Optimisation of b-values in MR diffusion-weighted acquisitions through information theory: a mathematical justification for consensus

Poster No.: B-0580
Congress: ECR 2014
Type: Scientific Paper
Authors: A. Alberich-Bayarri, R. Sanz-Requena, G. García-Martí, L. Martí-Bonmatí; Valencia/ES
Keywords: MR physics, Oncology, Abdomen, MR, MR-Diffusion/Perfusion, MR-Functional imaging, Technical aspects, Computer Applications-General, Technology assessment, Tissue characterisation, Multidisciplinary cancer care, Cancer
DOI: 10.1594/ecr2014/B-0580

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Purpose

Diffusion-weighted (DW) magnetic resonance (MR) imaging is today widely extended as a functional imaging technique to analyze the alterations of the thermally driven microscopic motion of water molecules in several tissues and organs within the body, with brain [1], abdomen [2], oncology [3], musculoskeletal [4] and cardiac reference applications [5].

A simple monoexponential signal decay model was initially used for the study of MR diffusion and the estimation of the apparent diffusion coefficient (ADC). However, the intravoxel incoherent motion (IVIM) theory demonstrated that the motion of blood water molecules flowing through capillary network had an influence in the diffusion signal intensities at low b-values, and therefore a bi-exponential curve of the signal decay was obtained if a dense b-value sampling scheme was used, allowing for the extraction of a pure diffusion coefficient (D), a pseudodiffusion coefficient (D*) representing perfusion and a perfusion fraction parameter (f) [6].

Nevertheless, it has been stated that ADC, D, D* and f measurements heavily depend on the choice of b values, which usually are reduced in order to maintain reasonable acquisition times [7, 8]. Although important consensus statements have been proposed from a qualitative perspective towards the standardization of the technique [9], the measurement biases of diffusion are still hindering the expansion of DW MR and IVIM modeling as a robust, precise and reproducible tool with an impact in clinical trials. A clear and justified b-value sampling scheme for a proper modeling of the full bi-exponential signal has still not been proposed. Therefore, the development of clinically suitable b-value sampling schemes providing the best modeling of the signal and minimizing the estimation errors is a challenging topic of research.

The goal of this work is to address the problem of b-value optimization in DW-MR as a signal compression problem in the frame of information theory and the properties of the Fisher information matrix (FIM), focusing on 4 optimum b-values that contain most of the information of the signal and provide minimum estimation error of the diffusion parameters.
Methods and materials

Particularization to IVIM

In order to analyze the amount of information of the biexponential signal decay model of diffusion, the Fisher information matrix (FIM) was calculated, which objectivizes the amount of information that an observation carries about unknown parameters. The diagonal of the FIM corresponds to information with respect to each parameter, and in optimal experimental design a model can be optimized if such information is maximized for the variable values [10].

The IVIM model used is expressed by the well-known Equation (1) [11]:

\[
\frac{S_b}{S_0} = (1 - f) \cdot \exp(-b \cdot D) + f \cdot \exp[-b \cdot (D + D*)], \tag{1}
\]

Fig. 1: IVIM equation

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where \(b\) is the so-called b-value, \(S_b\) is the signal at the given b-value, \(S_0\) the signal measured at b-value 0 s/mm\(^2\) (no diffusion weighting), and \(D, D^*, f\) are the IVIM parameters. In order to provide the real value of \(S_0\) and simplify the optimization problem to only \(D, D^*\) and \(f\) parameters, it was considered herein that the b-value 0 is always acquired.

