

Reliable estimate of lactate and lipid for newly-diagnosed gliomas patients using lactate-edited 3D ¹H-MRSI with ellipsoidal k-space sampling

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A robust and practical acquisition was developed in order to reliably estimate lactate and lipid levels in glioma patients. This combined J-difference modulation and reduced k-space sampling to obtain 3D ¹H-MRSI data. Thirteen pre-treatment glioma patients were studied. Preliminary results concerning the spatial distribution of lactate and lipid are presented and compared with estimates of rCBV obtained using dynamic perfusion weighted MR imaging.

INTRODUCTION

Lactate is a sensitive indicator of anaerobic glycolysis and reduced cellular oxygenation in living tissues. Mobile lipid resonance has been correlated with necrosis and cell breakdown. Reliable estimates of levels of lactate and lipid resonances are of interest for evaluating prognosis and hence guiding the clinical management of brain tumor patients. In the normal acquisition of ¹H-MRS data, lactate and lipid peaks overlap within the region from 0.9 to 1.3 ppm and are therefore hard to distinguish. Spectral editing that is based on J-difference modulation allows for simultaneous acquisition of the lactate doublet at 1.3 ppm and the uncoupled resonances of choline, creatine, NAA and lipids. This technique requires two separate acquisitions per phase-encode step and therefore reduced k-space sampling is beneficial to keep the total acquisition time practical for patient studies. The goal of this study is to explore a robust method for estimating lactate and lipid with a reasonable acquisition time.

MATERIALS AND METHODS

Thirteen newly-diagnosed patients with histologically classified glioma were studied. Eight had low grade gliomas (five pre-surgery and three post-surgery but prior to other treatment) and five had glioblastoma multiforme (all pre-surgery). MR data were acquired on a 1.5T GE Signa Echospeed MR scanner. The MRI protocol included axial FLAIR images (10000/147/2200) and post contrast agent T1-weighted volume SPGR images (27/6). All pre-surgery patients had perfusion data with T2*-weighted gradient-echo echo-planar images (1250/54/1) during the first pass of a bolus of contrast agent. PRESS localization was applied with 3D phase encoding and using dual BASING (band selective inversion with gradient dephasing) pulses. J-difference lactate edited MRSI was performed using a prior method [1] based on altering carrier frequency of BASING pulses to alternately include and then exclude the lactate methine resonances at 4.1ppm in the excitation passband while keeping TE as 144ms. Very Selective Saturation (VSS) pulses were employed to provide sharpen the PRESS-selected volume and to reduce chemical shift misregistration effects. With normal cubic k-space sampling, a total of 45 minutes acquisition including setting up parameters would have been needed. Reduced k-space sampling was applied in which only the centrally-located voxels in k-space within a defined ellipsoid were acquired and the corner voxels were zero-filled before spectra reconstruction. The radius in each axis was selected to have the same nominal voxel size as the cubic sampling acquisition (FOV as 120*120*80mm³, phase encoding matrix as 12*12*8). At TR 1s, the acquisition time was reduced to around 25 minutes including setting up parameters. Spectra data were quantified automatically using software developed in our lab [2]. Levels of choline, creatine, N-acetyl aspartate and lipid (Lip) were estimated using the sum of the two cycle data while lactate (Lac) was estimated from the difference spectra. Lac and Lip with height more than twice of the noise standard deviation were defined as significant and contours were generated. rCBV (regional Cerebral Blood Volume) was derived from the dynamic dataset and normalized to contralateral normal-look white matters [3].

RESULTS

Five out of the eight low grade patients showed significant increased Lac resonance with a volume ranging from 1.1 to 10.1 cc. Two of the patients were pre-surgery and three were post-surgery. One of the post-surgery patients also had significantly elevated lipid/macromolecules resonances at 1.3ppm with a volume of 9.9cc. All five GBM patients showed significant elevated Lip peaks with a volume ranging from 1.1 to 40.1 cc. All but one of the five GBM patients had significantly increased Lac with a volume ranging from 2.8 to 14.3cc. Two of them had Lac in the non-enhanced region within the T2-hyperintensity, which was different from the region with elevated Lip peaks. The latter tended to occur within the contrast enhancement and necrotic core, as in the example shown in Fig 1. Maximum rCBV was measured within the contours of elevated Lac and of elevated Lip. The maximum rCBV within the Lac contours was consistently smaller than 1.0 with median 0.86 and the value within the Lip contour was consistently higher than 1.0 with median 2.57.

DISCUSSION

Although the nominal voxel size of the reduced k-space acquisition used in this study was the same as that with cubic acquisition, simulations indicated that the true voxel size was around 40% larger than the latter and that less Gibbs ringing artifacts were obtained when imaging circularly limited objects such as the head [4]. Significantly elevated lactate was observed in a high proportion of the low grade patients, which suggests that it cannot be considered as a characteristic of just high grade gliomas. Increased lactate may occur when the lactate-producing anaerobic glycolytic pathway exceeds the capacity of the lactate-catabolizing respiratory pathways or when the cellular capacity for exporting lactate to the bloodstream is impaired. Thus lactate presence is expected to be a strong indicator of hypoxia or poor perfusion in the lesion. We hypothesize that high lactate levels in pre-treatment lesions will predict radio-resistance and provide a poor outcome. Mobile lipids were observed in all of the high grade lesions followed in this study. Higher rCBV was observed in the lipid regions and lower rCBV in regions with lactate. One possible explanation is that the hypoxia, as indicated by high lactate, occurs prior to tumor angiogenesis, whereas the lipid arises during and after angiogenesis and indicates the presence of macro- and micro-necrosis that can be induced by both tumor and treatment. This suggests that studying lactate and lipid signals may be important for providing information about tumor progression.

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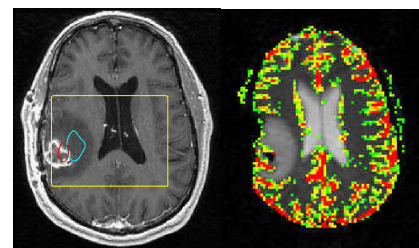


Fig 1. Contours of Lac and Lip (left. Yellow: PRESS box; Red: Lip; Blue: Lac) and rCBV map (right)