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Lesion Segmentation for MR Spectroscopic Imaging Using the Convolution Difference Method

Andrew A. Maudsley, Ph.D.

Department of Radiology, University of Miami School of Medicine, Miami, Florida

Abstract

Purpose—Delineation of lesion boundaries from volumetric MRSI metabolite ratio maps using a method that accounts for the spatial response function of the acquisition and variable spectral quality and is robust to signal heterogeneity within the lesion.

Methods—A novel method for lesion segmentation, termed Convolution Difference, has been developed that is robust to signal heterogeneity within the lesion and to differences in the spatial response function. Procedures are described for processing metabolite ratio maps and to exclude regions of inadequate spectral quality. This method was evaluated using computer simulations and results compared to an iterative thresholding technique that determines an optimal amplitude threshold, and to the use of a fixed amplitude threshold. These methods were evaluated for segmentation of volumetric MRSI studies of gliomas using maps of the choline to N-acetylaspartate ratio, and a qualitative comparison of lesion volumes carried out.

Results—Simulation studies indicated improved performance for the convolution difference method when applied to ratio maps. Variations in tumor volume were observed for the in vivo studies between the convolution-difference and the iterative thresholding methods; however, visual analysis indicates that both showed improved accuracy in comparison to using a fixed amplitude threshold.

Conclusion—This study reinforces previous reports indicating that the use of fixed threshold values for segmentation of maps with broad spatial response functions can result in errors in lesion volume definition. A novel segmentation method, termed Convolution Difference, has been introduced and demonstrated to be robust for segmentation of volumetric MRSI metabolite data.

Keywords

Magnetic Resonance Spectroscopic Imaging; MRSI; Brain; Lesion Segmentation; Convolution-Difference

1. Introduction

Proton MR Spectroscopic Imaging (MRSI) provides information on altered metabolite distributions associated with brain lesions (1) that is complimentary to clinical structural

imaging studies. Studies of brain tumors indicate that metabolic changes can be observed outside of regions with altered signal intensity from T1 contrast enhancement or T2 hyperintensity (2–5), and furthermore, that these changes may predict a subsequent recurrence (6,7). In light of these findings, methods have been proposed to delineate the boundaries of a metabolically-abnormal region to augment surgical or radiation treatment planning (8–12) or for deriving quantitative image features and treatment monitoring metrics.

The most widespread method for segmentation of metabolite images has been the use of fixed amplitude thresholds to the choline (Cho) to N-acetylaspartate (NAA) ratio map. Several methods have been used to determine the threshold, including a fixed value (8,11); the Cho/NAA ratio normalized to a contralateral region (13); a z-score regression analysis (14); or based on the mean and standard deviation from a normal tissue region (4). Validation of the thresholds used has been carried out by correlating Cho/NAA values with histological analyses of biopsy specimens (2,7,15,16) and these studies have reported an association of Cho/NAA with molecular markers of tumor infiltration. For example, Guo et al (15) determined that Cho/NAA values (defined as the ratio of the areas under each resonance) of 0.5, 1.0, and 2.0 had probabilities of 0.38, 0.6, and 0.9 in high-grade gliomas and 0.16, 0.39, and 0.87 in low-grade gliomas. However, these reports also indicate variability between studies and considerable variation between individual subjects (2,17).

The use of fixed amplitude thresholds has been shown to be inaccurate for lesion delineation using PET images (18,19), which have similar considerations to MRSI regarding the broad spatial response function (SRF) of the imaging system. These studies demonstrated that the optimal threshold value depends on the size of the lesion and the signal-to-background ratio (SBR), which is measured as the peak signal value within the lesion relative to the mean background signal outside of the lesion. Therefore, given the relatively broad SRFs of MRSI, lesion delineation using metabolite maps must also take these factors into account. An additional consideration of the broad SRF is that quantitative measures of metabolite values in and around the tumor should also account for signal contributions across neighboring compartments, which as yet has not been incorporated into the histological comparison studies. Additional considerations for segmentation of MRSI include the relatively low SNR of metabolite maps, the possibility of missing voxels due to localized regions of inadequate quality, and the impact of taking metabolite ratios.

