Avalanching Amplification of MRI Lesion Contrast by Nonlinear Feedback

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Introduction

The ability to generate sufficient image contrast based on small variations in local MR parameters is crucial for the noninvasive mapping of structure and function by MR microscopy and clinical MRI. The delineation of distinct internal structures becomes particularly challenging when the MR properties do not vary significantly, leading to imperceptible contrast changes. We present a new approach to MRI contrast enhancement that manipulates the intrinsic spin dynamics in the presence of nonlinear feedback interactions [1]. This approach yields robust image contrast sensitive to small variations in versatile MR parameters. We demonstrate avalanching amplification of MRI contrast due to small differences in spin density or resonance frequency under the feedback interactions of the distant dipolar field and/or radiation damping in phantoms and *in vitro* human brain tissue. Up to 20 times improved contrast is observed in epileptogenic lesions and malignant brain tumors, tissues with minimal contrast differences in routine MRI.

Theory and Methods

The basis of feedback-based contrast enhancement is outlined in Figure 1. To enhance the dependence of $\boldsymbol{m}(\boldsymbol{r},t)$ on specific MR properties, we employ a local field $\boldsymbol{B}(\boldsymbol{r},t)$ that explicitly depends on $\boldsymbol{m}(\boldsymbol{r},t)$ and renders the Bloch equations nonlinear. For solutions at high field with abundant high-gyromagnetic ratio nuclei, e.g., ^{1}H, magnetization-dependent contributions to $\boldsymbol{B}(\boldsymbol{r},t)$ mainly come from two feedback fields: the distant dipolar field, $\boldsymbol{B}_d(\boldsymbol{r},t)$, and radiation damping, $\boldsymbol{B}_r(t)$. A simple pulse sequence prepares the magnetization in an initial unstable configuration $\boldsymbol{m}(\boldsymbol{r},t_0)$ under the feedback fields. Subsequent evolution of $\boldsymbol{m}(\boldsymbol{r},t_0)$ under the MR parameters in the Bloch equations generates small variations in the resulting magnetization distribution $\boldsymbol{m}(\boldsymbol{r},t_0+\Delta t)$, which are reflected in the feedback field $\boldsymbol{B}(\boldsymbol{r},t_0+\Delta t)=\boldsymbol{B}(\boldsymbol{m}(\boldsymbol{r},t_0+\Delta t))$. $\boldsymbol{B}(\boldsymbol{r},t_0+\Delta t)$ acts on $\boldsymbol{m}(\boldsymbol{r},t_0+\Delta t)$ to bring it away from the initial unstable state with ever-increasing efficiency, such that changes in the magnetization distribution act back on the magnetization through the feedback field to amplify contrast in a positive feedback cycle. Contrast enhancement is triggered by the smallest changes in the magnetization distribution and builds up rapidly to reflect the underlying MR parameters, leading us to refer to such enhancement as "avalanching amplification."

All studies were conducted according to protocols approved by the UCLA institutional review board. The pulse sequence for feedback-enhanced contrast is shown in Fig. 2. MR microimaging experiments were performed on brain tissue samples excised from patients with epilepsy and malignant brain tumors. Images were acquired at 14.1-T on an MR microimaging unit using a 5-mm saddle coil optimized for ^{1}H sensitivity.

Results

Feedback-based contrast enhancement was demonstrated on mildly dysplastic *in vitro* unfixed brain tissue excised from the left posterior parietal-occipital lobe of a patient with cortical dysplasia (Fig. 2). Cortical dysplasia is linked to medically intractable epilepsy and is characterized by cortical laminar disorganization and blurring of the gray and white matter junction. The radiation damping field following the initial 175° pulse selectively excited the magnetization in different regions based on differences in magnetic susceptibility and hence resonance frequency between gray matter and white matter, resulting in an increase in contrast-to-noise ratio (CNR) of about 15 times compared to the T_2-weighted image.

The radiation damping feedback field was also used to distinguish tumor growth from surrounding healthy tissue in glioblastoma multiforme (GBM) (Fig. 3), the most common malignant primary brain tumor. Tumor cells surrounding the microvasculature were highlighted in the radiation damping-enhanced image (Fig. 3A), corresponding to an increase in CNR of 20 times over the T_2-weighted image. The hyperintense regions in Fig. 3A corresponded to differences in bulk susceptibility originating from variations in blood oxygenation level and increased water content in the compact extracellular space of the tumor. These clusters of malignant cells were not sufficiently vascular to enhance on the T_2-weighted image.

