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Accuracy and reproducibility of a quantitative magnetic resonance imaging method for concurrent measurements of tissue relaxation times and proton density

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ABSTRACT

Purpose: To evaluate the accuracy and reproducibility of a quantitative magnetic resonance (qMR) imaging method (QRAPMASTER) for simultaneous measurements of T1 and T2 relaxation times, and proton density (PD).
Materials and Methods: Measurements of T1, T2, and PD with qMR were performed using phantoms with different relaxation times and concentrations of heavy water. Healthy volunteers were examined with different head coils. Regional measurements were performed in normal-appearing white and gray matter from the healthy control subjects, and in multiple sclerosis (MS) patients.
Results: In phantom measurements, QRAPMASTER slightly underestimated T1, and T2 variations between repeated measurements were modest. PD was generally overestimated. The overall relative difference was $-1.2 \pm 5.3\%$ (T1), $-6.6 \pm 1.9\%$ (T2), and $0.7 \pm 5.1\%$ (PD). In healthy volunteers, there were no statistically significant differences of T1, T2 or PD using different head coils. Values of T1, T2, and PD obtained in healthy controls and MS patients were within reference ranges. However, significant differences were found in normal-appearing gray and white matter.
Conclusion: QRAPMASTER can be considered a sufficiently accurate and reproducible method for use in clinical practice. Neuropathology in normal-appearing brain tissue may be revealed using this MR method, with putative implications for quantification of tissue damage in neurological diseases.

1. Introduction

Magnetic resonance (MR) images used in clinical practice contain either quantitative or relative pixel values. The apparent diffusion coefficient (ADC) is an example of a quantitative MR image, while conventional T1, T2, and proton density weighted images (T1W, T2W, and PDW) represent examples of images containing relative pixel values.

The signal intensities in spin-echo (SE) images can be calculated for different settings of the repetition time (TR) and the echo time (TE) if the relaxation times (T1 and T2) and the proton density (PD) of the object are known. There is also an analytical relationship for the signal intensity in FLAIR (fluid attenuated inversion recovery) images, where an additional pulse sequence parameter TI (inversion time) is used for nulling the signal from cerebrospinal fluid (CSF). Thus, determination of tissue properties in terms of T1, T2, and PD enables direct calculation of synthetic FLAIR and SE images of different weighting.

As a consequence, development of techniques based on simultaneous acquisition of T1, T2, and PD may result in shorter examination times and provide new information, compared to conventional protocols. Furthermore, quantitative data may be considered as scanner independent.

In examinations of the brain using specialist software, quantitative data can be used for the calculation of contrast MR images. Additionally, automatic analysis of intracranial volume as well as characterization and volume estimation of gray matter, white matter, and CSF can be performed. Central nervous diseases such as multiple sclerosis (MS), Alzheimer disease and vascular dementia are associated with focal and global brain atrophy. Thus, reliable estimation of brain volume and quantification of cerebral tissue components could provide a useful tool in early diagnosis and individual follow-up [1].

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Today, several methods are available for quantification of T1, T2, and PD [2–4] or T1 and T2 [5]. Accuracy and clinically acceptable scanning times are crucial features in the development of such methods. However, accurate combined and simultaneous measurement of all three parameters within an acceptable scanning time remains a challenge. QRAPMASTER [3], a method for simultaneous quantification of T1, T2, and PD with correction of B1-field inhomogenities, has recently been described. The image data can be used for subsequent calculations of synthetic MR images that resemble conventional T1W, T2W, PDW, and FLAIR images. Since such calculations of synthetic images and quantification mapping rely on T1, T2, and PD, it is essential that the measurements are accurately reproducible. A recently published QRAPMASTER study on automatic quantification of intracranial volume with synthetic MR imaging software, showed results that were congruent with reference data [6]. In another study, quantification data obtained with QRAPMASTER were able to be used as a novel and robust method for brain tissue segmentation [7].

Although the quality of synthetic images is perceived to be inferior, diagnostic work-up has been suggested to be sufficient when compared to conventional MR images [8]. In most studies, the use of QRAPMASTER has been evaluated with conventional MR images acquired at the same time. In clinical practice, however, disease monitoring requires repeating examinations over time, which may imply the use of different receiver coils. Evaluation of accuracy and reproducibility is of the utmost importance for reliable comparisons of quantitative numbers over time. There are, to the best of our knowledge, no previous studies addressing these issues.

Hence, the aim of this study was to investigate the quantitative MR (qMR) method QRAPMASTER with different tests to clarify its applicability in clinical use. These tests included: the accuracy and reproducibility of T1, T2, and PD measured repeatedly over a longer period of time in phantom experiments; measurements from different coils used in the clinical setting in healthy individuals; and, comparison of measured relaxation times and PD in groups of healthy volunteers, and multiple sclerosis (MS) patients.

