# On the application of simultaneous dual contrast weighting using double echo 2in1-RARE in healthy subjects and multiple sclerosis patients

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**Target audience:** This work is of interest for basic MR researchers, imaging scientists and clinical scientists.

**Purpose:** 2in1-RARE is a dual contrast RARE variant that provides simultaneous anatomical (PD) and functional ($T_2^*$) contrast in a single scan [1]. 2in1-RARE presents an alternative to address scan time constraints frequently encountered during sequential acquisition of $T_2$, $T_2^*$ or proton density (PD) weighted RARE. It is conceptually appealing to pursue simultaneous PD and $T_2^*$ weighted imaging (i) for the assessment of multiple sclerosis (MS), (ii) for the differential diagnosis of MS versus orphan neuroinflammatory diseases based upon the detection of small perivascular veins and lesion conspicuity, and (iii) for the diagnosis and therapy of neurodegeneration with iron brain accumulation (NBIA). To approach this goal this work examines the applicability of 2in1-RARE for susceptibility weighted imaging, for $T_2^*$ mapping and for PD weighted imaging of the human brain including the detection of subtle MS lesions at 3 T. Point spread function (PSF) assessment was performed for 2in1-RARE and benchmarked versus conventional and split-echo RARE variants [2,3] to scrutinize 2in1-RAREs image quality and spatial resolution fidelity. Secondly, 2in1-RAREs capabilities for $T_2^*$ mapping were validated versus multi-echo gradient echo acquisitions. In-vivo 2in1-RARE experiments were performed in healthy subjects and in MS patients including susceptibility weighted imaging and $T_2^*$ mapping.

**Methods:** The underlying concept of 2in1-RARE is the strict separation of spin echoes (SE) and stimulated echoes (STE). This approach provides independent weighting of spin echoes and stimulated echoes and hence provides means for generating two images of different contrast simultaneously. An evolution time $\tau$ is inserted after the first refocusing pulse to impress $T_2^*$ weighting to the SE magnetization while the STE part remains PD weighted. Experiments were performed on a 3 T MR system (Magnetom Verio, Siemens Healthcare, Erlangen, Germany, $G_{max}$ = 40 mT/m, maximum slew rate: 200 mT/m/ms). The body coil was used for signal transmission and a 12 element head coil (Siemens Healthcare, Erlangen, Germany) was employed for signal reception. PSF assessment was performed in a $CuSO_4$ doped cylindrical agarose phantom. For this purpose, measurements with phase encoding gradients turned off were conducted using: TR = 1000 ms, TE = 25 ms, echo spacing (ESP) = 12 ms, echo train length (ETL) = 7, receiver bandwidth = 465 Hz/pixel, acquisition matrix = 1024 x 512, $FoV_{read}$ = 250 mm, slice thickness = 5 mm, $\tau$ = 15 ms. The full-width-half-maximum (FWHM) of the PSF was calculated as a measure for quality. To validate $T_2^*$ weighting in 2in1-RARE, a series of measurements with 14 $\tau$ values ranging from 0 ms to 50 ms was performed in the phantom. $T_2^*$ maps were generated by fitting the data points to a mono exponential decay. For comparison, $T_2^*$ mapping was conducted using 2D multi-echo gradient echo imaging (TR = 100 ms, 14 TE values ranging from 2.42 ms to 33.9 ms, equidistant $\Delta$TE = 2.42 ms, (0.7 x 0.7 x 5.0) $mm^3$). The performance of 2in1-RARE was also tested in-vivo including healthy volunteers and MS patients. The imaging parameters were identical to those used in the phantom with the exception of TR = 4000 ms. For $T_2^*$ mapping of the brain 13 equidistant evolution times $\tau$ ranging from 0 ms to 40 ms were applied. $T_2^*$ maps were calculated from the SE images. The STE images simultaneously derived from 2in1-RARE were averaged to create an anatomical image, for which whole brain SNR was calculated [4]. For comparison, $T_1$ weighted 3D GRE (MPRAGE) images were used as an anatomical reference for MS lesion detection.

**Results:** The minor PSF broadening of about 15% obtained for 2in1-RARE versus coherent RARE and split-echo RARE (Table 1) originates from the faster signal decay in the 2in1-RARE echo train, since secondary stimulated echoes (i.e. stimulated echoes that are generated past the third refocusing pulse) are discarded. For 2in1-RARE $T_2^* = (31.2 \pm 8.9)$ ms was obtained for a ROI covering the whole axial slice of the phantom. In comparison, $T_2^*$ mapping using conventional 2D multi-echo gradient echo imaging yielded $T_2^* = (29.1 \pm 13.5)$ ms for the same ROI, affirming the correct susceptibility weighting in 2in1-RARE. SNR analysis revealed a whole brain SNR of $66.4 \pm 11.2$ for the averaged anatomical PD weighted image (Fig. 1c). The delineation of two MS lesions with diameters of about 2 mm and 5 mm in images acquired with 2in1-RARE (Fig. 2b,c) demonstrates the feasibility of 2in1-RARE for depicting subtle pathological structures.

