Multimodality (MR/PET/CT) Monitoring Preoperative Systemic Therapy in Operable Breast Cancer

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INTRODUCTION: Preoperative systemic therapy (PST) is frequently used in patients with operable breast cancer [1]. Non-invasive imaging of breast lesions is feasible using techniques such as proton [2], sodium (23Na) [3] and PET/CT imaging [4]. We have evaluated the utility of combining these methods to provide new insights into the molecular and metabolite environment of breast tumors during PST and as a potential early predictive marker of response.

METHODS: Five patients with operable breast cancer undergoing PST were studied before beginning PST and after the first cycle of chemotherapy (days 7-8). MRI data were acquired on a GE Signa 1.5T MRI scanner. Fat-suppressed MRI T2 (TR/TE = 5700/102) and T1 FSPGR (TR/TE = 200/4.4ms) with FOV = 18x18cm, 256x192, slice thickness = 4mm were acquired. GdDTPA contrast agent (0.1 mmol/kg) was administered, and fat-suppressed 3D T1 FSPGR (TR/TE = 20/4, 512x160, 2mm) pre- and post-contrast images were obtained. Sodium MR images were obtained with Twisted Projection Imaging (TE/TR=0.4/120ms) [5,6]. Total data acquisition time was about 45 min. PET/CT data was acquired with GE Discovery LS following the i.v. injection of FDG at a dose of 0.22 mCi/kg. A 50-minute uptake period was followed by quantitative 2d PET imaging. After PST, patients had a clinical assessment of tumor response, e.g, complete, partial, or no response, and a pathological assessment of residual disease at the time of definitive surgery. Volumes were obtained with a semi-automated segmentation algorithm, the Eigenimage method [6]. Quantitative estimates of sodium content were made using an external reference technique [7]; SUV lean-max lesion data was measured from the PET/CT data [7]. Descriptive and ANOVA statistics are presented as mean and standard deviations.

RESULTS: Five patients (age, 44±16yr) diagnosed with adenocarcinoma of the breast received a taxane-based PST. Four had a pathologic partial response (pPR) and one had no response. Tumor volume decreased significantly between baseline and after cycle 1 (C1) by 43% in responders and 35% in nonresponders ($p<0.05$). Total sodium concentration decreased by 24% in responders and increased 3% in nonresponders ($p=0.06$). SUV lean-max significantly decreased by 37% in responders and 22% for nonresponders ($p<0.05$). Of note, one patient with invasive lobular histology and low FDG uptake before and after treatment had a large decrease in tumor volume and sodium concentration. Figure 1 demonstrates the application the methods to a 35 year old with an infiltrating ductal carcinoma. Conversely, Figure 2 demonstrates low FDG uptake on an invasive lobular breast cancer, that is clearly visualized using MRI. Similar trend were noted on MRI and the final histopathogical diagnosis was partial response.

DISCUSSION: We have demonstrated the feasibility of monitoring PST in patients with operable breast cancer using multi-modality proton, sodium MR, and PET/CT imaging. Significant decrease in tumor volume, total sodium, and SUV were observed. These methods provide a basis for a comprehensive evaluation of the complex tumor environment by examining the changes in volume and sodium and glucose metabolism in response to therapy. These data serve as proof of principle and suggest the potential utility of this technology to monitor PST and predict response.

REFERENCES:[1] Kaufman M et al *J Clin Oncol* 2005, in press, [2] Jacobs MA, *Radiology.* 2003;229 (1):225-232. [3] Jacobs MA, *Technol Cancer Res Treat.* 2004 3(6):543-50 [4] Wahl RL *J Clin Oncol.* 1993;11:2101-11. [5] Boada FE, et al. *MRM* 1997; 37:706-15. [5] Ouwerkerk R, *Radiology.* 2003;227:529-537. [6] Jacobs MA, *JMRI.* 2000;11(4):425-37. [7] Sugawara Y, *Radiology.* 1999;213:521-525.

ACKNOWLEDGMENT: Zaver Bhujwalla, PhD for helpful discussions. 1R01CA100184, P50 CA103175, 1R21CA95907-01, and CA-88843AV15

Figure 1. Combined multimodality images on a 35 y/o female. Baseline MR volume was 32cc, 28cc after C1, and 12cc before surgery. The sodium concentration within lesion before was 42.8mMol, after C1, 41mMol. SUV significantly changed from 6.7 to 3.15 after C1.

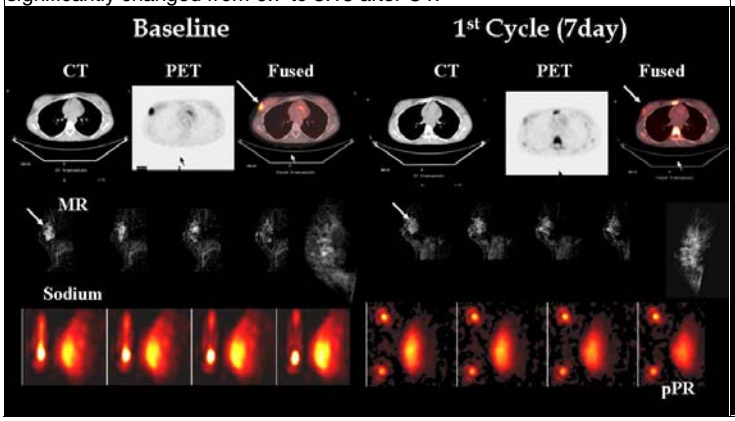

Figure 2. Demonstrates low FDG uptake on an invasive lobular breast cancer, that is clearly visualized using proton and sodium MR. Similar trends were noted on this case with the changes in MR and sodium volume and the patient had a pPR after PST.