Influence of the non-linear fitting approach on intravoxel incoherent motion (IVIM) MRI: A model selection study

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Introduction: Intravoxel incoherent motion (IVIM) MRI can be used to assess tissue microcapillary perfusion properties based on diffusion-weighted acquisitions by fitting a biexponential model function to the measured signal attenuation as a function of the diffusion weighting (b-value); the perfusion properties are reflected by the initial signal attenuation at small b-values between 0 and about 150 s/mm² [1,2]. Several strategies have been proposed for the fitting procedure including two-step linear-fit approaches applied to the logarithm of the signal attenuations or non-linear multi-parameter fitting using, e. g., the Levenberg-Marquardt algorithm. While the conventional fully biexponential model has 4 free parameters including the initial signal at b-value 0, several studies use only the signal attenuation relative to this initial value (e. g. [3]), thus artificially discriminating, the measurement at b=0 and at higher b-values. Therefore, the aim of the present study is to use a model selection approach based on the Akaike information criterion [4] to decide whether a biexponential model with 3 or 4 free parameters is more appropriate for typical IVIM data.

Materials and Methods: 12 athymic nude rats (Hsd:RH-Fox1mu) with implanted breast carcinoma tumors (MDA-MB-231) were examined in a 3-Tesla whole-body MRI system (Magnetom Verio, Siemens Healthcare, Erlangen, Germany) with a dedicated 4-channel small-animal surface coil (Rapid Biomedical, Rimpar, Germany). IVIM measurements were performed with a single-shot echoplanar imaging sequence with a 100×100 matrix and a field of view of 100×100 mm², 9 slices with thickness of 3 mm, TR/TE=2600/90 ms, 8 signal averages, and 10 b-values (0, 25, 50, 80, 150, 300, 500, 800, 1200, 1600 s/mm²). For ADC and IVIM evaluation, multi-slice regions of interest of homogeneous appearing tumor tissue (excluding necrosis areas) were defined. The signal attenuations were fitted with either a monoexponential (M): $S(b) = S_0 \cdot e^{-bD}$ or biexponential (B) model: $S(b) = S_0 \cdot [f \cdot e^{-b(D+D^*)} + (1-f) \cdot e^{-bD}]$ with a maximum of 4 free parameters: initial signal S_0, (apparent) diffusion coefficient D, pseudo diffusion coefficient D^*, perfusion fraction (PF) f. We compared 4 models with 1 (**M1:** D), 2 (**M2:** S_0, D), 3 (**B3:** D, D^*, f), or 4 (**B4:** S_0, D, D^*, f) free parameters (in **M1** and **B3**, S_0 was set to the measured value $S(0)$). An example for all 4 fits is shown in Fig. 1.

The quality of the fit and the appropriateness of the model were assessed using the Akaike information criterion and the corresponding Akaike weights, which describe the probability that a certain model is appropriate for given data [4].

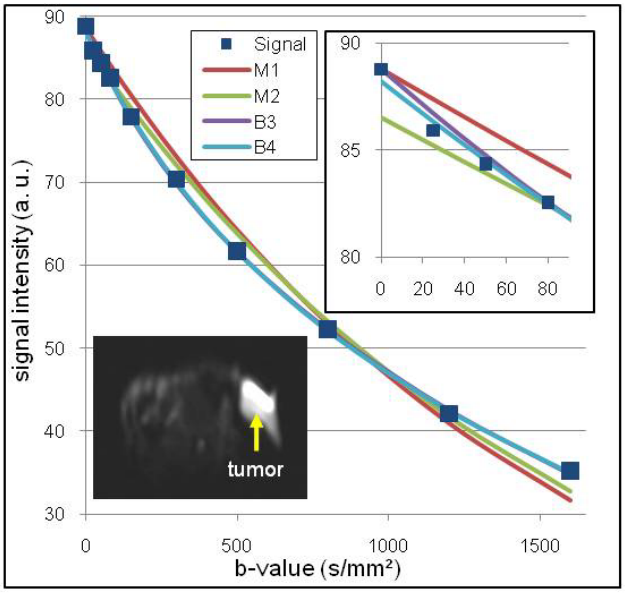

Fig.1: Signal attenuation and fitted models; inlay plots show zoomed view of data at small b-values and MRI data.

Results: Mean values and standard deviations of the model parameters are summarized in Table 1. In all 12 animals, the 3-parameter fit (**B3**) showed the highest Akaike weights ranging from 90.3% to 98.8%, and thus, is with very high probability the most appropriate model. The standard deviations of D^* and PF are slightly higher with **B4** than with **B3**. The monoexponential models exhibit very low Akaike weights typically below 1%.

Table 1: Mean values (std. dev.) of fit parameters and Akaike weights

Model	S_0 (a.u.)	D (10^{-3} mm²/s)	D^* (10^{-3} mm²/s)	PF f (%)	w_{Akaike} (%)
M1	–	0.717 (0.128)	–	–	0.2 (0.6)
M2	115 (77)	0.677 (0.113)	–	–	0.7 (1.7)
B3	–	0.562 (0.104)	4.73 (2.69)	13.1 (3.3)	**96.6 (3.0)**
B4	118 (79)	0.554 (0.101)	4.40 (2.75)	14.1 (4.3)	2.5 (2.4)

Conclusions: The evaluated tumor data show clear biexponential attenuation (as confirmed by the low Akaike weights for the monoexponential models). The comparison of the 3-parameter and 4-parameter biexponential models based on the Akaike weights results in a very strong preference of the 3-parameter model (with normalization to the signal at b = 0). With a 4-parameter model, the fits are only marginally improved (in terms of the sum of squares of the differences between data and model); at the same time, the parameter standard deviations of D^* and PF increase slightly. This indicates that, for our data, a 3-parameter model is sufficient and appropriate, the inclusion of S(0) as a fit parameter is not justified.

References: [1] Le Bihan D et al. Radiology 1988; 168: 497–505, [2] Koh D et al. AJR 2011; 196: 1351–1361, [3] Döpfert J et al. Magn Reson Imaging 2011; 29: 1053–1580 [4] Glatting G et al. Med Phys 2007; 34: 4285–4292