| | | FWHM [pixel] | |
|---|---|---|---|
| coherent | | 1.7 | |
| split-echo | odd/even | 1.7 | 1.7 |
| 2in1 $\tau$ = 0 ms | SE/STE | 2.0 | 2.0 |
| 2in1 $\tau$ = 15 ms | SE/STE | 1.6 | 2.0 |
| split-echo $\tau$ = 15 ms | odd/even | 1.5 | 1.6 |

**Table 1:** FWHM values in pixel for coherent, split-echo and 2in1-RARE. For split-echo RARE odd and even echoes were reconstructed separately. In comparison, for 2in1-RARE the echo is divided into SE and STE echo groups.

**Discussion:** 2in1-RARE combines anatomical information (PD weighting) and functional aspects ($T_2^*$ weighting) within a single acquisition. The applicability of 2in1-RARE was demonstrated for healthy volunteers and MS patients. To expand the range of clinical 2in1-RARE applications it would be beneficial to extend 2in1-RARE to $T_2$ weighted imaging by modifying the centric phase encoding scheme or by incorporating a $T_2$ preparation module [5]. The factor two in speed gain of 2in1-RARE over conventional RARE can be put to good use for simultaneous $T_2/T_2^*$ mapping and holds the promise to eliminate slice mis-registration artifacts frequently encountered in sequential acquisitions with RARE. The strict separation of SE and STE offers further possibilities for independent contrast manipulation. Diffusion weighting could be impressed to the SE magnetization, while the STE magnetization remains PD/$T_2$ weighted. This would be of great interest for stroke imaging. 2in1-RARE is not limited to brain imaging, but can also meet the needs of abdominal imaging and cardiac imaging.

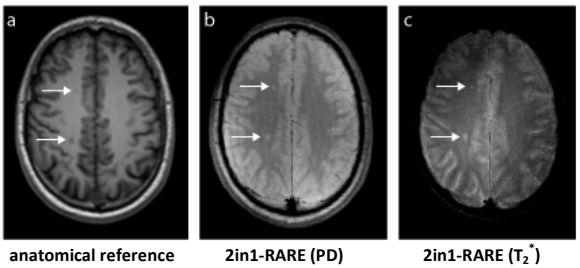


**Figure 2**: In-vivo brain images of a MS patient comparing $T_1$ weighted GRE (MPRAGE) **(a)** with PD weighted and $T_2^*$ weighted 2in1-RARE images **(b,c)**. The depicted slice comprises two lesions with diameters of about 2 mm and 5 mm.

**Conclusion:** 2in1-RARE provides dual contrast means for simultaneous $T_2^*$ mapping and proton density weighted imaging which holds the promise to be beneficial for the detection of subtle MS lesions, for the differential diagnosis of neuroinflammatory diseases and for brain iron quantification.

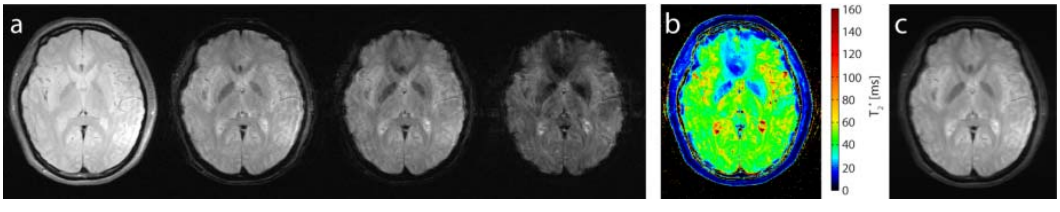


**Figure 1:** 4 out of 13 images reconstructed from the SE magnetization using evolution times ranging from $\tau$ = 0 ms to $\tau$ = 40 ms **(a)**. A $T_2^*$ map calculated from the series of 13 datasets is depicted in **(b)**. In addition to the $T_2^*$ weighted images 2in1-RARE simultaneously provides PD weighted data with **(c)** depicting an image resulting from the average of all 13 PD weighted datasets exhibiting a resolution of (0.5 x 0.5 x 5.0) $mm^3$.

**References:** [1] Fuchs et al, *Proc. Intl. Soc. Mag. Reson. Med. 21* (2013), p. 864; [2] Schick, *MRM* 1997, 38:638; [3] Norris et al, *MRM* 1992, 27:142; [4] Constantinides et al, *MRM* 1997, 38:852; [5] Brittain et al, *MRM* 1995, 33:689