

## Improving Contrast of delta relaxation enhanced MR (dreMR) Imaging

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**Target audience:** molecular imaging research, targeted contrast agents, field-cycled MRI, and dreMR contrast.

**Purpose:** Delta relaxation enhanced MR (dreMR) is an imaging technique that exploits the dependency of the relaxation rate ( $R_1$ ) of bound molecular probes on magnetic field strength as a source of contrast in MR images [1]. dreMR contrast is normally obtained subtracting magnitude MR images acquired at two different magnetic fields, which are created with additional magnetic field-cycling hardware that modulates the main magnetic field of a conventional MRI system [2]. Eddy currents resulting from the switching of magnetic fields make dreMR contrast derived by magnitude subtraction of images obtained with different field shifts highly susceptible to edge artefacts. The method presented here reduces these effects and improves dreMR contrast by compensating for phase differences between the source images and performing a subtraction of the full complex data.

### Methods:

**MRI:** Imaging was performed on a 1.5T GE Signa CVMR system (WI, USA) with an insertable dreMR field-cycling magnet for dynamic control of  $B_0$ . The main magnetic field was modulated  $\pm 0.221$  T with preparatory dreMR pulses of 300-ms duration before a conventional Fast Spin Echo (FSE) sequence. The imaging sequence had parameters of TR=500 ms, TE=9.4 ms, 1 average, echo train length of 2, isotropic in-plane resolution of 0.39 mm, and slice thickness of 4 mm.  $T_1$ - and  $T_2$ -weighted as well as dreMR images were obtained before and after the albumin-targeted contrast agent Ablavar (Gadofosveset trisodium, Lantheus Medical Imaging, Inc. N. Billerica, MA, USA, formerly known as MS-325) was injected into the animal [3].

**Image processing:** Phase difference of  $k$ -space data from positive and negative field modulation was minimized using a two-dimensional normalized cross-correlation function and performing, after the appropriate field normalizations, a complex subtraction of the complex data before obtaining the final magnitude dreMR image. All the image processing was performed using Matlab® tools (MathWorks, Natick, Massachusetts, U.S.A.)

**Phantoms:** In order to test the proposed method without any physiological effects, a grid phantom containing 4-mm NMR tubes with different concentrations of Ablavar and Rabbit Serum Albumin (RSA) was imaged (Figure 1). Additionally, two 4-mm NMR tubes with and without 4.0% w/v RSA were doped with 160 $\mu$ M of Ablavar. During the imaging session these two phantoms were placed at either side of the animal to serve as dreMR contrast controls.

**Animal:** A female NU/NU mouse was injected subcutaneously with  $2 \times 10^6$  PC-3M cells into each flank and a sufficient period of time was permitted for tumour growth. During the imaging session the animal was anesthetized with 2% isoflurane and placed on a custom water-heated bed in a Tx/Rx birdcage RF coil within the dreMR coil. Ablavar (0.1mmol/kg) was injected intravenously through the tail vein.

### Results:

Figure 1 shows the improvement on dreMR contrast by using phase correction and complex subtraction instead of magnitude subtraction only. The panels in Figure 2 present an axial slice of the mouse including significant tumour volumes, as indicated on the  $T_2$ -weighted image.  $T_1$ -weighted images of pre- and post-injection of the albumin-targeted gadolinium contrast agent are shown as well as a false-colour subtraction of them (lower left panel) to enhance those regions where gadolinium is present. The dreMR contrast images presented at the lower centre and right panels illustrate the differences between magnitude subtraction and the complex dreMR subtraction images.

### Discussion:

While the Pre – Post injection  $T_1$ -weighted images nicely define regions where the gadolinium contrast agent is present, dreMR images only show those regions where the contrast agent is bound to albumin. The method proposed here shows a significant improvement in the detection of those regions where the contrast agent is bound and shows a reduction of edge artefacts.

### Conclusion:

This proposed method produces improved dreMR contrast by introducing proper compensation of phase differences between the images acquired with opposite field shifts and the complex subtraction of those images. This method has been compared with the straightforward difference of magnitude-only images. These preliminary results show that the proposed method increases the specificity of the dreMR contrast, which may be useful for the differentiation of necrotic and non-necrotic tumours as well as leaky or solid tumours.

### References:

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- Alford J.K., et al., Magnetic Resonance Engineering 2009;35B(1):1-10.
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### Acknowledgements:

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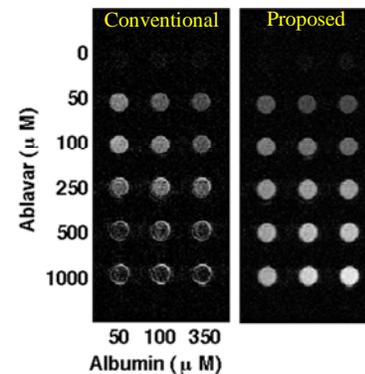


Figure 1.

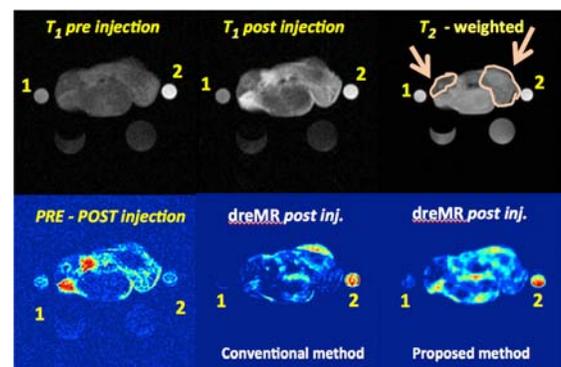


Figure 2. 1 = 160  $\mu$ M Ablavar only  
2 = 160  $\mu$ M Ablavar plus 4 % w/v Albumin