Supplementary Material

Water content based electrical properties tomography: results from a retrospective clinical study

Stefano Mandija[1,2], Sarah M. Jacobs[3], Jordi Kleinloog[1,2], Hongyan Liu[1,2], Oscar van der Heide[1,2], Anja G. van der Kolk[4], Alessandro Sbrizzi[1,2], Cornelis A.T. van den Berg[1,2]

1 Department of Radiotherapy, UMC Utrecht, Utrecht, The Netherlands,

2 Computational Imaging Group for MR Therapy and Diagnostics, UMC Utrecht, Utrecht, The Netherlands,

3 Department of Radiology and Nuclear Medicine, UMC Utrecht, Utrecht, The Netherlands,

4 Department of Medical Imaging, Radboud UMC, Nijmegen, The Netherlands

Correspondence: Stefano Mandija, University Medical Center Utrecht, 3508 GA, Utrecht, The Netherlands. Emil: s.mandija@umcutrecht.nl

Part 1: *wEPT conductivity validation in healthy volunteers*

In wEPT, the empirical relation linking water content to conductivity was previously validated in phantoms using probe measurements as a reference (Michel et al. 2016). Afterwards, we validated this relation *in vivo* (Mandija et al. 2018a) for WM conductivity reconstructions using Helmholtz based MR-EPT reconstructions (H-EPT) as independent reference. Here, as preliminary work, we extended this validation to *in vivo* GM using previously acquired data on eight volunteers (Mandija et al. 2018a, 2021).

MRI measurements were performed on eight healthy volunteers (6 females; mean age 21.7 years, standard deviation 2.3 years) following ethical protocols approved by the IRB of our institution. For these measurements, a clinical 3 T MR scanner (Achieva, Philips, Best, The Netherlands) and an 8-channel transmit/receive head coil were used.

As previously presented (Mandija et al. 2018a), first water content maps (W) were computed from image ratio (I_r) maps (T_1-weighted maps), obtained by dividing two T_1-weighted Spin-Echo magnitude images acquired with different TRs (700/3000 ms, respectively), according to (Michel et al. 2016): $W(\boldsymbol{r}) = w_1 e^{-w_2 I_r(\boldsymbol{r})}$, with w_1 = 1.527 and w_2 = 1.484 (mean of the w_1 and w_2 values computed by fitting literature water content values of WM, GM, and CSF to I_r values measured for each volunteer in these three brain regions). The other scan parameters were: TE = 6 ms, FOV = 240x240x90 mm^3, voxel size = 1x1x1.5 mm^3, slice gap = 1.5 mm, total acquisition time ~20 minutes.

Then, EPs maps were derived from water-content maps as described in the main manuscript, using the same $c_{1,2,3}$, and $p_{1,2,3}$ parameter values.

For an independent comparison, H-EPT reconstructions were performed according to (van Lier et al. 2012; Mandija et al. 2018b):

$$\varepsilon_r(\boldsymbol{r}) = \frac{-1}{\mu_0 \varepsilon_0 \omega^2} Re\left(\frac{\nabla^2 B_1^+(\boldsymbol{r})}{B_1^+(\boldsymbol{r})}\right) \quad [2]$$

$$\sigma(\boldsymbol{r}) = \frac{1}{\mu_0 \omega} Im\left(\frac{\nabla^2 B_1^+(\boldsymbol{r})}{B_1^+(\boldsymbol{r})}\right) \quad [3]$$

with ω: Larmor angular frequency, ε_0/μ_0: free space permittivity/permeability, and **r**: x,y,z-coordinates. The B_1^+ magnitude was measured using a dual-TR (AFI) sequence (Yarnykh 2007): FOV = 240x240x90 mm^3, voxel size = 2.5x2.5x3 mm^3, TR_1/TR_2/TE = 50/250/2.5 ms, flip angle = 65°.

