

# Contrast Enhancement by Feedback-Enhanced MRI

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## Introduction

Improving contrast is particularly important in medical imaging, where spatial-resolving contrast is crucial to the early diagnosis of disease. We present a new approach to MR contrast enhancement that manipulates the intrinsic spin dynamics in the presence of nonlinear feedback interactions. Evolution under the feedback 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.

## Theory and Methods

The basis of feedback-based sensitivity and contrast enhancement is outlined in Figure 1. To enhance the dependence of the magnetization  $m(r,t)$  on specific MR properties, we employ a feedback field  $B(r,t)$  that explicitly depends on  $m(r,t)$  and renders the Bloch equations nonlinear. For spectroscopic measurements, the solute spins are first detected by the solvent spins through various magnetization transfer mechanisms and serve as small "input" signals  $m(r,t_0)$  to perturb the solvent magnetization, which is prepared in an unstable state. The weakly detected signal is then amplified through subsequent nonlinear evolution of the solvent magnetization under the feedback field  $B(r,t)$ . For imaging experiments, contrast enhancement is triggered by the smallest changes in the magnetization distribution  $m(r,t)$  and builds up rapidly through positive feedback to reflect the underlying MR parameters.

## Results

The spin dynamics evolving under the RD feedback field are highly sensitive to small resonance frequency differences between tissues with different chemical environments or magnetic susceptibilities [1-3]. For example, RD-enhanced images are more sensitive to voxels with small differences in the underlying microscopic frequency distributions, especially when  $T_2$  is short. In the presence of strong local dipole fields, such as those set up by superparamagnetic iron oxide (SPIO) nanoparticles or blood, the RD field enables better visualization of image contrast by producing positive contrast, compared with the signal loss seen in  $T_2^*$  images (Fig. 2, arrows).

Feedback-enhanced contrast also yields robust image contrast that is sensitive to small magnetic susceptibility differences distinguishing tumor from surrounding normal tissue. *In vitro* images were acquired at 14.1-T on brain tissue samples excised from patients with the malignant brain tumor glioblastoma multiforme (GBM) using a 5-mm saddle coil. The intrinsic RD in the coil was used to distinguish tumor growth from healthy tissue in GBM (Fig. 3). Tumor cells surrounding the microvasculature were highlighted in the RD image, with an increase in CNR of 20 times over the  $T_2^*$  image, corresponding to variations in blood oxygenation level.

## Discussion and Conclusion

For most MR scanners, the receiver coil is not sufficiently sensitive to induce a strong RD field for *in vivo* imaging in animals and humans. An active radiofrequency (RF) feedback loop was developed to amplify and control the RD feedback field for *in vivo* imaging of mice. Mouse models infected with human lung adenocarcinoma cell line H447 were imaged on a 7-T wide-bore magnet using a 3.7-cm Helmholtz coil and a home-built active feedback device. Figure 4 shows that tumor and necrotic tissue could be distinguished from surrounding skeletal muscle, with features reflecting tumor heterogeneity. Feedback enhanced contrast can also detect developing, early-stage tumors not seen on  $T_1$  or  $T_2^*$  images (not shown). These results suggest that active feedback-enhanced contrast can reveal changes in tissue composition associated with early tumor growth, prior to appearance on conventional MRI.

We demonstrate significantly improved contrast in *in vitro* human brain tissue and *in vivo* mice. Feedback-enhanced MRI offer a conceptually new approach to practicing MR, leading to avalanching amplification of contrast.

## References

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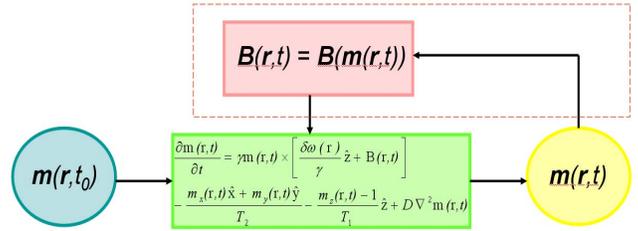


Fig. 1. Flowchart outlining feedback-enhanced MRI.

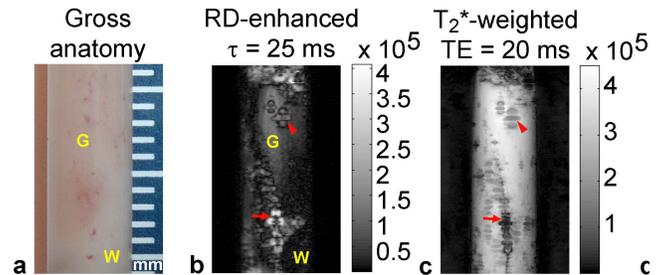


Fig. 2. *In vitro* feedback-based contrast enhancement in brain tissue removed from a patient with cortical dysplasia. (A) Gross anatomy, (B) radiation damping-enhanced ( $\theta = 175^\circ$ ,  $\tau = 25$  ms), (C)  $T_2^*$ -weighted experimental images.

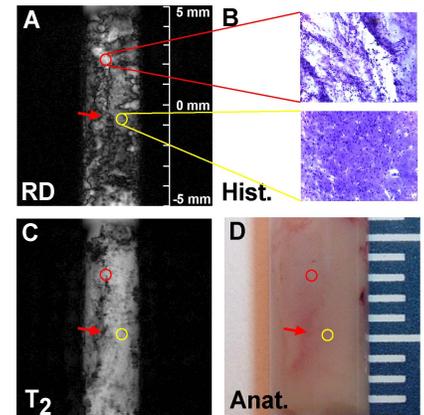


Fig. 3. (A) Feedback-enhanced MR image, (B) histopathology, (C)  $T_2^*$ -weighted MR image, and (D) gross anatomy of brain tissue taken from a patient with GBM.

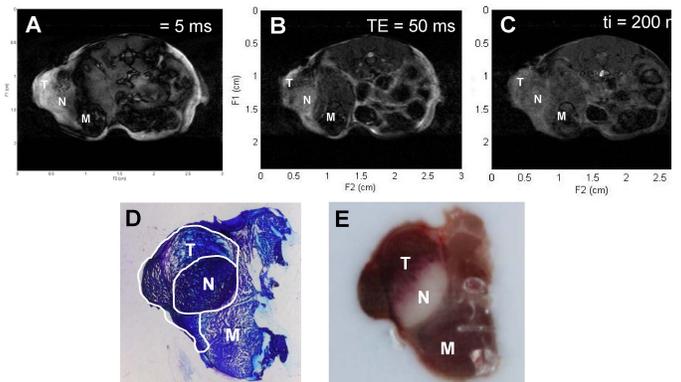


Fig. 4. (A) Active feedback-enhanced, (B)  $T_2$ -weighted, and (C)  $T_1$ -weighted MR images, with corresponding (D) histopathology and (E) gross anatomy of tissue taken from a mouse with lung tumor embedded in the leg. T = tumor; N = necrosis; M = muscle.