

5007

## A comparison of dynamic and static $B_0$ mapping approaches for correction of CEST MRI at 7T

Esau Poblador Rodriguez<sup>1</sup>, Philipp Moser<sup>1</sup>, Barbara Dymerska<sup>2</sup>, Simon Robinson<sup>1</sup>, Benjamin Schmitt<sup>3</sup>, Andre van der Kouwe<sup>4</sup>, Stephan Gruber<sup>1</sup>, Siegfried Trattnig<sup>1,5</sup>, and Wolfgang Bogner<sup>1</sup>

<sup>1</sup>High Field MR Centre, Department of Biomedical Imaging and Image-guided Therapy, Medical University of Vienna, Vienna, Austria, <sup>2</sup>Medical Physics and Bioengineering, University College London, London, United Kingdom, <sup>3</sup>Siemens Healthineers, Sydney, Australia, <sup>4</sup>Athinoula A. Martinos Center for Biomedical Imaging, Department of Radiology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, United States, <sup>5</sup>Christian Doppler Laboratory for Clinical Molecular MR Imaging, Vienna, Austria

### Synopsis

In contrast to established static  $B_0$  correction approaches which assume an invariant static field during a CEST MRI acquisition, we propose three methods which can track and compensate temporal  $B_0$  fluctuations by shifting each Z-spectral point separately before  $MTR_{asym}$  analysis. We show the benefit of the proposed dynamic methods in comparison to three established static approaches by assessing their performance in the absence/presence of an induced frequency drift. In addition, we investigate the reliability and reproducibility of CEST MRI at ultra-high field (7T) by evaluating the drift's impact on the  $B_0$ -corrected  $MTR_{asym}$  maps in the brains of five healthy volunteers.

### Introduction

Chemical Exchange Saturation Transfer (CEST) MRI benefits from ultra-high field due to increased spectral resolution. Local magnetic field inhomogeneities,  $\delta B_0$ , are more severe, however, complicating CEST quantification<sup>1</sup>. Static  $B_0$ -correction techniques are prone to errors since they assume negligible temporal  $B_0$ -fluctuations arising from system instabilities (such as frequency drifts) or involuntary subject movement. We propose and compare the in vivo performance of three different dynamic  $B_0$ -correction methods for CEST MRI which should lead to more reliable  $MTR_{asym}$  maps than three established static  $B_0$ -correction approaches in the presence of  $B_0$ -instabilities.

### Methods

The three  $\delta B_0$  mapping approaches for static CEST correction were:

- (A) CEST-minZ:  $\delta B_0$  from the minimum of the interpolated Z-spectra (intrinsic)<sup>2</sup>
- (B) WASSR:  $\delta B_0$  from high spectrally resolved Z-spectra without fat suppression (pre-scan)<sup>1</sup>
- (C) GRE-2TE:  $\delta B_0$  from a dual-echo gradient echo (GRE) readout reference scan (pre-scan)<sup>3</sup>

The three proposed  $B_0$  tracking approaches for dynamic CEST correction were:

- (D) CEST-GRE-2TE:  $\delta B_0(t)$  from a dual-echo GRE readout which replaces the single-echo GRE readout after the CEST-labeling module (intrinsic)<sup>4</sup>
- (E) CEST-GRE-1TE:  $\delta B_0(t)$  from a single-echo GRE readout after the CEST-labeling module. Additionally, coil phase offset maps need to be determined (intrinsic/pre-scan)<sup>5,6</sup>
- (F) NAV-EPI-2TE:  $\delta B_0(t)$  from a dual-echo multi-shot EPI readout that is interleaved with the CEST sequence (interleaved navigator)<sup>7,8</sup>

The study was performed on a whole-body 7T MR system (Magnetom, Siemens) with a <sup>1</sup>H 32-channel head coil (Nova Medical). The 2D sequences had a resolution of 2.1x2.1x6.0mm<sup>3</sup> for which image acquisition/analysis parameters were matched (details in Table 1). Image processing, coil combination,  $B_0$  map calculation and ROIs statistics were conducted in MATLAB (MathWorks).  $B_0$ -correction and asymmetric magnetic transfer ratio ( $MTR_{asym}$ ) analysis were performed voxel wise.

Initial phantom tests were performed to evaluate the consistency of the  $B_0$  mapping among the different methods and to establish their dependency on the CEST-labeling module.

