To Add Myelin Detection to Your Neuro Protocol Without Additional Scan Time

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SyntheticMR provides REMyDI (Rapid Estimation of Myelin for Diagnostic Imaging)[1], which was introduced on the Siemens Healthineers booth at RSNA 2016. REMyDI pro-vides a method of myelin detection in the brain, using a scan time of only 5 to 6 minutes. Based on the same sequence data, however, conventional images such as T1w, T2w and FLAIR can also be generated. If these images are taken for diagnosis, instead of acquiring them conventionally, valuable examination time is saved.

The secret behind this efficient way of data collection is MR quantification; a sequence is acquired that provides maps of physical properties of the patient, such as the T1 relaxation time, T2 relaxation time and Proton Density (PD). It is well known that these physical properties govern the signal intensity of MR images, but normally we can only speak in terms of weighting: an image is T1-weighted if the MR scanners parameters are set such that differences in tissue T1 relaxation result in contrast differences in image signal intensity. Similarly, an image is T2-weighted if the MR scanners parameters are set such that differences in tissue T2 relaxation result in contrast differences in image signal intensity. These conventionally weighted images, however, are arbitrarily scaled and do not provide a measurement of the actual T1 or T2 value. Without this absolute scale, radiologists are forced to interpret the images based on contrast differences only.

[1] REMyDI is currently under development at SyntheticMR and is not for sale in the US and in other countries. Its future availability cannot be ensured.

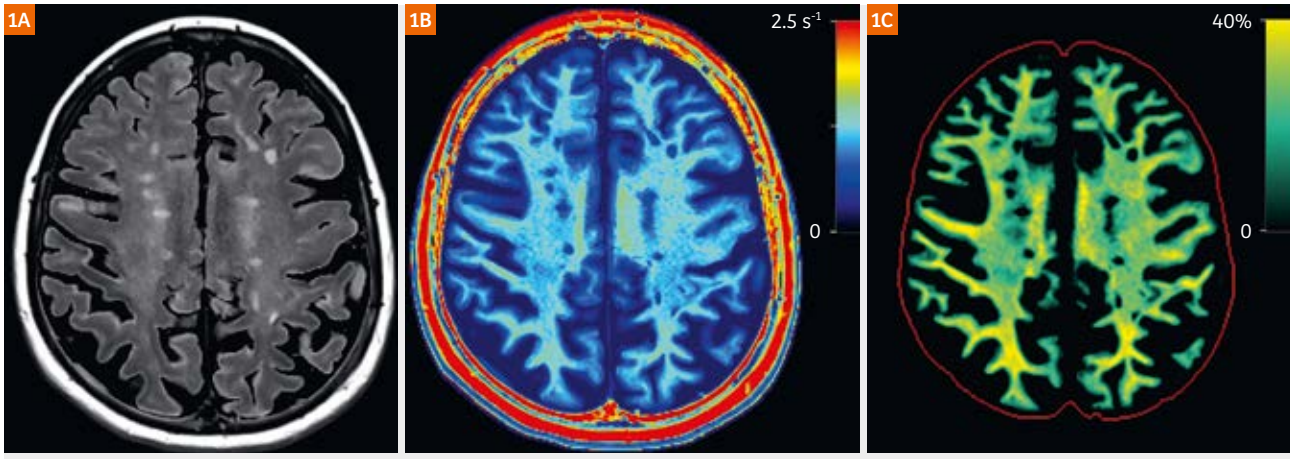

Figure 1:
Example images showing the application of REMyDI on a patient with multiple sclerosis (60-year-old female). A synthetic T2w-FLAIR of an axial slice of the brain is shown **(1A)**. This image is synthesized based on quantitative maps of R1 relaxation rate (shown on a scale 0–2.5 s^{-1} in **1B**, the R1 relaxation rate is the inverse of T1 relaxation time), R2 relaxation rate (1/T2) and proton density PD (not shown), together with virtual scanner settings TE/TR/TI = 100/15000/3000 ms. Using the same quantitative maps also myelin partial volume is calculated (shown on a scale 0–40% in **1C**). At the location of the MS plaques the myelin values are clearly lower than the surrounding normal appearing white matter. All images were generated on a 3T MAGNETOM Prisma system from a single acquisition of 5 minutes and 8 seconds.

