# Sensitivity of feedback-enhanced contrast to sub-voxel microscopic field variations

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## Introduction

Contrast enhancement based on nonlinear feedback interactions can highlight differences in tissue composition based on small resonance frequency variations arising from chemical shift or magnetic susceptibility differences [1]. For example, the radiation damping feedback field has been shown to highlight pathologic features in fresh *in vitro* human brain tissue samples excised from epileptogenic lesions and malignant brain tumors based on subtle variations in magnetic susceptibility and/or resonance frequency that are not apparent in conventional T1-weighted, T2*-weighted, and proton density images [2]. Whether the high selectivity of such feedback-based contrast enhancement for small resonance frequency variations still holds even in the presence of macroscopic field inhomogeneity is important for transitioning this new methodology into *in vivo* animal models in imaging systems with lower field strengths and homogeneity. Here we show that contrast enhancement under the radiation damping feedback field is sensitive to local, sub-voxel frequency or field variations while remaining robust to systematic background field inhomogeneities across the sample, which give rise to distortions in conventional frequency-sensitive images.

## Theory and Methods

Under radiation damping, different frequency components contribute to varying extents to the feedback field, resulting in sensitivity to microscopic field variations [1]. The evolution of the magnetization under radiation damping depends on the width and mean of the specified frequency distribution in a given voxel relative to that of all other voxels within the active region of the coil. While T2*-weighted images can distinguish voxels with substantial differences in the distribution of local microscopic field variations, radiation damping-enhanced images are more sensitive to voxels with small differences in the underlying frequency distributions. On the other hand, the dynamics under radiation damping can resist distortions to image contrast in the presence of systematic background field inhomogeneities if the field variation across the coil-sensitive region is smaller than or comparable to the field difference between the tissues of interest. Under radiation damping, minor distortions in the sample magnetization profile level out due to the distribution of frequencies created by the inhomogeneous field, leading to images that are more robust to systematic background field variations compared with conventional MRI methods.

## Results

To demonstrate the resistance of the magnetization evolution to distortions due to field variations across the sample, Fig. 1 compares one-dimensional profiles of experimental feedback-enhanced and conventional phase images taken on a simple two-frequency component phantom. The difference in frequency between the inner and outer regions is $\delta\nu = 8$ Hz, and a linear variation in frequency of $\pm\gamma G_x(l_x/2)/2\pi = \pm 4$ Hz is induced across the sample by adjusting the magnetic-field shims in the *x*-direction (Fig. 1A). The magnetization profiles following evolution under the feedback fields at short times (e.g., 20 ms) show slight distortions due to inhomogeneity but eventually smooth out after longer evolution under radiation damping.

As for sub-voxel frequency variations, while T2*-weighted images can distinguish voxels with substantial differences in the sub-voxel microscopic field distribution (e.g., T2' = 112 ms versus T2' = 27 ms in Fig. 2A), radiation damping-enhanced images are more sensitive to voxels with small differences in the corresponding T2' values, especially when the rate of static dephasing is large, or T2' is short. Such short T2' values may be encountered in the presence of strong local dipole fields, such as those set up by superparamagnetic iron oxide (SPIO) nanoparticles or blood. In these cases, the radiation damping field may enable better visualization of image contrast due to microscopic frequency variations. Radiation damping-based contrast enhancement can produce clear positive contrast due to local dipole fields compared with the signal loss seen in T2*-weighted images, as demonstrated through numerical simulations on magnetic dipole field distributions and experiments on blood in excised tissue (Fig. 3).

## Discussion and Conclusion

The dynamics under radiation damping can resist distortions to image contrast in the presence of systematic background field inhomogeneities across the sample while remaining sensitive to microscopic, sub-voxel field variations originating from internal, tissue-specific sources. The joint action of radiation damping and an additional feedback field, the distant dipolar field (DDF), is also sensitive to small local changes in resonance frequency between different tissue types and robust to systematic field inhomogeneity across the sample. The added presence of the DDF couples spins in neighboring voxels more strongly than distant spins, allowing the combined reaction fields to correlate regions with small differences in frequency more effectively, e.g., at the boundaries between different tissue regions. At the same time, the joint feedback fields remain relatively robust to background field variations compared with conventional frequency selective pulses, as coupling under the DDF is less effective over larger length scales and is essentially averaged out if the precession frequency difference is sufficiently large. We will also discuss how background inhomogeneity or applied magnetic field gradients can act in concert with radiation damping and the DDF to expedite refocusing of the magnetization helix [3] and improve differentiation of distinct tissue regions.

[1] S. Datta et al., J. Phys. Chem. B. **110**, 22071 (2006); [2] S. Y. Huang et al., Magn. Reson. Med. **56**, 776 (2006); [3] S. Y. Huang et al., *MAGMA* (in press).

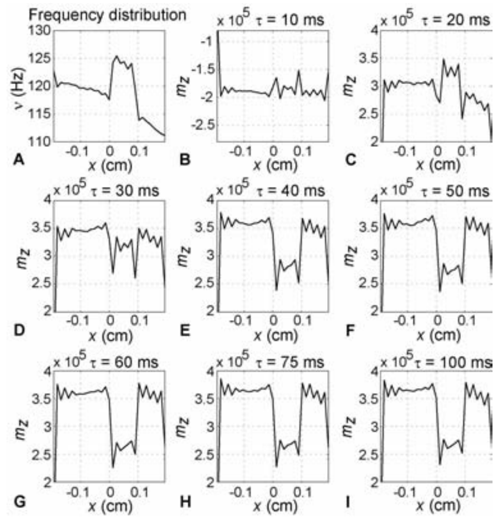


**Fig. 1.** Experimental frequency distribution and magnetization profiles for contrast enhancement in a two-frequency component phantom under radiation damping in the presence of macroscopic field inhomogeneity.

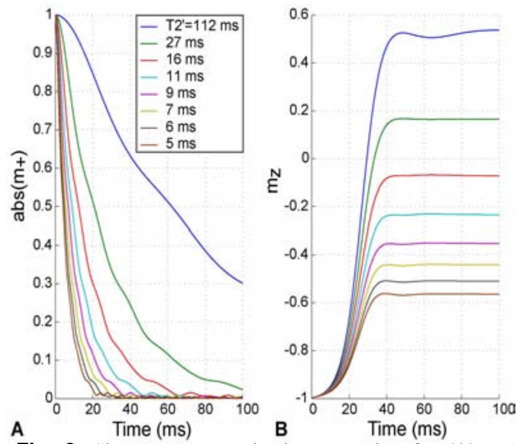


**Fig. 2.** Simulated magnetization evolution for **(A)** $T_2$*-weighted and **(B)** radiation damping-enhanced imaging based on Lorentzian frequency distribution centered at 0 Hz.

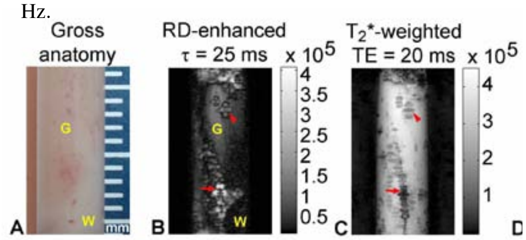


**Fig. 3.** *In vitro* feedback-based contrast enhancement in brain tissue removed from left posterior parietal occipital lobe of patient with cortical dysplasia. **(A)** Gross anatomy, **(B)** radiation damping-enhanced (θ = 175°, τ = 25 ms), **(C)** $T_2$*-weighted experimental images. Radiation damping-enhanced image showed intense positive contrast surrounding blood in regions with greater concentrations of deoxyhemoglobin (arrow).