# Fast absolute myelin water mapping without an external water standard

Thanh D Nguyen[1], Sneha Pandya[1], Pascal Spincemaille[1], Susan A Gauthier[1], and Yi Wang[1]
[1]*Weill Cornell Medical College, New York, NY, United States*

**Target Audience** Researchers and clinicians interested in brain imaging.

**PURPOSE** Myelin water mapping (1,2) can quantify myelin changes in multiple sclerosis (MS) (3), yielding results highly correlated with demyelination and remyelination measured by histopathology (4,5). However, the commonly used myelin water fraction (MWF)–defined as the ratio of myelin water signal and voxel water signal–can be confounded by changes in axonal and extracellular water in edematous lesions. It is possible to obtain absolute cerebral myelin water volume (CMV) by referencing the voxel signal to an external water probe attached to the head after correcting for differences in temperature, T1, receiver coil sensitivity and flip angle (6,7), at the cost of a complicated setup and long acquisition time. The objective of this study is to develop a fast method for CMV quantification which does not require the use of an external water standard.

**METHODS**: Our design is based on the Fast Acquisition with Spiral Trajectory with T2prep (FAST-T2) sequence (Fig.1) recently developed for whole brain MWF mapping (8). To obtain CMV from MWF, it is necessary to reference voxel water signal to the signal of a pure water standard. Here we propose to use CSF as the reference signal, thus eliminating the need for an external water probe. As water density and T1 vary significantly with temperature, another advantage of the proposed method is that it does not require temperature correction for the reference water signal.

FAST-T2 can be sensitized to T1 by swapping out T2prep and varying the saturation recovery time ($T_{SR}$), thus providing SNR efficient whole brain T1 mapping (FAST-T1). The receiver sensitivity of a multi-channel coil can be mapped by dividing the individual coil images by an image obtained with the reference body volume coil.

Six healthy volunteers were imaged on a GE 1.5T scanner with following typical imaging parameters: 1) FAST-T2 (4 min): 1.25x1.25x5 $mm^3$ resolution, 28 slices, 6 geometric TEs between 0-300 ms; 2) FAST-T1 (2 min): same coverage and resolution as FAST-T1, 5 saturation recovery times (200, 500 ms, 1, 2, 5 sec); 3) Reference body coil acquisition (1 min). Total CMV mapping time was 7 min. A water probe was attached to the head coil as a reference.

MWF maps were extracted using a multi-voxel spatially constrained nonlinear data fitting algorithm. T1 maps were calculated using the Levenberg-Marquardt algorithm. For CMV calculation with the external water probe, signal correction was performed to account for changes in water density and T1 (9) at body temperature (37.5°C) compared to room temperature (20°C). The proposed CSF based CMV calculation does not require such correction. Linear regression and Bland-Altman plots were used to assess the agreement between the two CMV mapping methods.

**RESULTS** Figure 2 shows an example of T1, coil sensitivity, and CMV maps obtained with the conventional and proposed CSF based methods, demonstrating similar depiction of WM tracts. The correlation between measurements obtained by ROI analysis from 12 WM and GM regions in all 6 subjects was excellent ($R^2$=0.983, slope=0.97). Bland-Altman plots reveals negligible CMV bias within narrow 95% limits of agreement of [-0.7%,0.4%] (Fig.3). Mean voxel water content was 72±4% in WM and 83±2% in GM with the proposed method, and 74±4% in WM and 84±3% in GM with the reference method (P<.001, n=6).

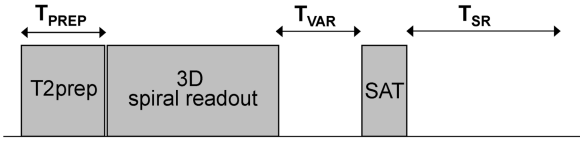


**Fig.1**. Schematic of the CMV mapping pulse sequence, consisting of a T2prep module followed by spiral data acquisition and a variable time delay $T_{VAR}$, and completed by a saturation pulse (SAT) to null the magnetization and a saturation recovery time $T_{SR}$. $T_{PREP}$ and $T_{SR}$ can be varied to sensitize tissue T2 and T1, respectively.

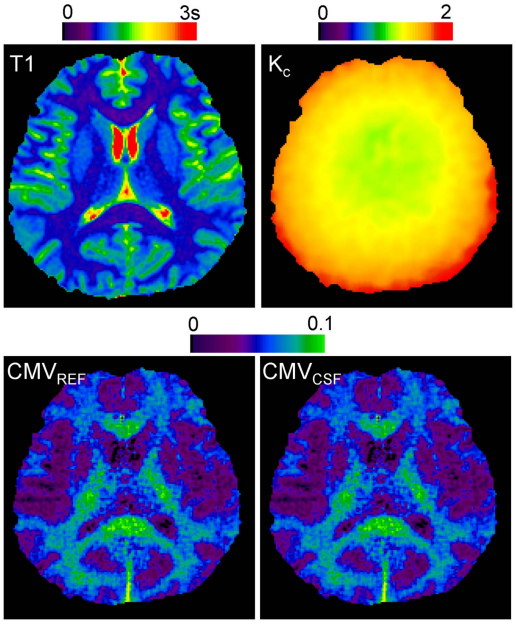


**Fig.2**. Example of T1 and sum-of-squares receiver coil sensitivity (Kc) maps and CMV maps obtained with the reference method (using an external water probe) and the proposed CSF based method.

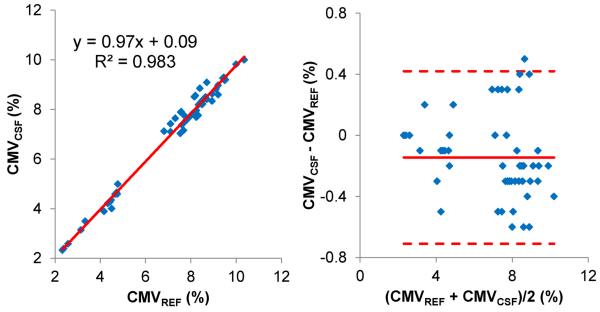


**Fig.3**. Scatter and Bland-Altman plots of regional CMV values obtained with the conventional (using an external water probe) and proposed CSF based methods, showing excellent agreement.

**DISCUSSION** Our preliminary data in healthy volunteers has demonstrated the feasibility of fast absolute myelin water quantification without the need for an external water probe. The estimated myelin and voxel water measurements were in good agreement with literature values (6). Further improvement in accuracy, scan time and SNR is possible by optimizing the proposed FAST-T1/T2 protocol for higher field strengths and by performing transmit B1 inhomogeneity correction. Future work will focus on demonstrating the clinical utility of CMV mapping for the monitoring of acute MS lesions.

**REFERENCES** 1. MacKay et al. MRM 1994;31:674. 2. Deoni et al. MRM 2008; 60:1372. 3. Laule et al. J Neurol 2004;251:284. 4. McCreary et al. Neuroimage 2009;45:1173. 5. Laule et al. Neuroimage 2008; 40:1575. 6. Whittal et al. MRM 1997;37:34. 7. Neeb et al. Neuroimage 2008;42:1094. 8. Nguyen et al. MRM 2012;67:614. 9. Tofts ed. Wiley 2003.