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# MRI CONTRAST ENHANCEMENT OF MAGNETIZATION PREPARED STEADY STATE SEQUENCE: AN OPTIMAL CONTROL FRAMEWORK

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## ABSTRACT

The present work investigates the possibilities of enhancing MRI contrast between two target tissues in a three-dimensional Magnetization-Prepared Rapid Gradient-Echo (MP-RAGE) based on relaxation time’s differences. The benefit lies in the adaptation of the GRAPE algorithm to the optimization of a magnetization preparation in a cyclic sequence without full recovery between each cycle. This numerical approach allows optimizing a magnetization preparation of an arbitrary number of radio frequency pulses to enhance contrast, taking in account the establishment of a steady state in the longitudinal component of the magnetization. *In vivo* validation on rat brain is performed at 11.7T and shows the benefit of an optimized T<sub>2</sub>Prep-IR compared to a simple inversion to enhance contrast between white and gray matter.

**Index Terms**— GRAPE, Optimal Control, MP-RAGE

## 1. INTRODUCTION

Since the early work of Mugler et al. [1], MP-RAGE is one of the most common sequence for T<sub>1</sub> weighted MRI of the brain. This sequence allows high spatial resolution and high contrast images in times adapted to a clinical context. A MP-RAGE sequence is typically divided into cycles (or segments). Each cycle contains three periods: (1) a time devoted to partial magnetization recovery, (2) a magnetization preparation period for contrast control, (3) several data acquisitions with a short time of repetition (TR) and low flip angle using a spoiled gradient echo scheme. Each cycle fills a fraction of the k-space. The establishment of the longitudinal steady state without any contribution of the transverse magnetization (due to the gradient echo excitation pulses) supposes to select coherent transverse pathway. In practice disrupting transverse coherence is achieved by incrementing the RF pulse phase and using gradient spoiler [2].

The optimization of the sequence remains a difficult numerical problem due to coupling between cycles. Mugler and al. [3] have developed a solution in the simple case of a

single RF pulse preparation. However, improvements can be made to increase the types and/or quality of contrast achievable. For example, one decade ago, Marques and al. [4] proposed an improvement of this sequence with the MP2RAGE which has two periods of acquisitions per cycle. In this context, our approach is to investigate the possibilities of enhancing contrast by modeling an arbitrary preparation inside the MP-RAGE. Our work is based on the recent optimal control framework proposed for the design of a preparation to optimize MRI contrast based on the relaxations differences [5-7].

This paper presents a novel use of the GRAPE algorithm in order to optimize a complex preparation within the establishment of a longitudinal steady state. It generalizes previous optimal control based algorithm in which full magnetization recovery was required. In addition, it presents the contrast improvement that can provide an optimized T<sub>2</sub>Prep-IR compared to a standard MP-RAGE on rat brain.

## 2. METHOD

### 2.1. Modeling of a T<sub>1</sub>w MP-RAGE

For a simple inversion-recovery preparation, the cyclic nature of the sequence with no-full recovery of the magnetization between each cycle leads to a stationary state quite easy to compute. The evolution of the longitudinal magnetization within one cycle,  $M_{z,j=1..4}^k$ , is described below:

