AUTOMATIC DETECTION OF BOLUS ARRIVAL TIME IN DYNAMIC MRI STUDIES

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Abstract: Methods for automatic detection of bolus arrival time in dynamic MRI studies (Dynamic Susceptibility Contrast) are presented. The first method uses gamma-variate function fitting to data and thresholding. The second method is based only on original signal thresholding. Results achieved for clinical data are presented and discussed. Presented methods are implemented in automatic maps synthesis software which is prepared for clinical trials.

Introduction

Parametric imaging become more and more popular. This includes Dynamic Susceptibility Contrast DSC-MRI [1], ASL MRI [2], dynamic PET/SPECT [3], dynamic active thermography [4], etc. Parametric images represents values of reconstructed parameters for assumed tissue/activity model. This extends the structural imaging towards functional imaging. Qualitative parametric imaging could be extremely useful technique, however quantitative imaging could be even much more powerful, especially using the same modality as used for structural imaging. This is a reason why DSC-MRI is an active area of research in quantitative cerebral perfusion. In this work we are investigating the automatic detection of bolus arrival time methods.
Automatic detection of BAT is important for automatic parametric imaging using DSC-MRI. Reliable detection of BAT can be used in an Arterial Input Function – AIF - detection (including local AIFs) and as a valuable clinical indicator of blood transport problems.

MRI-DSC imaging

In the DSC-MRI brain studies, after injection of a bolus of the contrast agent (Gd-DTPA), series of images are measured (fig. 1).

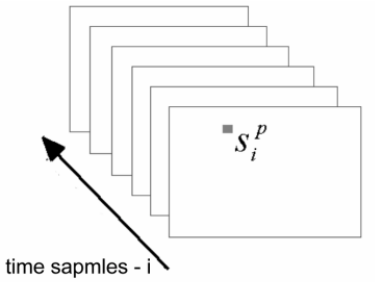

Figure 1: Measured series of images: a composition of 1D signals S for pixel number p.

This time-sequence data presents local voxel activity of the contrast (blood) flow and it's distribution. It is assumed, that measured MRI signal values are proportional to the contrast concentration [5]:

$$C_c(t) = -\frac{1}{k \cdot TE} \ln\left(\frac{S_c(t)}{S_0}\right), \qquad (1)$$

where:
C(t) – the tracer concentration in time,
TE – echo time,
S_0 - measured MR signal intensity without a tracer,
$S_c(t)$ - measured MR signal intensity after a bolus of the contrast agent injection,
k – a proportionality constant.

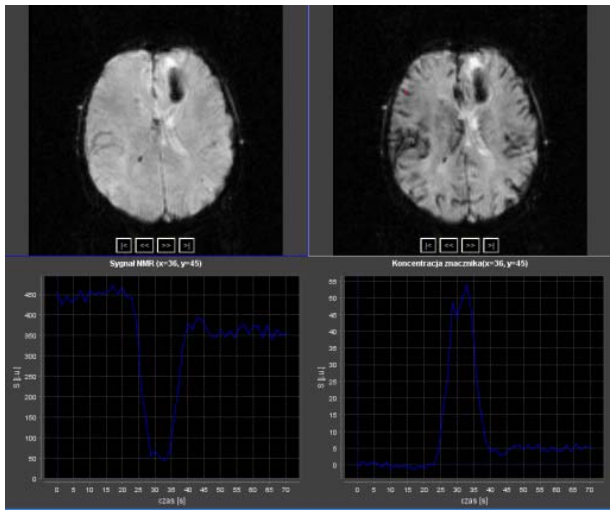

Figure 2: Signal to concentration conversion: (left – down) image before contrast arrival, image with

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maximum contrast presence, extracted signal intensity changes for a vessel, calculated contrast concentration in the same vessel.

