

Assessing the effects of radiation therapy on normal brain tissue in patients with glioma using Susceptibility-Weighted Imaging at 7 Tesla

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Introduction: Radiotherapy (RT) is an integral component in the management of patients with glioma, but its potential effect on neurocognitive ability and quality of life has recently become of great importance as new treatments extend survival in less malignant grades [1]. It has been reported that glioma survivors experience progressive decline in neuropsychologic function after irradiation, with patients treated with partial as opposed to full brain irradiation having improved outcome [2]. The histologic response to radiation includes vasculopathy, with progressive impairment in cerebral microcirculation and formation of cavernous angiomas that may slowly or acutely hemorrhage. Susceptibility-weighted imaging (SWI), in addition to visualizing microvasculature, is a powerful tool for imaging hemosiderin-containing microbleeds [3,4]. At 7T, heightened susceptibility effects provide enhanced sensitivity to these lesions, which could potentially be useful for examining changes in normal brain tissue after exposure to radiotherapy. The goal of this study was to use 7T SWI to evaluate the intermediate- and long-term effects of radiation therapy on normal-appearing brain tissue by assessing the number and location of the appearance of microbleeds as a function of time since treatment.

Methods: Twenty patients with stable gliomas (5 grade II, 13 grade III, 2 grade IV), scanned at 23 time points, were recruited for this study. Seventeen patients received prior external beam radiation therapy (x-RT), either with or without adjuvant chemotherapy, between 1 and 16 years prior to the time of imaging. Six patients treated with chemotherapy only from 1–6 years prior to imaging were scanned as controls. High resolution SWI was performed on a GE whole body 7T scanner with volume excitation and 8-channel phased-array reception, and employed a 3D SPGR sequence with TE/TR=16/50ms, flip angle=15°, BW=62.5kHz, 24x24cm² FOV, and 2mm slice thickness. To keep the scan time under 6 minutes, a GRAPPA-based parallel imaging acquisition was utilized with either a 2- or 3-fold reduction, 512x144 acquired matrix, and 16 autocalibrating lines [5]. Standard SWI post-processing was performed on the reconstructed k-space data for each coil, and then combined, intensity corrected, and projected through 8 mm-thick slabs. Phase imaging was also performed to confirm the absence of calcification in these lesions. Clinical pre- and post- gad T1-weighted SPGR and T2-weighted FLAIR images were acquired at 3T immediately after the 7T exam and used to identify regions of contrast enhancing lesion and T2-hyperintensity, respectively, which were then overlaid on the SWI images. Microbleeds were identified as discrete foci of susceptibility that did not correspond to vessels or hemosiderin staining of the surgical cavity on consecutive slices. The number of microbleeds was counted within the T2 hyperintense lesion excluding contrast-enhancing tumor (T2L), outside the T2L, and in the contralateral hemisphere of the original tumor. For three patients, radiation dosimetry maps were reconstructed on a Philips Pinnacle treatment planning system and fused with the 7T SWI data after alignment to the original treatment CT images using mutual information.

Results: 7T SWI scans revealed an increase in both the total number of microbleeds and the percent of which resided outside the T2 lesion with time from radiation therapy, as shown in Figures 1 and 2A. Patients who received solely chemotherapy did not exhibit microbleeds as far as 6 years from onset of therapy (Figure 1, top panel). Only 2 lesions in total were found in the 4 patients who received RT within 2 years of the scan date. Less than 10 microbleeds were observed in each of the 3 patients who received RT within 3 years of the SWI scan, 90% of which resided within the T2 lesion, and all were located in the same hemisphere as the initial tumor. In the one patient who was scanned serially at 1.6, 2.4, and 3.2 years post-RT (Figure 2B), no lesions were observed at 1.6 years, 6 were observed at 2.4 years, and 25 at 3.2 years, even though the tumor was stable. After 5 years post-RT, there was a larger variation in the number of lesions, which could be due to differences in the extent of radiation dose received to healthy brain tissue. Figure 2C demonstrates how the majority of these microbleeds reside within tissue that received 98% of the maximum dose for these two patients. No trends were found between the number of microbleeds and grade, pathology, or location of the tumor.

Conclusions: High-field SWI has potential for visualizing the appearance of hemosiderin containing microbleeds associated with long-term effects of radiotherapy on brain tissue. The prevalence of these lesions increases over time since receiving radiation therapy. The ability to visualize these lesions in normal brain tissue may be important in further understanding the utility of this treatment in patients with grade 2 and grade 3 tumors with longer survival rates. Future studies will investigate serial within-patient changes over time, and correlate the number and location of microbleeds with radiation dose and neuro-cognitive decline.