In 2008, an efficient method of MR quantification was introduced [1], where T1, T2 and PD could be obtained in 6 minutes, covering the entire head. The post-processing software SyMRI was created that did not only display these maps, but also had the ability to synthesize conventional T1w, T2w, FLAIR, PSIR and DIR images. The approach of synthesizing conventional images based on a single quantification sequence has been known since the eighties, but became clinically available only in the recent years. A large, prospective study on 109 subjects, rated by 7 neuroradiologists, showed the clinical viability of synthetic MRI [2]. The advantage of this approach is that radiologists can continue to interpret the images they are comfortable with, or even optimize the image contrast after the patient has left, while the imaging data actually consists of quantitative T1, T2 and PD maps. The maps reflect patient tissue properties only and hence are entirely independent of MR scanner settings and identical for all scanners at a specific field-strength. It is an important step towards more standardization in MR. Moreover, the maps provide a robust input for computer algorithms to automatically detect tissue. For example, in neuroimaging white matter, grey matter and cerebrospinal fluid can automatically be found, providing an accurate means to monitor brain atrophy in neuro-degenerative diseases [3].

Recently, a model was proposed, with which it is possible to detect myelin partial volume based on the T1, T2 and PD maps [4]. Owing to the magnetization exchange between the rapidly relaxing myelin water and surrounding intra- and extracellular water, the presence of myelin is inferred using the observed changes in relaxation