Contrast concentration as a function of time is measured for brain supported arteries. This function can be estimated as the arterial input function (AIF). Assuming ideal conditions this function should be an ideal impulse function, so measuring the output function (impulse response) one can specify properties of the object under study, including mass flow, mass volume, and mean transfer time. Since AIF is not an ideal impulse function (dispersion and delay) and because in DSC-MRI measurements are performed from a volume of interest (VOI), deconvolution should be used to calculate VOI impulse response F R(t) [6]:

$$C_t(t) = \frac{\rho}{Kh}\int_0^t C_a(\tau)\left(F\,R(t-\tau)\right)d\tau\,, \tag{2}$$

where:

$C_a(t)$ - contrast concentration in the artery (e.g., Middle Cerebral Artery) – Arterial Input Function AIF,

$C_t(t)$ - contrast concentration in the tissue,

$\frac{\rho}{Kh}$ - scaling factor (quantitative description)

ρ – mean tissue density of a brain, ρ=1.04 g/mol;

Kh – hematocrit ratio (large to small arteries) *Kh=(1-Hd)/(1-Hm); Hd=0.45*; *Hm=0.25*;

*F*R(t)* – scaled impulse response (residue function) inside VOI,

R(t) - represents fractional tissue concentration:

$$R(t) = 1 - H(t) = 1 - \int_0^t h(\tau)d\tau\,, \tag{3}$$

where:

h(t) – a transport function – an impulse response (an ideal instantaneous unit bolus injection).

Distribution of transit times through the voxel depends on the vascular structure and the flow. The model is based on tracer kinetics for non-diffusable tracers – contrast material remains intravascular.

Scaled impulse response can be calculated using deconvolution (with *FFT* or *SVD* to eliminate singularities). Since *R(t=0)* should be equal to 1, then $F \cdot R(t=0) = F = CBF$ (Cerebral Blood Flow).

Cerebral blood volume (proportional to the normalized total amount of tracer) can be calculated as

$$CBV = \frac{\int_0^\infty C_t(\tau)d\tau}{\frac{\rho}{Kh}\int_0^\infty C_a(\tau)d\tau}\,, \tag{4}$$

Based on central volume theorem, Mean Transit Time – MTT - (average time required for any given particle of tracer to pass through the tissue after an ideal bolus injection) can be estimated as

$$MTT = CBV/CBF. \tag{5}$$

Bolus Arrival Time describes quantitatively the moment when the bolus reached the measured VOI. The BAT distributions through the brain offer added value to diagnostics and the knowledge of the accurate BAT is extremely important e.g. in recognition of AIF, in MTT estimation, etc. Signal delays of 1 to 2 seconds (usually equal to sampling period) can introduce an approximately 40% underestimation of CBF and 60% overestimation of MTT [7]. In parametric imaging the typical manual BAT extraction is not useful (e.g. 256x256 signals). In [8] authors have proposed (declaring as the first approach– 2003) the automatic BAT recognition method based on piecewise continuous regression models.

Automatic detection of BAT is important for automatic parametric imaging using DSC-MRI. Calculated three types of quantitative parametric images (CBF, CBV, MTT), synthesized under strictly controlled procedure, offer additional and important information for brain studies.

Material

Based on the introduced description of quantitative limitations of DSC-MRI different simulations were performed using Mathematica (Wolfram Research) and Java prepared applications. The concentration signal was modelled as

$$C(t) = \begin{cases} K(t-t_0)^{\beta}\cdot e^{-\alpha(t-t_0)}, t > t_0 \\ 0, t \le t_0 \end{cases}; \tag{6}$$

where:

K, α, β model parameters (used β=3, α=2/3),

t_0 - bolus arrival time (BAT).

Recirculation component was included in C(t) as a scaled Gaussian function shifted in time and exponential component (1-exp(-t/T)). Resulted AIF was then convolved with residue impulse response function R(t), described by (3). MTT was set form the <1s,10s> range, resulting in different C(t) for simulated tissues.

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Material – clinical data

We collected images for in-vivo measurements (1.5T MRI SE-EPI with: 12 slices, 50 samples, TR=1.25-1.61s; TE=32-53ms; slice thickness 5-10 mm; 60 series - 3000 images). Images were collected for typical cases and for cases where Blood-Brain Barrier was damaged. Using own, created software we extracted signals and concentration curves for typical region of interests (ROI): arteries, grey matter (GM) and white matter (WM). Typical SNR values (defined as a ratio of a signal amplitude to a standard deviation of baseline noise) were 30 (arteries), 20 (GM) and 15 (WM). However for some cases (BBB disruption, low contrast dose) the SNR was reduced up to 3-5.

