Designing active feedback-based contrast enhancement for in vivo imaging

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Introduction

A new approach has recently been introduced for amplifying MRI contrast due to slight differences in MR parameters based on emergent, nonlinear feedback interactions [1-3]. Developing feedback-based contrast enhancement into a useful tool for in vivo imaging requires improved techniques that are robust to inhomogeneity and sensitive to subtle physiological variations. In addition to rational pulse sequence design that manipulates the underlying spin dynamics, hardware modifications are necessary for adapting feedback-enhanced contrast to small animal and ultimately human imaging at low fields. Here we propose and demonstrate newly designed pulse sequences and hardware that exploit active electronic feedback to target these challenges and augment the feedback leading to in vivo contrast enhancement. Up to 20 times improved contrast-to-noise ratios are attainable compared with conventional MRI sequences, as observed in small, cold-blooded animal imaging and at field strengths as low as 7 T.

Methods

The spin dynamics evolving under such feedback fields as radiation damping are highly sensitive to small resonance frequency differences between tissues with different chemical environments or magnetic susceptibilities. On the other hand, field inhomogeneity tends to be more pronounced in vivo due to local sources of field variation, e.g., microscopic capillaries, susceptibility differences at air-tissue interfaces. Since the feedback fields depend on the magnetization itself, dephasing of the transverse magnetization under such field inhomogeneity may reduce the strength of the feedback fields in vivo. Simulations and in vivo experiments on fish and frog embryos at 14 T were carried out to demonstrate robustness to field inhomogeneity of contrast enhancement under radiation damping and an additional feedback field, the distant dipolar field (DDF) (Fig. 1). In addition, the interplay of radiation damping and applied radio-frequency (RF) pulses was studied to enable better contrast enhancement compared with under radiation damping alone (Fig. 2). Finally, to bolster radiation damping at the lower fields (7 T) and probe quality factors typically used in small animal imaging, a modified circuit was constructed to generate and feed back an additional large-amplitude, phase-matched RF field to the sample (Fig. 3, top).

Results

Contrast enhancement under radiation damping alone as well as under the joint feedback fields highlighted anatomical features of a live guppy fish that were not discernable in the corresponding conventional T_2*-weighted, T_1-weighted, and proton density images (Fig. 1). In the simulated and experimental radiation damping-enhanced images (Figs. 1a and c), regions corresponding to the eyes appeared bright against the darker facial tissue, while in the simulated and experimental joint feedback field-enhanced images shown in Figs. 1b and d, the eyes appeared darker than the surrounding facial tissue. RF pulse sequences were also designed to improve radiation damping-enhanced contrast in experiments by directing the magnetization toward the unstable inverted state. Fig. 2 shows experimental MR images of a developing *Xenopus laevis* frog embryo demonstrating contrast enhancement under radiation damping combined with additional RF pulses. Fig. 2b highlighted the developing neural tube and outline of the jelly matrix in which the embryo was suspended, while Fig. 2c showed enhanced contrast distinguishing the darkened eye pigments (1), hypointense ear vesicles (2), and hyperintense gill areas (3), compared with the corresponding T_2*-weighted image (Fig. 2c). To adapt feedback-enhanced contrast for in vivo imaging at lower fields, the radiation damping field was actively reinforced through electronic feedback to the induced current. As a proof of principle, Fig. 3 shows active feedback-enhanced images of a phantom sample of water (outer tube) and ethanol solution (inner tube) at 7 T. The contrast enhancement develops as a function of evolution time following dynamics characteristic of radiation damping.

Discussion and Conclusion

The feedback-based methods presented here generalize novel, nonlinear spin dynamics to enhance in vivo contrast at lower fields and in the presence of field inhomogeneity. In this new approach, additional RF pulses and applied or intrinsic field gradients serve to amplify or suppress the feedback leading to contrast enhancement. Through a judicious choice of flip angles and evolution times in multiple-pulse sequences, the dynamics due to the interplay of radiation damping and RF perturbations were shown to highlight detailed internal structures in the frog embryo not seen in the conventional or radiation damping-enhanced images (Fig. 3). Simulation results also suggested that successive RF pulses could partially refocus dephasing of the magnetization under T2* relaxation and render the resulting contrast more robust to field inhomogeneity.

In the limit of fast pulsing by continuous RF irradiation, the magnetization may also be driven to different stable and unstable fixed points under radiation damping [23]. Furthermore, manipulation of the amplitude and/or phase of the radiation damping field could provide another means of adjusting the feedback field to lock or sustain the magnetization in a state that yields maximal contrast. The improved contrast provided by combining evolution under radiation damping with active feedback or additional RF fields may facilitate non-invasive characterization of development, physiology, and pathology in living organisms ranging from amphibian embryos to mice and ultimately humans.

[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).

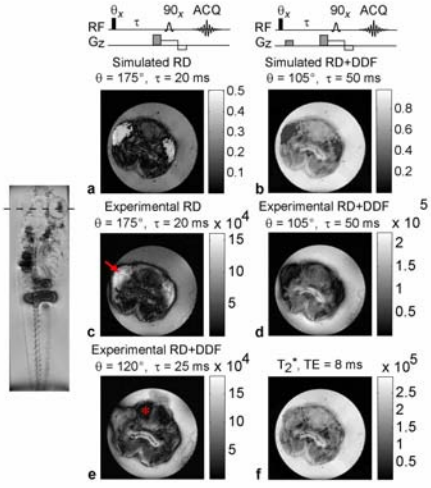

Fig. 1. *In vivo* feedback-based contrast enhancement in live guppy fish at 14 T.

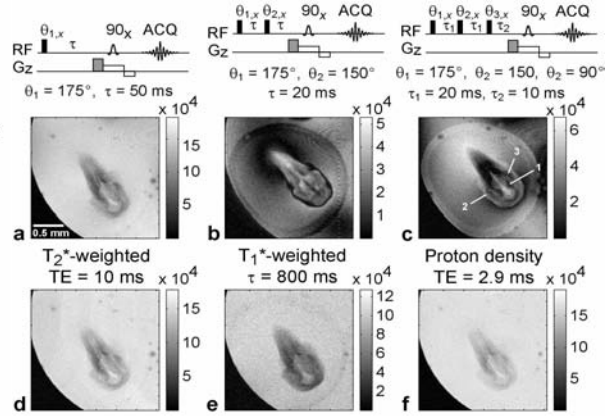

Fig. 2. *In vivo* contrast enhancement under radiation damping and added RF fields in live frog embryo at 14 T.

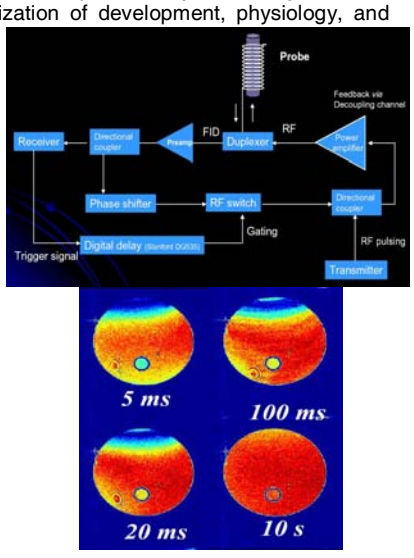

Fig. 3. Feedback-enhanced contrast on a water/ethanol phantom at 7 T with active electronic feedback (scheme at top).