For the B_1^+ phase, the transceive phase assumption was adopted, i.e. the B_1^+ phase was approximated with half of the transceive phase ($\varphi^{\pm}$) (van Lier et al. 2012, 2014). To obtain the transceive phase, we acquired two phase maps (φ) (single-echo Spin-Echo sequences) with opposite readout gradient

polarities. These were then combined ($\varphi^{\pm} = \frac{(\varphi_{\mathrm{spin\_echo\_1}} + \varphi_{\mathrm{spin\_echo\_2}})}{2}$) to minimize the impact of potential eddy-currents related artifacts (Mandija et al. 2015). For each sequence, the adopted parameters were: FOV = 240x240x90 mm^3, voxel size = 2.5x2.5x2.5 mm^3, slice gap = 0.5 mm, TR/TE = 800/6 ms, number of signal averages = 2. The total acquisition time for these three sequences was about 25 minutes.
Gibbs ringing correction and k-space Gaussian apodization were performed to reduce the impact of high frequency spatial variations in H-EPT reconstructions (Mandija et al. 2018b). H-EPT reconstructions were then performed using an in-plane 7×7 voxels derivative kernel (van Lier et al. 2012). For each volunteer, GM, WM, and CSF were first segmented in SPM12 (WTCN, UCL, London, UK) from one of the two Spin-Echo volumes used to compute the transceive phase. The voxels with P < 99% (affected by partial volume effects) were excluded. Then, these masks were eroded to remove boundary regions which would otherwise lead to erroneous mean conductivity values (Mandija et al. 2021).

For each volunteer, mean and standard deviation of the reconstructed conductivity values using wEPT were computed in the WM, GM, and CSF. For H-EPT reconstructions, this characterization could only be performed in the WM and GM (SI-Table S1), since CSF conductivity could not be reconstructed due to the severe boundary errors, as known from literature (Mandija et al. 2021).

The reported mean wEPT conductivity values agree with literature EPs values for healthy volunteers. Additionally, mean conductivity values in the GM and WM reconstructed using wEPT agree with the independently computed mean conductivity values reconstructed using H-EPT after boundary regions were excluded. Note that for H-EPT the conductivity contribution arising from through-plane second order derivatives is missing since this cannot be computed from phase data acquired using a multi-slice Spin Echo acquisition, leading to the observed small underestimation in the H-EPT reconstructed conductivity values with respect to literature values. Furthermore, the standard deviation values in wEPT reconstructions are much lower than H-EPT reconstructions, thus indicating higher precision.

In conclusion, as previously done for the WM (Mandija et al. 2018a), the model parameters used for wEPT-based conductivity reconstructions are verified *in vivo* in healthy volunteers for GM conductivity using H-EPT as independent measurement modality.

Supporting Table S1: Mean conductivity values and standard deviations for each volunteer and among all volunteers for wEPT and H-EPT.

	wEPT conductivity σ [S/m]						H-EPT conductivity *(after boundary erosion)* σ [S/m]			
Healthy volunteers	**GM** *mean*	*std*	**WM** *mean*	*std*	**CSF** *mean*	*std*	**GM** *mean*	*std*	**WM** *mean*	*std*
volunteer #1	0.62	± 0.16	0.35	± 0.02	1.79	± 1.52	0.54	± 0.68	0.32	± 0.24
volunteer #2	0.59	± 0.12	0.34	± 0.02	1.65	± 1.59	0.56	± 0.73	0.31	± 0.22
volunteer #3	0.56	± 0.14	0.34	± 0.02	2.56	± 3.16	0.55	± 1.05	0.29	± 0.26
volunteer #4	0.60	± 0.14	0.34	± 0.02	2.17	± 1.99	0.43	± 1.07	0.29	± 0.21
volunteer #5	0.58	± 0.12	0.34	± 0.02	1.95	± 1.97	0.54	± 0.65	0.31	± 0.20
volunteer #6	0.63	± 0.14	0.35	± 0.02	2.48	± 2.58	0.59	± 0.84	0.32	± 0.28
volunteer #7	0.68	± 0.18	0.35	± 0.02	2.15	± 1.80	0.55	± 0.79	0.31	± 0.18
volunteer #8	0.62	± 0.17	0.35	± 0.02	1.52	± 1.36	0.53	± 1.23	0.32	± 0.26
Mean	0.61	± 0.15	0.35	± 0.02	2.03	± 2.07	0.53	± 0.90	0.31	± 0.23
Literature	0.59		0.34		2.14		0.59		0.34	

Part 2 *– water content values*

Supporting Table S2: Mean water content values and standard deviations for each participant.