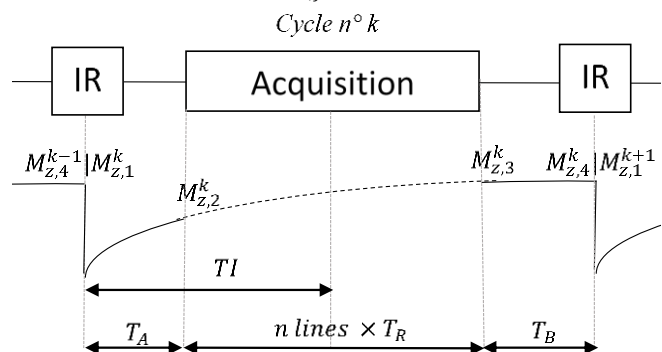


Fig. 1. Schematic diagram of the T<sub>1</sub> MP-RAGE sequence

$$M_{z,1}^{k+1} = -eff \cdot M_{z,4}^k$$

$$M_{z,2}^{k+1} = M_0(1 - EA) + M_{z,1}^{k+1}EA$$

$$M_{z,3}^{k+1} = M_0S_1(1 - K_1^n) + K_1^n M_{z,2}^{k+1}$$

$$M_{z,4}^{k+1} = M_0(1 - EB) + M_{z,3}^{k+1}EB$$

With:  $EA = e^{-\frac{TA}{T_1}}$ ,  $EB = e^{-\frac{TB}{T_1}}$ ,  $K_1 = \cos(\alpha) e^{-\frac{TR}{T_1}}$ ,  $\alpha$ : the flip angle (degrees),  $T_R$ : the time of repetition of the gradient echo scheme (ms),  $n$  the number of lines encoded per cycle,  $eff$ : the efficacy of the inversion and  $M_0S_1$ : the steady state associated to the gradient echo acquisition sequence,  $S_1 = \left(1 - e^{-\frac{TR}{T_1}}\right) / \left(1 - \cos(\alpha) e^{-\frac{TR}{T_1}}\right)$ .

By iteratively inserting the first equations in the last one, we find:

$$M_{z,4}^{k+1} = M_0(1 - EB) + M_0S_1(1 - K_1^n)EB + M_0K_1^nEB(1 - EA) - eff \cdot K_1^nEBEA M_{z,4}^k$$

Then writing  $M_{z,4}^{k+1} = M_{z,4}^k$  gives the steady state:

$$ss = M_0 \frac{(1 - EB) + S_1(1 - K_1^n)EB + K_1^nEB(1 - EA)}{1 + eff \cdot K_1^nEBEA} \quad (1)$$

More precisely, we also have the convergence:

$$M_{z,4}^k = ss + K^k (M_{z,4}^0 - ss), \quad K = -eff \cdot K_1^nEBEA$$

## 2.2. Modeling of an arbitrary MP-RAGE

In the presence of multiple pulses and delays in the magnetization preparation, the ratio between magnetization before and after the preparation is no more constant. We assume that the action of the preparation on the magnetization can be modeled by a transfer matrix. We can write:

$$M_{out} = \begin{pmatrix} A_u & q_u \\ 0 & 1 \end{pmatrix} M_{in}, \quad M_{out} = UM_{in}$$

$M_{out}$ : the magnetization after the preparation,  $M_{in}$ : the magnetization before the preparation.  $U$ : the transfer matrix, which can be decomposed as the product of  $N$  matrix, each modelling the action of a pulse followed by a time of relaxation. The magnetization vector is expressed along its homogeneous coordinates:  $(M_x, M_y, M_z, 1)$ .  $u$  refers to the parameters of the preparation which contains for each RF pulse its amplitude, its phase and the delay before the next RF pulse. Considering that any transverse magnetization is adequately spoiled ( $M_x = M_y = 0$ ), it follows that:

$$\begin{pmatrix} 0 \\ 0 \\ M_{z\ out} \\ 1 \end{pmatrix} = \begin{pmatrix} A_{u\ 1,1} & A_{u\ 1,2} & A_{u\ 1,3} & q_{u_1} \\ A_{u\ 2,1} & A_{u\ 2,2} & A_{u\ 2,3} & q_{u_2} \\ A_{u\ 3,1} & A_{u\ 3,2} & A_{u\ 3,3} & q_{u_3} \\ 0 & 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} 0 \\ 0 \\ M_{z\ in} \\ 1 \end{pmatrix}$$

We can retrieve the following transfer relation:

$$M_{z\ out} = A_{u\ 3,3}M_{z\ in} + q_{u_3} \text{ i. e. } M_{z\ out} = f(u)M_{z\ in} + h(u)$$

As  $f(u)$  and  $h(u)$  remain unchanged at each cycle, this allows updating the steady state (1) from the previous section:

$$M_{z,4}^{k+1} = M_0(1 - EB) + M_0S_1(1 - K_1^n)EB + M_0K_1^nEB(1 - EA) + K_1^nEBEA(f(u)M_{z,4}^k + h(u))$$

ss =

$$\frac{M_0 \times [(1 - EB) + S_1(1 - K_1^n)EB + K_1^nEB(1 - EA)] + K_1^nEBEA h(u)}{1 - K_1^nEBEA f(u)}$$

$$ss(u) = \frac{A + \lambda h(u)}{1 - \lambda f(u)} \quad (2)$$

$A$  and  $\lambda$  only depends on the acquisition parameters.  $h(u)$  and  $f(u)$  only depend on preparation parameters.

