Magnetization Transfer Ratio Imaging in Multiple Sclerosis – a comparison of 3D balanced steady-state free precession and 2D gradient echo sequences in clinical studies

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Introduction: There is a great need for techniques, that quantitatively assess subtle tissue changes beyond the gross pathology in multiple sclerosis (MS) patients. Such pathology is known to occurr, but current magnetization transfer ratio (MTR) techniques have various limitations. We evaluated a new balanced steady-state free precession (bSSFP) MTR protocol yielding maximal sensitivity to MT in human brain [1]. We compared this 3D-bSSFP technique with the commonly used 2D gradient echo approach in a clinical setup, and evaluated the advantages of bSSFP in a quantitative study on 20 multiple sclerosis patients. Protocols were adjusted to similar acquisition times while using optimized sequence settings for each of both approaches.

Methods: Data were acquired on a 1.5 T clinical MR system (Avanto, SIEMENS, Erlangen/Germany), and 20 patients w/ multiple sclerosis (5 male, mean age 51 (29-68) years, 17 RRMS/2 SCP/1 CIS, mean EDSS 2.7 (1.5-4.5)) were included in a clinical protocol. The MR protocol involved transverse double-echo PD- and T2-weighted TSE (TR/TE1/TE2 3980/14/108 ms, 40 slcs of 3 mm, rFoV 188x250 mm², MAT 224x256), sagittal 3D T1w-MPRAGE (TR/TE/TI 2080/3.9/1100 ms, 160 partitions of 1 mm, rFoV 235x250 mm², MAT 240x256), four scans for MT contrast, and transverse T1w-SE after contrast media injection (TR/TE 552/17 ms, 40 slcs, TH 3 mm, MAT 192x256). MT contrast images were acquired using 1) a commonly used approach of two transverse 2D gradient echo (GRE) sequences w/o and w/ MT saturation pulse (TR/TE 1000/12 ms, flip 20°, 28 slcs, 4 mm, FoV 250 mm², MAT 128x256, TA 3:11 min. twice, adiabatic rf-pulse 7.68 ms), and 2) two sagittal 3D scans of bSSFP (TR/TE 5.38/2.41 ms, TR/TE 3.58/1.49 ms, flip 40°, 160 partitions of 1 mm, FoV 250 mm², MAT 256x256, TA 4:25 & 2:56 min, rf-pulse durations 0.27 ms & 2.1 ms).
All volume stacks were skullstripped, both GRE and bSSFP series were registered to each other to correct for motion; bSSFP series were slightly Wiener-filtered (noise adaptive 3x3) to assimilate SNR in comparison to GRE. Finally MTR images were estimated according to $MTR=1-M_{sat}/M_0$. T1w 3D-MPRAGE was registered to GRE and bSSFP, resp., and subsequently segmented into CSF/GM/WM; atlas-based information of basalganglia was used to correct for misregistrations in GM & WM masks. MS lesions were digitally marked on PDw (hyperintense) and T1w (blackholes) and registered into GRE and bSSFP space. The registered lesion masks were then used to produce GM and WM masks w/o lesions. Additionally, a semi-quantitative T2-map was calculated from the registered (to 2D-GRE and 3D-bSSFP, resp.) dual-echo TSE series.
Quantitative evaluation was based on global histogram analyses due to the different spatial resolutions of GRE and bSSFP. Histograms (100 bins for MTR < 0.8, normalized) have been built from binary masks of GM w/o lesions, WM w/o lesions, lesions marked on PDw, and blackhole lesions marked on T1w, applied on MTR volumes of 2D-GRE and 3D-bSSFP. Furthermore, all specific histograms have been summed up across subjects, and corresponding mean and median values of the histograms were estimated. FWHM and maxima positions were deduced from a fit using a combination of a Gaussian and gamma-variate curve. Similarly, histograms were built applying the masks on the quantitative T2-maps in 2D-GRE and 3D-bSSFP space.