In general, methods for segmentation of brain tumors using high resolution structural MRI (20) cannot be directly applied to MRSI as they do not take into account the SRF of the imaging system. However, suitable methods have been proposed for segmentation of PET images (19,21). Of these, methods based on image intensity thresholds are generally simple and easy to implement, however, are sensitive to the SRF, lesion size, and relative signal strength (22). While other methods may not specifically include a priori information on the SRF (21), techniques such as convolutional neural networks make use of a training phase that will take the SRF into account (21). To account for the dependency of the threshold value on the lesion size and signal strength an iterative thresholding method has been widely used for PET studies (21,22) in which an optimal threshold value is obtained for each lesion volume and SBR, which are determined from a previous estimate. A revised amplitude

threshold value is then determined based on a priori information from a calibration measurement and the lesion estimation repeated in an iterative manner. Calibration measurements for PET studies have used experimental measurements in phantoms (22). For MRSI, however, the SRF can be easily calculated based on the k-space sampling distribution and any applied spatial filtering, therefore the calibration can be carried out computationally. There remain several limitations of this technique. First, the calibration must be carried out for an assumed object shape that simulates the lesion. A spherical object is typically chosen, though this will be a poor approximation to most lesion shapes. A second limitation is that the calibration measurement, whether done using phantom measurements or simulation, assumes a constant signal intensity within the object, which does not take into account signal heterogeneity within the lesion. A third limitation is that the threshold value is dependent on the SRF, therefore the calibration will have to be redone for any acquisition or processing variant that impacts the SRF. For volumetric MRSI the SRF is commonly different between the in-plane and through-slice directions, implying different threshold values are needed in each dimension. An additional consideration is that the SRF is only known a priori for maps of single metabolite distributions, however, this is not the case for maps of metabolite ratios where the SRF will depend on the relative amplitudes of the numerator and denominator maps.

In this report, the errors associated with intensity-based thresholding are first reviewed and extended to include considerations for metabolite ratio maps. A new segmentation method is then presented that utilizes a basic property of data smoothing to provide an image segmentation that is not strictly dependent on the SRF or assumptions of homogeneity within the high signal region. The method is compared to the iterative thresholding (IT) method using computer simulation and volumetric MRSI studies in the brain.

2. Theory

2.1. The Convolution-Difference segmentation method

In Figure 1 are shown simulations for a one-dimensional object with three higher signal intensity regions relative to a background signal. Two cases are considered: a) for a fixed width of the increased signal region with increasing magnitude; and b) with a fixed signal magnitude and varying width. The ideal profile is shown in black, together with profiles resulting from the application of two smoothing functions, representing differing SRFs, identified as S_1 and S_2 , and shown in blue and red, respectively. Data were simulated for 64 k-space sample points and zero-filled to 512 points prior to Fourier transformation. If a fixed intensity threshold of 2.0 is applied, the errors in the widths of the high signal regions relative to the true width of the simulated high-intensity region, are for the S_1 (blue) profile: a) -13%, 26%, and 39%, and b) 19%, 10% and 7%; and for the S_2 (red) profile the errors are larger at: a) -32%, 45% and 71%, and b) 38%, 20% and 13%. Similarly, using an object-specific threshold value based on 50% of the maximum data value within each of the high-signal regions results in errors of 32%, 13% and 6% for the S_1 profile and 84%, 32%, and 26% for S_2 . In agreement with previous reports (22,23), this demonstrates that fixed amplitude threshold values should not be used for lesion delineation and that the errors are dependent on the SBR, size of the region, and the SRF. Additional simulations (not shown)

also demonstrate that the errors are different for the ratio of two signals, for which they also depend on the relative magnitude of the numerator and denominator.

