New Partial Volume Estimation Methods for MRI MP2RAGE

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Abstract. Magnetic resonance imaging (MRI) is commonly used as a medical diagnosis tool, especially for brain applications. Some limitations affecting image quality include receive field (RF) inhomogeneity and partial volume (PV) effects which arise when a voxel contains two different tissues, introducing blurring. The novel Magnetization-Prepared 2 Rapid Acquisition Gradient Echoes (MP2RAGE) provides an image robust to RF inhomogeneity. However, PV effects are still an issue for automated brain quantification. PV estimation methods have been proposed based on computing the proportion of one tissue with respect to the other using linear interpolation of pure tissue intensity means. We demonstrated that this linear model introduces bias when used with MP2RAGE and we propose two novel solutions. The PV estimation methods were tested on 4 MP2RAGE data sets.

Keywords: MP2RAGE, Partial Volume Estimation, Bi-exponential model.

1 Introduction

Magnetic resonance imaging (MRI) is a commonly used modality for brain diagnosis and many morphometric methods have been developed to estimate brain atrophy [1,2,3]. However MRI has some limitations, which may affect the performance of several image processing steps and may hamper automated structural quantification if not taken into account. Among them, noise, the receive field (RF) inhomogeneity and partial volume (PV) effects.

The novel Magnetization-Prepared 2 Rapid Acquisition Gradient Echoes (MP2RAGE) sequence [4] has good signal-to-noise and contrast properties and is therefore an excellent candidate for image processing methods. The sequence also tackles the inhomogeneity of the signal across the scanned volume with a double acquisition approach. Two co-registered images are obtained and both are identically biased. A composite image is computed free of any RF inhomogeneity. MP2RAGE was also designed to maximise contrast-to-noise ratio per unit of time between brain tissues to

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facilitate segmenting the brain in main tissues: gray matter (GM), white matter (WM) and cerebrospinal fluid (CSF).

However, PV effects remain an issue in MP2RAGE. They occur when two different tissues, having different magnetic properties, contribute to the signal of a single voxel. PV estimation (PVE) consists in assigning a fractional content, *i.e.* a proportion, to each of the tissues composing a voxel labeled as a PV voxel. PVE has been shown to be useful in cortical thickness estimation [5,6,7] as the cerebral cortex, the GM, is surrounded by two different tissues: WM and CSF. Thus, the cortex is subject to two types of PV effects at its two interfaces: GM/WM and GM/CSF. Additionally, cortical thickness is of the same order of magnitude as the image resolution (typically a few mm). Its size and its convoluted structure make the cortex very sensitive to PV effects.

As cortical thickness reduction has been shown to be a good biomarker for many neurodegenerative diseases such as Alzheimer's [1], we focus this paper at estimating PV effects using MP2RAGE.

Previous works [8,9] rely on the same PV model [7] to estimate fractional contents and calculate PV maps. This model has not been validated on the particular MP2RAGE sequence yet. In this work, we evaluate the commonly used PV model on the composite image computed with the two acquisitions in MP2RAGE.

2 MP2RAGE

MP2RAGE is a recent sequence based on the popular MPRAGE sequence [10]. It starts with a magnetization preparation followed by two gradient echo blocks providing two co-registered and differently contrasted images S_1 and S_2 (Fig. 1(a) and (b)). MP2RAGE has the advantage of being robust to the RF inhomogeneities as a composite image U (Fig. 1(c)) is computed inline with the two images in a way that cancels the RF inhomogeneity:

