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A Quasi-Analytical Method for Relaxation Rate Distribution Determination of T_2-Weighted MRI in Brain

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***Abstract*— A quasi-analytical method for the determination of relaxation rate distribution functions in T_2-weighted MRI in brain is proposed. The method solves analytically the set of non linear polynomial equations on the assumption that the transversal magnetization decay in Carr-Purcell-Meiboom-Gill (CPMG) T2-weighted MR brain images can be decomposed in a finite number of exponential decays, each one corresponding to a particular tissue class. The proposed method was validated by numerical simulations and applied to the calculation of relaxation rate distribution functions of tumoral lesions in brain.**

I. Introduction

The determination of relaxation rate distributions for T_2-weighted Carr-Purcell-Meiboom-Gill (CPMG) MRI has been previously used [1], [2], [3] for tissue classification and tumor segmentation, particularly for obtaining nosologic maps of tumoral lesions in brain [4]. Those efforts relay on the application of simulated annealing and Metropolis algorithm to perform an inverse Laplace transform on relaxation data and whose details are discussed elsewhere [1], [3]. Even though these methods are extremely precise and robust for the determination of relaxation rate distributions, they are also extremely slow and require some adjustments and side processes to be applicable on a patient basis. The decay of pixel intensity through the set of CPMG T_2-weighted MR images can be modeled by a discrete sum of positive exponential functions [5]. The fact that pixel intensity sampling is made at equally spaced time intervals, transforms the initial fitting problem into a problem of finding the solutions of a set of non linear polynomial equations [6], [7]. In the present work, these equations are solved analytically and the solution is applied for the estimation of relaxation rate distributions in MR brain images.

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II. Materials and Methods

A. Image Measurement

Multi-echo T_2-weighted images were acquired using Carr-Purcell-Meiboom-Gill (CPMG) sequence with a total of 16 equally separated echoes, starting at TE = 22 ms. To cover the totality of the tumoral lesion, images for 8 axial slices were obtained, each one 5 mm thick. Pixel intensity is generally given by

$$p_n = p_O \exp(-nTER_2) \tag{1}$$

where $R_2 = 1/T_2$, n being the echo index and T_2 the transversal relaxation time.

B. The Partial Volume Problem

A common situation in MR images is that even when they exhibit a very high spatial resolution axially, i.e., over the 2D image, the spatial resolution in the longitudinal direction, i.e., related to slice width, could be very low. As a consequence, it can be assumed that there could be a mixture of tissues within the image voxel, i.e., a partial volume problem [8], [9], and in correspondence a mixture of relaxation rates R_2. In that case the image intensity in a voxel can be written as

$$p_n = b + \sum_{i=1}^{N} C_i \exp\left(-nTE\, R_2^{(i)}\right) \tag{2}$$

where C_i stands for the proportion of tissue i in the voxel, $R_2^{(i)}$ represents its characteristic relaxation rate, b is a baseline correction to the pixel intensity and N is the maximum number of tissues that could be present in the voxel.

C. Non Linear Polynomial Equations

Equation (2) can be written as:

$$p_n = b + \sum_{i=1}^{N} C_i\, X_i^n \tag{3}$$

where

$$X_i = \exp\left(-TE\, R_2^{(i)}\right) \tag{4}$$

The equally spaced sampling of the magnetization decay allows for a polynomial representation of each data point according to (3). If it is assumed [3], [4], that at most 3 tissues are present in each voxel; normal or unaffected tissue, lesion tissue and cerebrospinal fluid, CSF, a set of non linear polynomial equations [6], [7] can be written:

$$\begin{aligned} p_1 &= b + C_1X_1 + C_2X_2 + C_3X_3 \\ p_2 &= b + C_1X_1^2 + C_2X_2^2 + C_3X_3^2 \\ &\vdots \\ p_7 &= b + C_1X_1^7 + C_2X_2^7 + C_3X_3^7 \end{aligned} \tag{0}$$