Results: 2D-GRE and 3D-bSSFP differ considerably with respect to sequence parameters and image characteristics, esp. concerning spatial resolution (voxelsize 8:1) and SNR. The application of a Wiener-filter on bSSFP data provided comparable SNR while maintaining the advantage of high isotropic resolution in the 3D-bSSFP approach (Fig. 1). Common 2D-GRE yielded MTR values in accordance with literature (GM ≈ 0.44, WM ≈ 0.47; max position of accumulated histograms) [2], whereas for 3D-bSSFP mean values were reduced (GM ≈ 0.35, WM ≈ 0.41), Fig. 2.
The difference between mean MTR values for white and grey matter was larger in 3D-bSSFP ($MTR_{WM}/MTR_{GM} \approx 1.19$) than in 2D-GRE ($MTR_{WM}/MTR_{GM} \approx 1.11$) which is reflected by the considerable increase in white and grey matter contrast (see Fig. 1). As a result, histograms built from PDw- (hyperintense) and T1w-marked (blackholes) lesions were more clearly separated using the bSSFP approach. In addition, the analysis of joint histograms (MTR vs. T2, Fig. 3) gives detailed information on the dependencies of NAGM, NAWM, and lesions on MT and T2, beeing supported by the higher isotropic resolution and increased SNR of the 3D-bSSFP approach.

Discussion / Conclusion: The i) high isotropic spatial resolution, ii) whole brain coverage, iii) stronger contrast between grey and white matter, and iv) fast and robust quantification of MTR are provided by the 3D balanced steady-state free precession MTR technique and appear advantageous over the 2D-GRE approach. It provides a more elaborate characterization of NAWM, NAGM and lesion detail. Despite the quantitative nature of MTR, it must be kept in mind that absolute values strongly depend on sequence parameters: for 2D-GRE on TR and the number of slices, whereas for 3D-bSSFP on TR, TE and flip angles. Protocol parameters have been chosen in 2D-GRE to match commonly used protocols, and in 3D-bSSFP to provide an optimized saturation effect within the limits of spatial resolution and acquisition time.
The increase in grey-white matter MTR contrast is based on the stronger dependence on T1-relaxation in bSSFP sequences, whereas the 2D-GRE sequences hardly reveal any T1-dependence when used in an interleaved multi-slice prescription with long TR.

References: [1] Bieri O, et al., MRM, 58: 511-518 (2007); [2] Barker GJ, et al., Proc 5th Ann Meeting ISMRM, 5: 1556 (1997).

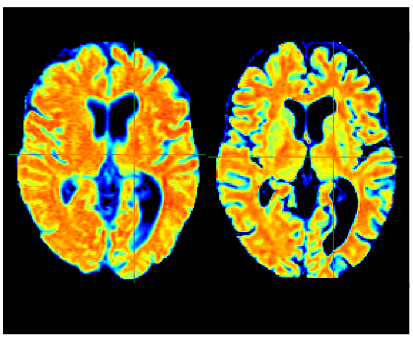

Fig. 1: Maps of magnetization transfer ratio (MTR) contrast derived from 2D gradient echo (GRE, left) and 3D balanced steady-state free precession (bSSFP, right) sequences.

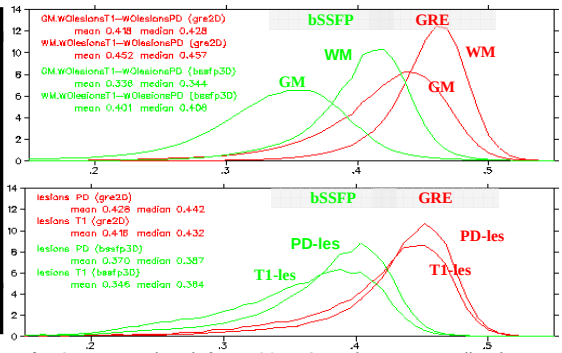

Fig. 2: Accumulated from 20 MS patients, normalized MTR histograms built from masks (GM, WM – top row, and PDw-, T1w-marked lesions –bottom row) applied on MTR contrast maps, derived from 2D-GRE (red) and 3D-bSSFP (green).
Separation of MT_{GM} vs. MT_{WM} is considerably larger for 3D-bSSFP due to stronger T1-relaxation dependence.

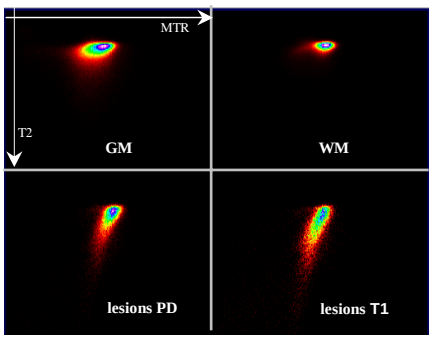

Fig. 3: Joint histograms MTR vs. T2 (single patient) built from tissue masks applied on MTR contrast maps, derived from 3D-bSSFP protocol.