Evidence for Need of Incorporation of MRSI Data in Radiation Treatment Planning of Brain Gliomas

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Introduction

Currently, the standard approach to define radiation target volumes for brain glioma treatment is to deliver a uniform dose to areas of imaging abnormalities determined from FLAIR MRI, post-contrast T1-weighted MRI, or CT scans, with an additional uniform margin of 1.5-2 cm. This often causes the target volume to either cover too much non-involved normal brain tissue or leave small areas of tumor infiltration untreated. Recently developed radiation delivery technologies allow the control of exquisitely conformal dose distributions that can simultaneously increase dose to certain portions of the tumor while sparing normal brain. Thus, it is critical that tumor heterogeneity and margins identified for different dose delivery are defined accurately.

3D proton MRSI techniques have been gaining popularity for the diagnosis and followup of brain tumors, offering clinically feasible metabolic assessment of the presence and extent of neoplasm based on levels of choline compounds (Cho) elevation and/or N-acetylaspartate (NAA) reduction in neoplasm relative to normal tissue. It has been demonstrated that compared to MRI, MRSI provides more reliable and complete pictures of grade and extent of disease, and that the radiation target volume defined by MRSI data can be significantly different from that defined by MRI (1-3). In this preliminary study, by comparing pre-radiation MRSI data with outcome of conventional imaging-based radiation planning and treatment, we sought to assess the need of incorporating MRSI information in radiation treatment planning for patients with brain gliomas.

Methods

Prior to radiation treatment, twelve patients with brain gliomas (6 low grade, 6 high grade) underwent 3D ^{1}H MRSI examinations in addition to the routine MRI protocol with contrast administration. The MRI/MRS studies were performed with a 1.5T GE Excite or LX whole-body MR system. The MRI protocol included axial FLAIR MRI and pre- and post-gadolinium contrast T1-weighted MRI. The FLAIR images were used as scouts for placement of MRSI excitation volume of interest extending beyond the suspected disease (hyperintense areas on FLAIR images) to include some normal brain tissue. The MRSI data were acquired using a PRESS sequence with TE=144 ms, TR=1000 ms, 1 cm slice thickness, and 3D phase encoding (8 x 8 x 8). The nominal voxel size ranged from 0.8 to 1.2 cc due to variation of the FOV of MRSI acquisition. Outer volume saturation bands were applied to avoid contamination from subcutaneous lipid signals. GE's FuncTool software was used to process the MRSI data, with interpolation in the superior-inferior direction to overlay the spectra onto the thinner (3 mm) FLAIR images. Using a method analogous to that introduced by Nelson and coworkers (1-3), ratios of Cho to total creatine (Cr), denoted as 'CCR' index, were calculated for each MRSI voxel and classified into four grades (Table). The CCR index maps with corresponding four image intensity levels (Table) were then co-registered with the FLAIR images using a home-built image fusion program (4).

During radiotherapy, these patients received uniform radiation dose in the suspected disease region: areas of imaging abnormalities in the FLAIR images, plus a uniform margin. Follow-up brain MRI protocol was performed post-treatment.

Results

CCR index	Grade	Image Intensity
<1	0	0
≥ 1-2	1	85
≥ 2-3	2	170
≥ 3	3	255

Fig. 1a shows MRSI spectra overlaid on a FLAIR image, revealing a focal lesion with hyperintensity. High Cho elevation was observed well beyond the hyperintense area, indicating the spatial extent of the malignancy and suggesting potential treatment failure by delivering uniform radiation dose to the hyperintense lesion area. Fig. 1b shows the co-registration of the CCR index map with the FLAIR image. We assigned CCR ≥ 3 to correspond to high grade tumor, CCR of 2-3 to non-enhancing tumor, CCR of 1-2 to low grade and microscopic disease, and CCR <1 to normal brain tissue.

