DIGITAL "PROXIMITY MAPPING" TO ASSESS RADIAL DEPENDENCE OF BREAST STROMAL ENHANCEMENT ASSOCIATED WITH RESPONSE TO NEOADJUVANT CHEMOTHERAPY.

C. Klifa[1], D. Newitt[1], C. Park[2], S. Suzuki[1], L. Wilmes[1], Y. Lu[3], and N. Hylton[1]

[1]**Radiology and Biomedical Imaging, University of California San Francisco, San Francisco, california, United States, [2]Department of Radiation Oncology, University of California San Francisco, San Francisco, California, United States, [3]Department of Health Research and Policy, Stanford University, Stanford, California, United States**

Introduction: Dynamic contrast enhanced (DCE) MRI of the breast can generate high quality 3D images from which quantitative breast tumor volume and perfusion characteristics can be calculated. There is growing interest in understanding and characterizing the role of normal appearing fibroglandular tissue (NAFT) surrounding breast tumors. Quantitative measures of NAFT may provide important information for local radiation treatment options and allow better monitoring of treatment response. While CAD systems have been developed to measure tumor pharmacokinetics or morphology from breast MRI data, most assessment of the normal tissue is performed qualitatively: this visual assessment lacks the robustness, objectivity and quantitative conclusions needed to accurately assess tissue changes in patients over time. We present a new technique that automatically assesses MRI-based functional properties of NAFT surrounding invasive breast tumors, based on closest proximity ("proximity mapping"). We applied this technique to study MRI characteristics of NAFT in a group of patients with invasive cancers.

Materials and Methods: We applied the proximity mapping technique to MRI data acquired for 46 women with locally-advanced breast cancer, enrolled in a study evaluating MRI for assessing response to neoadjuvant chemotherapy. The study was approved by our Institutional Review Board and all patients gave informed consent. The patient mean age was 47.2 years (range [32-63.8]). All patients underwent three MRI examinations: prior to treatment, after one cycle Adriamycin/Cyclophosphamide (AC) and at end of AC before surgery. We studied proximity-based measures of MRI parameters at baseline and after 1 cycle AC. For all patients, pathology and radiology reports and a disease free survival follow-up of 3 years were available. MR images were acquired on a 1.5 Tesla GE scanner using a dedicated bilateral phased-array breast coil. For DCE-MRI, T1-weighted images were acquired using a 3D fast gradient echo 3DFGRE sequence with the following parameters: TR/TE=8.4/4.2ms, NEX 2, 256x256 matrix, FOV 20cm, slice thickness 2mm. Gadopentetate dimeglumine (Magnevist, Bayer Health Care) was injected at a dose of 0.1 mmol/kg. Three time points were acquired: a baseline scan before injection followed by two post- contrast scans at 2.5 and 7.5 minutes [1]. The proximity mapping method allows the automated measure of structural or functional parameters in regions spreading radially from the edges of breast lesions via the following steps: 1) the breast tumor is automatically segmented from DCE-MRI images using an automated method based on the Signal Enhancement Ratio (SER) technique [2-3] (Figure 1a-c); 2) the breast fibroglandular tissue volume is separately extracted from adipose in the entire breast volume using semi-automated segmentation [4]; 3) a proximity map is created by labeling each voxel in the fibroglandular tissue mask with the shortest distance from any tumor voxel (Figure 2); 4) 3D shells surrounding the tumor are defined at different proximity ranges, e.g. 10-20mm from the tumor edge (Figure 1d). The proximity map was subsequently applied to measure mean enhancement values at increasing distances from the tumor edge and extending 60 mm radially.
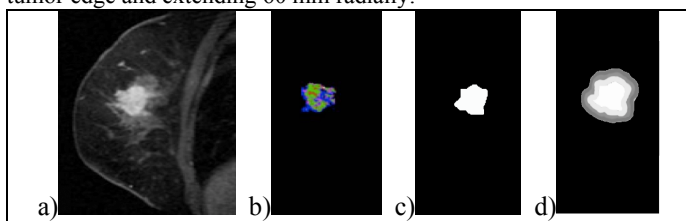

Figure 1: a) Original first contrast MRI volume showing an enhancing (bright) tumor region; b) Color-coded SER map of the tumor in a); c) tumor map (white); d) surroundings of tumor region (3D regions displayed are 10-20-30 mm from tumor border)
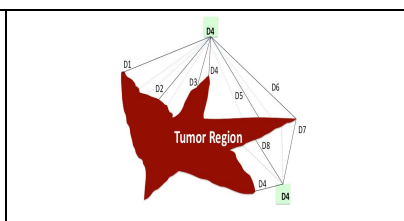
Figure 2: Schematic diagram showing proximity mapping of each voxel (gray square) with the shortest distance from the nearest tumor voxel
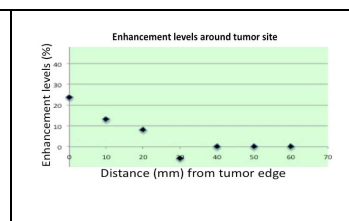
Figure 3: Enhancement levels around the lesion, for one patient

Results: A gradient of decreasing enhancement with increasing distance from the tumor was found for the radial regions of NAFT in all patients. Figure 3 shows the mean enhancement values in different tumor proximity ranges for one patient. In univariate analysis, the level of enhancement measured after the first cycle of therapy in normal breast tissue within 10mm from tumor, corrected for age, showed a trend toward being an independent predictor of disease free survival (p=0.058).

Discussion: A new proximity mapping technique was used to evaluate the radial dependence of low-level enhancement in non- affected fibroglandular tissue surrounding breast tumors. In contrast to a previous study of stromal enhancement using a manual approach, this study using proximity-based assessment was able to measure a radially-dependent association of stromal enhancement and patient outcome [3]. Proximity-mapping is a generalizable method that can be used to quantify the radial dependence of any functional property of stroma measurable by breast MRI, including mean apparent diffusion coefficient (ADC). Our results suggest that non-tumor tissue enhancement levels can potentially be used to better target local therapy and/or to monitor patients receiving cancer treatment. Future larger studies are needed to fully assess the role of the host tissue and tumor-adjacent tissue properties.

References: 1. Partridge SC et al. *MRI measurements of breast tumor volume predict response to neoadjuvant chemotherapy and recurrence- free survival.* American Journal of Roentgenology AJR 2005; 184:1774–1781. **2.** Hylton NM. *Vascularity assessment of breast lesions with gadolinium-enhanced MR imaging.* Magn Reson Imaging Clin N Am, 1999, 7(2):411-20. **3.** Hattangadi J.,et al. *Stromal enhancement by MRI is associated with response to neoadjuvant chemotherapy*, American Journal of Roentgenology AJR 2008, 190:1630-1636. **4.** Klifa C. et al**.** *Quantification of Breast Tissue Index from MR data using Fuzzy Clustering*, IEEE Engineering in Medicine and Biology Society, Vol. 3, p.1667-1670, 2004.