## 2.3. Optimization of the magnetization preparation in the MP-RAGE

The optimization of the preparation sequence requires the differentiation of the previously described steady state (2), with respect to  $u$ :

$$\nabla_{ss} = (A + \lambda h(u)) \frac{\lambda}{(1 - \lambda f(u))^2} \cdot \nabla f + \frac{\lambda}{1 - \lambda f(u)} \nabla h(u)$$

Recording that  $f(u) = \vec{e}_z U \vec{e}_z$  and  $h(u) = \vec{e}_z U \vec{e}_0$  where  $\vec{e}_z = (0\ 0\ 1\ 0)$  and  $\vec{e}_0 = (0\ 0\ 0\ 1)$ , the transfer matrix is:

$$U = \begin{pmatrix} * & * & * & * \\ * & * & * & * \\ * & * & f(u) & h(u) \\ 0 & 0 & 0 & 1 \end{pmatrix}$$

For an arbitrary  $N$ -pulse preparation:  $U = U_N \dots U_2 U_1$ .

$U_i = U(u_i)$  is the transfer matrix modeling the action of  $i$ -th pulse and delay whose parameters are regrouped into the vector  $u_i$ . So:

$$\nabla_{u_i} f = \vec{e}_z \frac{\partial U}{\partial u_i} \vec{e}_z \quad \nabla_{u_i} h = \vec{e}_z \frac{\partial U}{\partial u_i} \vec{e}_0$$

At this point, we have expressed the steady state and its partial derivatives with respect to the preparation scheme parameters. The standard GRAPE algorithm can thus be used: with the chain rule derivation, we can derivate any cost functions that are composite functions of  $ss(u)$ . The algorithm is coded on Matlab (*The MathWorks, Inc., Natick, MA, USA, R2019b*). A second order gradient descent is performed thanks to the Matlab function *fmincon*, to which gradient expressions derived in the previous equations are provided.

## 2.4 Numerical simulation to enhance contrast between gray and white matter

To validate the proposed method, we have compared our numerical results with those of Mugler and al. They optimized a preparation composed of a single non-selective radiofrequency pulse with flip angle between  $0^\circ$  and  $180^\circ$ . In their model, 32-step phase encoding is performed at each cycle with TR/TE of 10/4 ms. The goal is to optimize the signal intensity between white matter ( $T_1/T_2$ /proton density: 550/90 ms/0.65) and gray matter ( $T_1/T_2$ /proton density: 940/100 ms/0.75). There is no recovery between the end of the acquisition and the preparation pulse. The time between the pulse and the beginning of the acquisition is fixed to 140 ms to fulfill the constraint of acquisition time. They have found for each flip angle of the gradient-echo acquisition the best angle for preparation pulse to maximize white matter and gray matter signal difference (WGSD). For each flip angle used in the gradient-echo, they plotted the difference between the maximum WGSD obtained with the optimal preparation pulse and the WGSD without any preparation. To retrieve this result, we search the minimum of the following cost function thanks to our adaptation of GRAPE:

$$C = -|S_{WM}| + |S_{GM}| = -WGSD \quad (3)$$

$S_{WM}$  and  $S_{GM}$  are respectively the signal intensities of the white and gray matter at the center of the k-space containing  $n$  lines.

$$S = \left[ s + \left( \frac{ss(u) - (1 - EB)}{EB} - s \right) K_1^{-p} \right] \sin(\alpha) e^{-\frac{TE}{T_2}} \quad (4)$$

With  $s = M_0 S_1$ ,  $p = \frac{n}{2}$  or  $n$  for respectively centrally reordered or sequential phase encoding. Due to absolute value, the function of (3) is not differentiable in some points, which can lead to errors. In this specific case, the parametrization used in the optimization ensures to be in a domain where the gradient is defined. The computation of the gradient of the cost function is based on paragraph 2.3 and general rules of differentiation.

