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Fast generation of *T2** maps in the entire range of clinical interest: Application to thalassemia major patients

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ABSTRACT

*T2** maps obtained by the processing of multiecho MR sequences can be useful in several clinical applications. *T2** map generation procedures should join a processing time compatible with on-line image analysis with a good precision in the entire *T2** range of clinical interest. Fast generation of *T2** maps can be achieved by the estimation of the *T2** values by the weighted linear fitting of the logarithm of the signal (WLSL) method. This approach fails if the signal decay diverges from a pure exponential decay, as happens at low *T2** values where the rapid decay in the signal intensity leads to a plateau in the later echo times (*TE*). The proposed method implements the automatic truncation of the signal decay curves to be fitted in order to compensate for the signal collapse at low *T2** values, allowing the extension of the WLSL method through the entire clinical range of *T2** values.

Validation was performed on synthetic images and on 60 thalassemia major patients with different levels of myocardial iron overload. Phantom experiments showed that a 5% fitting error threshold represented the best compromise between *T2** value measurement precision and processing time. A good agreement was found between *T2** map pixel-wise measurements and ROI-based measurements performed by expert readers (CoV=1.84% in global heart *T2**, CoV=5.8% in segmental analysis). In conclusion, the developed procedure was effective in generating correct *T2** maps for the entire *T2** clinical range.

1. Introduction

Quantitative assessment of the tissue relaxation time has several applications in magnetic resonance imaging (MRI) [1], including the detection of superparamagnetic iron oxides [2] and the characterization of myocardial tissue in several pathologic conditions such as myocardial edema [3]. Inverse correlation between *T2* and *T2** values and the iron content was fully demonstrated [4,5], and *T2** relaxometry represents the only widely available, non-invasive methodology for cardiac, hepatic, and pancreatic iron overload (IO) assessment in patients with primary or secondary hemochromatosis [6–8]. To calculate the relaxation time, the MRI signal is monitored by acquiring images at several echo times (*TE*s) and the measured signal decay is fitted to a mathematic model.

Two main approaches have been proposed to fit the signal decay to the model: region-of-interest (ROI) approach and pixel-wise approach. In the ROI-based fit, the signal values of all the pixels within a ROI are averaged for each *TE* and the fitting is performed on the averaged decay curve, leading to a single relaxation time value taken as representative of the whole ROI. The procedure can be iterated among several ROIs to assess the spatial distribution of the *T2*/*T2** values, such as in the eight liver segments [9] or in the 16 left ventricle (LV) wall segments to obtain standardized LV segmentation [10,11]. The main advantage of the ROI-based approach is the increase of the signal-to-noise (SNR) ratio of the decay curve that improves the fitting quality. Moreover, as one or few fitting operations are performed, the processing time is low and the fitting quality can be visually assessed by plotting the decay curve together with the model.

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In the pixel-wise approach, the fitting is performed on the signal decay curves extracted from each pixel, yielding a complete relaxation time map. The obtained map allows for the visualization of the $T2/T2^*$ distribution with the same spatial resolution of the acquired images. To obtain a relaxation time measurement from a defined district, a ROI is defined on the map and the $T2/T2^*$ value of the ROI is obtained by computing the mean or the median of the $T2^*$ values inside the ROI. In the pixel-wise approach, the $T2/T2^*$ variations can be assessed with pixel-size resolution, exposing focal areas of artifact or pathology that might be missed using a ROI-based approach. The primary drawbacks of the pixel-wise approach are that it is computationally intensive, as the fitting operation must be performed for each pixel, and that the signal-to-noise (SNR) ratio for each individual decay curve is relatively poor. The difference in measurements performed by the ROI-based and pixel-wise approaches was demonstrated to be clinically irrelevant if the same signal decay model is adopted [12–14].

The simplest decay model adopted in the relaxation time computation is a pure exponential decay. The adoption of this model overcomes some of the drawbacks of the pixel-wise approach, allowing for the direct computation of the relaxation time value by a linear fitting of the logarithm of the signal [15]. The use of a simple two-parameter model also improves the convergence of the fitting algorithm in presence of a low SNR. However, the single exponential decay model is adequate only if the SNR is high enough at all *TE*s to neglect the background signal associated with the MR noise [16]. This condition is generally satisfied in quantitative $T2$ studies, as the $T2$ value in tissues is typically large. In $T2^*$ relaxometry, at low $T2^*$ relaxation times the signal at later *TE*s may collapse on the background MR signal, leading to a large $T2^*$ overestimation error [12,13]. Two main approaches were proposed in the literature to address this issue. The first approach (truncation model) consists of manually limiting the mono-exponential equation to few echo times [17]. The second approach consists of a non-linear fitting of the signal to an exponential plus a constant offset model that compensates for the noise plateau [12]. A more recent study includes the Rician distribution of the MRI noise in the fitting model. The method could improve the fitting procedure performance when the noise component is dominant, as in liver images of patients with severe iron overload [18]. Truncation and offset models were well validated in ROI-based analysis, but they present important issues in $T2^*$ map generation as the manual truncation of the pixel-related decay curves is impractical due to the number of curves to be processed and the need for the non-linear fitting of the pixel-wise decay curves will dramatically increase the processing time. In this study we propose a method for $T2^*$ map generation that exploits a linear fitting algorithm with automatic truncation of later *TE*s for low $T2^*$ values. The method was validated on a generated synthetic phantom mimicking real MR data and on thalassemia major patients with different levels of iron overload.

