NeuroImage 63 (2012) 540–552

Contents lists available at SciVerse ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Quantitative proton density mapping: correcting the receiver sensitivity bias via pseudo proton densities

Steffen Volz [a,*], Ulrike Nöth [a], Alina Jurcoane [b], Ulf Ziemann [c], Elke Hattingen [b], Ralf Deichmann [a]

[a] Brain Imaging Center, University Frankfurt, Germany
[b] Department of Neuroradiology, University Frankfurt, Germany
[c] Department of Neurology, University Frankfurt, Germany

ARTICLE INFO

Article history:
Accepted 28 June 2012
Available online 14 July 2012

Keywords:
Proton density
Spin density
Water content
Receiver sensitivity profile
T1

ABSTRACT

Most methods for mapping proton densities (PD) in brain tissue are based on measuring all parameters influencing the signal intensity with subsequent elimination of any weighting not related to PD. This requires knowledge of the receiver coil sensitivity profile (RP), the measurement of which can be problematic. Recently, a method for compensating the influence of RP non-uniformities on PD data at a field strength of 3 T was proposed, based on bias field correction of spoiled gradient echo image data to remove the low spatial frequency bias imposed by RP variations from uncorrected PD maps. The purpose of the current study was to present and test an independent method, based on the well-known linear relationship between the longitudinal relaxation rate R1 and 1/PD in brain tissue. For healthy subjects, RP maps obtained with this method and the resulting PD maps are very similar to maps based on bias field correction, and quantitative PD values acquired with the new independent method are in very good agreement with literature values. Furthermore, both methods for PD mapping are compared in the presence of several pathologies (multiple sclerosis, stroke, meningioma, recurrent glioblastoma).

Introduction

Among the various techniques employed in magnetic resonance imaging (MRI), the goal of quantitative MRI (qMRI) is the direct measurement of tissue parameters, in particular the relaxation times, the diffusivity, and parameters describing magnetization transfer phenomena (Tofts, 2003). Recently, there has been increasing interest in mapping the proton density (ρ). This parameter refers to the density of MRI-visible protons, most of which are located in tissue water. There is also a large pool of non-aqueous protons (about 30% in white matter), which, however, are in general not visible in MRI (Tofts, 2003). Thus, the proton density ρ is often used to measure brain tissue water contents, assuming that fat and macromolecules do not contribute to the observed signal (Neeb et al., 2008). Various clinical applications of quantitative ρ-mapping have been described, e.g. in multiple sclerosis (Laule et al., 2004), hepatic encephalopathy (Shah et al., 2008), ischemia (Ayata and Ropper, 2002), and for obtaining absolute metabolite concentrations in MR spectroscopy (Gasparovic et al., 2009).

In general, quantitative ρ-values are derived directly from local image intensities in a data set acquired with sufficiently high signal-to-noise ratio (SNR) and spatial resolution. To achieve pure ρ-weighting, the data must be corrected for all secondary effects affecting the signal, such as weighting with respect to relaxation times and distortions of the static magnetic field B0 and the transmitted radio-frequency (RF) field B1. Thus, quantitative ρ-mapping requires several sub-experiments for mapping all parameters that may influence signal intensities. For gradient echo (GE) imaging, these parameters comprise T1, T2*, and B1 (Warntjes et al., 2007). The corrected image intensities yield a multiplication factor (MF) map, which is the product of the actual ρ-map, the receiver sensitivity profile (RP) of the RF coil used for signal reception, and an unknown scaling constant which mainly depends on the receiver gain and the algorithm used for image calculation. If RP is known, MF values can be corrected and scaled, resulting in a ρ-map with a value of 1 in cerebro-spinal fluid (CSF). Scaling is either based on an external water reference (Neeb et al., 2008) or on the average signal inside CSF (Gasparovic et al., 2009).

One of the main problems with quantitative ρ-mapping is the fact that the determination of RP can be problematic. Most techniques for RP mapping are based on the reciprocity theorem (Hoult and Richards, 1976). This theorem is often applied in its most basic approximation, assuming that for an RF coil operating both in transmit and in receive mode the receive sensitivity profile RP is identical to the transmit profile B1, which can be measured with standard techniques. Even for separate transmit and receive coils, this method can still be applied indirectly for determining RP (Neeb et al., 2008). However, a strict mathematical description (Hoult, 2000) shows that this approximation does not hold exactly, in particular at high magnetic field strengths, where the RF wavelength is not considerably larger than the object

* Corresponding author at: Brain Imaging Center, University Hospital, Schleusenweg 2-16, 60528 Frankfurt, Germany. Fax: +49 69 6301 3707.
E-mail address: volz@med.uni-frankfurt.de (S. Volz).

1053-8119/$ – see front matter © 2012 Elsevier Inc. All rights reserved.
doi:10.1016/j.neuroimage.2012.06.076

investigated. In fact, it was shown recently that deriving RP maps from B1 maps at 4.7 T requires the introduction of a spatially non-uniform correction factor (Watanabe et al., 2011). Thus, an alternative method was proposed for RP mapping which is based on subjecting the MF map to a bias field correction algorithm, assuming that the bias field reflects RP variations. It could be shown that this method, which had previously been proposed for quantitative B1 mapping (Weiskopf et al., 2011), yields more reliable ρ-values than the method based on the reciprocity theorem (Volz et al., 2012). In particular, a comparison of the maps obtained with both methods showed that ρ-values based on the bias field correction (1) were free from any residual spatial bias; (2) did not depend on the subject's position, and (3) allowed for a clear distinction between brain tissue types when represented in histograms. However, the question remains if this method, which basically removes any intensity variations with low spatial frequencies from anatomical brain images, does maintain effects of interest such as physiological or pathophysiological proton density variations. Thus, it would be beneficial to develop a different method of ρ mapping for testing the reliability of the bias field method. Another problem may arise from the fact that the performance of any bias field correction technique and therefore the accuracy of ρ maps obtained with the bias field method depends on the algorithm and parameters used. Thus, an independent reference method would be helpful for testing the suitability of a given bias field correction algorithm for RP mapping and for optimising the respective parameters. The purpose of the present study was to propose an alternative method for RP mapping based on a different concept, and to compare the results obtained with the new method and the method based on bias field correction. The new method exploits the frequently observed relationship between T1 and ρ in brain tissue.

