Proton-Decoupled 31P MR Spectroscopic Imaging of Radiation-Induced Temporal Lobe Necrosis

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Introduction
Late delayed radiation-induced injury of the brain is one of the most serious complications of radiation therapy (RT) for brain tumors and tumors at the skull base. It is generally irreversible and progressive and may be fatal [1]. The etiological mechanisms have not been resolved but endothelial damage and injury to oligodendrocytes have been implicated [2]. Late radiation-induced temporal lobe (TL) necrosis is one of the most serious complication of radiation therapy in the treatment of nasopharyngeal carcinoma (NPC), with an incidence of 4 to 18%. Previous evaluation on proton (H) magnetic resonance spectroscopy (MRS) has shown that morphologically more severe injury on imaging tended to have lower N-acetylaspartate (NAA)/creatine and NAA/choline (Cho). A significantly higher Cho/creatine (Cr) was also observed in the most severe necrosis, in which lactate might be present [3]. The objectives of the present study were to evaluate: (i) the feasibility of proton-decoupled 31P phosphorous spectroscopic imaging (31P SI) in the evaluation of radiation-induced TL necrosis and (ii) the bioenergetic and phospholipid metabolites in radiation-induced necrosis.

Methods
Fourteen patients with NPC treated by RT and complicated with radiation-induced TL necrosis for at least two years were recruited. The nasopharynx and adjacent regions were irradiated to the equivalent of at least 66 Gy. In vivo 2D 31P SI was performed on a 1.5 T whole-body system (Philips, ACS-NT) using a 31P head coil. The VOI was chosen using T1W survey images and oblique axial images (Fig. 1).

Results
Spectra obtained from a patient with severity grades of 3 and 4 in the temporal lobes and the morphologically normal occipital lobe are shown in Fig.2.

Fig. 1. Oblique axial image of a patient with right TL overall grade 3 and left TL overall grade 4. 31P spectra were acquired using TR 2250 ms, FOV 230 mm, matrix 8x8, slice thickness 30 mm, NEX 16 and 1024 samples.H-decoupling was implemented using a WALTZ sequence and nuclear Overhauser enhancement (NOE) was employed. Spectra at the TLs and the occipital lobes were selected and the FIDs were processed with a convolution difference to remove broad 31P signals. Spectra were analyzed in the time domain using VARPRO [4]. Conventional MR imaging was performed to assess the morphological severity of TL necrosis and an overall lesion severity category from 1 to 4 was assigned to each TL according to the method described in ref. [3].

Fig. 2. Spectra obtained from the TLs and from the normal occipital lobe shown in Fig.1. The pH of radiation-induced TL necrosis of all severity grades was within normal. Adenosine triphosphates (ATP)/inorganic phosphate (Pi) ratio and PCr (phosphocreatine)/Pi ratio showed no significant change with different lesion severity. No significant difference was observed when compared to metabolite ratios in the morphologically normal occipital lobes. Phosphoethanolamine (PEth)/glycerol-phosphoethanolamine (GPE) ratio, phosphocholine (PCho)/glycerophosphocholine (GPC) ratio, phosphomonoster (PME)/phosphodiesters (PDE) ratio and PCho/Ptotal ratio (Ptotal = sum of all visible phosphates) showed a decreasing trend with increasing severity of radiation necrosis (Fig. 3). All ratios in lesions with morphological severity grade 4 showed significant differences from ratios obtained in the occipital lobes.

Discussion
No significant pH changes was detected in radiation necrosis in temporal lobes when compared to the morphological intact occipital lobes. In a study of cellular energetics by 31P SI in multicellular tumor spheroids, Freyer et al found no correlation between the intracellular pH, the nucleotide triphosphate/Pi ratio or the PCr/Pi ratio and the size of tumor spheroids or the amount of central necrosis [5]. Absence of correlation of 31P MRS spectral energy-related parameters with necrotic areas in tumor has also been shown in vivo [6]. Metabolite changes in phospholipid metabolism was noted. A mild increasing trend of the PEth/PCho ratio with increasing severity of radiation necrosis was observed. This may be due to a decreasing PCho with increasing morphological severity of radiation necrosis or an increasing PEth with morphologically increasingly severe radiation necrosis. Using 31P MRS, Freyer et al showed that the PEth/PCho ratio was positively correlated with experimental tumor spheroid size, implying an elevation of PEth relative to PCho with increase in area of necrosis in the spheroids [5]. A decreasing PME/PDE ratio with increasingly severe grade of radiation necrosis implies the predominance of catalytic phospholipid membrane changes over anabolic changes. The decrease in PME/PDE ratio is consistent with the nature of pure radiation necrosis. The decreasing trend of PEth/GPE ratio and PCho/GPC ratio with increasing severity of radiation necrosis is also evidence for the catalytic predominance over anabolic change with regard to PME constituents and their glycerol-derivatives when the radiation necrosis becomes severe. In conclusion, our study has shown the lack of bioenergetic metabolite and pH changes in radiation necrosis. Increased phospholipid membrane catabolism with increasing severity of radiation necrosis is shown by the relative increase of PDE to PME and GPE and GPC to their precursors, PEth and PCho.

References