An additional observation from Fig. 1 is that the two smoothed profiles coincide at the edges of the simulated object. Therefore, the true extent of the high signal region corresponds to the region where $S_I > S_2$. This introduces the proposed lesion segmentation method that is based on subtraction of a smoothed version of the data, i.e. the binary result, R , defined over the image dimensions $\bar{r}$, is:

$$R(\bar{r}) = \begin{cases} 1, & (S_I(\bar{r}) - S_2(\bar{r})) \geq 0 \\ 0, & (S_I(\bar{r}) - S_2(\bar{r})) < 0 \end{cases} \quad (1)$$

where the signal S_I represents the acquired data and S_2 is a smoothed version of S_I . Since an image corresponding to S_2 can be derived by convolution with a smoothing function the method is identified as Convolution-Difference (CD) image segmentation.

For the noise-free one-dimensional simulation shown in Fig. 1 this operation results in correct segmentation for all except the most narrow example in Fig. 1b, which has a width smaller than the width of the SRF, but which was still identified with a relatively small error of 5%. However, this method breaks down in the presence of noise and ringing resulting from truncated spatial sampling. This is illustrated in Fig. 2, which shows a noisy signal, S_I , and a smoothed version of this signal, S_2 , with the primary crossover point of these two signals occurring at a value C . Note that C is not a fixed value and may vary around the object depending on the local SBR. Several points can be seen in the high signal regions where $S_I < S_2$ and conversely in the background where $S_I > S_2$, which would result in false negative and positive segmentations respectively. To avoid including these regions upper and lower limits need to be imposed, as indicated by the horizontal lines labeled T_H and T_L . The algorithm first determines these two parameters, with the values representing a balance between incorrect classifications if T_H and T_L are too high or low respectively, and limiting the range for the search for the correct crossover point if T_H and T_L are too close to C . Both values can be empirically determined, and will generally be easier to determine for higher SNR and SBR values.

For this study, the amplitudes for T_H and T_L were set relative to an initial estimate of the value of C and these three values were determined as follows:

Crossover determination—Regions where $S_I \cong S_2$ are identified using the operation $|(S_I - S_2)/S_2| < 0.05$. To eliminate background regions of the image the signal S_2 is differentiated and the results of the previous operation are limited to the region close to the maximum value of this derivative. The mean value of the S_2 signal taken over voxels that meet the above two criteria is then taken as C .

Lower Threshold Determination—The lower threshold was set as:

$$T_L = \bar{B} + n \times \sigma \quad (2)$$

where $\bar{B}$ and σ are the mean and standard deviation of the background signal and n is a constant. For the analyses presented in this report, n was set to 3.0 for single metabolite maps, corresponding to less than 0.2% probability of misclassifying noise as a signal, assuming that the noise is normally distributed. This threshold was modified for ratio maps as described below. Ideally, the maximum value of T_L should be limited to $T_L < C$, however, this was found to increase the number of false classifications for low SNR cases and was therefore not used, with the tradeoff being an underestimation of segmentation volumes for the low SNR cases. The mean value of the background signal was determined from a dilated volume around an initial estimate of the high signal region, with this initial estimate obtained using an intensity threshold of $C * 0.8$. That result was then dilated to further reduce the contribution of voxels near the lesion to the background estimation.

Upper Threshold Determination: This value was set as:

$$T_H = C + (S_{1,M} - C) * 0.25 \quad (3)$$

where $S_{1,M}$ is the median value of S_I calculated over the center of the high signal region. The use of the median value was chosen over the maximum value to reduce sensitivity to outlying values, which is particularly important for ratio maps; however, this also has a disadvantage in that it requires that a volume be defined over which the median value is calculated. For this study, this region was determined using a previously-obtained estimate of the high signal region volume, which was then reduced using a three-dimensional erode operator with a size of the half-width of the SRF, while requiring a minimum of 64 voxels.

