Evaluation and Reduction of Variability in Quantitative R2* Measurement of the Human Brain

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Introduction

The R_2* parametric mapping has been utilized for quantification of tissue iron *in vivo* [1-2]. However, a large degree of variability in measuring of R_2* limits its clinical utilization [1-2]. It is important to systematically examine the influence of the basic data acquisition parameters on quantitative R_2* measurement so that a standardized protocol can be established. This study is designed to address the experimental issues of R_2* quantification using a well-controlled phantom and validate those results with R_2* mapping of human brains.

Methods

R_2 Phantom*

The phantom consists of a series of test tubes containing media with T_2 and T_1 relaxation characteristics similar to human brain tissues at 22 ºC in 3.0 T (Fig. 1). Each tube contains a mixture of agar and gadolinium at the appropriate concentrations. The R_2* of the phantom is controlled by titration of Fe concentration using $FeCl_3$ ranging from 0 to 240 µg/g wet weight to encompass tissue iron concentrations in the human brain.

MRI protocol

A series of T_2* images were obtained with the phantom using a multi-echo GESEPI sequence [3] on a Bruker MedSpec S300 3.0 T system and a birdcage coil for RF transmission and reception. The R_2* maps were obtained using 12 echo images acquired with echo spacing = 4.23 ms, TR / TE / FA = 322 ms / 8 ms / 50º, bandwidth = 100 kHz, FOV = 25 × 25 × 0.8 cm^3, matrix = 256 × 192 × 16 and two 8-mm-thick axial slabs. For human studies, 2 healthy subjects (34 and 64 years old) received a similar R_2* mapping protocol.

Data processing and analysis

A series of R_2* maps were generated using a variable number of echo images (from the first 4 to 12 echo images) using the same set of multiple gradient-echo images and linear regression. R_2* values and its variability from each test tube in the phantom were measured with the mean and standard deviation (SD) from a circular ROI (Fig. 1). In order to quantify the relative differences of R_2* measurement with respect to sampling length (number of echo images), Effect Size (ES) [4] of R_2* with a given sample of the free induction decay (FID) is defined as:

$$ES = (\overline{R_2^*}_{n\_echoes} - \overline{R_2^*}_{12\_echoes}) / SD_{R_2^*{}_{12\_echoes}}$$

where *n* is the number of echo images used for calculation of a R_2* map. Here the R_2* map calculated with 12 echo images is used as a relative standard. This is true for the phantom sample study because the sample is uniform and SNR is sufficiently high for all the echo images. In this case, $SD_{R2^*\,12\_echo}$ represents the minimal variability of a set of measurements of R_2* (all the pixels in the given ROI) in a uniform sample. ES as defined can, thus, be used as a statistic quantity for evaluation of measurement methods.

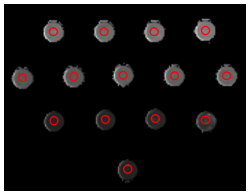

Figure 1. The R_2* map of the phantom. The red circles are the regions of interest used for calculation.

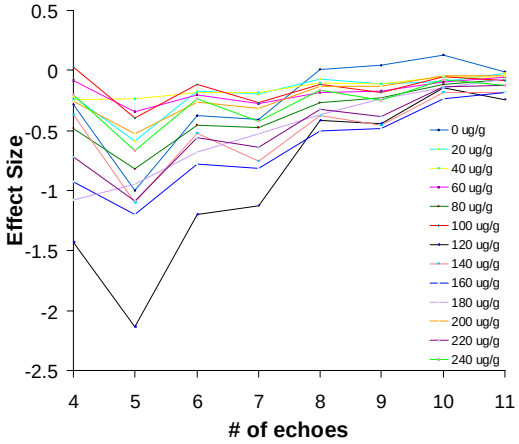

Figure 2. The Effect Sizes of 4 to 11 echoes compared to 12 echoes mGESEPI R_2* measurement on the phantom.

Results

Figure 2 shows the Effect Sizes of R_2* obtained with 4 – 12 echo images from the phantom. There is an apparent trend of decreasing in ES with increasing number of echo images used for R_2* calculation. With eight or more echo images used, the ES was smaller than 0.5 for all the iron concentrations ranging from 0 to 240 µg/g wet weight. This indicates that a sampling length of R_2* curve less than 37 ms with 8 echo images will lead to significant inaccuracy. Figure 3 shows ES of R_2* of six brain structures from the 34 years old subject, which presents similar characteristics to the phantom data.

Discussion

R_2* is traditionally estimated with only two gradient-echo images acquired at different TE. As demonstrated in this study, a large variability is expected with this approach. To reliably measure R_2*, the FID should be sampled equal to or longer than one T_2* period with adequate sampling points (number of echoes).

R_2* conveys rich information about tissue physiological state (oxygenation, calcification, and iron content, etc.). However, R_2* mapping is underutilized clinically due to its large variability and the influence of magnetic field inhomogeneity artifact. This study systematically evaluated and traced the sources of the variability in R_2* measurement. The data presented are essential for establishing a standardized protocol for clinical quantitative analysis with R_2* mapping.

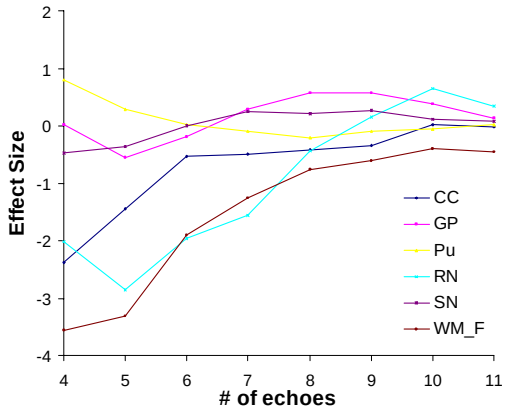

Figure 3. The Effect Sizes of 4 to 11 echoes compared to 12 echoes mGESEPI R_2* measurement on a 34 years old man. Caudate nucleus: CC, globus pallidus:GP, putamen: Pu, red nucleus, RN, substantia nigra: SN, frontal white matter: WM_F.

Reference

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