Discussion and Conclusion

The simple preparation sequences shown here belie the complexity of the underlying dynamics and introduce a novel approach to designing MR pulse sequences. In this new approach, evolution under the reaction fields allows the spins themselves to play an active role in determining and differentiating their subsequent evolution, thereby improving the distinction between regions with different MR properties. The feedback interactions become more pronounced under conditions developed for high-sensitivity MR imaging and microscopy, i.e., high fields, sensitive probes, and/or highly polarized samples. Such feedback fields are thus readily adapted for contrast enhancement in *in vitro* and *in vivo* preclinical studies by MR microscopy and may be generalized to lower fields through careful consideration of the experimental system, pulse sequence design, and imaging hardware.

Feedback-based contrast enhancement is sensitive to small differences in endogenous MR parameters that correlate with versatile physiological origins. For example, limited variations in the concentrations of oxyhemoglobin, deoxyhemoglobin, and methemoglobin in healthy, tumor, and necrotic tissues are highlighted based on differences in bulk magnetic susceptibility. These findings suggest that feedback-based contrast enhancement may lead to improved lesion characterization, among other potential biomedical applications.

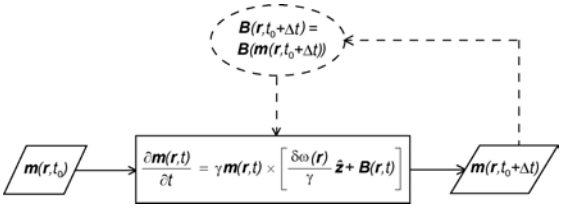

Fig. 1. Flowchart of feedback-based contrast enhancement.

Fig. 2. (right) (A) Radiation damping-enhanced (τ = 75 ms) and **(B)** T_2-weighted MR images (TE = 20 ms) at 14.1 T of brain tissue excised from a patient with cortical dysplasia. **(C)** Histopathology and **(D)** gross anatomy. Feedback-enhanced image shows amplified contrast between gray matter (*) and white matter (^), with corresponding contrast-to-noise ratios (CNRs) of 60.5 in **(A)** and 4.2 in **(B)**.

Fig. 3. (far right) (A) Radiation damping-enhanced MR image, **(B)** histopathology, **(C)** T_2-weighted MR image, and **(D)** gross anatomy of brain tissue taken from a patient with GBM. Regions of enhanced signal intensity in **(A)** correspond to tumor cells surrounding the microvasculature (red circle) compared with normal tissue (yellow circle) (CNR=42.6 in **(A)** versus CNR=2.2 in **(B)**).

[1] S. Y. Huang *et al.*, Science 2005; submitted.

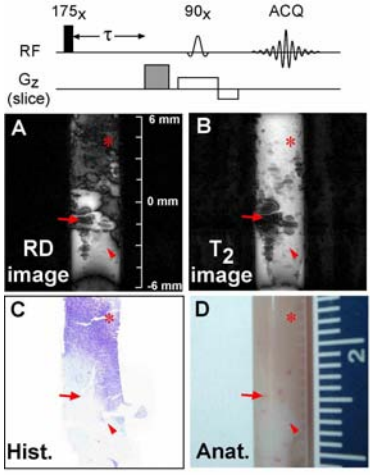

Figure 2

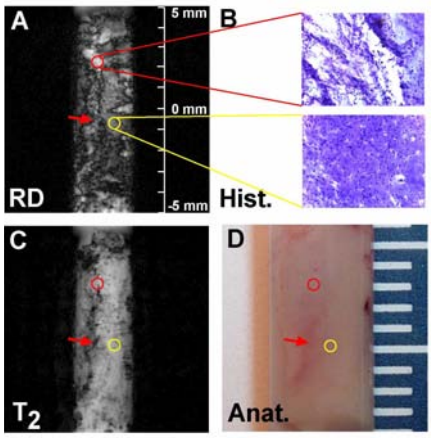

Figure 3