3. Methods

The CD and IT segmentation methods were implemented using IDL (Harris Geospatial Solutions, Inc.) and integrated into the MIDAS software (24). Processing time for both methods for volumetric MRSI data was under one second.

3.1. Simulation Studies

A computer simulation study was carried out to evaluate the performance of the CD segmentation method. Data was created that corresponded to acquisition parameters used for volumetric MRSI of the brain (25), and which consisted of a high-signal region within a larger background signal. Noise was added and SNR varied by changing the amplitude of the high signal region. The volume identified using the CD segmentation method was then compared to the known object size using the Dice similarity coefficient (26). Results were also compared to the IT method, which was implemented as previously described (22) with the exception that the median data value within the lesion, derived as previously described for the CD method, was used to calculate the SBR.

Data were simulated for a non-isotropic k-space distribution with $50 \times 50 \times 18$ encodings over $280 \times 280 \times 180 \text{ mm}^3$. The simulated object was initially created at $256 \times 256 \times 128$ points to improve accuracy for the volume measurement. This was then inverse Fourier transformed, the central k-space points retained and zero-filling applied to $256 \times 256 \times 128$ k-space points. Spatial smoothing was applied by multiplication of the k-space data with a Gaussian filter function as $\exp(-\sigma^*(2k/K)^2)$, for $-K/2 \leq k \leq K/2$, where K is the number of k-space points and σ is the smoothing factor of value 2.0. The resultant full-width-half-maximum of the SRF was 9.84 mm in-plane and 15.47 mm through-plane. Simulations were carried out for SBR values of 2, 3, 5, and 10; object sizes from 2 to 20 point diameter; three objects with differing signal variations; single value maps and image ratio maps; and results averaged over 20 instantiations of the noise. The three object definitions were: i) a solid homogeneous sphere; ii) a solid sphere with a linearly varying signal intensity in one dimension that reached 50% on one edge; and iii) a hollow sphere with a wall thickness of 50% of the radius and the same signal intensity variation as described for the second case. Examples of the three simulation objects, each displayed using a different SBR value, are shown in Fig. 3, which also illustrates increased variability on the ratio maps relative to the single value maps. For each simulation the SNR was measured using the ratio of the median signal value within the high signal region to the standard deviation of the background noise. It is noted that the noise distribution for the ratio maps is not normally distributed.

The IT method requires calibration of the optimum intensity threshold as a function of object size and SBR. This was carried out by finding the value in a simulated MRSI result at the known edge of the simulated object, for a homogeneous spherical object definition and MRSI parameters as previously described. A table of threshold values was generated for object volumes from 0.46 cc to 516 cc and SBR values from 2 to 50. Example results for selected SBR values are shown in Supporting Figure S1, which illustrates the association of the optimal image intensity threshold on the SBR and object size, as has previously been described for segmentation of PET images (22,23). In Fig. S1a is the result using the maximum data value, which becomes modified when the median value within the high signal volume is used, as shown in Fig. S1b. These values were then used to derive the optimal threshold value based on a previous estimate of the SBR and object size. No differences were found for simulations based on a single metabolite or a metabolite ratio, therefore this same calibration result was applied to both cases.

3.2. Extension to volumetric data and metabolite ratios

Initial evaluation of the CD method indicated that the relationship between the original and smoothed versions of the data, S_1 and S_2 , was altered for volumetric data in comparison to the one-dimensional simulation. This is illustrated in Fig. 4, which shows the edge profile from a high-intensity object using simulations in one and three dimensions. While the one-dimensional case shows the S_1 and S_2 signals crossing at the exact location of the edge of the high-signal region this is not the case for the three-dimensional case. In addition, the mismatch between the crossing point and the edge of the object is dependent on the object size and SBR. This mismatch occurs because the smoothing for S_2 is applied in all three dimensions, meaning that additional modification of the edge profile is taking place in the orthogonal directions. Additional simulations were carried out with smoothing applied in