The impact of the method of  $B_0$  determination on the  $MTR_{asym}$  was assessed in five healthy volunteers. To show the performance of the dynamic compensation methods versus the static methods in the presence of scanner instabilities, a  $\sim 4$ Hz/min frequency drift was induced during the CEST re-scan (protocol flow in FIG.1). This is consistent with previous reported drifts at 3T<sup>9-11</sup>.

### Results

The dynamic correction methods successfully tracked the  $B_0$  evolution to independently correct each Z-spectral point before  $MTR_{asym}$  analysis. The intrinsic dynamic methods CEST-GRE-2TE and CEST-GRE-1TE were not corrupted by the RF saturation prior to the CEST readout for  $\Delta\omega \gg |0.24|$ ppm. FIG.2 shows the effect of the  $B_0$  determination on the corrected  $MTR_{asym}$  curves among the different correction methods. In the presence of an induced  $\sim 4$ Hz/min drift, the established static methods resulted in severely underestimated ( $\sim 1/3$  for CEST-minZ) or overestimated ( $\sim 3$  times for WASSR and GRE-2TE) ratios compared to the stable case. CEST-minZ estimated  $B_0$  approximately at the end of the CEST scan ( $\delta B_{0(12min)} \approx 48$ Hz) in contrast to the pre-scans WASSR and GRE-2TE ( $\delta B_{0(0min)} \approx 0$ Hz).

The resulted color-coded  $MTR_{asym}$  maps are presented in FIG.3. Among the dynamic correction methods, NAV-EPI-2TE and CEST-GRE-2TE provided closest  $B_0$ -corrected contrasts between the two CEST acquisitions (stable conditions VS induced drift). CEST-GRE-1TE showed some deviations, but was still better than all static methods.

To investigate the CEST scan-rescan reproducibility, a comparison among five healthy volunteers was performed. The results provided by NAV-EPI-2TE, presented in FIG.4, show highly consistent  $MTR_{asym}$  maps. CEST-GRE-2TE achieved similar uniform results among volunteers with the exception of frontal

and periventricular discrepancies in volunteer V2.

## Discussion and Conclusion

The current study focused on the  $MTR_{asym}$  integration range  $\Delta\omega=\pm[0.24-1.18]$ ppm, to test the performance of the proposed correction methods for the most challenging frequencies due to the high slope of the Z-spectrum<sup>1</sup>.

The proposed dynamic method CEST-GRE-2TE tracks the  $B_0$  field intrinsically from a dual-echo CEST scan requiring no additional measurements, making it widely applicable. CEST-GRE-1TE shortens the measurement time by allowing a single-echo CEST scan, at the expense of a negligible ~1s long pre-scan. The implementation of NAV-EPI-2TE is more complex since it requires interleaved  $B_0$  maps via a navigator, but it is completely insensitive to the RF saturation applied for CEST-labeling.

The proposed dynamic methods could be additionally combined with real-time motion correction by extending the navigator to 3D as previously shown for MRI and MRSI<sup>7,8;12;13</sup>. Such techniques will be assessed in further work to, on top of  $B_0$ -instabilities, readily correct for motion-induced  $\delta B_0$ .

This study provides an excellent basis for reliable clinical CEST MRI in presence of temporarily fluctuating  $B_0$ -inhomogeneities, offering more accurate water resonance determination, avoiding the need of lengthy pre-scans (required for WASSR) and shortening the measurement time by allowing the use of fewer Z-spectral points (as required for CEST-minZ).

## Acknowledgements

This material is based upon work supported by Christian Doppler Laboratory for Clinical Molecular MRI and the Austrian Science Fund (FWF) under Grant KLI-718.

Special gratitude to Vladimir Mlynarik for his guidance and assistance.