Method

In [8] authors proposed (declaring as the first approach– 2003) the automatic BAT recognition method based on piecewise continuous regression models. They verified the method based only on synthetic, simulated data using (6) as a signal model. We verified the BAT detection method with clinical data described earlier. The resulted BAT (in ~60% off all normal cases) were shifted in time in comparison to true BATs (marked by experts). Almost 10% of the BATs were shifted by two sampling periods (TR). We conclude the reason as curvature of the gamma-variate function near the BAT does not describe accurately the real signal. This is especially a case in the global gamma-variate function fitting to DSC-MRI concentration signals (overall fitting quality is high, but not for BAT).
The proposed method is based on the following assumptions:

- SNR of the MR signal (not concentration signal as in [8]) > 3 ,
- a signal enhancement duration is at least 10 seconds;
- the baseline is measured at least 10s before BAT (noise estimation).

The first step of the BAT detection is a gamma-variate (4 parameters including BAT) function fitting (6) to MR signal data (after baseline shift and negation). Since most experiments (similarly to performed experiments using piecewise continuous regression) produced underestimation of BAT (lower than the true BAT as in [8]) thus we apply the next step. Then we apply threshold operator

$$BAT1 = \min\{t : S_{fitted}(t+1) > T\}, \qquad (7)$$

where:

T – the threshold value based on the SNR of the baseline signal $S_c(t)$;

T=mean($S_c(t)$)+stddev($S_c(t)$).

We propose to use original signal instead of the derived concentration function (1) to eliminate any non-linear modifications. The thresholding is performed on fitted signal so a noise is assumed to be filtered (assumed original signal recovered using the process model).
The method requires the fitting operation which is costly. In parametric imaging we are processing all signals from the region of interest, usually the image. This leads to the total number of signals equals to the total number of pixels.
Calculation reduction requires to eliminate fitting operation. Keeping in mind assumptions (i.e. high SNR) the modified threshold operator can be proposed as:

$$BAT2 = \min\{t : each\ S(i) > T; i \in \{t+1..(t+nTR)\} \qquad (8)$$

where:

TR – sampling interval,

n – number of samples in the enhancement region, usually *n TR*=10-25s.

The second method can be theoretically justify because signals with very low SNR (according to the previously defined SNR for this study) are no reliable and medical diagnosis based on such signals is a risk.

Results

Both BAT detection method variants were applied to measured data and synthetic data constructed using gamma-variate signal model (4 parameters, including BAT). In case of clinical data we tested randomly chosen signals from three compartments: vessel, grey matter and white matter. Signals were extracted and presented as one dimensional charts using linear interpolation between samples.
Almost all detected BAT values were in agreement with the expert evaluation. Only in one case (for typical DSC-MRI data, SNR>5) there was a difference in detected BAT values (i.e., BAT2<BAT1). However the difference was only 1 TR.
In case of data sets for lower SNR (<5) 30 percent of BAT values were overestimated (i.e. greater than true BAT). In this case the fitting procedure improves results only in 10% cases. The reason was that the fitting procedure for other signals was not successfully competed. Similar results were obtained for simulated data. In case of high SNR the all BAT values were detected properly. This could be expected since the simulation model and fitting model are the same.
In figure 3 different signals are presented with detected BAT values presented as values related to the beginning of the measurement.

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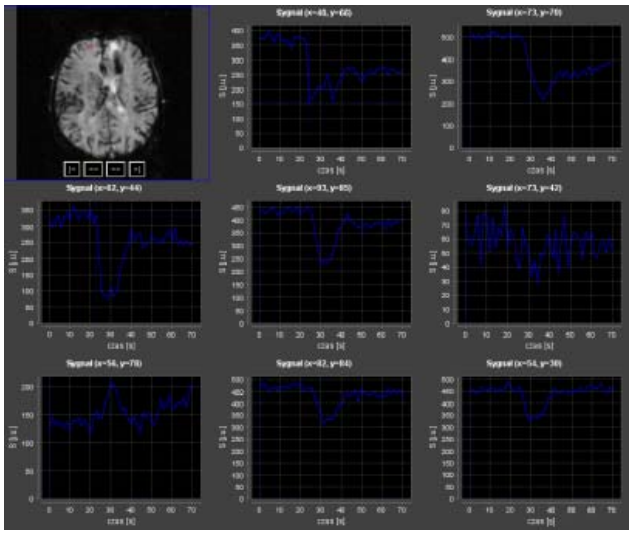

Figure 3: BAT detection for different kind of signals (including low SNR) indicated within the object: (left-down) BAT=21.45; 24.31; 22.88; 24.31; 27.17; 17.16; 25.74; 24.31.

