Monitoring Primary Systemic Therapy in Locally Advanced Breast Cancer using Proton and Sodium Magnetic Resonance Imaging

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INTRODUCTION: Preoperative systemic therapy (PST) is increasingly being used in patients with locally advanced breast cancer (LABC) as part of combined multimodality therapy[1]. In vivo assessment (tissue acquisition and imaging studies before and after PST) is likely to improve decision-making and outcome. Non-invasive imaging of breast lesions is feasible using techniques such as proton and sodium (23Na) imaging[2-4]. We have evaluated the use of these MR methods to provide new insights into the molecular and metabolite environment of breast tumors during PST.

METHODS: Five patients with LABC undergoing PST with an anthracycline-based regimen (with or without taxanes) were studied. MR data were acquired on a GE Signa 1.5T MR scanner. Fat suppressed MRI T2 spin echo (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. A 3-turn 23Na solenoid coil was built to fit in the MR breast coil. 23Na images were obtained with Twisted Projection Imaging (TE/TR=0.4/120ms)[5]. Total data acquisition time was about 45 min. After PST, patients had a mastectomy or lumpectomy with pathological assessment of tumor response. Volumes and vector characteristics were obtained with an unsupervised segmentation algorithm, the Iterative Self-Organizing Data Analysis Technique (ISODATA)[6]. Quantitative estimates of sodium content were made using an external reference technique[7]. Descriptive statistics are presented as mean and standard deviations.

RESULTS: We have applied our methodology to five patients receiving PST therapy for adenocarcinoma of the breast. Two patients had pathologic complete response, two had a pathologic partial response, and one had progressive disease during chemotherapy. Volume size of the tumor decreased between baseline and after the 1st cycle of PST by 49% for responders and 31% for nonresponders. Total volume changes between baseline and last cycle of PST was 80% for responders and 69% for nonresponders. Normal volunteer sodium concentration was 17.4±1.6mM for fatty and 39.5±10 for glandular. Figure 1 demonstrates the application the methods to a 54yr receiving PST. Her initial histological result was infiltrating ductal carcinoma. Baseline MR volume was 33cc, 11cc after the 1st treatment, and 3.9cc before surgery. There were significant changes in sodium concentration within lesion (61.8 mMol/kg) after the 1st treatment (48.9mMol/kg) and remained constant until surgery. Moreover, the ISODATA vector characteristics significantly changed during treatment, glandular tissue = 13.4° (baseline), 14.2°, 1st cycle, and 6.3° before surgery. Similarly, the lesion ISODATA angle was 16.6° (baseline), 30.7°,1st cycle and 20.3° before surgery.

DISCUSSION: We have demonstrated that monitoring PST in patients with LABC is feasible using multiparametric proton and sodium MR imaging. By combining these MR data into the ISODATA model will enable us to further investigate the biophysical environment of a breast lesion in the clinical setting by defining the different tissue signatures in breast lesions. These methods provide a basis for a comprehensive interrogation of the complex tumor environment by examining the changes in volume and sodium and tissue signature vector characteristics. In conclusion, The results of these studies should improve our understanding of the factors affecting efficacy of PST intervention and may yield potentially useful information to guide therapy in breast cancer patients.

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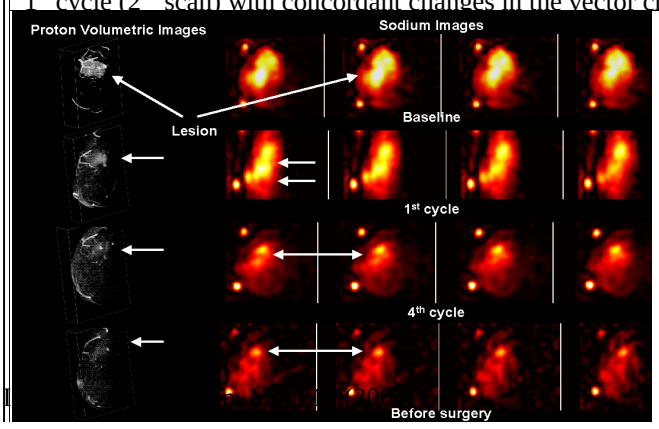
Fig 1. A 54 y/o patient that underwent PST. The lesion is clearly visible in the baseline sodium MR and proton volumetric images. However, there was a significant decline in both volumes and sodium concentration after the 1st cycle (2nd scan) with concordant changes in the vector characteristics.



MR Scan	MR Volume	Sodium mMol/kg	ISODATA Angle
Baseline	33 cc	61.8	16.6
1st Cycle	11 cc	48.9	30.7
Last	4 cc	48.1	20.3

Final Diagnosis: Complete pathological response