## References

- Kim M, Gillen J, Landman BA, Zhou J, van Zijl PC. 2009. Water saturation shift referencing (wassr) for chemical exchange saturation transfer (cest) experiments. *Magn Reson Med.* 61(6):1441-1450.
- Zaiss M, Schmitt B, Bachert P. 2011. Quantitative separation of cest effect from magnetization transfer and spillover effects by lorentzian-line-fit analysis of z-spectra. *J Magn Reson.* 211(2):149-155.
- Kawanaka A, Takagi M. 1986. Estimation of static magnetic field and gradient fields from nmr image. *Journal of Physics E: Scientific Instruments.* 19(10): 871.
- Visser E, Poser BA, Barth M, Zwiers MP. 2012. Reference-free unwarping of epi data using dynamic off-resonance correction with multiecho acquisition (docma). *Magn Reson Med.* 68(4):1247-1254.
- Robinson S, Grabner G, Witoszynskij S, Trattnig S. 2011. Combining phase images from multi-channel rf coils using 3d phase offset maps derived from a dual-echo scan. *Magn Reson Med.* 65(6):1638-1648.
- Dymerska B, Poser BA, Barth M, Trattnig S, Robinson SD. 2018. A method for the dynamic correction of b0-related distortions in single-echo epi at 7t. *NeuroImage.* 168:321-331.
- Hess AT, Tisdall MD, Andronesi OC, Meintjes EM, van der Kouwe AJ. 2011. Real-time motion and b0 corrected single voxel spectroscopy using volumetric navigators. *Magn Reson Med.* 66(2):314-323.
- Bogner W, Hess AT, Gagoski B, Tisdall MD, van der Kouwe AJ, Trattnig S, Rosen B, Andronesi OC. 2014. Real-time motion- and b0-correction for laser-localized spiral-accelerated 3d-mrsi of the brain at 3t. *NeuroImage.* 88:22-31.
- Harris AD, Glaubitz B, Near J, John Evans C, Puts NA, Schmidt-Wilcke T, Tegenthoff M, Barker PB, Edden RA. 2014. Impact of frequency drift on gamma-aminobutyric acid-edited mr spectroscopy. *Magn Reson Med.* 72(4):941-948.
- Rowland BC, Liao H, Adan F, Mariano L, Irvine J, Lin AP. 2017. Correcting for frequency drift in clinical brain mr spectroscopy. *Journal of neuroimaging : official journal of the American Society of Neuroimaging.* 27(1):23-28.
- Lee CY, Choi IY, Lee P. 2018. Prospective frequency correction using outer volume suppression-localized navigator for mr spectroscopy and spectroscopic imaging. *Magn Reson Med.*
- Hess AT, Andronesi OC, Tisdall MD, Sorensen AG, van der Kouwe AJ, Meintjes EM. 2012. Real-time motion and b0 correction for localized adiabatic selective refocusing (laser) mrsi using echo planar imaging volumetric navigators. *NMR in biomedicine.* 25(2):347-358.
- Alhamud A, Taylor PA, van der Kouwe AJ, Meintjes EM. 2016. Real-time measurement and correction of both b0 changes and subject motion in diffusion tensor imaging using a double volumetric navigated (dnav) sequence. *NeuroImage.* 126:60-71.

## Figures

		TR	TE1	TE2	BW	FA	Echo Train	Miscellaneous
		[ms]	[ms]	[ms]	[Hz/Px]	[°]	Length	
STATIC	CEST-minZ	9.5	1.74	-	780	6	128	$T_s=700$ ms, $B_1^{rms}=2.0$ $\mu$ T, $\Delta\omega=0.08$ ppm
	WASSR	9.5	1.74	-	780	6	128	$T_s=100$ ms, $B_1^{rms}=0.2$ $\mu$ T, $\Delta\omega=0.013$ ppm
	GRE-2TE	9.5	1.74	5.16	780	6	128	
DYNAMIC	CEST-GRE-2TE	9.5	1.74	5.16	780	6	128	$T_s=700$ ms, $B_1^{rms}=2.0$ $\mu$ T, $\Delta\omega=0.08$ ppm
	CEST-GRE-1TE	9.5	1.74	-	780	6	128	$T_s=700$ ms, $B_1^{rms}=2.0$ $\mu$ T, $\Delta\omega=0.08$ ppm
	NAV-EPI-2TE	15	5.4	9.0	2442	5	4	

Table 1. Summary of relevant parameters for each of the  $B_0$  acquisition methods evaluated. Static methods correct for  $B_0$  inhomogeneities by shifting the entire Z-spectrum and hence assuming no drift or fluctuation in the static field throughout the CEST measurement. Dynamic methods, on the other hand, track its temporal  $B_0$  evolution to shift each Z-value (at certain saturation frequency offset  $\Delta\omega$ ) independently.

