Quantitative MRI with shorter scan times

By I Hachette & Dr. M Warntjes

Clinically important information, such as the brain volume and degree of myelination can now be efficiently quantified through a single 6-minute acquisition MRI scan. This article summarizes the principles and applications of SyMRI, that is commercially available from the Swedish company, SyntheticMR

Conventional MRI images are acquired using the image signal contrast between tissues and are not based on absolute signal intensities. The long scanning times of conventional MRI are both expensive for the hospital and tiresome for, and disliked by the patients.

With SyMRI, a product from the Swedish company SyntheticMR, a rapid image acquisition sequence of six minutes can produce eight of the most common image contrasts defined in the clinical protocol. This can significantly shorten examination times in daily practice. In addition, SyMRI provides quantitative data on brain tissues such as white and gray matter and cerebrospinal fluid, as well as a reliable assessment of brain parenchymal volume and the fraction of the intracranial volume. SyMRI includes industry first FDA-cleared myelin measurements, which show great potential in pediatrics and in the assessment of patients with neurodegenerative diseases.

SyMRI has regulatory approval in several countries, including the US and European countries, and is compatible with GE, Philips and Siemens MRI platforms.

Brain structures and tissues on MR images are characterized by the gray scale contrast in the images, which, depending on the settings of the scanner being used, can highlight and differentiate tissue components and biomarkers. Although conventional contrast-weighted images provide good anatomic detail, the signal intensity is not absolute. Assessment of such images relies on the subjective view of the radiologist, as well as the specific behavior of the MRI scanner being used [1]. Qualitative measures such as hyper-intense, hypo-intense or iso-intense only provide a relatively crude scale for image interpretation. Therefore, depending on the individual skills of the radiologist and the variability between individual MRI systems being used, the tissue under examination may be reported differently. Assessment becomes even more challenging when there are tissue changes as a result of pathology and/or over time, such as in neurodegenerative diseases or in the developing pediatric brain [2, 3].

In such clinical application areas, there is a great potential for quantitative MRI. Objective measurements of tissue volumes could enable the radiologist to quickly assess patient status and enable comparisons with a healthy cohort. Follow-up of the patient's development over time could then be expressed quantitatively. This approach would remove some of the existing uncertainty and provide a valuable tool to aid radiologists in their daily work. The choice of treatment and monitoring can then be based on objective measurements and data, so providing an additional level of confidence for clinicians. As for the patient, the approach would lead to a faster and more reliable diagnoses.

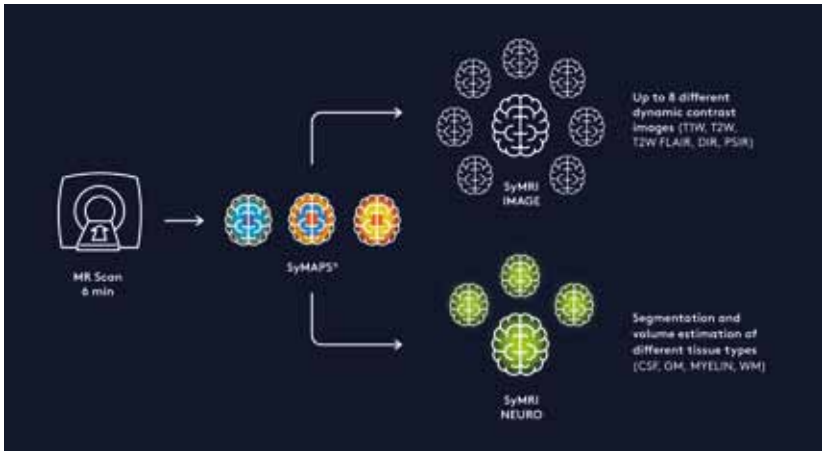

Fig. 1. SyMRI workflow. SyMRI creates the parametric SyMaps, from which eight different contrast images and tissue segmentations are created.

SHORTER SCAN TIMES WITH SYNTHETIC CONTRASTS

Tissue relaxometry is a quantitative method that measures MR imaging parameters such as R1 and R2

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relaxation rates (the inverse of T1 and T2 relaxation times), as well as the proton density (PD). In many cases this technique is very time-consuming and requires multiple sequences, which may not be feasible in a routine clinical setup.

SyMRI provides an efficient way of integrating quantitative MRI into the clinical work flow [Figure 1]. The quantitative measures are based on the absolute quantification of physical parameters of the patient that govern the image signal intensity in MRI, R1 and R2 relaxation, and proton density [4]. From these values it is possible to differentiate tissue and synthetically recreate contrast-weighted images that are independent of scanner settings.