In 1986, a strong correlation between T1 and ρ-values of human brain tissue was described (MacDonald et al., 1986). In a subsequent publication, a linear relationship between T1 and ρ was proposed (Bell et al., 1987) and verified experimentally, performing T1 mapping in vivo on tumour patients and determining ρ-values in surgically excised tissue samples of the same patients by means of gravimetry. A more detailed analysis was provided (Fatouros et al., 1991), deriving theoretically a linear relationship between 1/ρ and 1/T1 and verifying this finding experimentally on cat brains. In a subsequent publication (Fatouros and Marmarou, 1999), a similar measurement was performed for human brain tissue in tumour patients at 1 T, separately for white matter (WM) and grey matter (GM). T1 and ρ were determined in vivo before tissue resection and ρ was measured gravimetrically in excised tissue samples. The results showed that the two parameters (slope and intercept) describing the linear relationship between 1/ρ and 1/T1 are almost identical for WM and GM, but dependant on the magnetic field strength. A similar linear relationship was found by (Gelman et al., 2001) who employed qMRI techniques for measuring both T1 and ρ in the human brain at 3 T. Linear fitting was performed for GM only, and the authors showed that T1 variations across different GM areas are concomitant with respective ρ variations. Furthermore, they showed that WM data could be included with high accuracy, using the same slope and intercept. Due to these findings, some researchers chose to calculate ρ-values directly from T1-maps, rather than performing actual ρ-mapping (Andersen, 1997; Kover et al., 2004). This procedure will yield reliable ρ-values for normal brain tissue, but the question arises if results inside pathological areas are correct. The method proposed here overcomes this problem in the following way: first, a "pseudo proton density" map (ρ_p) is calculated from local T1 values, assuming that ρ_p corresponds to the actual ρ-values at certain "sample points" inside the brain, i.e. positions where normal brain tissue is found. Thus, the quotient of MF and ρ_p will yield correct RP values at these sample points. Since RP is a smooth function, values for all other areas (in particular pathological areas) can be obtained via interpolation, based on polynomial fitting. This results in a smooth RP map covering the whole brain, so the global ρ-map can be calculated from the quotient of MF and RP. Since the parameters describing the linear relationship between 1/ρ and 1/T1 are not necessarily known, a recursive procedure is proposed, using results obtained from the literature as starting values which are updated after each recursion.

In summary, the goals of this study were:

(1) To apply the method described above to in vivo data acquired on healthy volunteers and to test if convergence is achieved for the slope and intercept values during the recursive process, independent of the starting values.
(2) To compare the final values of slope and intercept with values known from the literature.
(3) To compare the final RP maps to results obtained with the method based on bias field correction.
(4) To demonstrate how the new method can be used to obtain RP maps in the presence of brain areas, which are involved in a pathological process. This demonstration is based on data obtained on a patient with multiple sclerosis (MS), a patient with an old infarct and transient ischemic attacks, and two patients with brain tumours (meningioma and recurrent glioblastoma).

Theory

In most methods presented so far, maps of the proton density (ρ) are derived from a fast gradient echo sequence such as FLASH (Haase et al., 1986) which is acquired with the repetition time TR, the echo time TE, and the nominal excitation angle α. Due to inhomogeneities of the transmitted radio frequency (RF) field B1, the actual excitation angle will show local deviations from the nominal value and is given by B1·α. (Please note that in this work B1 is given in relative units, assuming a value of one where the actual and the nominal excitation angles are identical). The image signal is given by

$$S = MF \cdot ST \cdot \exp\left(-TE/T2^*\right). \quad (1)$$

In this equation, ST determines the steady state magnetization. If transverse magnetization components are spoiled after each signal acquisition, ST is given by (Haase, 1990):

$$ST_{theo} = \frac{1-\exp(-TR/T1)}{1-\cos(B1\cdot\alpha)\cdot\exp(-TR/T1)}\cdot\sin(B1\cdot\alpha). \quad (2)$$

The multiplication factor (MF) is given by:

$$MF = C\cdot\rho\cdot RP \quad (3)$$

where RP is the receiver coil sensitivity profile and C is a spatially invariant scaling constant.

In general, ρ-mapping is performed as follows (Warntjes et al., 2007): in addition to the FLASH acquisition described above, the parameters T1, T2*, and B1 are measured with suitable mapping methods. Thus, the steady state can be calculated from Eq. (2) and MF can be obtained from the signal intensities in the FLASH data set according to Eq. (1). However, the conversion of the MF map into a ρ-map still requires knowledge of RP. The RP mapping method presented in this work is based on the following concept:

The relationship between T1 and ρ-values in WM and GM as frequently reported in the literature (Fatouros and Marmarou, 1999; Fatouros et al., 1991; Gelman et al., 2001) can be expressed by:

$$\frac{1}{\rho} \approx A + \frac{B}{T1}. \quad (4)$$

As T1 has to be determined anyway to calculate the steady state in Eq. (2), a recursive operation is performed. Each recursion consists of