A POSITIVE CONTRAST METHOD FOR MR-LYMPHOGRAPHY USING SUPERPARAMAGNETIC IRON OXIDE NANOPARTICLES

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Introduction: Superparamagnetic iron oxide nanoparticle (SPION) has been widely used in magnetic resonance (MR) lymphography taking advantage of the ability of macrophages to accumulate nanoparticles in lymph nodes [1]. SPIONs lead to hypointense artifacts in conventional MR-lymphography due to magnetic field distortion, creating negative contrast in normal lymph nodes. However, several other sources can also cause negative contrast such as voids, motion or calcification, which make it difficult to discriminate lymph nodes accumulated with SPIONs from some other tissues. Several positive contrast methods have been proposed to produce positive contrast signal at SPIONs using protocol modification or post-processing methods [2-4]. Post-processing method has the advantage of generating both original image and positive contrast image at one scanning time. In this work we propose a positive contrast method based on post-processing techniques and apply it in lymph nodes imaging.

Methods and Materials: We only consider the linear part (gradient) of magnetic field inhomogeneity caused by the different susceptibility of SPIONs. The echo position (maximum value in k-space) appears at the time of complete phase cancellation from imaging gradient G^{im} and susceptibility gradient of SPIONs G^{su}. Therefore, susceptibility gradient leads to an echo position shift that is determined by $\Delta = -G^{su}TE/((G^{su}+G^{im})\cdot\tau)$, where τ is the sampling time. The expression indicates that susceptibility gradient is in direct ratio to echo position shift when $G^{su} << G^{im}$. That relation provides a criterion to discriminate SPIONs region from other regions. The positive contrast procedure is listed below: (1) Divide a 2D complex image into small square regions and do short-term Fourier transform to the region [4]; (2) Measure the distance from the maximum point to the center of Fourier domain image; (3) Define a range [min, max] for filtering. If the distance is inside the range, the region is considered as sub-image of interest otherwise not; (4) Add all the sub-images of interest together and do inverse Fourier transform to obtain the enhanced spatial image.
Phantom and animal experiments were implemented on 4.7T Varian animal MRI system. Phantoms were made by pouring 2% boiling agar solution into a plastic bottle and cooled to room temperature. Three cylinder shaped holes were carved in the phantom and filled with SPIONs (Resovist) at different iron concentration: 20, 10, and 5.0 μmol Fe/ml. The direction of magnetic field is perpendicular to the cylinder holes. Animal experiments were performed according to permitted protocols. Wistar rats (n=2) were injected with SPIONs at concentration of 200μmol Fe/kg from tail vein. MRI scanning was performed at general anesthesia status of rats 24 hours after injection. Gradient echo pulse sequence was used for scanning, with TE=10ms for phantom, TE=7ms for rats, TR=100ms, FOV=4×4cm^2, N_x=N_y=128. K-space data were collected after scanning.

Results and Discussion: In Fig. 1 (A), three cylinder holes are filled with (a) 20, (b) 10, (c) 5.0 μmol Fe/ml iron respectively. SPIONs regions show hypointense signal while the other parts with homogenous magnetic field show intense signal. In positive contrast image (B), signals from high iron concentration regions *a* and *b* get enhanced while signal from low iron concentration region *c* is suppressed. In rats MR image (C), hypointense signal appears at the popliteal lymph nodes. In corresponding positive contrast image (D), SPIONs produce intense signal which separates them from other regions. This positive contrast method uses the spatial image to highlight the region with magnetic field gradient rather than use k-space shift value directly. Therefore, noise in void or background that also contributes large echo shift is not enhanced by this method due to its small magnitude. In addition, the method allows using a fixed minimum size of sub-image (3×3) which results in high resolution in the enhanced image.

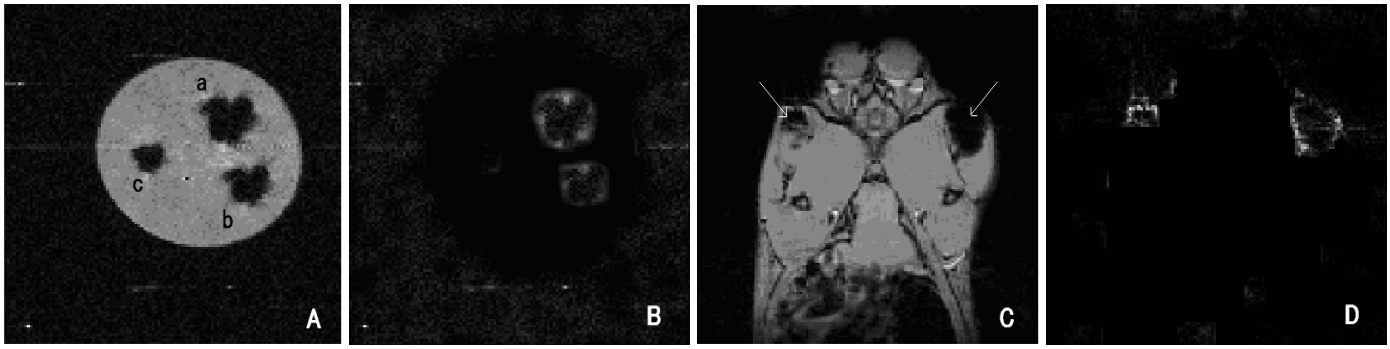

Figure 1: (A) Magnitude image of the SPIONs phantom; (B) Positive contrast image of the SPIONs phantom (min=50); (C) Magnitude image of rat popliteal lymph nodes 24 hours after SPIONs injection; (D) Positive contrast image of rat popliteal lymph nodes (min=50).

Conclusion: The post-processing method for positive contrast in this work is feasible for all gradient echo based protocols and can be easily integrated into image processing software. Positive contrast MRI of lymph nodes targeted by SPIONs can provide additional information in lymphography. Future work will focus on the discrimination of normal lymph nodes from metastasis lymph nodes that have lost the ability to accumulate SPIONs.

References: [1] R. Weissleder, et al. (1994), Radiology. 191(1):225-230; [2] V. Mani, et al. (2006), Magn. Reson. Med. 55(1):126-135; [3] P. Balchandani, et al. (2009), Magn. Reson. Med. 62(1): 183-192; [4] H. Dahnke, et al. (2008), Magn. Reson. Med. 62(3): 595-603.