The SyMRI multi-dynamic multi-echo (MDME) acquisition sequence has a total scan time of around 6 minutes, after which the R1, R2 and PD maps are calculated. Once these maps are generated any contrast-weighted image can be synthesized, with a free choice of echo time TE, repetition time TR and inversion delay TI. Hence, standard contrasts such as T1W, T2W and FLAIR images, but also Double Inversion Recovery (DIR), Phase Sensitive Inversion Recovery (PSIR) and Short Tau Inversion Recovery (STIR) can be synthesized using the same scan data [5].

DIR and PSIR images are known to be useful in the detection and monitoring of Multiple Sclerosis plaques, specifically in the cortical or mixed white matter – gray matter areas [6]. In conventional MRI, adding DIR and PSIR sequences generally increases examination time beyond clinically acceptable levels. With SyMRI, all these contrasts are acquired simultaneously in the same single sequence.

An additional advantage with synthetic MRI is that the algorithms remove scanner imperfections such as coil sensitivity, B1 field inhomogeneity and RF pulse profile effects. As a result, synthetic images will appear nearly identical on any MRI scanner system, no matter from which MRI vendor. [Figure 2]

TISSUE SEGMENTATION AND VOLUMES

Tissue segmentation derived from a conventional scan is based on differences in contrast between tissues, a process which requires provisional filters and normalization of signal intensities. Quantification of tissue volumes can thus vary depending on vendor and system settings.

With SyMRI, it is possible to obtain co-registered quantitative data from a single scan. The use of parametric maps as input for the segmentations removes much of this variability and delivers quantitative data largely independent of scanner settings. The resulting values are robust and can be compared over time and across different systems. The narrow inter-scanner variability can thus aid larger institutions who may have several different scanner models and manufacturers, as well as facilitating multi-center studies.

The resulting segmentation in SyMRI has been shown to be robust and precise. Automatic segmentation of white matter, gray matter CSF, and myelin is expected to be of importance in the clinical workflow in the future [7].

SyMRI can also measure the brain parenchymal fraction (BPF), i.e. the ratio of brain volume to intracranial volume. This measurement is showing great promise as a means of measuring atrophy in patients with neurodegenerative disorders. Patients with multiple sclerosis have been shown by SyMRI to have significantly lower BPF than healthy age-matched controls [8].

MYELIN SEGMENTATION

Myelin is the membrane segmented along the nerve fibers, and which enhances signal speed. The content of myelin in the brain can be estimated from R1, R2 and PD as quantified by SyMRI. The myelin model assumes four compartments for modelling the brain, where myelin is one part, and the other three compartments are described by water in cellular, free and parenchymal partial volumes [1]. The proportionality of the myelin partial volume as determined by SyMRI to the actual myelin volume has been validated *in vitro* and by histopathological examination [9].

Myelination is the last stage of white matter development. In the pediatric developing brain, the fibers continue to mature in a specific directional pattern, referred to as spatiotemporal development. This development process of spatiotemporal myelination is believed to be associated and correlated with normal function and behavior in children, whereas delayed myelination is shown in children with developmental delay. Many psychiatric disorders such as autism, attention deficit disorder and schizophrenia have recently been connected to myelination problems [10].

MULTIPLE SCLEROSIS

Multiple sclerosis is a neurodegenerative disease that involves myelin loss. Although MRI is a sensitive method for

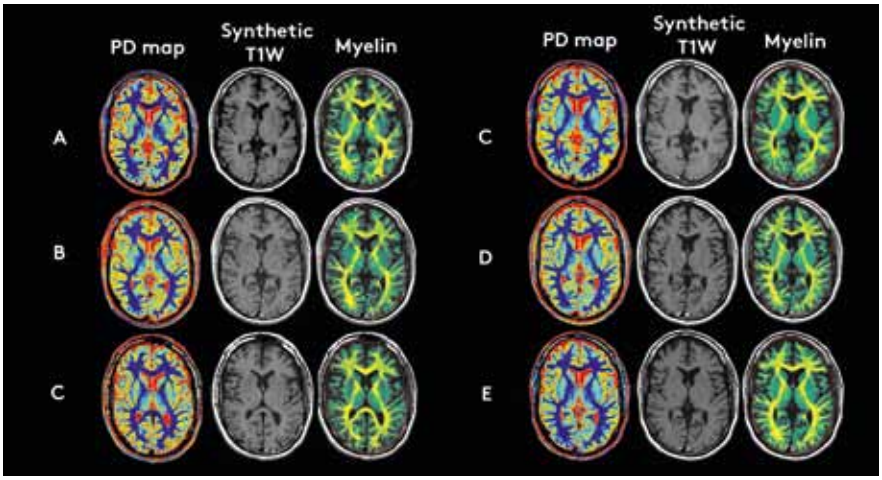

Fig. 2. Cross system reliability. SyMRI has been shown to deliver robust volumes across different systems, between different field strengths and manufacturers for (A) Philips 3T, (B) GE 3T, (C) Siemens 3T, (D) Philips 1,5T, (E) GE 1,5T and (F) Siemens 1,5T. This can aid institutions with several different systems, as well as facilitate multi-center studies.

