Phase Gradient Mapping (PGM) for Positive Contrast Generation

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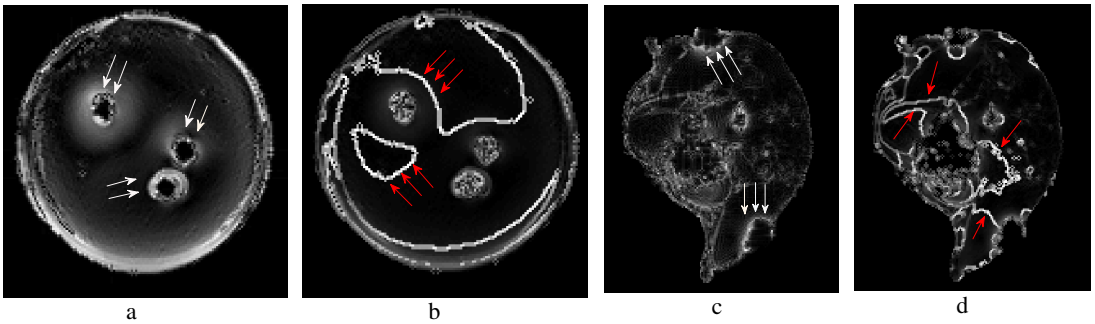
Introduction: Detecting paramagnetic contrast agent *in vivo* can be used in many applications such as cell tracking. Traditional T2-weighted sequence generates a signal loss appearing as a dark spot, referred to as negative contrast, at the site of paramagnetic contrast agent. Recently, there have been many efforts [1,2] to generate a positive contrast image by modifying pulse sequences. Liu et al [3] proposed a post-processing method referred to as the SGM (Susceptibility Gradient Mapping) without pulse sequence manipulation. In this study, a new post-processing method, referred to as PGM (Phase Gradient Mapping), is proposed to obtain a positive contrast image. The proposed method is different from the SGM in that the SGM measures a susceptibility induced echo-shift in the k-space, whereas the PGM does so in the image space by measuring the derivative of a phase map.

Theory: Paramagnetic contrast agent introduces local field inhomogeneity because of the susceptibility difference from its surroundings. This susceptibility gradient can be detected by measuring an echo-shift in the k-space, which is the core of the SGM. It is noted that an echo shift in the complex k-space can be represented as a spatial phase shift in the image space. This can be shown through the Fourier shift theorem: $\hat{\rho}_{shift}(x) = F^{-1}[s(k - m_{shift})] = exp[i2\pi m_{shift} x]F^{-1}[s(k)] = exp[i2\pi m_{shift} x]\rho(x)$,where $\rho(x)$ is a real spin density function, $s(k)$ is the k-space signal, and F represent the Fourier transform. The phase derivative can be obtained using the Fourier transform [4] described by the following equation: $\partial\varphi(x,y)/\partial x = -i\overline{\rho}^{*}(x,y)\partial\overline{\rho}(x,y)/\partial x$,where $\partial\overline{\rho}(m,n)/\partial m = \sum i2\pi p / N_x^2 \, DFT(\partial\overline{\rho}(p,n))exp[i2\pi mp / N_x]$ and $\overline{\rho}(x,y)$ is a normalized image. The advantage of the Fourier-based calculation is that no phase unwrapping is required before the derivative is calculated.

Data Acquisition and Results; Three plastic cylinder vials (1cm in diameter) which contain iron oxide nanoparticles (Fe_2O_3) in the enclosed gel were embedded into a large, cylindrical agarose phantom (20 cm in diameter). Experimental MR measurements were taken using a 3.0 T GE SIGNA HDX MR scanner (GE Medical Systems, Milwaukee, WI) and a birdcage transmit/receive head coil. 2-D Gradient refocused echo (GRE) scans were taken with the following parameters, TR=150 ms, TE=7 ms, Flip angle = 90 degree, slice thickness of 4mm, field of view (FOV) =22cm, and 128 x 128 acquisition matrix. For *in vivo* 3-D mouse data, C6 glioma cells (ATCC, Manassas, VA, USA) were labeled with ferumoxides (Berlex Lab, Wayne, NJ,USA) and implanted into a nude rat. Images were taken using Philip Achieva clinical MR scanner. The mouse was scanned using a three-dimensional fast field echo sequence (3DFFE) with 256x256 matrix size, 36 slices, slice thickness=0.7mm, and FOV=70mm.



a b c d

Figure1. a) PGM result (SPIO-embeded vials are indicated by white arrows) and b) Direct phase derivative (note the boundary of wrapped phase area indicated by red arrows in 1-b and 1-d) for the phantom data, c) PGM result and d) Direct phase derivative for the mouse data (tumor areas are indicated by white arrows).

Positive contrast map was generated using the PGM and compared with direct phase derivative for the phantom and mouse data. The PGM shows positive contrast around the boundary of the three vials (Fig. 1a) and the tumor area labeled with SPIO (Fig. 1c). The lines shown in the direct phase derivative (indicated by red arrows) are caused by the phase wrapping in the original phase map.

Discussion: We demonstrated that the PGM can detect SPIO nanoparticles in the phantom and *in vivo* SPIO-labeled tumor. The PGM detects the echo-shift introduced by field inhomogeneity from the SPIO nanoparticles by measuring the derivative of a phase image but it doesn't require any phase unwrapping procedure. Further study will be needed to differentiate positive contrast from SPIO and other sources such as air/interface boundary.

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Reference: [1] JH Seppenwoolde et al, MRM 2003;50:784-790. [2] Venkatesh et al, MRM 2006;55:126-135. [3] Liu et al, NMR Biomed, 2007. [4] Z.-P. Liang, *IEEE Trans. MI,* vol. 15, pp. 893-897, 1996.