

# Direct Protein Imaging of Inflammation in the Human Hand

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**Introduction** The first example of direct protein imaging in a human volunteer is presented here. We use a new form of image contrast termed *delta relaxation enhanced MR* (dreMR) which exploits the strong magnetic field dependence of slowly tumbling paramagnetic (gadolinium) contrast agents, particularly at fields around 1.5T<sup>1,2</sup>. The dreMR method allows one to directly differentiate MR image intensity due to bound contrast agent from all other sources of image intensity by dynamically modulating the strength of the applied magnetic field through the use of an insertable shielded electromagnet.

Contrast arising from both native biological tissue and from fast-tumbling imaging probes, like GdDTPA, show little to no magnetic field dependence in the 1.5T range. Conversely, protein-bound probes like the FDA-approved contrast agent gadofosveset (MS-325, Ablavar) have a very strong field dependence with  $\Delta r_1 = 24.6 \text{ mM}^{-1} \text{ s}^{-1} \text{ T}^{-1}$  about 1.5T<sup>4</sup>. See Fig. 1. By modulating the B<sub>0</sub> field about 1.5T and taking T<sub>1</sub>-weighted images, the difference image yields signal solely attributable to the slow tumbling pool.<sup>2</sup> Unbound probe (rapidly tumbling) and the inherent T<sub>1</sub> of tissues will show very little dependence and therefore produce minimal image contrast.

**Methods** A volunteer with a broken finger was imaged twice. First, anatomical images with 0.18-mm isotropic resolution were acquired on a Siemens 7T Magnetom MRI system. Next, the volunteer was intravenously injected with 0.03mmol/kg MS-325. In humans, the biological half-life of this agent is 18 hours<sup>4</sup>. Approximately 24 hours following injection, the volunteer was imaged using a modified 1.5T Siemens Avanto system that was outfitted with an auxiliary electromagnetic insert (dreMR insert) to produce magnetic field shifts for dreMR imaging. To maximize SNR, a transmit/receive surface coil was placed directly beneath the volunteers fingers. T<sub>1</sub>-weighted images were acquired at relaxation fields of 1.35 and 1.65T. Following baseline correction for differences in M<sub>0</sub> between 1.35 and 1.65T, the images were processed to obtain magnetic field dependent contrast.

**Results** The fracture in the finger is clearly shown on a high-resolution, 7T anatomical image (Fig 3, arrow). On the dreMR images, regions of interest were drawn in the joint near the break, labeled (a), and a region proximal to the break, labeled (b). ROI analysis showed a 14% change in image intensity in region (a), but only a 2% change in image intensity in the control region (b). An overlay map of the dreMR image on top of the corresponding anatomical image is shown in Fig 4. The dreMR map highlights tissues displaying magnetic field dependence, which is indicative of albumin-bound contrast agent.

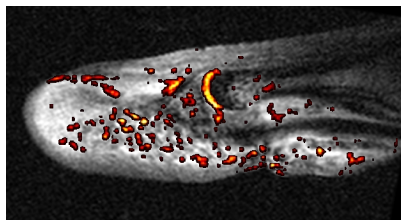


Fig 4. dreMR albumin map is false color overlaid on 1.5T anatomical image. Resolution: 0.2x0.2x2mm, TR = 60ms.

**Conclusion** dreMR imaging enables direct detection molecular imaging of albumin in living human using an approved targeted agent.

## References

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- 3) Caravan P, et al. J Am Chem Soc. 2002;124:3152-3162
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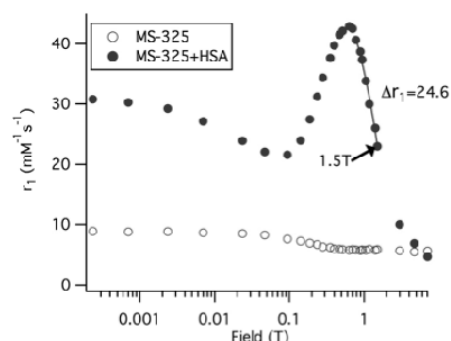


Fig 1. Magnetic field dependence of MS-325 relaxivity shows little field dependence when tumbling rapidly, but steep field dependence about 1.5T when bound to albumin (HSA).<sup>3</sup>

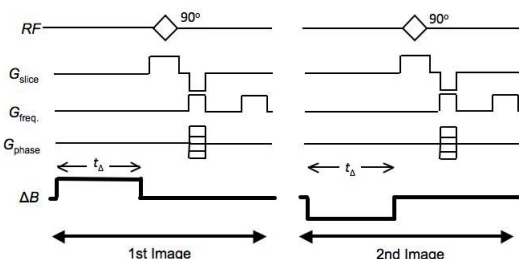


Fig 2. The dreMR pulses are applied only during the relaxation portion of the pulse sequence. In the first image the magnetic field was increased by 0.15T in the second image the field was decreased by 0.15T.

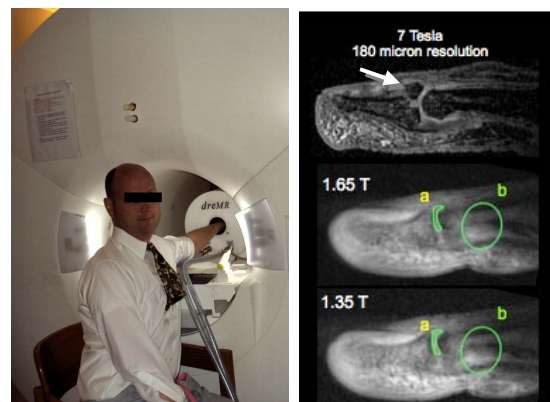


Fig 3. Left: human imaging using 2<sup>nd</sup>-generation dreMR coil. Right (top): high-resolution 7T image showing site of finger fracture. Right (middle and bottom) images obtained with the dreMR coil. ROI (a) in inflamed region near the break showed a 14% change in image intensity (1.35 - 1.65T), while ROI (b) had only a 2% change in image intensity.