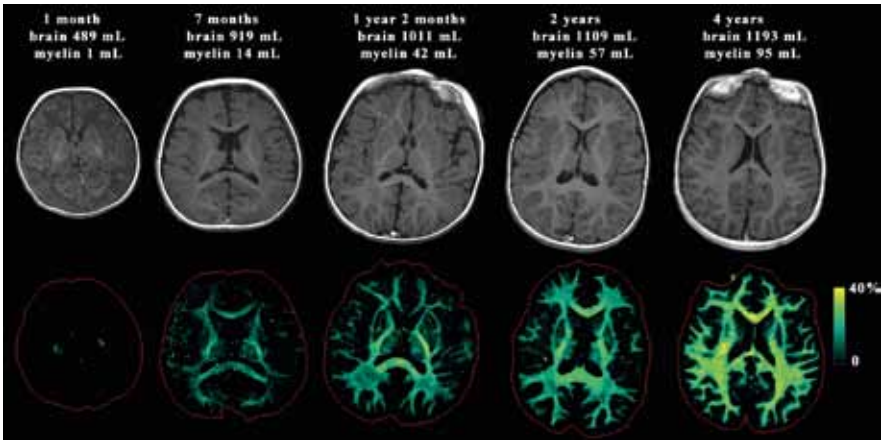

Fig. 3. Example of the application of SyMRI in the pediatric realm. Scanning was performed on children of various ages between 0 and 4 years old. A T1W image was synthesized (top row). Based on the same data a myelin volume map was created (bottom row). The red line indicates the intracranial volume. It is clear that the total myelin increases both in density and volume during these years (Images from Cincinnati Children's Hospital Medical Center).

detecting MS plaques, the correlation between the number of plaques and disease severity is not clear, a phenomenon known as the "clinico-radiological paradox" [11]. Here, quantitative MRI could be a solution. For example, glutamate and glutamine levels have been found to be increased in the normal white matter of MS patients, and could thus be a biomarker of tissue damage and disease severity, independent of the number of plaques. Quantitative MRI with SyMRI has shown decreased R1 and increased PD values in the normal appearing white matter of MS patients when compared with white matters in control groups [12].

Since multiple sclerosis involves myelin loss, the most straightforward biomarker for MS would seem to be myelin, but finding reliable measurements of myelin volumes has so far been challenging. The application of SyMRI is an industry first in enabling the measurement of myelin partial volumes and offering a validated method ready for clinical use. Myelin can be automatically calculated, quantified and visualized in SyMRI [1, 4].

THE PEDIATRIC DEVELOPING BRAIN

The rapid maturation of the brain at young age is associated with large changes in image contrast and various scanner MRI settings may be required as a function of age in order to distinguish brain features or to assess healthy brain development. Since the synthetic contrast images are independent of scanner settings, it is possible to retrospectively generate new contrasts specific to the patient. Using a single sequence to acquire multiple contrast images could also help accelerate the imaging process and reduce the need for anesthesia or sedation in older children, while lowering the sedation time for young children [10].

Quantifying brain tissue volumes shows great promise in pediatrics, where abnormal volumes may indicate pathology or developmental delays. Reference curves could be used to quickly and accurately assess the child's development, which could not only accelerate the assessment process but also provide additional information to the child's parents.

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SYNTHETICMR AT RSNA 2018:

• **Wednesday 28th Nov**

12:15-12:45 Poster, Station #4, Hye Jin Baek *et al.,* Initial Clinical Experience of Synthetic MRI as a Routine Neuroimaging Protocol in Daily Practice: A Single-Center Study

12:45-13:15 Poster, Station #3, Hye Jin Baek *et al.*, Synthetic Brain MRI Obtained from T1 and T2 Imaging

• **Thursday 29th Nov**

10:30-12:00, S503AB; Marcel Warntjes *et al.*, Synthetic MRI in 3D

• **Education**

Digital Education Exhibit, Neil M. Kumar, MD, Synthetic MRI for the Musculoskeletal Radiologist: A Primer

Hardcopy Backboard, Shohei Fujita, MD, How to Read Contrast-Enhanced Synthetic MRI of the Brain

Digital Education Exhibit, Marta Drake Perez, MD, Synthetic MRI in Neuroradiology: Imaging Findings, Clinical Applications, and Pitfalls