	Water content [%]								
	WM			GM			CSF		
Healthy volunteers	*mean*		*std*	*mean*		*std*	*mean*		*std*
volunteer #1	0.69	±	0.04	0.80	±	0.04	0.98	±	0.01
volunteer #2	0.69	±	0.04	0.82	±	0.04	0.98	±	0.01
volunteer #3	0.69	±	0.04	0.80	±	0.04	0.98	±	0.01
volunteer #4	0.68	±	0.04	0.81	±	0.04	0.98	±	0.01
volunteer #5	0.68	±	0.04	0.80	±	0.04	0.98	±	0.01
volunteer #6	0.69	±	0.04	0.83	±	0.04	0.98	±	0.01
volunteer #7	0.70	±	0.04	0.84	±	0.04	0.98	±	0.01
volunteer #8	0.67	±	0.04	0.80	±	0.04	0.98	±	0.01
volunteer #9	0.70	±	0.04	0.83	±	0.04	0.98	±	0.01
volunteer #10	0.69	±	0.04	0.82	±	0.04	0.98	±	0.01
NAT in tumor patients	*mean*		*std*	*mean*		*std*	*mean*		*std*
patient #1 (glioma Gr 2)	0.68	±	0.04	0.78	±	0.05	0.98	±	0.01
patient #2 (glioma Gr 2)	0.69	±	0.04	0.79	±	0.04	0.98	±	0.01
patient #3 (glioma Gr 2)	0.68	±	0.04	0.81	±	0.04	0.98	±	0.01
patient #4 (meningioma Gr 1**)**	0.69	±	0.04	0.80	±	0.04	0.98	±	0.01
patient #5 (meningioma Gr 2)	0.70	±	0.05	0.81	±	0.05	0.98	±	0.01
patient #6 (glioma Gr 3)	0.69	±	0.04	0.79	±	0.04	0.98	±	0.01
NAT in MS patients	*mean*		*std*	*mean*		*std*	*mean*		*std*
patient #7	0.69	±	0.05	0.80	±	0.04	0.98	±	0.01
patient #8	0.72	±	0.04	0.82	±	0.04	0.98	±	0.01
patient #9	0.68	±	0.04	0.79	±	0.04	0.98	±	0.01
patient #10	0.68	±	0.04	0.82	±	0.05	0.98	±	0.01
patient #11	0.69	±	0.04	0.80	±	0.04	0.98	±	0.01
patient #12	0.68	±	0.04	0.81	±	0.04	0.98	±	0.01
patient #13	0.69	±	0.04	0.81	±	0.04	0.98	±	0.01
patient #14	0.69	±	0.04	0.82	±	0.04	0.98	±	0.01
patient #15	0.68	±	0.04	0.80	±	0.04	0.98	±	0.01
Literature[1]	0.69		-	0.83		-	0.98		-

[1] Reference for the reported water content values in the WM, GM, and CSF. These values were used as reference in the calibration procedure to compute water content maps from either T1 maps (main manuscript) or image ratio (T1-weighted) maps (supplementary materials).

Supporting Table S3: Mean water content values and standard deviations in pathological tissue.

	Water content [%] in pathological tissue		
Tumor patients	*mean*		*std*
patient #1 (glioma Gr 2)	0.78	±	0.04
patient #2 (glioma Gr 2)	0.84	±	0.06
patient #3 (glioma Gr 2)	0.80	±	0.06
patient #4 (meningioma Gr 1**)**	0.86	±	0.05
patient #5 (meningioma Gr 2)	0.84	±	0.04
patient #6 (glioma Gr 3)	0.90	±	0.04
MS patients	*mean*		*std*
patient #7	0.79	±	0.07
patient #8	0.79	±	0.06
patient #9	0.77	±	0.08
patient #10	0.79	±	0.09
patient #11	0.78	±	0.07
patient #12	0.78	±	0.10
patient #13	0.77	±	0.06
patient #14	0.78	±	0.09
patient #15	0.78	±	0.08

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