Solutions to the set (0) must fulfill the following conditions:

$$\begin{aligned} &C_i > 0 \\ &0 \le X_i < 1 \end{aligned} \tag{5}$$

In order to reduce the number of equations, the set (0) is combined in the following way:

$$p_i - p_{i+1} \equiv q_i \tag{6}$$

also defining:

$$u_i = C_i\left(1 - X_i\right) \tag{7}$$

the new set can be written as:

$$\begin{aligned} q_1 &= u_1X_1 + u_2X_2 + u_3X_3 \\ q_2 &= u_1X_1^2 + u_2X_2^2 + u_3X_3^2 \\ &\vdots \\ q_6 &= u_1X_1^6 + u_2X_2^6 + u_3X_3^6 \end{aligned} \tag{I}$$

The set (I) can be further reduced by combining equations such that the variable u_1 is eliminated, this can be accomplished by the transformation:

$$q_{i+1} - q_iX_1 \tag{8}$$

and the definition:

$$v_i = u_i\left(X_i - X_1\right) \tag{9}$$

obtaining:

$$\begin{aligned} q_2 &= q_1X_1 + v_2X_2 + v_3X_3 \\ q_3 &= q_2X_1 + v_2X_2^2 + v_3X_3^2 \\ &\vdots \\ q_6 &= q_5X_1 + v_2X_2^5 + v_3X_3^5 \end{aligned} \tag{II}$$

A similar transformation can be applied to eliminate v_2:

$$q_{i+1} - q_iX_2 \tag{10}$$

with the definition:

$$w_3 = v_3\left(X_3 - X_2\right) \tag{11}$$

obtaining:

$$\begin{aligned} q_3 &= q_2\left(X_1 + X_2\right) - q_1X_1X_2 + w_3X_3 \\ q_4 &= q_3\left(X_1 + X_2\right) - q_2X_1X_2 + w_3X_3^2 \\ &\vdots \\ q_6 &= q_5\left(X_1 + X_2\right) - q_4X_1X_2 + w_3X_3^4 \end{aligned} \tag{III}$$

Finally, elimination of w_3 by a similar transformation:

$$q_{i+1} - q_iX_3 \tag{12}$$

yields:

$$\vec{Q} = \tilde{M}\,\vec{Z} \tag{IV}$$

with:

$$\vec{Q} = \begin{bmatrix} q_4 \\ q_5 \\ q_6 \end{bmatrix} \tag{13}$$

$$\tilde{M} = \begin{bmatrix} q_3 & -q_2 & q_1 \\ q_4 & -q_3 & q_2 \\ q_5 & -q_4 & q_3 \end{bmatrix} \tag{14}$$

$$\vec{Z} = \begin{bmatrix} X_1 + X_2 + X_3 \\ X_1X_2 + X_2X_3 + X_1X_3 \\ X_1X_2X_3 \end{bmatrix} \tag{15}$$

The solutions of (IV) determine a set of non linear algebraic equations:

$$\begin{aligned} Z_1^* &= X_1 + X_2 + X_3 \\ Z_2^* &= X_1X_2 + X_2X_3 + X_1X_3 \\ Z_3^* &= X_1X_2X_3 \end{aligned} \tag{V}$$

Solutions of set (V) can be obtained as the roots of the cubic equation:

$$X^3 - Z_1^*X^2 + Z_2^*X - Z_3^* = 0 \tag{16}$$

The rest of the variables can be calculated by replacing the solutions of (15) into the initial set (0).

D.Simulations.

Some considerations have to be made when applying this method to real data using it as an exploratory tool to

determine relaxation rate distribution functions: Firstly, pixel intensity is assumed to be composed of three exponential decays; this situation is not always valid since it depends on the actual tissue composition in the pixel and as a consequence some of the roots of equation (15) must be either complex or negative if the actual pixel composition involves less than 3 tissue types or equivalently less than 3 relaxation rates; somewhat the assumption of forcing the model for the pixel intensity decay to be a linear combination of 3 exponential decays leads to unphysical results, i.e., complex relaxation rates, when applied to real data. Secondly, in order that conditions (5) are completely fulfilled, C_i must be positive. Tests performed with synthetic data composed of linear combinations of up to 3 exponential functions demonstrated that solutions of equation (16) subjected to conditions (5) always yielded the right number of exponentials. For the simulations, a set of 3 relaxation rates was chosen according to those expected for tumoral lesions in brain [3], [4], i.e., 2 s^{-1} for necrosis or CSF, 7 s^{-1} for tumoral tissue and 12 s^{-1} for normal or unaffected tissue. The results of the simulation assuming that each relaxation rate exhibits a Gaussian distribution around its mean value are shown in Figure 1.