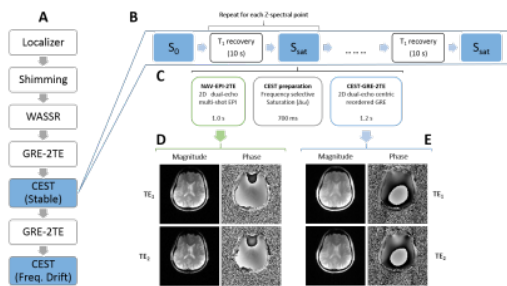


FIG. 1: An overview of the experimental protocol followed to compare 6  $B_0$ -correction methods (A). Scheme of the CEST measurement (B), in which a delay for T1 recovery of water signal is interleaved with  $S_0$  and  $S_{sat}$  acquisitions, each of them consisting of three blocks (C): an EPI navigator with dual-echo readout scan generating magnitude and phase images per echo time (D); a CEST-labeling period in which the magnetization is saturated by a train of Gaussian pulses at a sweeping frequency offset  $\Delta\omega$ ; and a GRE with dual-echo readout scan generating magnitude and phase images per echo time (E).

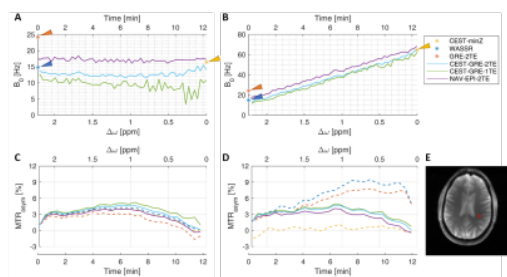


FIG. 2: Impact of a  $\sim 4$ Hz/min frequency drift within an ROI for volunteer V1 (E). ROI-averaged  $B_0$  tracking without (A) and with (B) an induced drift. The top x-axis represents the time after the “GRE-2TE” pre-scan was acquired and the bottom x-axis the frequency at which the saturation pulses were applied at the time instant when each  $B_0$  sample was determined. Differences in  $MTR_{asym}$  curves among  $B_0$ -correction methods under stable (C) and drifted (D) conditions are shown in the bottom row. The proposed methods CEST-GRE-2TE (light blue), CEST-GRE-1TE (green) and NAV-EPI-2TE (purple) succeeded to track and correct the induced drift  $\delta B_0(t)$ .

	CEST-minZ	WASSR	GRE-2TE	CEST-GRE-2TE	CEST-GRE-1TE	NAV-EPI-2TE	$MTR_{asym}^{2\tau-1.5\tau}$ [%]
Stable							
	2.02±1.02 %	0.80±1.39 %	2.17±1.97 %	3.11±1.70 %	3.08±1.65 %	3.11±1.04 %	$MTR_{asym}^{2\tau-1.5\tau}$ [%]
Induced drift							
	-1.23±1.48 %	11.00±3.97 %	13.95±2.85 %	3.70±1.62 %	3.70±1.76 %	3.26±1.72 %	$MTR_{asym}^{2\tau-1.5\tau}$ [%]

FIG. 3: Effect on the  $MTR_{asym}$  maps of a linear induced frequency drift for volunteer V2. The top row shows color-coded maps for the different correction methods in the absence of drifts, the bottom row depicts maps in which there was a  $\sim 4$ Hz/min drift. The static method CEST-minZ overestimated  $B_0$ , resulting in decreased map values, while WASSR and GRE-2TE show the opposite effect, since both scans took place before the field drift was applied. Among the dynamic methods, NAV-EPI-2TE compensates this drift most efficiently, providing the closest values within the delineated ROI (in black) between acquisitions, being closely followed by CEST-GRE-2TE.

	Volunteer V1	Volunteer V2	Volunteer V3	Volunteer V4	Volunteer V5	NAV-EPI-2TE
Stable						
	3.11±1.04 %	3.04±1.78 %	3.65±0.94 %	3.05±0.92 %	3.12±1.67 %	$MTR_{asym}^{2\tau-1.5\tau}$ [%]
Induced drift						
	3.06±1.03 %	3.26±1.72 %	3.62±0.95 %	2.92±1.12 %	3.39±1.87 %	$MTR_{asym}^{2\tau-1.5\tau}$ [%]

FIG. 4: Comparison of the correction performance of the proposed dynamic method NAV-EPI-2TE for all subjects (V1-V5):  $B_0$ -corrected maps in the absence (top row) and in the presence (bottom row) of the induced  $B_0$  drift during the CEST measurement. A ROI along each volunteer’s brain border was manually drawn (delineated in black) and the  $MTR_{asym}$  mean  $\pm$  standard deviation values within this ROI are shown at the bottom of each map. The  $MTR_{asym}$  maps are highly consistent between the CEST scans with and without the induced frequency drift in all cases.