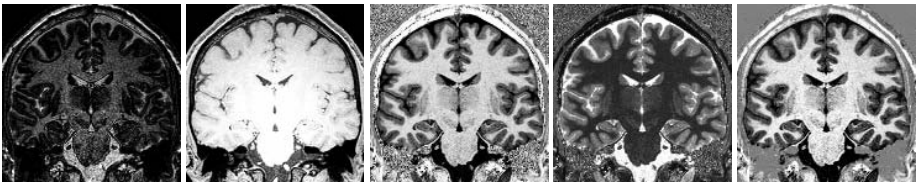
$$U = \frac{Real(S_1^* S_2)}{|S_1|^2 + |S_2|^2} \tag{1}$$

where the symbol * stands for the complex conjugate, more details regarding this equation can be found in [4]. Eq. (1) constrains the possible values in U between -0.5 and 0.5. U is not linear with respect to S_1 and S_2. This sequence also has the advantage of producing a high resolution T1 map (Fig. 1(d)). For tissues with a long longitudinal relaxation time T1, the short first inversion time in MP2RAGE results in negative signals. The sign information associated with S_1 was estimated by assuming that S_2 has positive signals due to the late second inversion time for the brain tissues considered, and therefore the sign of U is a good estimator for the sign associated with S_1. This allows using the entire dynamic range of S_1 in a new image called $S_1^{\pm}$ (Fig. 1(e)).

$$S_1^{\pm} = \frac{U(S_1^2 + S_2^2)}{S_2} \tag{2}$$

3 Methods

PV classes are often modeled as a linear mixture of two normal distributions modeling two pure tissues [11,7,5]. Under this assumption, the maximum likelihood estimation



(a) S_1 (b) S_2 (c) U (d) $T1$ map (e) $S_1^{\pm}$

Fig. 1. MP2RAGE images shown in a coronal plane. The sequence measures S_1 and S_2. U is computed inline with the two acquisitions with Eq. (1). The $T1$ map is also estimated inline. Our preprocessing includes reconstructing $S_1^{\pm}$ with the sign information contained in U.

of the mixture coefficient is a linear interpolation of tissue intensity means. In this section, the traditional linear model for PV effects will be investigated for the MP2RAGE sequence. The purpose of this paper is PVE only, in other words, the fractional content calculation. We assume that the brain tissues have already been segmented from the composite image U into GM, WM and CSF using an established and well validated method [11]. In this paper, we want to compare the GM fractional content estimated with three PVE methods at the GM boundaries. The explanations on the PVE models are concerned with a GM/WM voxel for the sake of clarity, but a similar reasoning can be applied to a GM/CSF voxel. The unknown GM fractional content is called $\alpha \in [0, 1]$.

3.1 Linear Interpolation of Intensity Means (LIMe)

In the majority of previous works on PVE, regardless of the sequence, the signal s_{gw} of a voxel composed of GM and WM is modeled as a linear combination of intensity means (μ_g and μ_w) of pure tissues

$$s_{gw} = \alpha\mu_g + (1 - \alpha)\mu_w \tag{3}$$

The model is parameterized by pure tissue intensity means. The fractional content calculation is done by interpolating the signal s_{gw} as following. f restricts the value of α in $[0, 1]$:

$$\alpha = f(\frac{\mu_w - s_{gw}}{\mu_w - \mu_g}) \tag{4}$$

The linear PV model could be independently applied to S_2 or $S_1^{\pm}$ but RF insensitivity and the optimized contrasts between cerebral tissues obtained in U would not be exploited. Given that the composite image is not linearly obtained, the well-known linear PV model (Eq.(3)) introduces errors. Assuming that partial voluming is linear in α in images $S_1^{\pm}$ and S_2, the linear model could be applied independently to both images. We call g_1 and g_2 (respectively w_1 and w_2) the intensity means of pure GM (respectively WM) in $S_1^{\pm}$ and S_2. Thus, given Eq. (1) and neglecting the noise, the GM/WM PV signal U_{gw} obtained in U can be expressed as:

$$\begin{cases} s_{1gw} = \alpha g_1 + (1 - \alpha)w_1 \\ s_{2gw} = \alpha g_2 + (1 - \alpha)w_2 \end{cases} \Rightarrow U_{gw} = \frac{s_{1gw}s_{2gw}}{s_{1gw}^2 + s_{2gw}^2} \tag{5}$$

$$U_{gw} = \frac{\boldsymbol{\alpha^2}(g_1g_2 + w_1w_2 - g_1w_2 - w_1g_2) + \boldsymbol{\alpha}(g_1w_2 + w_1g_2 - 2w_1w_2) + w_1w_2}{\boldsymbol{\alpha^2}((g_1 - w_1)^2 + (g_2 - w_2)^2) + 2\boldsymbol{\alpha}(g_1w_1 + g_2w_2 - w_1^2 - w_2^2) + w_1^2 + w_2^2} \tag{6}$$

From Eq. (6), it is clear that partial voluming in U is not linear but quadratic in α. Assuming a linear PV model for $S_1^{\pm}$ and S_2 results in a non-linear model for U. We propose in the next sections new models that reduce this error.