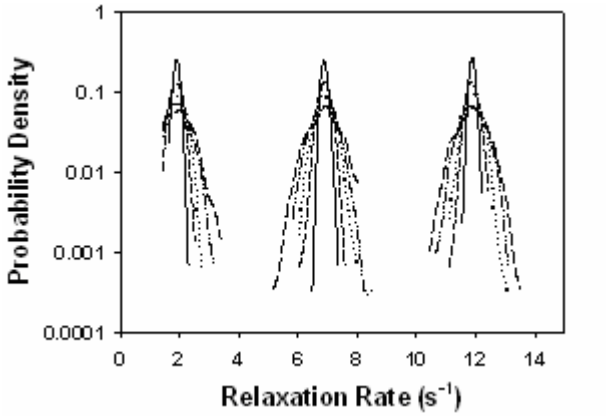

Fig. 1. Distribution functions obtained for synthetic data. Line types correspond to different dispersions of relaxation rates (0.1 to 0.5 s^{-1}). Relaxation rates used for the simulations were 2, 7, 12 s^{-1}, corresponding respectively to liquid or necrosis, tumoral tissue and normal or unaffected tissue [3], [4].

It has to be noticed that the distribution functions obtained by application of the method resembled quite well those used for the composition of synthetic data, i.e., dispersions, relaxation rate mean values and amplitudes are preserved.

III. Results

The method was applied on CPMG T_2-weighted images of tumoral lesions in brain. All the analyzed images were certified by histopathological results.

Regions of interest covering the entire lesion were compared with regions corresponding to unaffected or non pathological tissue, i.e. gray or white matter, and CSF, in order to discriminate relaxation rates associated to tumoral tissue leading to the segmentation of tumoral lesion. An example of this comparison is shown in Figure 2.

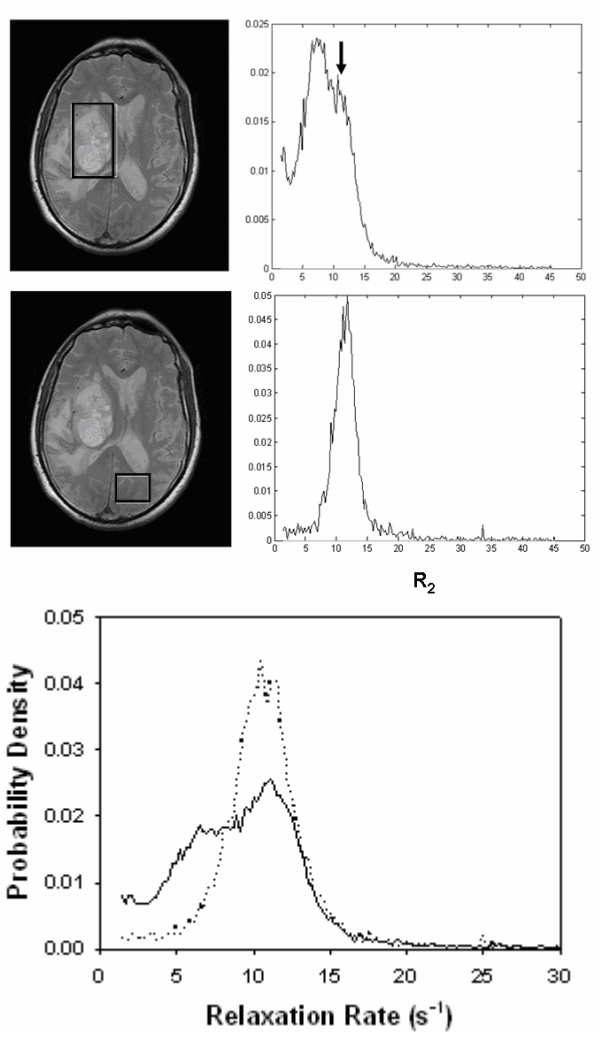

Fig. 2. Top, relaxation distribution function obtained for two different ROIs, shown on left side. The arrow indicates the position of the peak corresponding to unaffected tissue. Bottom, comparison of the relaxation rate distributions coming from different ROIs, solid line: ROI includes tumoral lesion completely; dotted line, contra lateral ROI. Images correspond to a glioblastoma multiforme.