only one dimension; however, resulted in increased errors in the segmentation. Therefore, to account for this effect a correction factor was applied to increase S_2 prior to applying the subtraction, i.e. Eq. 1 was modified as:

$$R(\vec{r}) = \begin{cases} 1, & (S_1(\vec{r}) - c \cdot S_2(\vec{r})) \geq 0 \\ 0, & (S_1(\vec{r}) - c \cdot S_2(\vec{r})) < 0 \end{cases} \quad (4)$$

where c is the correction factor. Using the method previously described for the optimal threshold calibration, this factor was calculated for the same range of SBR and object sizes as previously described for the IT method. Example values for four SBR values are shown in Fig. 5, which demonstrates that the correction increases for smaller object sizes and SBR values, though remains a relatively small effect, of under 5%, for larger object sizes and smaller SBR values.

An additional observation was that errors of the lesion segmentation occurred when the algorithm was applied to maps of a metabolite ratio. However, this only occurred if the smoothing was applied to the ratio map and did not occur when the smoothing was applied to the individual metabolite maps before taking the ratio. This is illustrated for the one-dimensional profile example in Supporting Fig. S2. Therefore, all ratio maps were calculated after smoothing.

A final modification used for segmentation of ratio maps was to increase the factor n used to calculate T_L in Eqn. 2 to 5.0, to account for the different noise distributions found in these images.

3.3. In Vivo MRSI Studies

The performance of the CD and IT segmentation methods was evaluated for 11 volumetric MRSI studies of gliomas acquired at 3 Tesla. Data were selected from an existing study, for which the acquisition methods and subject selection have been previously described (27). Processing using the MIDAS package (24) resulted in an interpolated voxel volume of 0.107 cc whereas the estimated final effective voxel volume following spatial smoothing was 1.46 cc.

Lesion volumes were segmented from the Cho/NAA map using the CD method, the IT method, and using a fixed threshold of the concentration ratio of 0.66, which is equivalent to a peak integral ratio of 2:1. For all methods, voxels with a linewidth >14 Hz were excluded, with this value obtained from the spectral fitting, which used a common linewidth for all resonances (28). In a few cases the quality maps were manually edited to include voxels that showed minimal metabolite resonances but a narrow water resonance, which were located in necrotic regions. In addition, lesion segmentation maps were manually modified to remove false positive results that commonly occur in the cerebellum and brain stem, for which the normal Cho/NAA ratio is increased (24). An additional region that has increased values of Cho is the white-matter surrounding the atrium of the lateral ventricle and positive

segmentation results in these regions were removed if not clearly associated with the observed location of the tumor.

Two steps were used to avoid outlying voxel values in metabolite ratio maps due to division by small NAA values. First, the denominator value was limited to a minimum value of 10% of the median value of all voxels within the brain that passed the quality evaluation. Second, a standard-deviation filter was applied that replaced voxels that exceeded the mean value plus six times the standard deviation, measured over the surrounding $5 \times 5 \times 3$ voxel array, with the mean value from the surrounding voxels. An additional filter was applied to the final segmentation map, for all methods, to remove isolated voxels that did not have at least three voxels within a connected volume that were classified as lesion.

Segmentation results were analyzed by integration of the resultant volume and associations with maximum and median values of the Cho/NAA within the segmented volume were examined.

4. Results

4.1. Simulation Studies

Plots of the Dice coefficient as a function of the object size are shown in Fig. 6 for the CD and IT methods, for simulation of the solid sphere with a 50% intensity gradient, and for a single value and a ratio (corresponding to the examples shown in Figs. 3b and 3e). Results for the single parameter indicate comparable performance for larger objects, though improved performance for the CD method for lower SNRs. Some advantage of the CD method is indicated for ratio images, for all SNR and object size (Fig. 6b). Results for the homogeneous solid sphere (not shown) show a similar trend and comparable performance of both methods. The Dice coefficient for the IT method reached 0.99 for the solid sphere but was slightly decreased to 0.96 for the sphere with the varying amplitude, whereas the results for the CD method were 0.975 for both simulation objects, indicating that the IT method is more strongly affected by non-homogeneous signal amplitudes within the high signal volume. Results are shown in Supporting Fig. S3 for the hollow sphere with an intensity gradient (corresponding to Figs. 3c and 3f), which shows the same trend as shown in Fig. 6, although with reduced performance of both methods for the ratio image.

