Automated Selection of Arterial Input Function (AIF) Pixels in DCE-MRI

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Introduction: Dynamic contrast-enhanced (DCE) MRI in combination with pharmacokinetic modelling allows the estimation of tissue perfusion, which is considered to be a capable tool for monitoring diagnostic changes during oncologic therapy [1]. To reliably detect changes in perfusion between consecutive measurements all other sources of variability must be minimized. While variations in contrast media injection can be avoided by using an automated injection pump, variations in cardiac output can be dealt with by measuring the arterial input function (AIF) during each perfusion measurement.

One of the biggest challenges in estimating the AIF from a dynamic T1w images series is to identify the most adequate arterial pixels that will define the blood uptake curve. The method used for the pixel selection is crucial for guaranteeing a high reproducibility. The generally used manual outlining of ROIs is naturally prone to introducing large variations, so that recently more sophisticated automated AIF detection methods have been developed [2-9]. These methods are either based on descriptive scores (peak, slope, time of peak, etc) derived from the pixel's signal-time-curve (STC) [2,3,5,6,8,9] or employ sophisticated mathematical techniques, such as independent component analysis [4] or fuzzy clustering [7].

Score/threshold based methods tend to be somewhat arbitrary, are often very specific and thus difficult to apply to other imaging locations, and complicated mathematical techniques are not easily implemented. Therefore, there is still a need for a simple, robust, and versatile AIF detection technique. We have developed a simple algorithm that reliably selects AIF pixels, while using available prior information (shape and position of artery) and requiring only minimal user interaction.

Materials and Methods: ***Imaging.*** T1-w images were acquired on a 1.5 T scanner (Siemens Magnetom Sonata) before, during, and after contrast media injection (Magnevist, Schering, Berlin, 0.15ml/Kg, 40–60s) every 3 s over a period of 7–8 minutes using a rapid spoiled GRE sequence (SR-TurboFLASH: TR/TE/TI/FA = 7.0ms/3.86ms/120ms/12°, FOV/TH/matrix = 350mm/7mm/256x192). When necessary, image registration was performed (*TurboReg* [10] plugin of *ImageJ*) prior to applying the AIF algorithm, which was developed in MATLAB (v6.5.1, The Mathworks, Inc., Natick). ***Algorithm.*** Our AIF algorithm consists of the following steps:

1. User places a seed in the most relevant artery. – *Eliminates need to search whole image.*
2. Search for pixels with highly correlated STC in concentric ring-shaped masks of increasing radius. – *Ensures adaptiveness and flexibility of method.*
3. Terminate search when ring contains no highly correlated pixels. – *Utilizes known artery shape.*
4. Define AIF as mean of half of the detected pixels with highest signal enhancement. – *Eliminates partial volume effects.*

Searching the whole image for AIF pixels [5,6,8,9] is inefficient for two reasons: (I) much effort is required to reject false positives in remote regions and (II) ideally only one relevant feeding artery should be detected rather than all arteries. The position of such an artery can easily be identified by the user in most DCE-MRI situations. Hence, the only user interaction required by our algorithm is placing a seed (rigid 3x3 pixel ROI) at the centre of the relevant artery.

The mean STC of the seed is then used to search within its proximity for pixels with a highly correlated STC, making the algorithm adaptive and versatile. To reduce noise a simple moving average filter (MAF, 9pt kernel, kernel size should be optimized for given time resolution and SNR) was applied to all STCs. The algorithm successively evaluates the pixels in ring-shaped masks of increasing radius (Δr must equal diagonal of a pixel) that are concentric around the seed, utilizing the circular nature of arteries. The search terminates when a mask contains no highly correlated pixels, where a correlation < 0.95 was used a rejection criteria.

The above criteria will select all pixels that contain arterial blood, i.e. also those containing part plasma part vessel wall. Methods that select almost all arterial pixels (e.g. Rijpkema *et al* [9]) are susceptible to partial volume and flow artefacts, so that some approaches select only the highest scoring single pixel [5,6] or 25 pixels [3]. The number of pixels selected must be optimized to balance susceptibility to these artefacts and SNR. Maintaining adaptiveness, we defined the AIF as the mean of the 50% of the detected pixels with the highest relative enhancement. The relative enhancement, $RE = (SI_{max} - SI_{min}) / SI_{min}$, was determined after extensive noise reduction filtering (MAF, 9pt, 3x) to guarantee robustness.