## 2.5. Maximization of the contrast between cortex and corpus callosum

On the assumption that exploiting  $T_1$  and  $T_2$  may enhance contrast, we used our algorithm to maximize contrast between cortex and corpus callosum on a rat brain at 11.7T. We consider that the best cost function to enhance contrast between two tissues aims at saturating the signal from one tissue while maximizing the signal from the other. Thus, we chose the following cost function:

$$C = \alpha \cdot S_1^2 - \text{sign}(S_2) S_2^2 \quad (5)$$

$\text{sign}$  : is added to force solution with positive value for the signal of species 2 in the center of the k-space.  $\alpha$ : a weighting coefficient (10 in our case).

We implemented the solution on a preclinical 11.7T scanner (Bruker). The objective was to optimize the best parameters to saturate the cortex ( $T_1/T_2$ : 1945.0/34.2 ms) and maximize the signal of corpus callosum ( $T_1/T_2$ : 1710/31.2 ms).  $T_1$  and  $T_2$  values have been estimated on the basis of the values measured by de Graaf and al. [7] and the application manual of the constructor. We considered in a first approximation the proton densities for both tissues as equal to 1. The duration of the sequence was constant. Main parameters of the sequence are summarized in the following table:

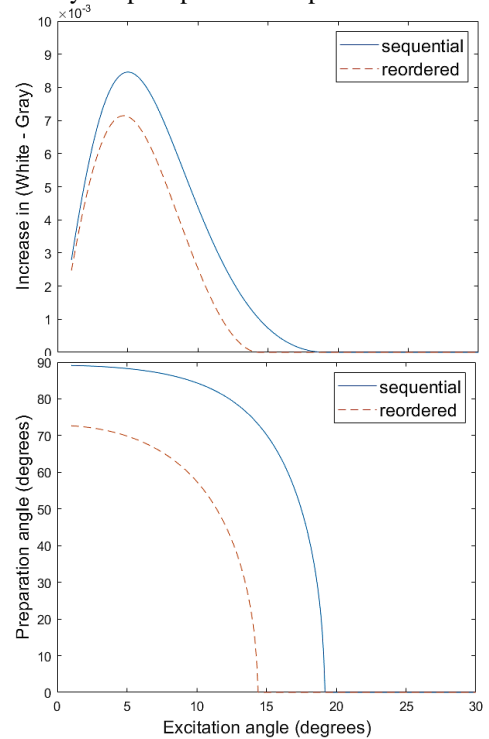
Number of lines per cycle	64
TR/TE/Angle of excitation	6.5 ms/2.2 ms/13°
Time of a cycle	3000 ms
Number of accumulations	8
Time of acquisition	438 s
Phase encoding	sequential
FOV/slice thickness	35×35 mm /6 mm
Matrix size	128×128×8

Table 1. Acquisition parameters

## 3. RESULTS

### 3.1. Numerical simulation to enhance contrast between gray and white matter: results

The results below obtained with our optimization well agree with the previous results of Mugler and al. [3]. This, somehow, validates the efficiency of the proposed approach for a relatively simple optimization problem.



**Fig. 2.** In the top graph, maximum WGSD minus WGSD without preparation as a function of the flip angle of the gradient echo acquisition. The ordinate in units of normalized transverse magnetization. In the bottom graph, preparation flip angle yielding the maximum WGSD as a function of the flip angle of the gradient echo acquisition.

### 3.2. Maximization of the contrast between cortex and corpus callosum: *in vivo* results

Considering the optimization of a single-pulse preparation, the optimal solution is a standard MP-RAGE with an inversion pulse ( $180^\circ$ ) followed by an inversion time of 925 ms (from the pulse to the first excitation).

Considering the optimization of a two-pulse preparation, the optimal solution is  $90^\circ - 17\text{ms} - 90^\circ - 646\text{ms}$  - first excitation. In order to counter the effect of  $B_0$  inhomogeneities, which are not taken into account in the optimization, a refocusing pulse is inserted between the two pulses. The final preparation results in an optimized  $T_2\text{Prep-IR}$ .

In both case, we numerically find a similar contrast of 0,93 ( $C = \frac{I_{max} - I_{min}}{I_{max} + I_{min}}$ ) and a signal 10 % higher with the two-pulse preparation.

*In vivo*, we verify the saturation of the cortex and the enhancement of the corpus callosum (**Fig. 3.**). As expected, the  $T_2\text{Prep-IR}$  solution gives a higher signal -to-noise ratio. This is explained by the fact that the proposed scheme uses  $T_2$  relaxation (in addition to  $T_1$ ) to generate contrast, which is inherently faster than using only  $T_1$ . For a similar contrast to IR,  $T_2\text{Prep-IR}$  is shorter. This provides more time to the magnetization recovery before the preparation and so a better signal dynamics.