Among the twelve patients, conventional radiotherapy was confirmed by pathological analysis to have failed to treat six patients (4 high grade and 2 low grade gliomas) effectively (50% failure rate). One example of such failure is a patient with brain stem glioma. Pre-radiation post-contrast T1-weighted MRI (Fig. 2a) showed no contrast enhancement. The treatment planning was based on the hyperintense area shown on the FLAIR image (Fig. 2b). The follow-up post-contrast MRI (Fig. 2c) revealed regions of contrast enhancement, indicating tumor recurrence. These regions matched well with those showing grade 3 CCR index from the pre-treatment MRSI data (Fig. 2b), suggesting that the inadequate radiation dose delivered to these areas was the reason for treatment failure. If the MRSI data were taken into account during treatment planning, three contours would have been drawn to define three tumor regions for different dose delivery (dose painting) (Fig. 2d): the red contour circling the region of grade 3 CCR index, the yellow contour circling the region of grade 2 or above CCR index, and the orange contour circling the region of grade 1 or above CCR index. This would have allowed an escalated radiation dose to be delivered to the gross tumor volume (grade 3 CCR index) to treat the cancer more effectively, while the less malignant tumor regions would also have receive adequate doses.

The radiation target volumes and shapes for the twelve patients all changed significantly compared to MRI-based radiation planning when the MRSI data were incorporated in defining tumor regions.

Discussion

The high failure rate of the conventional imaging-based radiotherapy suggests that it may be helpful to incorporate MRSI data in planning for radiation treatment of gliomas. Compared to MRI, MRSI provides better delineation of tumor heterogeneity, such as regions of higher grade elements in low grade tumor and regions of microscopic disease, thus allowing more accurate prescription of radiation dose painting to treat gliomas more effectively while preserving normal brain tissue. One limitation of the MRSI technique is its spatial resolution, which may cause uncertainties in contouring different tumor regions based on CCR index. This can be improved by employing higher field magnet, such as 3T, to reduce voxel size while retaining reasonable signal-to-noise ratio. We are also exploring the possibility of incorporating relevant functional MRI data in treatment planning to redirect the angles of radiation beams to avoid important functional cortex areas.

References 1. Graves EE et al., *Image Anal. Stereol.* **21**, 69 (2002). 2. Pirzkall A et al., *Int. J. Radiat. Oncol. Biol. Phys.* **53**, 1254 (2002). 3. Pirzkall A et al., *Int. J. Radiat. Oncol. Biol. Phys.* **50**, 915 (2001). 4. Chang J et al., *Int. J. Radiat. Oncol. Biol. Phys.* **60** (1) Supplement, 223 (2004).

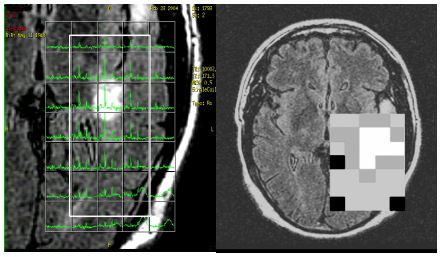

Fig. 1a **Fig. 1b**

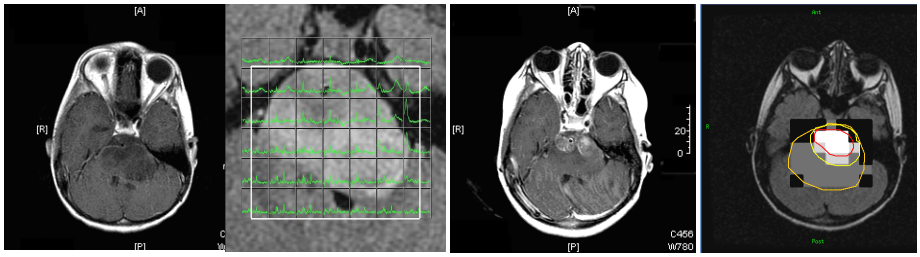

Fig. 2a **Fig. 2b** **Fig. 2c** **Fig. 2d**