3.2 Quadratic Interpolation of Intensity Means (QIMe)

The first solution that we propose to address PVE in U is an extension of LIMe, using a Quadratic Interpolation of Intensity Means (QIMe). As the PV signal in U appears to be quadratic, finding α is equivalent to solving a second order equation with the following reformulation of Eq.(6):

$$\begin{aligned} U_{gw} = \tfrac{N_{gw}(\alpha)}{D_{gw}(\alpha)} &\Leftrightarrow N_{gw}(\alpha) = U_{gw}D_{gw}(\alpha) \\ &\Leftrightarrow N_{gw}(\alpha) - U_{gw}D_{gw}(\alpha) = 0 \\ &\Leftrightarrow P_{gw}(\alpha) = 0 \end{aligned}$$

Finding the fractional content is equivalent to finding the roots of a second order polynom for every PV voxel. This polynom is parameterized by the signal U_{gw} and the intensity means of pure tissue in $S_1^{\pm}$ and S_2. When the discriminant of P_{gw} (Δ) is negative, there are no computable solutions so α is set to the closest tissue in terms of intensity in U (0 for WM, 1 for GM). When $\Delta > 0$, the closer root to the LIMe solution is chosen as the evolution of α as a function of a PV signal appears to be almost linear.

3.3 Bi-Exponential Model (BiExp)

Duché et al. [12] proposed a bi-exponential model (BiExp) to estimate PV from MP2RAGE. In BiExp, the parameters contributing to the signal are expressed: the tissue properties and the sequence parameters. Hence, the signal measured in a voxel is weighted by the longitudinal magnetization of the protons population M_0. Consequently, the two PV signals in $S_1^{\pm}$ and S_2 are defined as a linear combination of two pure signals:

$$\begin{cases} s_{1gw} &= M_{0g}s_1(T1_g) + M_{0w}s_1(T1_w) &= M_{0g}s_{1g} + M_{0w}s_{1w} \\ s_{2gw} &= M_{0g}s_2(T1_g) + M_{0w}s_2(T1_w) &= M_{0g}s_{2g} + M_{0w}s_{2w} \end{cases} \tag{7}$$

where $T1_g$ and $T1_w$ are the $T1$ values of pure GM and WM. They are estimated in the T1 map produced by MP2RAGE. The signals s_1 and s_2 have been described by Marques *et al.* [4], they are functions of the many sequence parameters and magnetic properties of the tissues. The assumption of this model is the uniqueness of T1 value per tissue. This simplifies the system as the signals s_1 and s_2 can then be computed for particular T1 values, resulting in the estimation of the constant $s_{1g}, s_{2g}, s_{1w}, s_{2w}$. They represent the pure GM and WM signals in $S_1^{\pm}$ and S_2 for $M_0 = 1$.

This voxel-wise linear system can be solved for (M_{0g}, M_{0w}) which are the amounts of respective pure tissues in the voxel, they represent the same physical information in

both co-registered MP2RAGE images. The fractional content of GM is calculated as $\alpha = \frac{M_{0g}}{M_{0g}+M_{0w}}$. This model is parameterized by the T1 values of pure tissues. T2 has a limited impact on α and the proton density values of the tissues are taken from the literature [13,14].

Table 1. Summary of the three presented PV estimation methods (first column). The second column names the required parameters for the method and recalls the image(s) they are extracted from. The last column contains the image(s) in which the PV estimation is done.