	Intensity mean $\pm$ standard deviation			Contrast to noise : $\frac{I_{max} - I_{min}}{Noise}$
	CC <sup>1</sup> :	CX <sup>2</sup> :	Noise :	
TI	1610 $\pm$ 467	710 $\pm$ 329	359 $\pm$ 93	2,5
$T_2\text{Prep-IR}$	2441 $\pm$ 492	978 $\pm$ 422	363 $\pm$ 95	4,03

1: corpus callosum, 2: cortex.

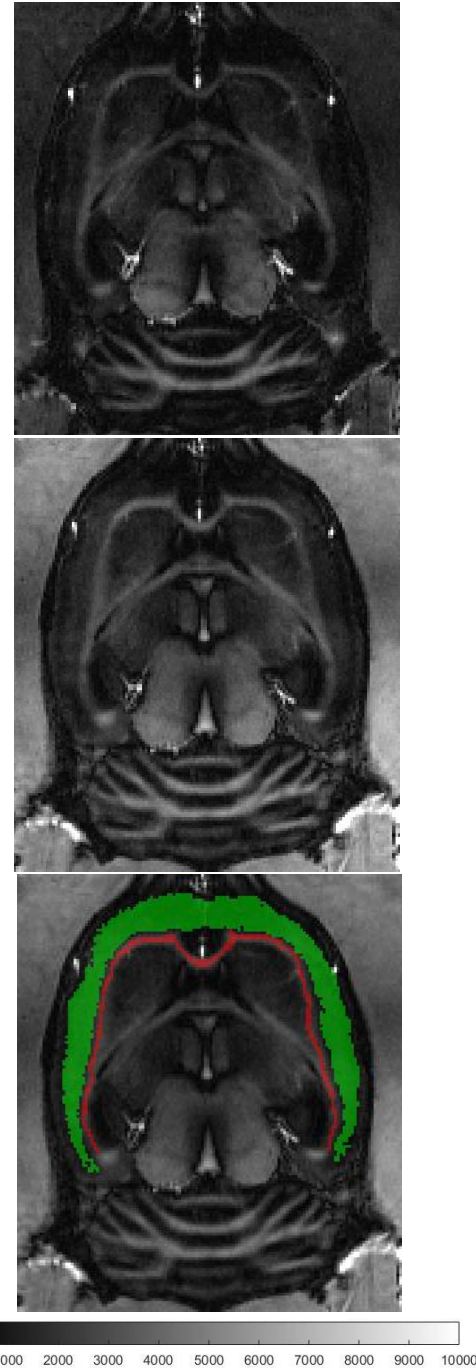
**Table. 2.** Intensity and Contrast-to-noise ratio *in vivo*

## 5. CONCLUSION

We have developed a new tool based on the GRAPE algorithm to optimize an arbitrary preparation in a MP-RAGE, with the aim to improve contrast between two target tissues. We validated our approach by numerical results and *in vivo* acquisitions. In the *in vivo* application, the resulting preparation sequence is an optimized  $T_2\text{prep-IR}$ , which significantly improves both signal and contrast-to-noise ratio compared to the standard IR strategy.

The novelty of our algorithm with respect to previous optimal control algorithms is the inclusion of the steady state in the optimization. Our framework is general and could be applied to complex contrast problems, particularly involving more

than two targeted tissues. In addition, the proposed framework could be applied to other rapid MRI sequences, with some adaptations that are currently under consideration.



**Fig. 3.** In the top image: Standard MP-RAGE with inversion recovery ( $TI = 925\text{ ms}$ ) aiming at saturating the cortex and maximizing the corpus callosum (results of one pulse optimization as described below). In the middle image: MP-RAGE with  $T_2\text{Prep-IR}$  aiming at saturating the cortex and maximizing the corpus callosum (results of two pulses optimization as described below). In the bottom image: segmented cortex (green) and segmented corpus callosum (red).

## 6. ACKNOWLEDGEMENTS

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## 8. COMPLIANCE WITH ETHICAL STANDARDS

*In vivo* studies were conducted in accordance with ethical compliance (agreement C69266 1401).