Results and Discussion: We tested the developed AIF detection algorithm on DCE-MRI data from rectum and oesophagus carcinomas, lower limb osteosarcomas, Wilm's tumours, and lymphomas. The search algorithm stages are illustrated for sample data in *Fig. 1*. Selecting the top 10,..,50% detected pixels usually did not have a great effect on the AIF (*Fig. 1c*), hence 50% was chosen for better SNR. The seed size requires the artery to cover at least nine (3x3) pixels.

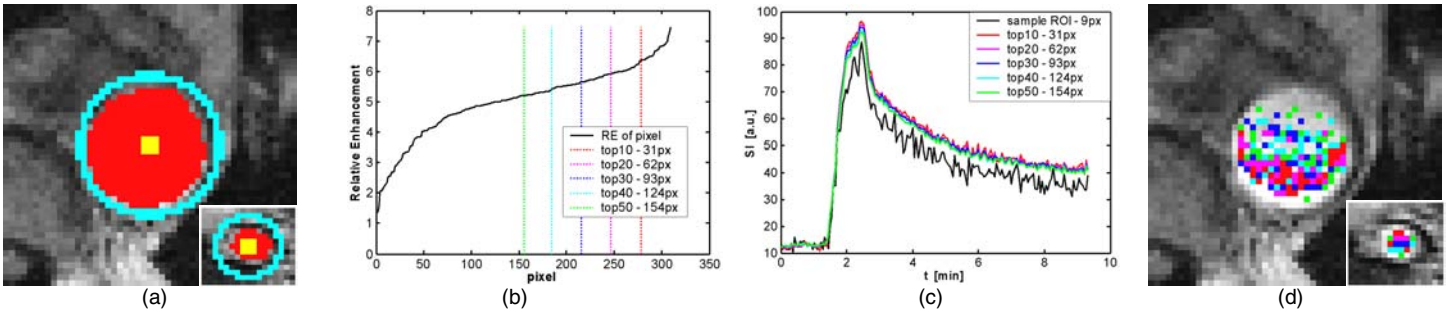

Fig. 1: *Examples of use on a large (a-d) and small artery (insert a,d).* ***a)*** *MR image showing the seed (yellow), the detected pixels (red), and the first 'empty' ring mask (cyan),* ***b)*** *the relative enhancement for all detected pixels, with indicators for the top 10, 20, 30, 40, 50 %,* ***c)*** *the unfiltered STC for the five ROIs corresponding to the top 10-50% pixels as well as the STC of the seed (black),* ***d)*** *MR image with the selected 50% AIF pixels marked in colour (according to them being in the top 10-50%).*

The algorithm was successfully used to extract the AIF from 138 DCE data sets with slice positions in the neck, thorax, abdomen, and lower extremities with false positives in only 2 of 138. In some cases other arteries are very close to the user marked artery, which will result in several arteries being detected. Hence a useful addition to the described algorithm is to automatically select only the subset of pixels that are part of the *4-connected* object overlapping the centre of the seed (use MATLAB's *bwselect*). We also included the option to manually exclude detected pixels, but the automatic subset selection worked in 98% (135/138) of the cases. The reproducibility was assessed by analyzing three data sets repeatedly (10 times), and calculating the coefficient of variation of *AIF(t)* for each *t*, giving excellent values (mean ± stdev) of c_v = 0.050% (±0.029), 0.040% (±0.021), and 0.047% (±0.031).

Previous studies have shown that the accuracy and sensitivity of DCE-MRI analyses to change can be improved by use of automated AIF identification methods [2,3,5-8]. The new method described here is easy to implement, ensures a high reproducibility, but is also robust and flexible enough to be suitable for various imaging targets. Therefore, it may help to improve the accuracy of DCE-MRI tumour perfusion imaging on its way to becoming a more reliable clinical diagnostic tool.

References: [1] Knopp MV *et al* (2003) Mol Cancer Ther, 2(4):419-26. [2] Ashton EA *et al* (2004) Proc ISBI, 824-27. [3] Ashton EA *et al* (2004) Proc ISMRM, 12:147. [4] Calamante F *et al* (2004) MRM, 52:789-97. [5] Carroll TJ *et al* (2001) Proc ISMRM, 9:1578. [6] Carroll TJ *et al* (2003) Radiology, 227:593-600. [7] Murase K *et al* (2001) JMRI, 13:797-806. [8] Reishofer G *et al* (2003) Proc ISMRM, 11:2190. [9] Rijpkema M *et al* (2001) JMRI, 14:457-63. [10] Thévenaz P *et al* (1998) IEEE Trans Image Proc, 7(1):27-41.