HIGH RESOLUTION BREAST DWI TO EVALUATE THE TUMOR-STROMAL BOUNDARY IN PATIENTS RECEIVING NEOADJUVANT CHEMOTHERAPY

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Introduction: Increasing evidence shows that the tumor microenvironment influences many steps of tumorigenesis. Tissue structures at the tumor-stroma border of breast tumors, such as collagen density and alignment, play a role in tumor formation [1,2], invasion [1,3], and patient outcome [4]. We hypothesized that DWI may be sensitive to the macromolecular effects of collagen alignment as it forms larger mechanical structures at the tumor-stroma border, as well as changes in these structures in response to treatment. We recently reported results [5] using a high resolution (HR) DWI sequence for the breast that decreases the detected voxel size by six-fold, resulting in finer spatial resolution of water mobility within the breast tissue. In this study, we investigated the changes in diffusion measurements relative to distance from the tumor boundary in patients receiving neoadjuvant treatment.

Materials and Methods: MRI data were collected for patients with locally advanced breast cancer enrolled in an IRB-approved study at UCSF; all patients signed informed consent. All patients had pathology-confirmed invasive breast cancer and underwent neoadjuvant chemotherapy using taxane-based therapy (T) followed by doxorubicin cyclophosphamide (AC). Patients had MRI scans before (V1), early during T (V2), following T, before AC (V3), and after neoadjuvant chemotherapy (V4). MRI data were collected on a 1.5 T GE Signa scanner LX (GE Healthcare) using a bilateral 8-channel phased array coil (Sentinelle Medical, Toronto, Canada). In addition to a standard fat-suppressed T1-weighted dynamic contrast enhanced (DCE) MRI, HR DWI was acquired with an echo planar imaging sequence [6] and the following parameters: TR/TE=4000/64.8ms, FOV=70x140mm, matrix=28x64, b=0,600, and voxel size=1.1x1.1x4.0mm.
HR DWI images were manually segmented into tumor and non-enhancing, surrounding stromal tissue on all slices. A proximity mapping method developed in house [7] was used to assign each stromal voxel a distance to the nearest tumor voxel. These distances were used to calculate the mean apparent diffusion coefficient (ADC) for the voxels in 1 mm shells, starting at 10 mm into the tumor (-10 mm) and ending at 20 mm away from the tumor. Mean ADC was calculated for three distance ranges as shown in Figure 1A: -5 to -2 mm (blue), 2 to 5 mm (green), and 10 to 13 mm (purple), called tumor (ADC_tumor), proximal exterior (ADC_prox), and distal exterior (ADC_dist), respectively. Differences in ADC – ΔADC_edge (ADC_prox - ADC_tumor, orange arrow) and ΔADC_stroma (ADC_dist - ADC_prox, red arrow) – were then calculated. For the purposes of this study, we defined volume response as the percent change in DCE MRI measured volume from V1 to V3.

Results: A subset of ten patients with HR DWI at V1 were evaluated; seven of those patients also had HR DWI scans at V2. For all patients, ΔADC_edge was positive; however, the value varied among patients. Variable ADC patterns were seen in the stroma, with patients showing stable, decreasing, or increasing exterior ADC values as seen in Figure 1B. At V2, ΔADC_edge had decreased for six of the seven patients. In four of those patients, the ΔADC_edge decrease was primarily due to increases in ADC_tumor. Although ΔADC_stroma changed from V1 to V2, no trend was observed. Figure 2B shows the percent change in ΔADC_edge from V1 to V2 versus the volume response of the patient. In this subset, larger changes in ΔADC_edge appear to be associated with larger volume response.

Discussion: These preliminary studies show that tumors and surrounding tissue had variable ADC patterns at V1 and V2, suggesting that water mobility properties vary among tumors. Our early results suggest that a decrease in ΔADC_edge from V1 to V2 may identify tumors that will respond. This study is ongoing, and we plan to further investigate the correlation between these phenomena and other tumor characteristics in additional patients.

References: [1] Provenzano PP, et al. BMC Medicine 2008; 6: 1-15. [2] Lopez JI, et al. Integr. Biol. (Camb.) 2011; 3: 910-921. [3] Provenzano PP, et al. BMC Medicine 2006; 4: 1-16. [4] Conklin MW, et al. Am. J. Path. 2011; 178: 1221-1232. [5] Singer L, et al. Acad. Radiol. In press. [6] Saritas EU, et al. Magn. Reson. Med. 2008; 60: 468-473. [7] Klifa C, et al. ISMRM abstract Proc. Intl. Soc. Mag. Reson. Med. 2011.

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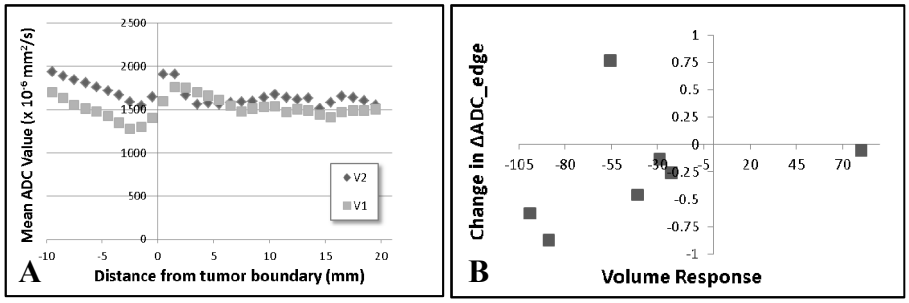

Figure 2: A) The mean ADC values of a representative patient at both V1 and V2 are plotted as a function of distance from the tumor boundary. B) The change in ΔADC_edge versus the volume response is plotted for all patients.

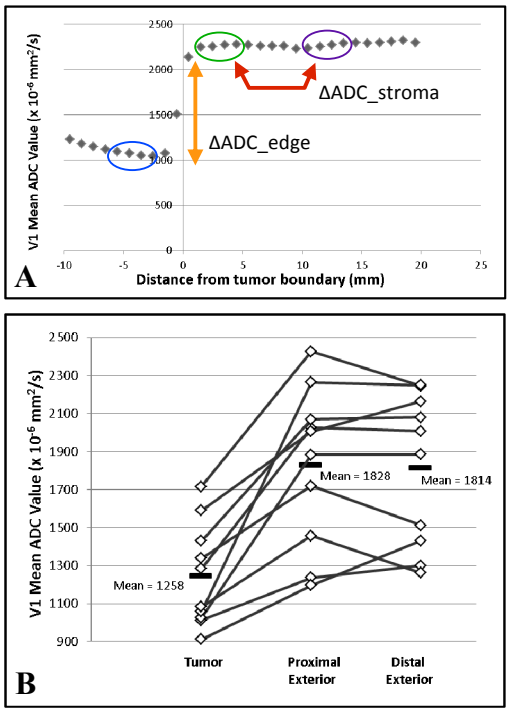

Figure 1: A) The mean ADC values are plotted as a function of distance from the tumor boundary for a patient at V1. B) The V1 mean ADC values for tumor, proximal exterior, and distal exterior are shown for all patients.