Improving fluorine imaging through optimized acquisitions and advanced reconstruction techniques

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Purpose: Fluorine-19 (19F) is an attractive second nucleus for contrast-enhanced MRI. However, for 19F cellular and molecular imaging, in order to achieve useful image resolution in reasonable scan times, methods must be developed to efficiently generate and utilize signal arising from small volumes of contrast agent. Here, we seek to improve 19F imaging of cardiac inflammation through a three-pronged approach: first, through pulse sequences optimized to maximize SNR; second, by incorporating side information from proton images in a constrained iterative reconstruction; finally, by exploiting the underlying sparsity of 19F images using model-based image reconstructions. We use these methods for rapid 3D imaging of monocyte/macrophage infiltration after myocardial infarction.

Methods: We performed a systematic comparison of the SNR efficiency of six different pulse sequences for cardiac 19F MRI: 2D and 3D GRE, bSSFP, and TSE using a phantom consisting of serial dilutions of 19F-containing nanoparticles. All sequences used the same acquisition bandwidth, voxel size, and number of averages. Image SNR was calculated for the vial containing the lowest concentration (0.07 μmol/voxel) of 19F and SNR efficiency was calculated assuming 40% gating efficiency for GRE and bSSFP sequences. Data presented previously [1] was used to further explore advanced reconstruction methods. Briefly, myocardial infarction was surgically induced in C57Bl/6 mice by a one hour occlusion followed by reperfusion. PFC-containing nanoparticles were administered following infarction, and imaged after macrophage infiltration into infracted tissue with 2D and gated 3D TSE sequences. Images were reconstructed first using a standard iFFT, then with a model-based iterative reconstruction with various combinations of regularizing constraints:

$$\hat{f} = \arg\min_{f} \left\| y - Af \right\|_2 + \beta_{L1} \left\| f \right\|_1 + \beta_R \sum_{i=1}^{N} w_i \left(f_i - f_{i-1} \right)^2$$

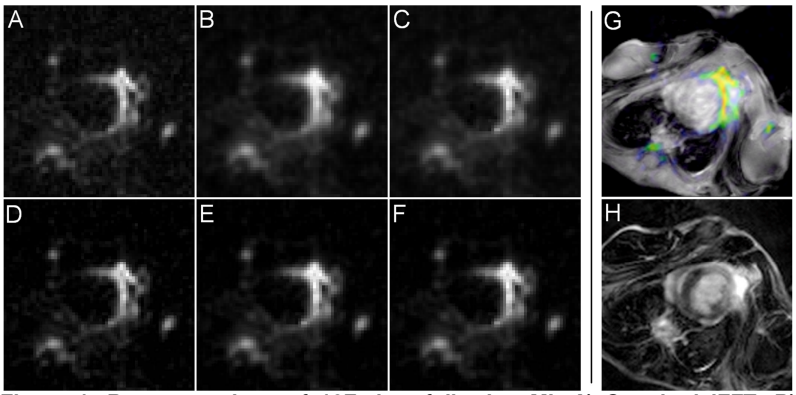

Figure 1. Reconstructions of 19F data following MI. A) Standard iFFT. B) Iterative Reconstruction with Smoothness Constraint (SC). C) SC plus edge information derived from proton image. D) Sparsity constraint through L1-norm constraint. E) SC plus L1-norm. F) SC plus L1-norm plus edge information. G) Image A superimposed onto a high-resolution proton image to show spatial distribution of 19F signal. H) LGE image showing extent of infarct.

First, a simple quadratic penalty was applied in order to promote image smoothness. Next, myocardial edge information was incorporated using a mask manually segmented from an anatomical proton image, acquired with a standard GRE localizer, accounted for by the weights, w_i, in the equation above. Image sparsity was enforced through an L1-norm regularizer, both with and without the additional smoothness and edge constraints. SNR and image sharpness of the myocardium were quantified. Sharpness was defined as the maximal value of the image gradient across the myocardium.

Table 1: SNR of Myocardium

	iFFT	SC	SC+Edge
No Sparsity	14.3	20.9 (+46%)	22.4 (+57%)
L1 Norm	19.5 (+36%)	24.7 (+73%)	28.7 (+100%)

Table 2: Sharpness

	iFFT	SC	SC+Edge
No Sparsity	0.0953	0.0744 (-22%)	0.1048 (+10%)
L1 Norm	0.1002 (+5%)	0.0862 (-10%)	0.1099 (+15%)

Results: Because of the long T_1 and T_2 of the perfluorocarbon used in this study, the bSSFP sequence resulted in the highest SNR (11.1) and SNR Efficiency (25.5). However, the TSE method was more robust than the SSFP method in the presence of field inhomogeneity (not shown), and also displayed good SNR (7.0) and SNR efficiency (8.0). Figure 1 shows the various reconstructions applied to an example short-axis 19F image. The fluorine signal correlates with LGE images (not shown), indicating specific recruitment of labeled macrophages to the damaged areas. SNR can be improved over a standard reconstruction through a smoothness constraint, which effectively averages signal locally at the expense of resolution. Incorporation of secondary edge information preserves resolution and may further improve SNR (Tables 1 and 2). The natural sparsity present in 19F images can be exploited to further improve image quality.

Discussion: The combination of high SNR and resistance to artifacts make the 3D TSE sequence a good choice for large-volume gated 19F imaging. Maximizing SNR is critical for 19F imaging, as the sensitivity of the MR experiment is inherently low and the volume of 19F contrast agent that can be delivered to an area of interest is likely to be small when in vivo labeling is desired. Signal can be improved without loss of resolution by utilizing additional information from concurrently-acquired proton data as well as by enforcing sparsity in the resulting images.

Conclusion: High-resolution 3D 19F images of monocyte/macrophage infiltration after myocardial infarction can be acquired in less than 15 minutes using an optimized cardiac-gated 3D TSE pulse sequence and image reconstruction methods that use information from proton images and exploit image sparsity.

References: [1] Fielden, et al. ISMRM 2012 (2540).