Breast Cancer Evaluation using Diffusion Weighted MR-Imaging – Prior to and Following Chemotherapy Can DWI Predict Chemotherapeutic Response?

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Introduction:

Pre-operative adjuvant chemotherapy for treatment of breast malignancy has become a standard approach attacking this disease, but has variable success in reducing or eliminating macroscopic cancer. MRI has been shown to be superior to other methods for assessment of amount of tumor size reduction (1,2).and several studies have suggested contrast enhanced MRI performed during chemotherapy can predict outcome (3,4). However, no MR (or other) technique has reliably predicted eventual tumor response a priori. We and many other investigators have assessed the utility of Diffusion Weighted MR-Imaging (DWI) of breast cancer, finding an enticing difference in Apparent Diffusion Coefficient (ADC) of malignant vs. benign or normal breast tissues (5,6). These ADC differences are thought to relate to a combination of factors including cell density, structure, necrosis, fibrosis and vascularity. In each study, there was clearly also significant variability between malignant lesion's ADC values (50-60%) that could potentially correlate with a tumor's resistance to chemotherapy. We have evaluated women with advanced stage breast malignancy, prior to, during, and following cytotoxic chemotherapy to determine if DWI was predictive of tumor shrinkage prior to treatment.

Methods:

The primary malignancy and normal breast parenchyma in 12 patients was assessed using DWI and MR-imaging performed prior to and after each of 3 cycles of chemotherapy (doxorubicin and cyclophosphamide). Comparison was made between ADC values for each tumor and the amount of volume reduction that occurred by the end of treatment. Tumor volume was determined using contrast enhanced MRI measurement before and during treatment and histologic measurement after definitive surgery. Exams were performed on a Philips 1.5T Intera using 4-element breast coil (MRI-Devices, Inc.). The diffusion-weighted single-shot spin-echo SENSE EPI 5mm axial slices covered the entire breast. Parameters included TR/TE/FA = 1600ms/43ms/90°, FOV=22cm, matrix=96×128, 4avgs. and SENSE X2 reduction factor = 48sec scan. The 60mT/m gradient option was employed to minimize TE. Prone positioning and oblique transverse phase-encoding direction minimized respiratory and cardiac motion. Diffusion-gradients were employed along 3 orthogonal directions with b values of 0, 400, 700, 1000 s/mm^2 A co-registration of DWI images carried out using unwarping technique that corrected for eddy current-induced distortion[6]. Regions of interest (ROI) were determined using b=0 DWI and standard images. A main magnetic field homogeneity map image was acquired before each DWI sequence and used to provide optimal correction of field distortion prior to ADC calculation. Image co-registration, ADC map calculation, and further analysis were performed off-line using IDL program (Research Systems Inc).

Results:

Prior to therapy, the ADC values of breast malignancy averaged 1.33 x 10^{-3} mm^2/s (range = 0.95-1.62) and normal parenchyma averaged 1.76 (range = 1.49-2.31). Of the 10 patients who have had surgery and histologic proof of results, half had tumor volume reduction of greater than 90% and half had poor response of less than 50% reduction (ADC averages 1.19 vs. 1.42 respectively). The lowest ADC for a poor-responder was 1.28. In these same two groups, average change in ADC (pre-chemotherapy vs. last post-chemotherapy) was about +20% for both, with a wide range (0 to +44%). The alteration of ADC values of normal parenchyma was minimal, with the average changing no more than 5% throughout chemotherapy. Assessment of the initial ADC ratios of each lesion compared to its adjacent normal parenchyma suggested no correlation with subsequent chemotherapy response.

Discussion:

Breast cancer is known to be a highly heterogeneous disease; histological variants abound. Against this backdrop, it is clear that a single imaging method of assessment will likely fail to deliver accurate predictions concerning each lesion's character and its response to therapy. A battery of imaging (and potentially other) tests may be needed to assess the wide range of malignancies encountered. Use of DWI is promising as a tool within a battery of MR-Imaging tests since many malignancies have ADC values that are far below the lowest values registered for normal tissue (only 2 cancers had "crossover" in our study). To our knowledge, no attempt has been made to use DWI techniques to predict outcome of breast cancer response to cytotoxic chemotherapy. This limited pilot-study suggests a correlation between lower ADC values and subsequent positive response to therapy. The number of patients assessed at this date is too small to draw firm conclusions. However, the range of ADC values for breast cancer determined in this study is nearly identical to those we have previously encountered using a similar DWI technique 2 years prior, indicating that this type of data is reproducible. Unfortunately, our technique is still known to be at least slightly inaccurate due to the significant perfusion effect that occurs using low b-values and other factors we have documented previously. Multiple improvements in technique (both DWI and specific measurement methods) will be needed to allow this to be used as a reliable tool in the imaging arsenal we require to diagnose and combat breast cancer.

Conclusions:

1. Breast malignancies with very low ADC values are more likely to respond to this cytotoxic chemotherapy.
2. DWI breast lesion to parenchyma ratios are not predictive of a positive or negative response to chemotherapy.
3. Use of DWI data for discrimination of malignant vs. benign disease is more accurate in a background of dense breast parenchyma, the scenario that often causes more difficulty for other imaging methods.

References:

1. Weatherall PT, Evans GF, Metzger GJ, et al. *J Magn Reson Imaging* 13:868-875 (2001).
2. Schott AF, Roubidoux MA, Helvie MA, et al. *Breast Cancer Res Treat*, 92:231-238 (2005).
3. Pickles MD, Lowry M, Manton DJ, et al. *Breast Cancer Res Treat*, 91:1-10 (2005).
4. Rieber A, Brambs HJ., Gabelmann A., et al. *Eur Radiol*, 12:1711-1719 (2002).
5. Woodhams R, Matsunaga K, Kan S, et al. *Magn Reson Med Sci*, 4:35-42 (2005).
6. Kuroki Y, Nasu K, Kuroki S, et al. *Magn Reson Med*

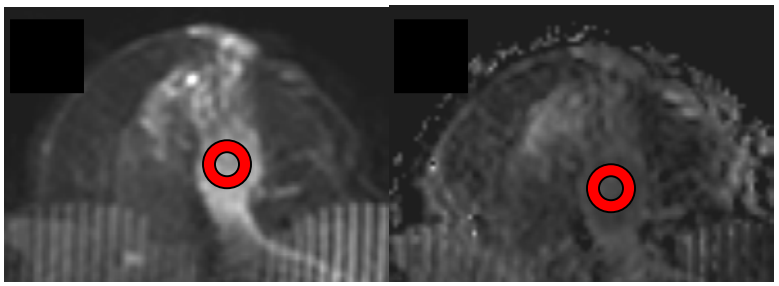

Figure 1: Transaxial DWI b=0 image (A) and ADC map (B) with Region Of Interest (ROI) drawn in the tumor area anterior to obvious artifacts.