Discussion and conclusion

Proposed methods produced very good BAT detection results. Even for rare, very low SNR almost 70 percent of BAT values were estimated accurately. This is very interesting result since usually SE-EPI method (used in this study) in DSC-MRI is characterized by lower SNR than GE-EPI.
Other methods were investigated based on signal filtration (fig. 4). However the best results were achieved using gamma-variate model fitting and thresholding. Especially after data reduction (i.e. reduction of data samples after the signal maximum or a few samples after) the better fitting quality was observed in the BAT region. Further studies will be performed on clinical data measured from other MRI-DSC devices. We are looking forward to measure image sequences with sampling time lower that 1s.

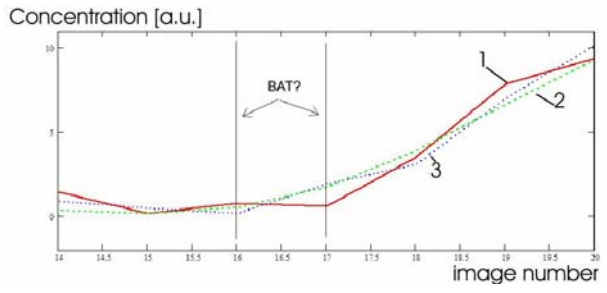

Figure 4: The role of data pre-processing in BAT detection: 1- measured signal (linear interpolation between samples), 2 – signal filtered using wavelets (soft thresholding), 3 - signal filtered in frequency domain (low pass).

Performance tests showed than the modified BAT2 method runs extremely fast. The tests performed on Pentium IV 2,66GHz, 1G RAM, Windows XP indicated that the average time required to process all image signals (a sequence) was lower than 1 ms.
The method has been implemented in the DSC-MRI brain analysis software. After prototyping algorithms were implemented in DSC-MRI software package created in Java (Sun JDK 1.5). The software operates on original DICOM image data, extracts user-defined time series, allows to enhance and analyse images and generates parametric maps (BAT, rMTT, rCBV, rCBF) with legends (colour lookup table description). In Fig. 5 the screen capture is presented as an example of the graphical user interface and image presentation.

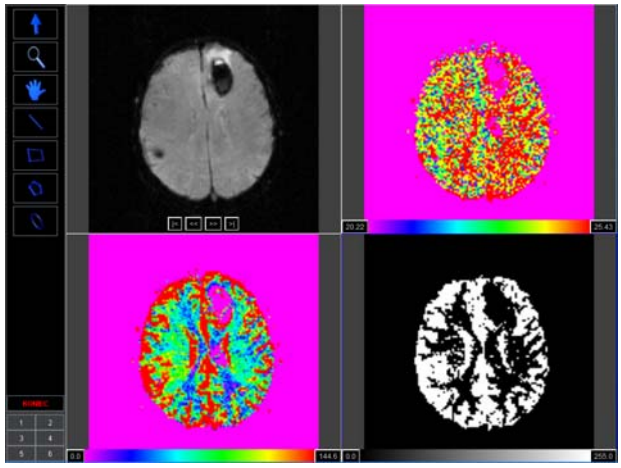

Figure 5: An example of the graphical user interface and image presentation (left top to right down): original image time series presented slice by slice, BAT image, rCBV image, image mask generated in the pre-processing stage in AIF detection

Currently the software is prepared for clinical research. There are many unsolved problems for standardization of parametric imaging and visualization of DSC-MRI data which is extremely important for clinical use. Some of them are: value ranges and units for semi-quantitative description, colour lookup tables, etc.

Acknowledgements

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