2. Materials and methods

In phantom studies, accuracy and reproducibility of the T1, T2, and PD measurements were investigated using substances with known values. Evaluation *in vivo* was performed in two steps. Firstly, the level of agreement was evaluated between two subsequent acquisitions in healthy volunteers obtained from two different head coils used in clinical settings. Secondly, measurements in normal-appearing white and gray matter from healthy volunteers and age-matched MS-patients were assessed.

2.1. MR protocol

All MR measurements were carried out on a Philips Achieva 1.5 T system (Philips Medical Systems, Best, The Netherlands) using the QRAPMASTER pulse sequence [3]. This sequence is a multi-slice, multi-echo and multi-saturation delay saturation recovery SE acquisition method where the images are collected for different combinations of echo time (TE) and saturation delay time (TD). Based on these images the T1, T2 and PD can be calculated using a post-processing algorithm. The algorithm, in brief, first uses the images of multiple TE to determine the T2 relaxation time. Then the images with different TD are used to get a first estimate of T1 and PD by performing an exponential fit to Eq. [3] found in reference [3]. A recalculation and refinement of T1 and PD is then finally performed by using the local effective flip angles of the saturation and excitation RF pulses. In this study QRAPMASTER was set to generate four different saturation delays (106, 602, 1992 and 4274 ms) based on four dynamic scans. A multi-echo readout was used to provide acquisitions for each saturation delay at TE = 15, 30, 45, 60, and 75 ms. The following imaging parameters were used in all acquisitions (both in phantom measurements and *in vivo*) similar to clinical MR-protocols for MS [9]: FOV = 230 mm, TR = 4360 ms, slice thickness = 3 mm, slice gap = 0.3 mm, in-plane resolution (1.5×1.5 mm^2), and an acceleration factor (SENSE [10]) of 1.2. The images were sampled to give a resolution of 0.9×0.9 mm^2. The number of slices was set to 44 so as to encompass the whole brain. The total scan time for this setting of the QRAPMASTER pulse sequence was 6 minutes and 20 seconds. In order to maintain an equal signal-to-noise ratio (SNR) and acceptable scanning time with whole brain coverage, as would have been the case using the parameter setting with 5 mm slice thickness as in reference [3], a decreased in-plane resolution and a reduced SENSE-factor were required.

QRAPMASTER pulse sequence data were used to calculate T1, T2, PD, and B1 maps at each slice position. Thereafter, the quantitative maps were used for subsequent calculation of the synthesized MR images T1W, T2W, and FLAIR. The quantitative T1, T2, and PD maps were obtained using the SyMRI software (Version 7.0.2, SyntheticMR AB, Linköping, Sweden), which was integrated in the PACS system (IDS 7, version 14.3.14.2, SECTRA Medical Systems, Linköping, Sweden).

The clinical MR protocol used in MS patients includes: axial and sagittal FLAIR (TR 11000 ms, TE 140 ms, TI 2800 ms, axial slice thickness/gap 3 mm/0.3 mm, sagittal axial slice thickness/gap 5 mm/1 mm); axial T2W fast spin echo (TR 9780 ms, TE 110 ms); and, gadolinium enhanced axial T1W sequences (TR 475 ms, TE 12 ms, slice thickness/gap 3 mm/0.3 mm).

Fig. 1 displays an example of T1, T2, and PD maps as well as synthetic T1W, T2W, and FLAIR images obtained from QRAPMASTER, and calculated with SyMRI, for one patient with MS, compared to conventional T1W, T2W, and FLAIR images as part of the clinical MR protocol.

2.2. Phantom measurements

A Eurospin II-(TO5) phantom (Diagnostic Sonar, Livingston, Scotland) was used as the reference for T1 and T2 relaxation times [11]. It consists of 18 gel-filled test tubes (gadolinium doped agarose gel) with known values for T1 and T2. Eleven test tubes with different T1 and T2 relaxation times were selected and included in the study (see Table 1). Furthermore, 12 test tubes with different mixtures of water (H_2O) and heavy water (D_2O) with a relative H_2O content of 50%, 55%, 60%, 65%, 70%, 72.5%, 75%, 80%, 85%, 90%, 95%, and 100% served as references for PD. The tubes were placed in a glass cylinder, filled with copper sulphate solution.

T1, T2, and PD measurements were taken with QRAPMASTER at 11 separate occasions over a ten-week period, with a minimum interval of at least one day between two adjacent measurements. All phantom measurements were performed in an 8-channel SENSE head coil set-up.

2.3. In vivo examination

Seven healthy volunteers (7 male, mean age = 36 years, range 29–43) underwent QRAPMASTER examinations using an 8-channel SENSE head coil and a 16-channel SENSE neurovascular coil, as used in clinical practice. The examinations were performed with the different head coils on the same occasion for each individual.

A group of 22 MS patients diagnosed according to the revised McDonald criteria [12] (7 male and 15 female, mean age = 36.6 years (range 29–43), median disease duration = 7.6 years (range 0.9–20.3), and median Expanded Disability Status Scale (EDSS) [13] score 2 (range 0–6.5), 19 patients had relapsing remitting