Radiation Toxicity to the Normal Brain Detected by Echoplanar Spectroscopic Imaging in Patients with Brain Metastases Treated with Whole Brain Radiation Therapy

S. Chawla[1], S. Wang[1], S. Sheriff[2], L. Desiderio[1], A. Lin[3], H. Quon[3], R. Rengan[3], E. R. Melhem[1], A. Maudsley[2], and H. Poptani[1]
[1]Radiology, University of Pennsylvania, Philadelphia, PA, United States, [2]Radiology, University of Miami, Miami, FL, United States, [3]Radiation Oncology, University of Pennsylvania, Philadelphia, PA, United States

Introduction: Whole brain radiotherapy (WBRT) is used to improve neurological symptoms and prolong median survival in patients with multiple brain metastases[1]. Serial magnetic resonance spectroscopy (^{1}H MRS) studies have been used to monitor response to radiation therapy from the tumor site in patients with brain metastases[2-4]. However, normal brain parenchyma is also affected by WBRT and these patients may experience cognitive impairment[5]. Therefore, it is pertinent to evaluate the extent of radiation-induced injury in normal brain regions affected by WBRT. Unfortunately, the single voxel or single slice multivoxel ^{1}H MRS methods used currently encompass only a small area of brain and thus are limited in assessing the whole brain. Echo planar spectroscopic imaging (EPSI) has recently been developed to map metabolite distribution throughout the brain with excellent spectral resolution and quality[6,7]. We thus sought to determine the potential of EPSI in detecting the metabolite alterations in tumors as well as normal brain parenchyma in patients irradiated with WBRT in the present study.

Methods: Three patients (mean age =64.66±5.13, 2M/1F) with multiple metastases were irradiated with fractionated WBRT (total dose=3000-4000cGy). These patients underwent magnetic resonance imaging and EPSI on a 3 Tesla MR system at three time points (pre-radiation, one month and three months post irradiation). Conventional imaging protocol included acquisition of T2, T1, PD and post contrast T1 weighted images with standard parameters. The spin echo EPSI data was acquired with chemical shift-selective (CHESS) water suppression pulses and lipid inversion nulling using an inversion time of 198 ms. The typical acquisition parameters were: TR/TE=1710/70ms, 50x50x18 phase encoding steps, excitation angle=73°, voxel size=5.6x5.6x10mm^3, field of view=280x280x180mm^3. The sequence also included an interleaved water reference acquisition scan obtained using a gradient-echo acquisition with 20°excitation angle and echo time =6.3 ms. Data were processed offline using the automated MIDAS tool described previously[8]. Area under the curves for N-acetylaspartate (NAA), total creatine (Cr) and total choline (Cho) were measured from multiple voxels involving contrast-enhancing region of the tumor. Non-neoplastic regions of the brain, such as bilateral dorsolateral prefrontal cortex (DLPFC), hippocampus (Hip), basal ganglia (BG), thalamus (Th), cingulate gyrus (CG) were also assessed. The averaged metabolite ratios (NAA/Cr and Cho/Cr) from each region were computed and compared between baseline and post-irradiation period.

Results and Discussion: Representative summed voxels and corresponding spectra from different locations of a brain metastasis patient prior to WBRT are shown in Fig 1. A decrease in NAA/Cr (9 - 21%) was observed from the BG, Hip, CG and Th from baseline to post-irradiation in two patients. A 7-11% decrease in Cho/Cr from Hip and CG was also observed in these patients, while the DLPFC showed an increase in the Cho/Cr ratio. Due to the poor quality of the baseline spectrum in the third patient, a similar analysis was not possible, however, a trend was observed in this patient that it showed a 10-14% decrease in NAA/Cr from the BG and Th from the second to the third time point indicating a steady decline in NAA/Cr over time. In addition, a 22% increase in Cho/Cr was also observed from CG in this patient. Reduction in NAA/Cr may be due to radiation-induced damage to neurons in these regions while alterations in Cho/Cr may be due to membrane turnover caused by neurodegeneration. These preliminary findings suggest that EPSI can be used to assess metabolite alterations and radiation toxicity in normal brain regions of patients with brain metastases undergoing WBRT and that EPSI may assist in better radiation planning.

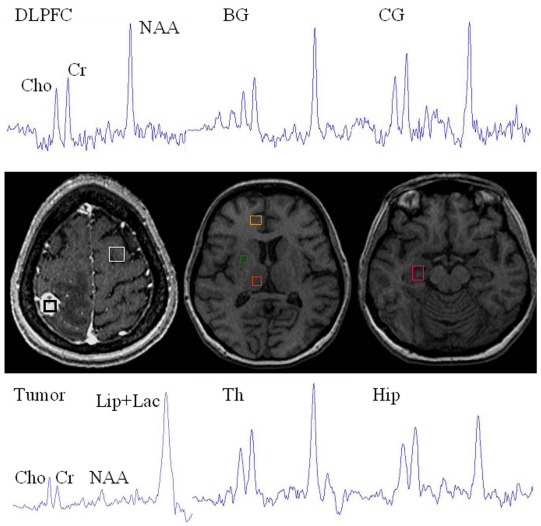

Fig 1. T1 weighted images demonstrating voxels from tumor (black), DLPFC (white), CG (yellow), BG (green), Th (orange) and Hip (Red). Corresponding spectra from these different regions are also shown.

References:

1. Davey P, et al. CNS Drugs 16:325-38,2002.
2. Yoshino E, et al. Stereotact Funct Neurosurg 66:240-59,1996.
3. Chernov M, et al. Minim Invasive Neurosurg 48:228-34,2005.
4. Chernov MF, et al. Brain Tumor Pathol 21:63-7,2004.
5. Shaw EG, et al. J Clin Oncol 24:1415-20, 2006.
6. Ebel A, et al. Magn Reson Med 46:1072-78;2001.
7. Maudsley AA, et al. Magn Reson Med 61:548-59;2009.
8. Maudsley AA, et al. NMR Biomed 19:492-503;2006.