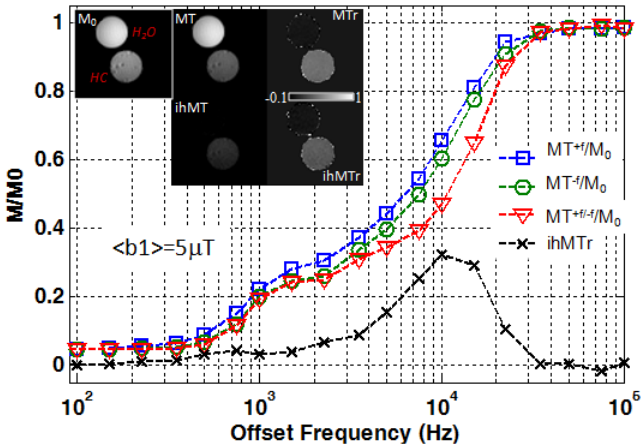
Specific inhomogeneous MT contrast in mouse brain white matter

Guillaume Duhamel[1], Olivier M. Girard[1], Gopal Varma[2], Patrick J Cozzone[1], Virginie Callot[1], and David C. Alsop[2]
[1]*CRMBM / CNRS 7339, Aix-Marseille University, Marseille, France,* [2]*Department of Radiology, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, United States*

Target audience: MR physicists and physicians interested in novel endogenous contrast mechanisms and specific white matter imaging

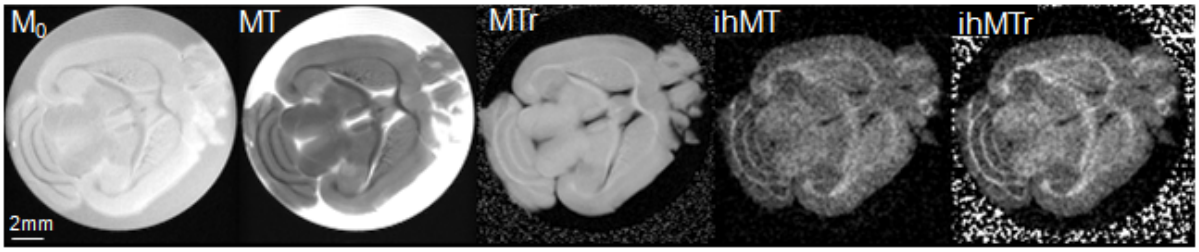
Introduction: Specific imaging able to provide quantification of myelin concentration would be a very valuable tool for clinical and preclinical studies of white matter pathologies (e.g. multiple sclerosis). While several advanced MR techniques are used to assess myelin content (short T_2 imaging, Myelin Water Fraction (MWF), Magnetization Transfer (MT), Diffusion Tensor imaging (DTI), quantitative Susceptibility Weighting Imaging (qSWI) or ultrashort TE imaging), they all are affected by confounding factors which limit their specificity to myelin. On the other hand, a previously reported new MT approach[1-3], able to specifically image the inhomogenous component of the MT spectrum, appeared to be selectively sensitive to tissue with myelin. This MT experiment, called inhomogenous MT (ihMT), was performed on human at 3T. In this study, we investigated the specificity of ihMT in mouse brain at very high magnetic field (11.75T).

Methods: The ihMT contrast was obtained from 3 images, acquired with different off-resonance irradiation. One image is acquired with off-resonance saturation at a positive frequency offset (MT^{+f}), one at the negative of this frequency offset (MT^{-f}) and one image is acquired with equal total power but divided between positive and negative offsets ($MT^{+f/-f}$). The ihMT image is given by $ihMT=MT^{+f} + MT^{-f} - 2MT^{+f/-f}$ and the ihMT ratio by $ihMTr=ihMT/M_0$, with M_0 being the image without irradiation. Additionally, the standard MTr is given by $MTr= 1-(MT^{+f})/M_0$. Experiments were performed at 11.75T on a vertical MR system (Bruker, AV 500WB, transmit/receive volume coil: ∅ 2cm, length 3cm) on a MT-phantom (commercially available Lamellar Liquid Crystals (hair conditioners)[4], on a fixed brain and, *in vivo*, on anaesthetized mice (C57BL/6j, 10 weeks, weight 25±1g). The ihMT off-resonance irradiation was performed with 2ms Hann shaped pulses applied every 2.3ms at either positive or negative offset, during 1.2s prior to image acquisition (single-slice FSE readout). A full Z-spectrum was acquired for the phantom (19 frequencies offsets and average RF power of b_{1ave}=5μT). For fixed brain and *in vivo* experiments, frequency offsets ±f=±10kHz and a b_{1ave} value of 5μT were used.