The CD correction factor presents a potential source of error, since this depends on an estimate of the lesion volume and SBR, similar to the IT method. To examine the potential impact of an imprecise estimate of this correction factor a comparison was made of the Dice coefficients obtained with and without application of the correction, i.e. representing a worst-case situation. In Supporting Fig. S4 are shown the Dice coefficients and the error in the volume measurements for the solid sphere. This result indicates a modest reduction in the Dice coefficient, by approximately 0.13 for smaller object sizes to comparable performance for larger objects. As expected from Fig. 4b, there was an overestimation of the volumes if no correction was applied.

4.2. In Vivo Studies

In Table 1 are listed the selected studies, with tumor grade, segmented volumes, and maximum and median values of Cho/NAA over the segmented volume. In Figs. 7 and 8 are shown example Cho/NAA maps and lesion segmentations, for subjects #6 and #10. Fig. 7 indicates general agreement of all segmentations with the volume of enhancement, seen on the underlying post-contrast T1-weighted MRI, although it is apparent that the fixed threshold method (Fig. 7c) resulted in a larger lesion volume. The study in Fig. 8 shows two lesions, with the more posterior having a large Cho/NAA signal, whereas the second, which contained a cystic core and only a limited contrast enhancement, shows an only slightly elevated Cho signal, but with increased Cho/NAA due to the absence of NAA. The IT method, which used a fixed threshold over the whole image, performed poorly in comparison to the CD method. An additional result is shown in Supporting Fig. S5, which is an example with a smaller increase of Cho/NAA with a well circumscribed lesion that is clearly defined on the post-contrast T1-weighted MRI. For this example, the IT and fixed threshold methods resulted in incomplete sampling of the volume indicated by the T1 contrast enhancement.

Segmentations using Cho/Cr and Cho (normalized to tissue water) were also investigated. For the grade III and IV cases, which all showed increased Cho, the resultant segmentations using Cho/Cr were very similar to those obtained from Cho/NAA. An example for the Cho/Cr segmentation for the same study shown in Fig. 7 is shown in supplementary Figure S6. All four grade II studies had minimal increase of Cho, resulting in poor segmentations, using either Cho or Cho/Cr maps, that included considerable contribution from normal appearing brain regions. For comparison, the Cho/NAA and Cho/Cr maps are shown for three subjects in Supporting Figure S7. In consideration of the variability in the segmentations from the Cho/Cr maps these were not included in this study.

Examination of Table 1 indicates that volumes from the fixed threshold method differ from those of the CD and IT methods with a dependency on the Cho/NAA amplitude. In Supporting Fig. S8 is plotted the difference between the volumes from the CD and fixed threshold methods and the median value of the Cho/NAA signal. This shows a strong association, with $R^2=0.8$, between the difference in volumes with the signal amplitude. Similar associations were obtained for differences with the IT method ($R^2=0.82$). While the true volume of the lesion is not known, in light of the simulation studies (Fig. 1) this result further demonstrates the limitations of using fixed amplitude thresholds.

5. Discussion

This report has addressed methods for delineation of brain lesion volumes using MRSI metabolite maps, for which it is essential to account for the relatively broad SRF of this imaging modality, and has presented a new lesion segmentation method. This convolution-difference method determines a local intensity threshold, which may vary over the lesion volume, and remains relatively insensitive to the shape of the SRF and signal heterogeneity within the lesion. This method was then compared to the iterative thresholding segmentation method, which has been widely implemented for PET studies, using computer simulations and in vivo MRSI data of gliomas. For the in vivo studies a fixed intensity threshold was

also evaluated, using $\text{Cho}/\text{NAA} > 2.0$, which has been proposed as indicative of abnormal pathology. Results demonstrate comparable performance of the CD and IT segmentation methods, although with an indication of improved performance for the CD method in the presence of signal heterogeneity and for ratio maps.

