Tracking Water diffusion in the Mammary Ductal Trees with MRI: A novel Method for Breast Cancer Detection

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The functional breast tissue is composed of many systems/lobes, which are highly variable in size and shape. Each system has one central duct with its peripheral branches forming a ductal tree and their associated glandular tissues. This architecture is very challenging to study in its entirety particularly *in vivo*. Mammary malignancies develop from the epithelial cells of the ducts, and spread within the ducts and infiltrate the ducts walls. Consequently, in ductal structures with malignant growth, the diffusion properties (direction and coefficient in each direction) are modulated. We have developed and applied magnetic resonance diffusion tensor imaging (MR-DTI) of the breast for tracking the anisotropic water diffusion in the mammary ductal trees. This innovative approach provided us with a means for detecting breast cancer due to the ducts blockage by malignant growth.

The experimental protocol of diffusion tensor imaging at 3 Tesla involved recording axial, bilateral diffusion weighted images at high spatial resolution (2x2x2 mm^3), using twice-refocused SE-EPI with field gradients at 64 different directions and at two diffusion gradient strengths. Calculation of the diffusion tensor per voxel and construction of parametric maps of the diffusion characteristics required several steps in which special algorithms were developed and applied. The final output of this analysis yielded voxel resolution maps of the 3 eigenvectors defining the diffusion directions (ν_1, ν_2, ν_3), and their corresponding eigenvalues defining the diffusion coefficients (λ_1, λ_2, λ_3).

The fibroglandular breast tissues in healthy volunteers (n=23) exhibited anisotropic water diffusion in the ductal regions with ν_1 aligned towards the nipple and an average first diffusion coefficient (λ_1) and anisotropy factor (λ_1-λ_3) of $2.1\pm0.2\times10^{-3}$ and $0.7\pm0.1\times10^{-3} mm^2/sec$, respectively. Cancerous tissues (13 cancer lesions in 10 patients) were clearly distinguished from normal fibroglandular tissue in the λ_1 parametric maps and exhibited a significantly, ~2 fold lower, λ_1 and λ_1- λ_3 values ($p<0.0001$) , as well as a disordered vector alignment in the ν_1 vector map due to the ducts blockage. Thus, the simultaneous presence of low 1st diffusion coefficient, low anisotropy factor and disordered orientation of the 1st eigenvector derived from DTI analysis enabled unequivocal delineation of breast malignancy. The proof of principle resulting from this study indicates that this fast, fully non invasive and safe method has the potential to meet the challenge of tracking the mammary trees *in vivo* and to be applied for breast cancer screening.