

Onset estimation for dual input DCE-MRI liver data : information criteria used to determine statistical optimality of global or pixel-wise onset estimation

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Introduction

Fitting a dual-input kinetic model to DCE-MRI data from liver is necessary to accurately capture the concentration time-course (CTC) behaviour seen in this organ. A parameter is therefore required to describe the relative arterial and portal contributions of the dual-input contrast delivery to each voxel, and typically the onset time of contrast enhancement is also estimated for each voxel. In practice, estimates of the arterial-portal fraction parameter and the onset time are largely influenced by only a few data points close to the onset time, so errors in these parameters are typically highly correlated. Therefore, reducing errors in the onset time estimates will tend to reduce errors in the arterial-portal fraction parameter.

The variability in the onset time estimates can be reduced by modelling and estimating the onset time as a single global parameter derived from all voxels simultaneously. Assuming this reduces the error in the onset estimate, it will also reduce the error in the arterial-portal fraction parameter estimates. The key question is therefore whether the differences between the true onset times and the global onset estimate are larger or smaller than the errors on voxel-wise onset time estimates. Since ground-truth is not available for in-vivo data this question cannot be answered directly, and so must be answered using statistical methods.

Theoretically there will be variations in the enhancement onset time over the liver, and *a priori* this is likely to be more pronounced in diseased states. However, from a statistical viewpoint, it is the relationship between the data sampling rate and the onset time variation that determines the need to model the onset time as a local voxel-wise parameter or as a single global parameter for the whole organ, or region of interest. In this abstract we propose using various statistical information criteria to determine whether the onset time should be modelled as a global or local parameter for DCE-MRI liver data acquired using two specific time-sampling protocols.

Methods

Data Acquisition Protocol DCE-MRI data were acquired coronally on a 1.5T Siemens Avanto using a 3D FFE sequence under sequential breath-hold at expiration, which gives highly reproducible registration of the liver¹. For protocol A₁, each breath-hold image was acquired in 5.6 sec, followed by a 6.4 sec breathing gap, and 20 images were acquired giving a total time of 4 minutes. For protocol A₂, two image volumes were acquired in 6 sec followed by a 6 sec breathing gap, and 40 images were acquired during the study. The imaging parameters for A₁ were TR/TE = 4.36/1.32 ms, FA = 24°, 20 slices @ 5mm thick, and for A₂ were TR/TE = 3.28/1.10 ms, FA = 18°, 12 slices @ 5mm thick, and for both NSA = 1, IPAT = 2, FOV = 350mm, 128x128 interpolated to 256x256 matrix. The dynamic scan was preceded by a calibration scan with the same parameters except FA = 2° to enable the dynamic sequence to be converted to contrast agent concentration.

Kinetic Model The dual-input model is given by $c_p(t) = \gamma c_A(t) + (1 - \gamma)c_V(t - t_p)$, where $c_A(t)$ and $c_V(t)$ are the arterial and portal CTCs, γ is a partitioning term with $0 < \gamma < 1$, t_p is the portal delay time and $c_p(t)$ is the overall input function curve. The input function components are modelled using a raised-cosine model² whose parameters are estimated from averaged patient data, as is t_p . The CTC uptake is described using a single compartment model, $c_i(t) = v_c k_{ep} c_p(t) \otimes \exp(-k_{ep}(t - \tau_0))$, which neglects any contribution from contrast agent in the blood plasma.

Data Fitting For the voxel-wise onset estimation, the parameters v_c , k_{ep} , γ and τ_0 are estimated by least-squares fitting of the CTC from each voxel in turn. During the optimisation v_c and γ are constrained to the interval [0,1] and k_{ep} is constrained to be positive. For the global onset estimation the optimization is stratified into two stages. In the inner stage v_c , k_{ep} and γ are estimated voxel-wise using least squares fitting for a given global τ_0 , and the sum of the residuals for all voxels is returned. The outer stage then uses the sum of the residuals as a cost function over which to optimise the global τ_0 .

Model Selection The Bayesian³ (BIC), corrected Akaike⁴ (AICc), and Hannan-Quin⁵ (HQIC) Information Criteria are used to indicate which model is statistically preferable. These are defined by:

$$\text{BIC} = -2 \ln(L) + k \ln(n), \quad \text{AICc} = -2 \ln(L) + 2nk / (n - k - 1), \quad \text{HQIC} = -2 \ln(L) + 2k \ln(\ln(n)),$$

where L is the value of the likelihood function (related to the least-squares residual), n is the total number of data values and k is the total number of parameters in the model. These criteria are designed using information theoretic arguments to trade off the quality of fit to the data with the number of parameters in the model. The given criteria differ in the second term which penalises over-parameterised models. With N_p voxels and N_T time-points per CTC, for the voxel-wise onset model $n = N_p \times N_T$ and $k = 4 \times N_p$, while for the global onset model n is the same and $k = 3 \times N_p + 1$.

Results All three information criteria were computed using both voxel-wise onset fitting and global onset fitting for 10 data sets – four acquired using protocol A₁ (patient IDs 1-4), six using protocol A₂ (patient IDs 5-10). The CTCs in each case were obtained from a ROI drawn around the whole liver in the central slice, and contained between 3,700 and 13,000 voxels. The figure shows the difference between the information criteria for the voxel and global onset fitting, so that a preference for global fitting is indicated by a negative value. It is important to stress that the value of these information criteria *should not* be used to indicate the strength of the preference, but only which of the two models is statistically preferable.

Conclusions The BIC is known to most strongly penalise over-parameterised models, and in this case it unanimously supports the global onset model. The HQIC prefers the global onset model in 8/10 cases, and for the two cases where the voxel-wise model is preferred, one is from data acquired with protocol A₁, the other with A₂. The corrected AIC is equally split in preference for the two onset models, and once again around half of each group are with A₁ data, the other with A₂ data. Only the BIC is unambiguously prefers the global onset model, but overall these data indicate that for both data acquisition protocols the global onset estimation model is to be preferred.

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References

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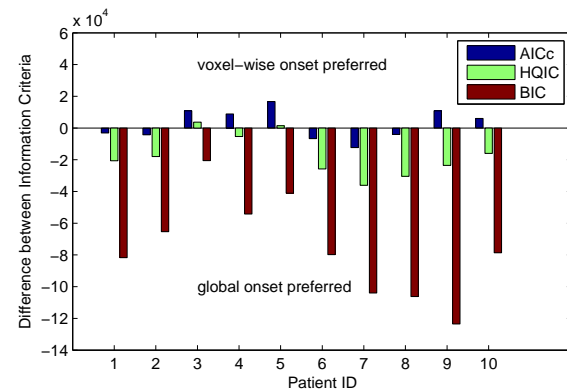


Figure 1 : Difference between various information criteria for voxel-wise and global onset estimation for 10 cases.

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⁵Hannan EJ, *Annals of Statistics.* 1980; **8**, 1071-1081.