabolite ratios were derived by peak integration between specified peak boundaries (7). Relative metabolite concentrations derived in the context of this study included choline (Cho), creatine (Cr), and N-acetylaspartate (NAA). The following metabolite ratios were calculated: Cho/Cr, Cho/NAA and NAA/Cr. The full set of standard metabolite ratios were calculated for each of the 42 regions of interest.

Two sets of metabolite peak boundaries were used in the calculation of relative metabolite concentrations and ratios for each dataset. One set included the preset peak boundaries generated by the software for each loaded dataset; the resulting metabolite ratios were labeled as the "default" metabolite ratio values. The second set included the peak boundaries defined after manual adjustment for each loaded dataset; the resulting metabolite ratios were labeled as the "adjusted" metabolite ratio values. Manual adjustment of peak boundaries was performed under the guidance and supervision of an experienced neuroradiologist and spectroscopist (P.C.S.). This involved manual definition of peak boundaries after visual inspection of the spectral set, using a feature of the same commercially available software (Functool 2000, version 2.6.0). The same group of spectra was also analyzed using an offline in-house curve-fitting routine written in IDL 6.0 (RSI Inc, Boulder, CO). Curve fitting was based on adjustment of Gaussian peak location, area, and width to match spectral Cho, Cr, and NAA resonances by an error minimization Marquardt-Levenberg routine similar to that used by others (8). The resulting metabolite ratios were labeled as the "curve-fit" metabolite ratio values. The curve-fitting routine also provided an estimate of fit parameter uncertainty and metabolite ratio uncertainty, which served as an indicator of spectral quality.

Six spectra per subject were obtained; spectra were extracted from either normal white matter or from regions near an enhancing tumor. All spectra, whether normal or pathologic, were analyzed in the same way. Very poor quality spectra as indicated by a high uncertainty in curve-fit ratio (>50%) were excluded leaving 30, 41, and 34 spectra suitable for Cho/Cr, Cho/NAA, and NAA/Cr ratio calculations, respectively.

Data Analysis

Each of the metabolite ratio sets included in the study was divided into three (nearly) equal groups based on the curve-fit metabolite ratio value. Cho/Cr ratios were, for example, divided into a group with Cho/Cr ratios <1.3