This study reiterates previous observations from lesion delineation using PET images of the errors in volume measurements that can occur when fixed intensity threshold values are used, and additionally demonstrates the importance of this consideration for MRSI. This concern is particularly problematic in light of the considerable signal heterogeneity in metabolite ratio maps and variability with different tumor types and between subjects (2,17). The proposed method is based on features within the metabolite image and will therefore provide comparable performance for a wide range of image intensities. A further limitation of the use of fixed amplitude threshold values is that studies examining associations between MRSI-derived signal intensities and histological findings (2,7,15,16) must also account for partial volume signal contributions.

Lesion delineation for brain MRSI is most readily implemented using the Cho/NAA ratio map due to the large signal contrast, which is strongly driven by low NAA values. Additional observations of this study include that calculation of this ratio must include steps to avoid extreme signal outliers, and that use of the Cho map or the Cho/Cre ratio can be less effective due to the presence of similar signal intensities in normal tissues. Even for the use of the Cho/NAA ratio it was necessary to exclude the brain stem and cerebellum and to be aware of increased values in peritumoral white-matter.

Limitations of the IT segmentation method include that this requires a calibration of the optimal threshold value, which is obtained using a simplistic assumption of the shape of the high signal volume as well as the assumption of signal homogeneity within the signal volume (23). Similarly, the CD method also makes use of a calibration to derive a correction factor; however, the magnitude of this calibration is relatively small for most object sizes. This effect would also be reduced when applied to 2D MRSI acquisitions.

A limitation of this study is that measurements in phantoms or realistic simulation models, where results can be compared to the known volume, were not included. For in vivo studies the true extent of a metabolically altered tissue volume is not known and precise boundaries cannot be defined due to infiltration into surrounding tissue. Therefore, it is not possible to state which segmentation methods had the greatest accuracy. For this reason, and given the small number of subjects and considerable variability of lesion types evaluated, a statistical comparison of the results from the differing methods has been deferred to a future study. A further limitation includes that the method has not been evaluated for 2D SI acquisitions; however, the full FOV or “whole brain” MRSI method offers significant advantages for mapping of tumor volumes and would be considered the preferred method for this purpose.

Potential applications of automated lesion delineation from MRSI include longitudinal measurements to monitor treatment and for definition of radiation treatment volumes. The clinical potential for these measurements remains to be evaluated; however, initial studies that have been carried out for image-guided resection (10), radiation treatment (12), and

treatment response assessment (11,29) indicate considerable benefit from incorporating the MRSI information. A limitation for more widespread use for clinical studies remains the quality and reliability of the MRSI data acquisition. While the method used in this study samples some of the largest brain volumes in comparison to other published methods, on average it still fails to sample approximately 30% of the brain volume (25), which inevitably means that some portion of the tumor volume may not be fully sampled. Therefore future studies must also examine potential improvements to MRSI acquisition methods.

6. Conclusions

This report has demonstrated that partial volume effects must be accounted for when using MRSI metabolite maps for delineation of lesion volumes and has presented a new lesion segmentation method. The results highlight that large errors in volume measurements occur if fixed threshold values are used for delineation of tumor volumes from MRSI.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1. Simulation of a one-dimensional object having three high signal regions, for a) equal width and varying intensity, and b) equal height and varying width. The ideal profile is shown in black together with two versions of a smoothed profile, shown in blue and red.

Figure 2.

Simulation of a one-dimensional object with two high signal regions in the presence of noise and ringing due to truncated spatial sampling. The ideal profile is shown in black (with reduced relative amplitude) and the profile corresponding to the spatial response function of the acquisition together with added noise is shown in blue and identified as **S1**. The result after smoothing of this signal is shown in red and identified as **S2**. To avoid incorrect classification the determination of the crossover point, **C**, is restricted to be within an upper and lower threshold values, **TH** and **TL**.