First of all, the method can be used as a tool to establish a correlation between relaxation rate and tissue, i.e., relaxation rate tissue classification, by analyzing different ROIs for which the tissue class is known by other means, i.e., stereotaxic biopsy, *in vivo* MR spectroscopy or nuclear medicine imaging, and use the correlation for the determination of nosologic maps with appropriate segmentation procedures [4]. Also, it is possible to evaluate the whole extension of the lesion by comparing its distribution function to the one obtained from ROIs corresponding to normal or unaffected tissue coming from the same patient, bottom of Figure 2. This opens the possibility of obtaining a sort of "lesion relaxation rate distribution" through a subtraction method that can be used for lesion evaluation.

The method is also applied to a 3D image set to analyze the lesion by using a volume of interest or VOI than is constructed from identical ROIs taken over the stacked

image set. In this way, a relaxation distribution function can be determined for each slice, allowing for determination of lesion tissue heterogeneity, a result which is very helpful in radiotherapy treatment planning, particularly in defining the gross tumor volume or GTV. These results are shown in Figure 3.

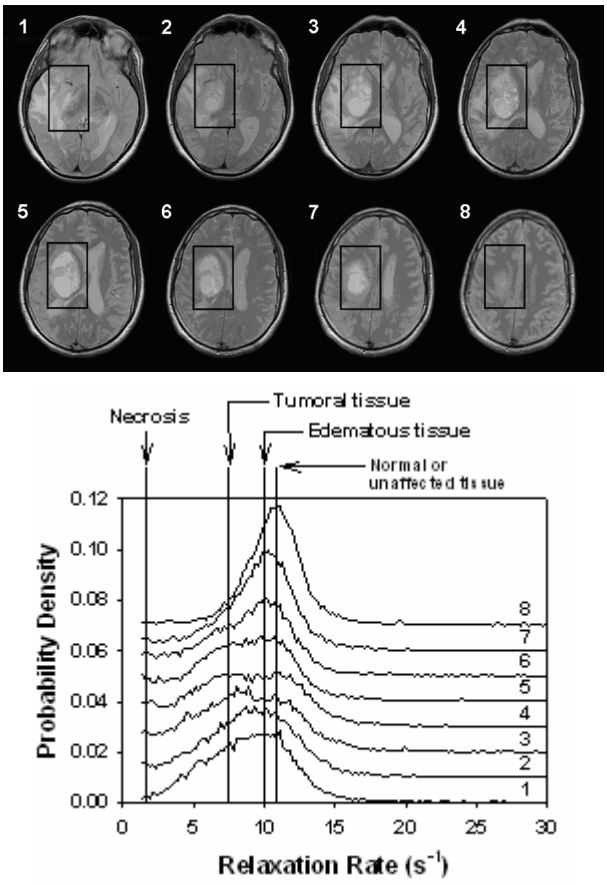

Fig. 3. Relaxation rate distribution functions from different slices (1-8). Lines indicate the mean relaxation rate for different tissue types. Analysis of the relaxation rate distributions allows for tissue classification and composition within the 3D image set.

IV. Conclusions

The quasi-analytical method developed in this work allows for a fast and reliable determination of relaxation rate distribution functions of tumoral lesions in brain over 2D or 3D image sets. Compared to other methods, based on the inversion of data by non linear regression analysis or inverse Laplace transform algorithms, the proposed method is extremely faster but it is limited to the assumption of a small number of exponential decays composing the image voxel data, i.e., the condition number increases with the number of exponentials considered. Nevertheless, for the signal to noise ratio in images used in this work and the typical relaxation rates values present in tumoral lesions in brain, allows for the reliability of the determination. The application of this method to other organs should be tested first. Future work is addressed to overcome the numerical stability problem by the application of some kind of regularization of the data in order to open the possibility of its application noisy data or to other organs. An immediate extension, in brain, is the application of the method to diffusion weighted MR imaging of tumoral lesions and other pathologies, such as Alzheimer disease and multiple sclerosis, for determination of nosologic maps used in treatment planning and monitoring.

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