2. Materials and methods

2.1. Patients' data

Images from 60 patients (34 males, age 29.4 ± 6.8 yrs) enrolled in the Myocardial Iron Overload in Thalassemia (MIOT) network [6,19] were retrospectively analyzed. The study was approved by the local ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All patients involved gave their informed consent prior to their inclusion in the study.

Cardiac MR acquisition followed a previously published protocol [6]. Briefly, multislice multiecho $T2^*$ MR was performed using a 1.5-T MR scanner (General Electric Healthcare, Waukesha, WI) at the MIOT network core-lab. An eight-element cardiac phased-array receiver surface coil was used for signal reception. Three parallel short-axis views (basal, middle, and apical) of the left ventricle were obtained by a $T2^*$ GRE, ECG triggered, multiecho sequence [10]. Each single short-axis view was acquired at ten echo times (2.0–22 ms, with an echo spacing of 2.26 ms) in a single end-expiratory breath hold to ensure image alignment. The acquisition time covered the end-diastolic phase, which was when the heart motion can be negligible. The image analysis procedure employed in the MIOT network (HIPPO MIOT software) [10] involved the calculation of segmental $T2^*$ values in the left ventricle wall following the AHA 16-segments standardization [20]. The global heart $T2^*$ value was obtained by averaging all segmental $T2^*$ values and the $T2^*$ value in the mid-ventricular septum was obtained by averaging $T2^*$ values in the mid-anterior septum and the mid-inferior septum. Segmental $T2^*$ values were calculated by ROI-based analysis and fitted to a pure exponential model with manual truncation. On the basing of the global $T2^*$ value, three groups of 20 thalassemia major patients each were identified using the $T2^*$ value thresholds adopted in clinical practice [21]: patients with no myocardial iron overload (MIO) (global $T2^*$ value > 20 ms), patients with mild to moderate MIO (global $T2^*$ value between 20 and 10 ms), and patients with severe MIO (global $T2^*$ value < 10 ms).

2.2. Synthetic phantom

As the true relaxivity value in tissues is generally unknown, a synthetic phantom was developed in order to assess the accuracy of the algorithm examined in this study. The synthetic phantom was composed by a sequence of images mimicking real signal intensities of myocardial tissue at different *TE*s using the patients' data set involved in the study as base of knowledge for the realization of the model. To generate the sequence, each pixel in the image was characterized by its $T2^*$ value and $S0$ value, where $S0$ was defined as the theoretical MR signal value at $TE=0$. The $S0$ value was randomly drawn from a Gaussian distribution with the mean and standard deviation (SD) inferred from measurements on real MR images of the patients. Signal decay in tissues was modeled by a pure exponential: $S=S0 \exp(-TE/T2^*)$ and sampled at N echo times. Generalized Rician noise was simulated for an 8-channel coil, with noise statistics inferred from measurements in the background of MR images of the patients [22]. The resulting signals were approximated to the nearest integer value to meet the DICOM format specifications used in real MR images. Hence, the developed phantom was able to simulate realistic decay curves dependent upon imposed $T2^*$ and image background SD values.

2.3. $T2^*$ map computation

The process for $T2^*$ map computation is schematized in Fig. 1. The relaxation time map computation follows an iterative process and includes three main steps. At the beginning of the procedure, each image pixel is classified as "in process" and the related signal decay curve is extracted (Fig. 1a). In the first step (background filtering, Fig. 1b), a procedure described in the following tests if the pixel should be classified as a background pixel (i.e., a pixel without a significant MR signal) or not. The background pixels are marked as "background pixels", a conventional $T2^*$ value (e.g., 0) is written in the $T2^*$ map, and are no further processing occurred. If the pixel is not classified as background, then step 2 is executed (Fig. 1c). The relaxivity value of the pixel is then computed, exploiting the whole range of the *TE* samples, by fitting the decay curve extracted from the pixel with an appropriate model and by computing the fitting error (Fig. 1d). A threshold (E_{max}) for the fitting error is