Figure 3.

Example cross-sectional images through the center slice of the three simulation objects used, with single metabolite maps having a signal-to-noise ratio of 3.0, 5.0 and 10.0 in a), b) and c), respectively, and the ratio maps for the same object definitions in d), e) and f), calculated with numerator and denominator values of 2.25/0.75, 2.5/0.5, and 5/0.5 respectively.

Figure 4.

Illustration of the edge profile from a high-intensity object using simulations in one (a) and three (b) dimensions. Each profile shows the ideal profile in black and two different levels of spatial smoothing, S_1 and S_2 , shown in blue and red. The three-dimensional profile was generated for a solid sphere and the edge profile is shown for two sizes of that sphere.

Figure 5. Plot illustrating the range of the correction factors applied to the smoothed dataset for the Convolution-Difference segmentation method. This is plotted as a function of the object diameter as a fraction of the full-width-half-maximum (FWHM) of the spatial response function (SRF), for four signal-to-background (SBR) values.

Figure 6.

Plots of the Dice coefficient showing the degree of agreement for the volume determination for a high signal region, simulated as a sphere with a 50% change in intensity along one dimension. The results are shown for segmentation of a single simulated metabolite map (a) and for a ratio (b). Each plot shows values for the convolution difference (CD) method in blue and the iterative thresholding (IT) method in red, for three different SNR values, as indicated, and plotted as a function of the object diameter as a fraction of the FWHM of the SRF.

Figure 7.

Example Cho/NAA map and segmentation results for a glioblastoma. a) The choline to N-acetylaspartate ratio (Cho/NAA) map is shown in a color scale with a contour indicating the edge of the region that passed the spectral quality evaluation. Data are shown for every second slice (11.25 mm interval). b) The T2-weighted MRI, shown for the center of the thicker MRSI slice. In rows c), d) and e) are shown the segmentation results for the CD method, the IT method, and the fixed threshold method, respectively. Results are shown as an overlay superimposed on the post-contrast T1 MRI selected from the center of the displayed metabolite map.

Figure 8.

Example Cho/NAA map and segmentation results for a grade III glioma that includes two regions with differing intensity of the Cho/NAA map. (a) The Cho/NAA map, shown for every second slice and with the edge of the quality map indicated using a grey contour; b) the T2-weighted MRI corresponding to the center of the thicker MRSI slice. In rows c), d) and e) are shown the segmentation results for the CD method, the IT method, and the fixed threshold method, respectively, superimposed on the post-contrast T1-weighted MRI.

Table 1

List of subjects used in the analysis together with the lesion volumes measured by the CD, IT, and fixed threshold methods. Also shown are the maximum data value and the median value calculated within the volume defined by the CD-segmented volume.

	Diagnosis	Grade	Segmented Volume, cc			Cho/NAA	
			CD	IT	Thresh	Maximum	Median
1	Astrocytoma	II	26.1	25.6	19.2	2.22	0.89
2	Astrocytoma	II	55.4	38.8	34.5	4.16	0.90
3	Glioma	III	28.4	30.5	11.4	1.82	0.59
4	Oligoastrocytoma	III	61.8	49.1	88.3	6.05	1.60
5	Glioblastoma	IV	73.2	52.9	63.8	4.47	1.10
6	Glioblastoma	IV	85.5	55.3	116.0	8.72	2.33
7	Astrocytoma	II	47.3	39.2	38.4	3.52	1.16
8	Glioblastoma	IV	78.9	45.5	75.3	4.17	1.09
9	Astrocytoma	II	75.0	72.4	46.1	2.31	0.71
10	Glioma	III	73.7	41.0	40.7	4.05	0.76
11	Glioblastoma	IV	48.0	34.7	42.4	5.20	1.34