Considering that the FIM expression for each \(i_j^{th}\) element adapted to DW MR images is the observed in Equation (2) [10]:

\[
F_{ij} = \frac{1}{\sigma^2} \sum_b \left( \frac{\partial S(b)}{\partial \theta_i} \cdot \frac{\partial S(b)}{\partial \theta_j} \right), \tag{2}
\]

Fig. 2: Equation for an element of the Fisher Information Matrix

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where \(\sigma\) is the standard deviation of the noise and, \(\theta_i, \theta_j\), are given by \(D, D^*\) and \(f\), respectively.
Thus, the expressions related to the amount of information from the main diagonal for D, D* and f parameters can be written as in Equations (3), (4) and (5), respectively:

\[
F_{11} \propto \frac{\partial S(b)}{\partial D} \cdot \frac{\partial S(b)}{\partial D} = S_0^2 \cdot (-b \cdot f \cdot \exp[-b \cdot (D + D^*)] - b \cdot (1 - f) \cdot \exp[-b \cdot D])^2
\]

\[
F_{22} \propto \frac{\partial S(b)}{\partial D^*} \cdot \frac{\partial S(b)}{\partial D^*} = S_0^2 \cdot (-b \cdot f \cdot \exp[-b \cdot (D + D^*)])^2
\]

\[
F_{33} \propto \frac{\partial S(b)}{\partial f} \cdot \frac{\partial S(b)}{\partial f} = S_0^2 \cdot (\exp[-b \cdot (D + D^*)] - \exp[-b \cdot D])^2
\]

**Fig. 3:** Equations for F11, F22 and F33, diagonal elements of the Fisher Information Matrix

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By considering biological and tissue-related values of the diffusion parameters, these expressions were used to obtain the b-value range that provided the highest information and hence the minimum error in the calculation of each parameter.

**Extraction of diffusion tissue characteristics**

In order to determine the distributions of D, D* and f values through different organs and parenchyma, a systematic literature review of relevant IVIM DW studies in brain, breast, abdomen, pelvis and musculoskeletal tissues was performed and can be appreciated in table 1. The variation ranges to be used in the optimization were extracted by calculating the minimum - 2 x maximum standard deviation and the maximum + 2 x maximum standard deviation for each parameter, considering a minimum value of 0 for D, D* and f. In the case of missing D* values, which are not calculated in some IVIM studies, a standard range of [0, 50mm$^2$/s] was used. By this approach, a range to cover the possible biological situations in the different tissues was obtained.

**Optimization of b-values**

The determination of the 4 optimum b-values that achieved a proper fit of the IVIM model was performed by considering the b-value 0 s/mm$^2$ in conjunction with the 3 b-value ranges providing the maximums of the 3 FIM diagonal elements F11, F22 and F33, namely, those b-values that accumulate the maximum information about the
biexponential curve (Fig 1). The biological value ranges of $D$, $D^*$ and $f$ previously extracted for each specific anatomy were used for the calculation of the optimum b-value series. Thereafter, a histogram analysis of the calculated optimum b-values permitted the evaluation of the intervals that concentrate the maximums of information. The full width at half maximum (FWHM) of the peaks was calculated as a measure of the best b-value range. All the calculations were performed in Matlab R2013a (The MathWorks, Inc., Natick, MA, USA).
Fig. 5: Variability in the diffusivity measurements depending on a mono exponential or bi-exponential fitting.

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Fig. 6: Fisher Information Matrix basics

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Results

The optimum b-values obtained for brain were 0, 15, 65 and 682s/mm$^2$; for breast 0, 8, 41 and 390s/mm$^2$; for abdomen 0, 10, 50, 351 s/mm$^2$; for pelvis 0, 25, 110, 674s/mm$^2$; musculoskeletal 0, 24, 110, 657s/mm$^2$. 
Fig. 7: Distribution of the Information for the different b-values (blue curve). Signal bi-exponential decay (red curve).

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Conclusion

Information theory was introduced by Claude E. Shannon 1948 and is a branch of applied mathematics, electrical engineering and computer science involving the quantification of information. The idea behind b-value selection is to optimize the amount of information conveyed by the measurements in the b-values about the IVIM parameters to be estimated. Optimal information can be defined in various ways, such as maximum response of the measurements to diffusion alterations in tissues, minimum uncertainty in the estimated parameters, or maximum orthogonality between the measurements.

An optimum set of b-values according to information theory was obtained for different regions and biological situations in the body. The results together with a validation currently being performed with clinical data will add relevant insight into consensus over a standardized b-value sampling scheme in DW-MR.
References