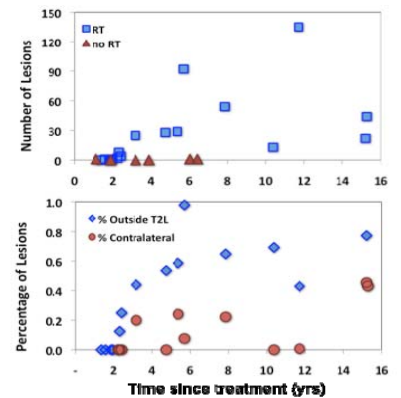


Figure 1: Number of microbleeds as a function of time since RT or chemo-therapy (top) and percentage of total that extended beyond the T2 lesion or into the contralateral hemisphere (bottom)

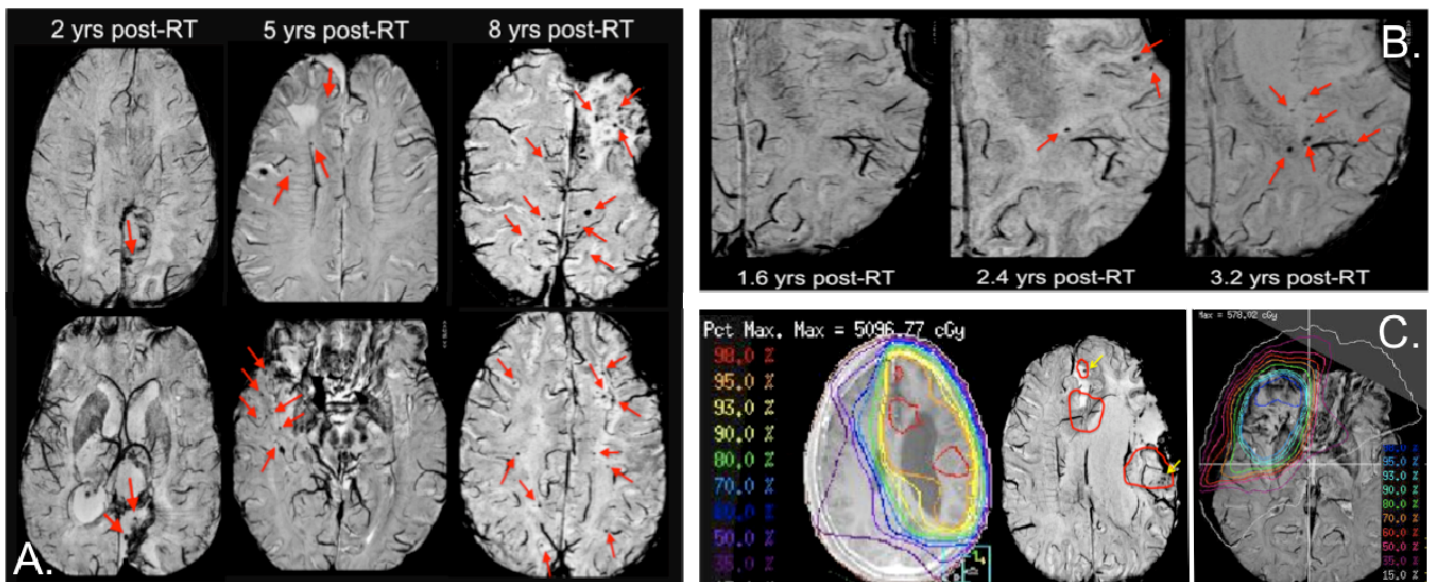


Figure 2: (A) 7T SWI images of 3 different patients scanned at 2, 5, and 8 years post-RT, (B) Example of a patient with a grade 3 oligodendroglioma scanned serially at 8 month intervals post-RT, and (C) Radiation dosimetry maps overlaid on 3T T1 post- gad images (left) and 7T SWI images (middle & right) for a grade 3 oligodendroglioma 3 years post-RT (left panel) and a grade 2 oligoastrocytoma 5 years post-RT. Red and yellow arrows denote microbleeds.

References: [1] Karim A et al. Int J Radiat Oncol Biol Phys 2002;52(2):316-324, [2] DeAngelis et al. Neurology 1989;39(6), [3] Haacke EM et al. MRM 2004; 52(3). [4] Haacke EM et al. AJNR 2007;28(2):316-7. [5] Lupo JM et al. MRI 2009 May;27(4):480-8

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