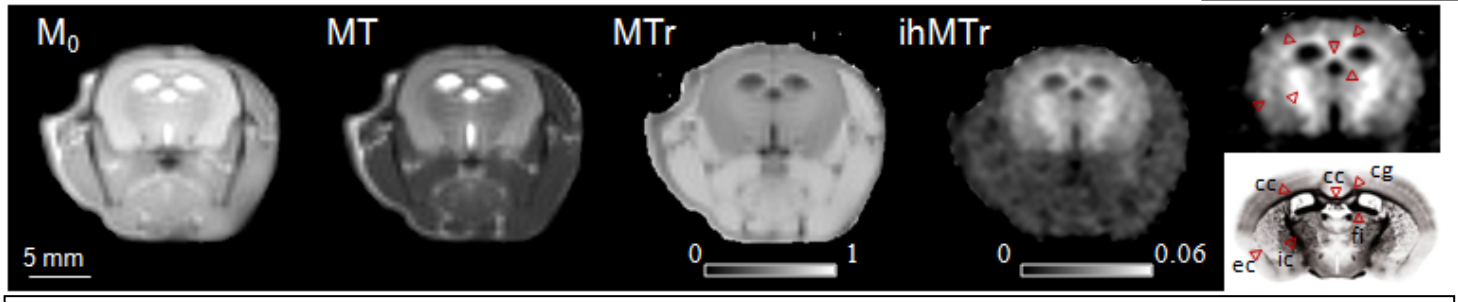


MT & ihMT images, Z-spectra and ihMTr measured in the MT-phantom (Hair Conditioner (HC)). Inhomogenous component is characterized by the ihMTr peak signal at f=±10kHz.

Results and Discussion: Fig1 shows an ihMTr peak signal at a frequency offset of 10 kHz in the hair conditioner phantom. This peak is the signature of an inhomogenous component (lipid bilayer structures composing hair conditioner) which can be isolated because, for the same total RF power, the saturation at separate positive and negative offsets transfers differently to the free water pool than irradiation at positive and negative offset simultaneously on such inhomogeneously broadened lines. Since the membranes that form myelin sheaths are made up from bilayer structure, ihMT appeared more selectively sensitive to white matter tissue, as illustrated on figures below. Whereas MT images show non-specific contrast (MTr^{cortex}=59±1%, $MTr^{internal\ capsule}$ =62±1%), ihMT images clearly highlight myelinated mouse brain structures (e.g. corpus callosum (cc) ihMTr=3.5±0.2%, internal capsule (ic) ihMTr=4.1±0.1%, fibria (fi) ihMTr=3.0±0.1%) relative to gray matter structure ($ihMTr^{cortex}$=2.5±0.2%) for both fixed brain and *in vivo*.



Fixed brain ihMT: ETL 8, mtx 128x128, FOV 1.5x1.5cm², ST 0.75mm. 100 NEX (Acq.time: 4hours). ihMTr image shows similar results than myelin mapping obtained with manganese-enhanced MT[5].



In vivo ihMT:ETL 64, mtx 64x64,FOV 2.5x2.5cm², ST 1.5mm. 32 NEX (Acq.time: 30mins). Despite low in-plane resolution, the specificity of ihMT to WM structures can be appreciated by comparison with the myelin stain image (far right images).

Conclusion: This preliminary study performed at 11.75T on mouse fixed brain and *in vivo*, highlighted the specificity of ihMT to myelinated tissue. The measured ihMTr values were however 50% smaller than those measured on humans[2,3] (~9% vs ~4%). Potential sources of explanation (magnetic field effect, T_2 effect) and sensitivity enhancement are under investigation. Nonetheless, the specificity of this technique towards WM tissues along with its very simple post-processing hold great promise for preclinical studies of brain pathologies such as MS or brain trauma.

***References*:** *[1] Alsop et al, Proc. ISMRM 2004; p2324 [2] Alsop et al, Proc. ISMRM 2005; p2224 [3] Alsop et al, Proc. ISMRM 2007; p2188 [4] Swanson et al, Proc. ISMRM 2012; p1378 [5] Watanabe et al, Neuroimage 2010*