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Protocol status: Working
 The protocol was tested on 15 MF diseased mice with 37 test-retest pairs. It is applied to ongoing preclinical MF studies.

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PIP MRI Magnetization Transfer Ratio (MTR) Measurement of Myelofibrosis in Mouse Tibia V.1

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DISCLAIMER

The PIP MTR claims hold when:

- Scanner hardware, diffusion weighted image (DWI) data acquisition method and parameters, image reconstruction, and data-reduction procedures are equivalent (or superior) to those detailed in section III.
- Use of the same animal model and interventions to induce myelofibrosis are performed as detailed in section V.
- ADC change is assessed on an individual animal basis where each animal undergoes identical procedures on the same MRI system over longitudinal timepoints.

Keywords: preclinical imaging protocol, magnetization transfer ratio, technical repeatability, mouse tibia, myelofibrosis bone marrow

ABSTRACT

The goal of this Co-Clinical Imaging Research Program (CIRP) pre-clinical imaging protocol (PIP) is to provide detailed description of key steps used to achieve a stated level of technical repeatability (precision) embodied in “Claims”, for MRI measurement of magnetization transfer ratio (MTR) in tibia bone marrow of myelofibrosis mouse models. This pre-clinical imaging procedure document will be referred to as a “profile” and adheres to a PIP MRI template provided in:

<https://www.protocols.io/workspaces/pre-clinical-imaging-protocols>.

Here we treat MTR as a “quantitative” metric, although numerical MTR results are a strong function of multiple experimental parameters and MRI hardware conditions. This profile will adopt the common practice to express MTR values in on a 0 to 1 scale. Empirically, MTR reflects fraction of visible signal loss due to application of off-resonance saturation RF energy depleting magnetization in the semi-solid (invisible) macromolecular matrix thus reducing magnetization replenishing visible signal. Simple fluids free of macromolecules should have an $MTR \gg 0$, whereas macromolecule-rich semi-solid tissues such as myelin, muscle, scar and collagen exhibit relatively high MTR (> 0.5). This document details procedures for MTR measurement in MF mouse tibia to achieve stated performance claims. Tibia bone marrow composition in MF mouse models has gradation going from proximal to distal ends of the tibia, therefore separate claims are made for volume of interest (VOI) analysis of ADC maps for each of three distinct sections along the length of the tibia (see Figure 1):

Section 1 (proximal)° VOI ($\sim 4\text{-}5\text{mm}^3$) within 9mm of proximal end of tibia

Section 2 (transition)° VOI ($\sim 0.4\text{-}0.5\text{mm}^3$) from 10 to 12mm of proximal end of tibia

Section 3 (distal)° VOI ($\sim 0.1\text{-}0.2\text{mm}^3$) from 13 to 14mm of proximal end of tibia

Claim 1: A measured change in the mean ADC in Section 1 VOI of MF mouse model tibia that exceeds $\pm 0.037\mu\text{m}^2/\text{ms}$ indicates a true biological change has occurred in the tibia bone marrow with 95% confidence.

Claim 2: A measured change in the mean ADC in Section 2 VOI of MF mouse model tibia that exceeds $\pm 0.087\mu\text{m}^2/\text{ms}$ indicates a true biological change has occurred in the tibia bone marrow with 95% confidence

Claim 3: A measured change in the mean ADC in Section 3 VOI of MF mouse model tibia that exceeds $\pm 0.030\mu\text{m}^2/\text{ms}$ indicates a true biological change has occurred in the tibia bone marrow with 95% confidence

ATTACHMENTS

[UMich_MTR_SOP-Profile_20230214.pdf](#)