Improving SNR and Sensitivity of 3D Fluorine Imaging With a Side-Information-Constrained Regularized Reconstruction

Introduction: "Hot spot" fluorine imaging with MRI benefits from 3D imaging, both from a signal localization point of view and a desire to maximize signal sensitivity. A 3D acquisition necessitates efficient sampling of the fluorine signal, and it is tempting to take advantage of the long T_2 of fluorine by using a long echo train to efficiently distribute the persistent fluorine signal across *k*-space. Indeed, this method has been used by [1] very effectively in 2D to image macrophage encroachment into damaged tissue after myocardial infarction. However, in cases where motion is present, this strategy will either fail entirely or else require a large number of averages to suppress motion artifacts. A better strategy is to gate the acquisition to the heart cycle and only image when the heart is quiescent. In this manner, the sensitivity advantages of a 3D acquisition can be leveraged to shorten scan time while increasing field of view and resolution. Here, we apply these ideas and, to our knowledge, show gated 3D TSE fluorine images of *in vivo* labeled macrophages for the first time.

Despite this boost, the fluorine signal is inherently small due to the generally low concentrations of fluorine present at tissues-of-interest for cellular and molecular imaging. Haldar et al [2] incorporated anatomical information into constrained reconstructions of low-SNR MR data, and Dewaraja et al [3] showed that incorporating boundary information from CT images into iterative SPECT reconstructions can improve the resultant images. Here, we apply the same concepts to improve reconstructed fluorine images by incorporating boundary information from anatomical proton MRI localizers and show that SNR and sensitivity benefit from this approach.

Methods: Myocardial infarction was surgically induced in C57Bl/6 mice by a one-hour occlusion followed by reperfusion. A 300 µl volume of perfluoro-15-crown-5-ether nanoparticle emulsion was injected intravenously 24 hours post-surgery. The nanoparticles had a mean diameter of 143 nm and had a surface lipid coat which consisted of a 50/50 mixture of DOPC and DSPC. Imaging was performed 4 and 8 days post-surgery to allow time for macrophage phagocytosis of nanoparticles and recruitment into damaged myocardium. The study was performed on a Bruker 7T small animal system with a dual-tuned 19F/1H coil. For fluorine, a 2D TSE sequence was prescribed as closely to that described by [1] as possible for comparative purposes. Scan parameters were: resolution 0.5×0.5 mm^2, slice thickness 2 mm, 3 slices, TR/TE=4500/5 ms, 256 averages, scan time 19:12 minutes, and no cardiac gating. Next, a gated 3D TSE sequence was applied with scan parameters: resolution 0.5×0.5×0.5 mm^3, TR/TE=3000/2.5 ms, 5 averages, scan time 11:44 minutes, and the sequence was run on the subsequent cardiac trigger following wait time TR. All animal care and protocols were in accordance with institutional guidelines.

To incorporate boundary information into the regularized reconstruction, the myocardium was manually segmented from the anatomical proton image, acquired with a standard GRE localizer. The edges of this myocardial mask control the weights, *w*, in the following regularizer [3] for a regularized least squares (RLS) reconstruction:

$$R(\mathbf{x}) = \beta \sum_{j=2}^{N} w_j (x_j - x_{j-1})^2$$

For simplicity, the regularizer above is written in 1D, the extension to 2D (or 3D) is straightforward. The weighting value *w* takes a 0 or 1 value depending on whether or not an edge is present in the mask. Conceptually, the weights prevent smoothing across boundaries, but allow smoothing elsewhere, with the regularizing parameter, β, controlling the amount of smoothing.

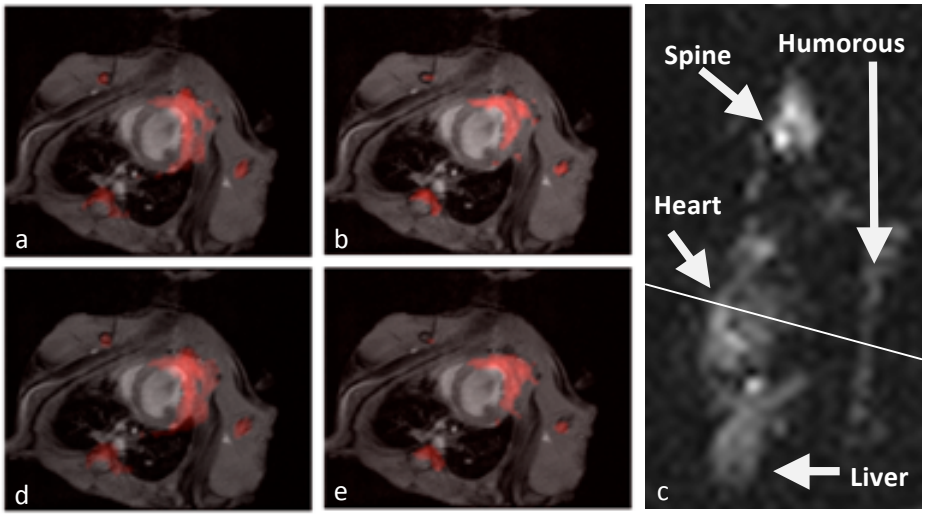

Figure 1. Macrophage tracking with fluorine nanoparticles in an infarct model. a) 2D TSE fluorine scan(red) overlaid on proton localizer. b) 2D reslice from 3D TSE fluorine scan. c) Coronal MIP of 3D TSE fluorine scan showing 2D reslice location for (b). Macrophage uptake of the nanoparticle formulation used in this work is also observed in the liver and bones. d) Regularized 2D reconstruction incorporating boundary information. e) Regularized 3D reconstruction. Note that the regularized 3D reconstruction shows a greater fluorine signal extent, which better matches 2D data.

Results and Discussion: Figure 1a,b shows standard Fourier transform reconstructions of the 2D and 3D datasets at day 8. Fluorine signal in the myocardium in both the 2D and 3D images correlates with LGE images (not shown), indicating specific recruitment of labeled macrophages to the damaged areas. The 3D sequence has a finer spatial resolution, took less time, and has a far greater field of view in the through-plane direction than its 2D counterpart while maintaining sensitivity to fluorine signal (Fig 1c). Figure 1d,e show the result of an RLS reconstruction of the same slice for both the 2D and 3D scan. Incorporating boundary information improves the SNR of the fluorine in the myocardium from 15 to 23 in the 2D data, and from 8.1 to 15 in 3D. RLS reconstruction shows greater fluorine extent in 3D, suggesting this approach works best in low-SNR regions. In the future, we could trade this SNR/sensitivity performance for better resolution, shorter scans, or utilize it for more difficult molecular targets.

Conclusion: Low SNR cardiac fluorine imaging benefits from gated 3D sequences and incorporating boundary information from proton images can further improve SNR and sensitivity.

References: [1] Flögel, et al. Circulation (2008) 118:140-148. [2] Haldar, et al. MRM (2008) 59:810-818. [3] Dewaraja, et al. Phys Med Biol (2010) 55(9):2523-2539.