PVE Method	Parameters (extracted from)	PV estimated with
LIMe	μ_g, μ_w, μ_c (U)	U
QIMe	$g_{1,2}, w_{1,2}, c_{1,2}$ ($S_1^{\pm}, S_2$)	U
BiExp	$T1_g, T1_w, T1_c$ ($T1$ map)	$S_1^{\pm}, S_2$

4 Experiments

4.1 Simulations

The three tissues were simulated with the T1 measured in the experimental data. Each GM interface was discretized with intermediate PV values where the signal was modeled as a linear combination of two pure tissue signals. The noiseless two echoes and composite signals were simulated. The three methods were applied to estimate the fractional content α. PVE by the various methods was expressed as a function f_s of the ground truth (GT) α.

4.2 Experimental Data

Two healthy volunteers were scanned twice in a 3T Siemens Scanner with a 20-channel head coil. A 3D isotropic (1mm^3) MP2RAGE protocol was used. Each MP2RAGE data underwent identical pre-processing that included brain extraction and automated segmentation of GM, WM and CSF. These masks were eroded to estimate parameters for the three PVE methods, the erosion allows to avoid a large number of voxels subject to PV effects at the boundaries. The parameters estimations were done in the same regions for the three methods. GM PV maps were calculated with the three methods presented in section 3. Boundary masks (GM/WM and GM/CSF) were extracted by taking the intersection of the dilated segmentations. This ensures to define regions in which a majority of the voxels are subject to PV effects. In these boundaries voxels, the three PV methods were compared with the same population of voxels.

Experimental results from the four scans were gathered for the analysis. The GM voxels were separated in two classes resulting in about 1 million GM/WM voxels and 1.5 million GM/CSF voxels. Fractional content estimates from two different PV methods were plotted and treated as a joint probability distribution. These 2D histograms were integrated to get an average function. These experimental functions f_e were compared with the function f_s obtained in the simulation.

5 Results and Discussion

Results from the simulations and experimental data are summarized in Fig. 2. The first row shows the MP2RAGE U image and the extracted GM boundaries. In the second