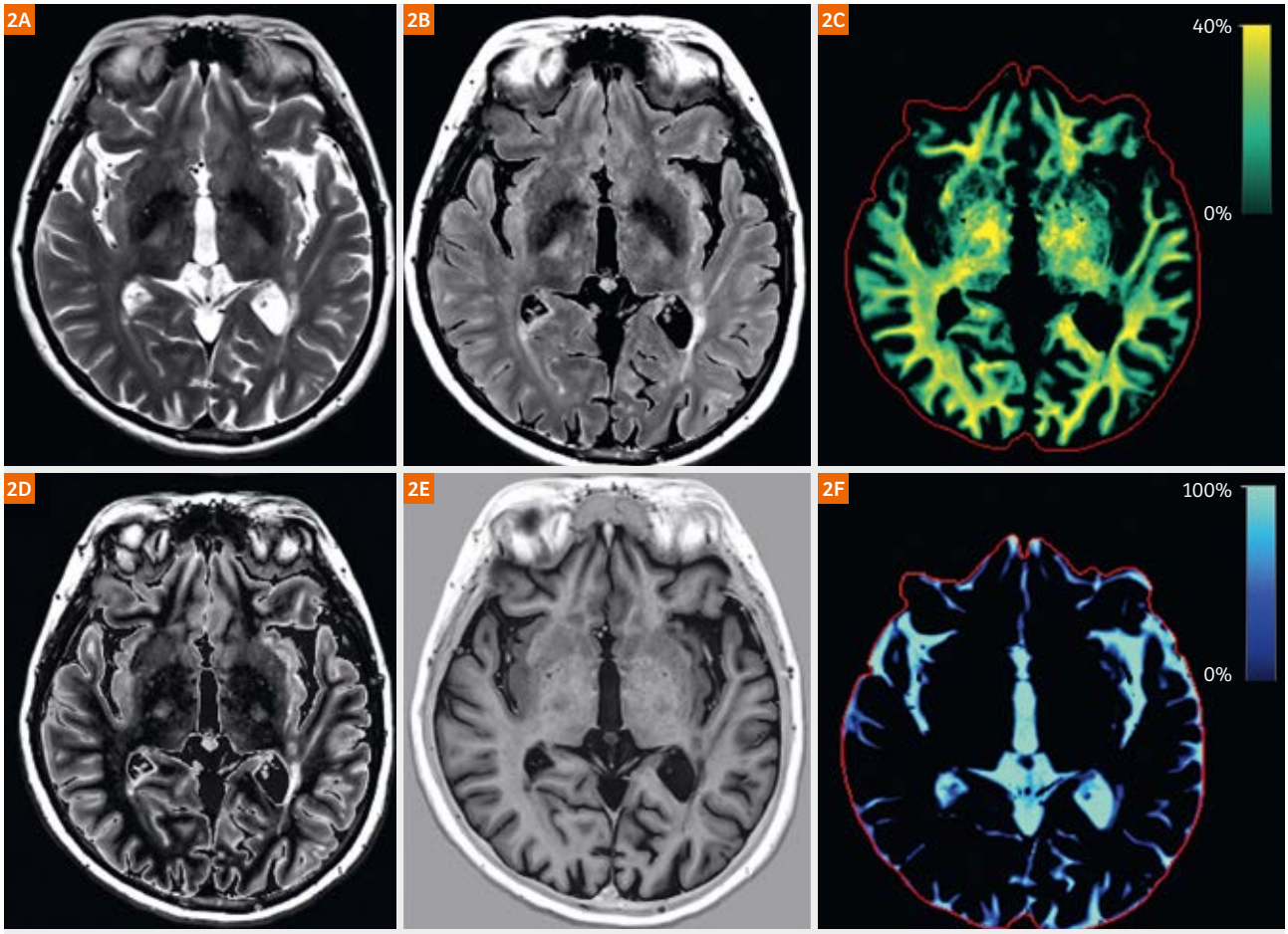

Figure 2:
An example of a subcortical MS plaque in the right temporal lobe. The synthetic T2-weighted image **(2A)** and T2w-FLAIR **(2B)** show the lesion well, but the contrast is actually higher in the synthetic Double IR **(2D)** and Phase-Sensitive IR **(2E)** images, facilitating detection. The myelin map **(2C)** clearly shows lower values at the location of the MS plaque. The intracranial volume is indicated by the red line. CSF segmentation **(2F)** in combination with the ICV provides the brain volume. The total myelin volume of the patient was 154 mL, the brain volume was 1214 mL and the intracranial volume was 1595 mL, meaning that myelin was 12.7% of the brain, and the brain was 76.1% of the ICV. All images were generated on a 3T MAGNETOM Prisma system from a single acquisition of 5 minutes and 8 seconds.