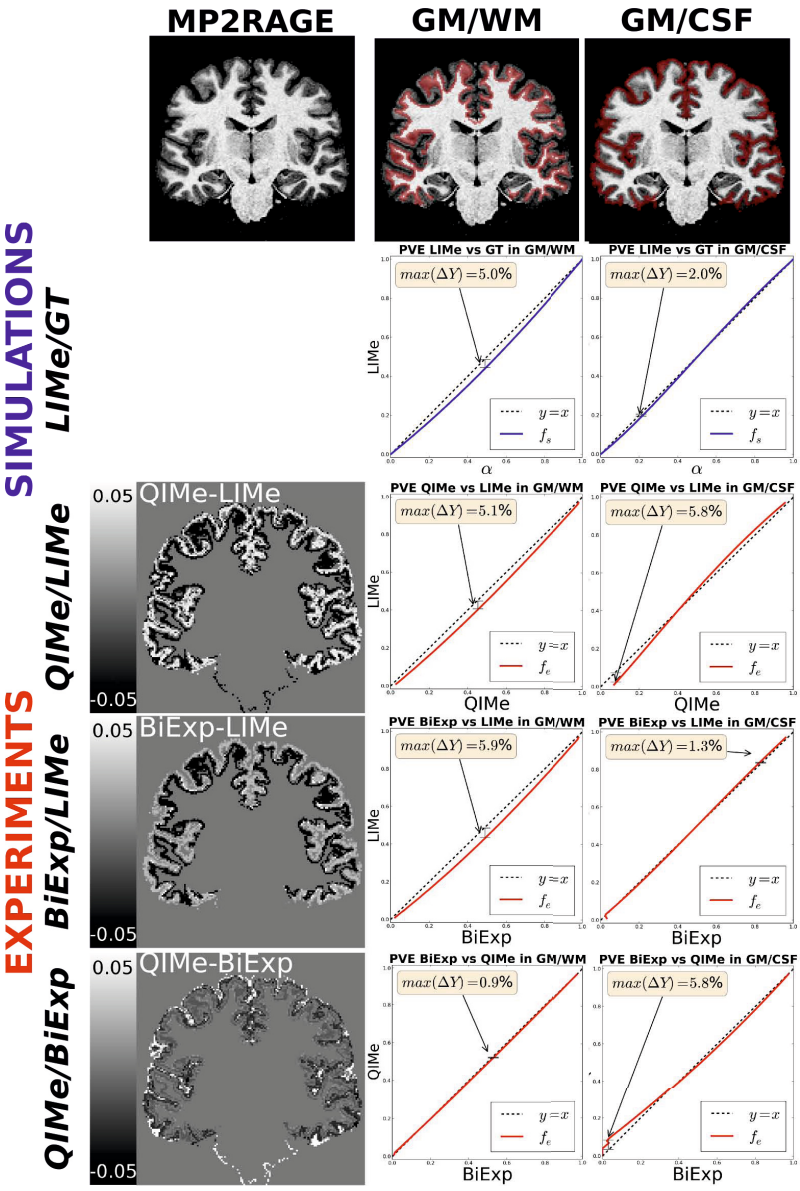


Fig. 2. Summary of the results. The first row shows the input and the two GM interfaces of interest where fractional content estimates are extracted from. The second row shows the results of the simulations for LIMe. For the experimental results, every row is the comparison of two PVE methods, the image is the difference of the PV maps.

row, f_s, expressing the LIMe PV GM fractional content estimate is plotted as a function of the GT α, is plotted in blue for the two boundaries. These graphs confirm the systematic errors made on the fractional content estimate with the linear PV model. It also suggests that the theoretical maximal cumulated error on both boundaries can go up to 7% of the voxel resolution used. For a 1mm^3 resolution and a cortical thickness of 3mm, this represents a maximal error of 2.33%.

In the "Experiments" part of Fig. 2, each row represents the comparison of two PVE methods as indicated on the left side by a vertical text. The image is the difference between the computed GM PV maps. The graphs exhibit the plot of f_e in red, expressing the average fractional content estimate of the first method as a function of the fractional content estimated with the second method for a large population of PV voxels.

For the GM/WM PV voxels, the experimental functions f_e for QIMe and BiExp are very similar to the noiseless simulated f_s confirming the error that we expected from using the linear model. Our results suggest that QIMe and BiExp are good PV models for MP2RAGE. When comparing QIMe to BiExp (last row), almost no difference was observed on the GM/WM boundary.

At the GM/CSF interface, the results obtained with QIMe are less consistent with the simulations when $\alpha \to 0$, *i.e.* when the voxel tends to be pure CSF. We hypothesized that this could be due to the low CSF SNR. BiExp seems more consistent with the expected behaviour of a good PV model.

QIMe and BiExp use the two echoes and are not subject to RF inhomogeneity. QIMe has the advantage of being self-contained, there are no assumptions on the T2 nor the proton density of the tissues. BiExp has the advantage of taking into account MR acquisition parameters and therefore could be extended to incorporate a model of a transmit field (TF) inhomogeneity map. The knowledge of the actual flip angle induced to the protons could be incorporated voxel-wise in the model as the signal equations are fully expressed.

The unique processing of the information contained in U (LIMe) results in underestimating the GM proportion in PV voxels. This undererestimation is systematic in the GM/WM interface. These results may explain the systematic measurement of a thinner cortex with MP2RAGE compared to MEMPRAGE found in [15]. Our work may be an answer to the missing tailored tissue segmentation method needed by MP2RAGE as Fujimoto *et al.* pointed out.

6 Conclusion

We investigated the well known problem of PVE with the novel MP2RAGE sequence. The well established linear model for PVE is prone to errors on both interfaces surrounding cortical GM. Our experiments suggest that PV can not be correctly estimated with the unique analysis of combined image U, the information contained in the two images $S_1^{\pm}$ and S_2 must be exploited. We proposed two solutions which led to similar results. Both methods provide a way forward to improve the accuracy of cortical surface reconstruction with MP2RAGE. Future work will include measuring the impact of the PVE error in GM with LIMe on cortical thickness estimation.

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