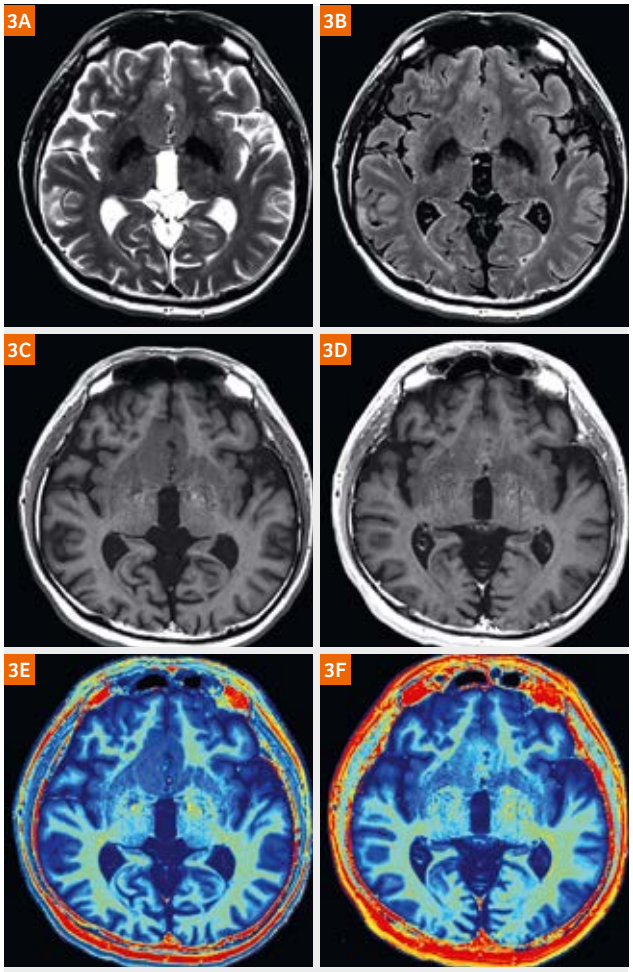

Figure 3:
An example of glioma, prior to and after Gadolinium administration. The synthetic T2-weighted image **(3A)** and T2w-FLAIR **(3B)** shows a hyper-intense lesion spreading to bilateral frontal lobes. Subtle contrast enhancement is shown in the synthetic T1w image before **(3C)** and after contrast administration **(3D)**. The shown T1w images are synthesized with a TR of 100 ms, which increases the T1w contrast with about a factor 2 in comparison to the more normal TR of 500 ms. The R1 relaxation maps (pre-Gd in **3E**, post-Gd in **3F**) show that the mean R1 value in the lesion increases from 0.83 s^{-1} before to 0.99 s^{-1} after Gd, corresponding to a decrease in T1 relaxation of 1210 ms to 1001 ms.

times and PD. The model was later verified on 12 human cadavers, where the results of the myelin model were compared with slices of the brain that were histologically stained with Luxol Fast Blue during autopsy [5]. The myelin detection algorithm was introduced into the SyMRI product as REMyDI. Myelin volume measured by REMyDI has been shown to increase according to age in children, especially ages under 3[1], indicating that this method correlates with normal myelination [6].

At Juntendo University Hospital all aspects of SyMRI – quantification, synthetic imaging and automatic brain segmentation –, were evaluated on various scanner models [7]. Our initial investigation showed that REMyDI had a very low error (coefficient of variation, 0.59% for 0.8 mm in-plane resolution) for estimation of whole brain myelin volume [8]. In addition, we have shown that REMyDI correlated well with magnetization transfer imaging, which is considered to be a criterion standard of myelin imaging [9]. These studies show the reliability of REMyDI. Indeed, REMyDI does not increase the scan time because contrast-weighted images can be created based on the same acquired quantitative values, which is an advantage over other myelin imaging methods.
We have examined the use of REMyDI in patients with multiple sclerosis (MS) and Sturge-Weber syndrome. ROI analysis provides a value for myelin partial volume per voxel. We have shown that myelin values are reduced in MS plaques in comparison to normal-appearing white matter. In addition, we have also revealed that even peri-lesional white matter has lower myelin values than normal-appearing white matter. This suggests that the myelin detection method is sensitive to pathological changes that are difficult to discern on conventional images [10, 11]. An example of a patient with MS is given in Figure 1.

Sturge-Weber syndrome is a neurocutaneous disorder and known to show white matter abnormality on the affected side in pediatric populations, and this phenomenon is presumably due to accelerated myelination. We recently reported that the affected side of the brain in a 4-month-old patient[1] with Sturge-Weber syndrome showed decreased T1, T2 and PD values, and increased myelin [12, 13]. Although this case does not have definite pathology, we think this report showed the potential utility of REMyDI for revealing pathophysiology of Sturge-Weber syndrome.

Synthetic MRI can create any combination of TE, TR and inversion delay TI, even more exotic combinations such as DIR and PSIR images, which generally are not acquired routinely due to scan time constrains. DIR and PSIR images are known to be sensitive to cortical and subcortical MS plaques. Previously, we reported that synthetic MRI with DIR and PSIR is more sensitive than conventional MRI with comparative scan times [14]. Figure 2 shows a representative case of DIR and PSIR images, clearly showing a subcortical MS plaque. In our study, we adjusted the DIR images to each patient by

[1] MR scanning has not been established as safe for imaging fetuses and infants less than two years of age. The responsible physician must evaluate the benefits of the MR examination compared to those of other imaging procedures.

changing the virtual inversion time after image acquisition. The synthetic DIR images had better lesion-to-white matter contrast than conventional DIR images.

When all myelin partial volumes of the entire brain are added up, REMyDI can also show whole myelin volume of the brain, which provides an objective means of patient monitoring. In Figure 2 the volumes of myelin, brain and intracranial volume are indicated. These values can be compared with an age-matched healthy group and over time.

Quantification of absolute R1, R2, and PD values is a strong advantage of this method. We view this as an important step towards more standardization in MR imaging. Currently we are investigating the quantitative enhancement of lesions after Gd administration, which is usually evaluated using conventional T1-weighted images. Quantitative R1 maps may provide us with a more direct and objective evaluation of contrast enhancement (Fig. 3). We are looking forward to more investigations and clinical application of SyMRI in the future.

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