AUTOMATED DETERMINATION OF THE ARTERIAL INPUT FUNCTION FOR MR PERFUSION ANALYSIS

E.D. Morris (morris@sensor.com), T.A. Tasciyan, J.W. VanMeter, J.M. Maisog, T.A. Zeffiro
Sensor Systems, Sterling VA20164

ABSTRACT

GOAL To develop an automatic algorithm for identifying arterial voxels in dynamic susceptibility-contrast MRI data for constructing the arterial input function (AIF).

INTRODUCTION Parametric maps of CBF and MTT can be derived from dynamic susceptibility changes by curve-fitting the “first-pass” tissue response then numerically deconvoluting it from the AIF. Deconvolution yields a “residue function” which is scaled by CBF. The singular value decomposition deconvolution, however, is sensitive to the shape of the AIF. Thus, the accuracy of the input curve may determine the quality of the deconvolution, and the quality of the CBF and MTT maps. AIF is typically determined by manual identification of “arterial” pixels in the images according to their anatomic location. This task is made difficult by the poor spatial resolution and poor blood-to-tissue contrast of dynamic EPI scans. Although the image data are acquired as low resolution in space due to acquisition constraints, they have high tissue-contrast, temporally. Thus, we discriminate arterial from non-arterial voxels by inspecting their signals in time.

We present a two-stage method for automatically deriving an AIF from the dynamic image data based on expected characteristics of arterial concentration curves. Candidate input functions are generated by maximizing three “arterial-likelihood” metrics. The “best” of the three candidate curves is chosen by a scoring system based on the first four moments of the AIF distributions. After fitting, AIF curves chosen automatically and manually appear comparable and yield comparable CBF results.

Our automated algorithm is integrated into MEDx v3.3 (Sensor Systems).

RESULTS

PERFORMANCE OF THE ALGORITHM

1. TEST DATA
Below, are some moderately noisy dynamic susceptibility contrast data used to test the automated algorithm. For this data set the algorithm selected 24 arterial voxels (a fixed fraction of the number of voxels in the brain). The AIF was created by averaging the time courses of these top voxels. In contrast to the data shown in the middle column, the highest scoring metric was M1.

2. ARTERIAL MAPS
Some of the automatically and manually selected arterial voxels are shown below. The auto- voxels are shown on an M1 map because it was deemed optimal. The manual voxels are shown on a comparable peak-height map (because it is generally best for visual location of voxels). At the right are plots of the respective AIF data (auto, manual) the mean tissue curve (blue) and the curves fitted to the pre-recirculation points. In this case, the manual curve is quite a bit higher but the timing is similar.

3. CBF MAPS
CBF maps created by both auto and manual methods are shown. The maps have been scaled by their respective global means. Agreement is quite good save for a scaling factor. We can quantify the similarity/differences in the maps with some simple statistical parameters.

4. COMPARISON MAPS
The correlation between the maps can be characterized by the correlation coefficient, r. In the case of the CBF maps, above, r = 0.996. Given the large degrees of freedom (corrected for spatial smoothness) the probability of this correlation occurring by chance is 0. Nevertheless, the measure is meaningful. If we use a square wave as wide as the mean tissue curve as our AIF, the r value drops to 0.8. Another way of confirming the correlation of the images is via their ratio which is shown at left with its histogram overlaid. The absolute differences between the images are gauged via the $X^2$ parameter. $X^2 = 409$ but again, with a large df, the chance of this or a larger $X^2$ value occurring is 1. The local $X^2$ map is created by calculating the $X^2 = \frac{[\text{manual} - \text{auto}]^2}{\text{manual}}$, at every pixel and then blurring with a 3x3 filter in-plane. No prominent clusters of difference are apparent. We have analyzed noisier data with similar results.

SUMMARY

- An automatic method is desirable for its ease of use and reproducibility.
- Multiple arterial metrics are robust for finding an input curve even in very noisy data.
- The high correlation between the auto- and manual perfusion maps demonstrates that CBV/CBF analysis is possible without operator intervention.

The authors thank Drs. J. Frank and S. Warach of NIH and Dr. G. Harris of MGH and their colleagues for use of their data.

STRATEGY

ALGORITHM DESIGN

Our interest is in designing an algorithm for finding AIFs that is fast and robust. Therefore we restrict ourselves to those methods that:

- Do not require curve-fitting (or other iterative procedures) at each voxel.
- Do not fail in the presence of very noisy data.

ALGORITHM EVALUATION

We evaluate our automated AIF algorithm both visually and by its impact downstream on the perfusion maps. That is, we want to locate arterial voxels but we are primarily concerned with whether or not the resultant CBF and CBV images made automatically are distinguishable from those made by selecting arterial voxels manually. Specifically, we ask:

- What is the correlation (r) between auto- and manual images?
- What is the difference ($\chi^2$) between auto- and manual images?

METHODS

PRE-CONDITIONING OF IMAGE VOLUMES

1. MOTION CORRECTION - OPTIONAL
Any algorithm that processes pixels across time is sensitive to subject movement. The greatest effect occurs at the edges of the image.

2. MASKING - REQUIRED
Masking is needed to remove non-brain voxels which can interfere with the automated AIF algorithm. It can also be used to trim the images of edge pixels that are corrupted by motion artifacts. The mask is made from a mean image which is thresholded to remove the background and filtered via morphological opening to eliminate non-brain clusters.

3. ARTERIAL ALGORITHM FOR ARTERIAL CURVES

3.1. ARTERIAL LIKELIHOOD METRICS
Each voxel in the image is evaluated for its “arterial-ness”. Three Arterial Maps are made — one for each map metric based on one or more characteristics of the concentration-time curve at each voxel.

\[
\text{Metric}_0 = \frac{1}{\omega} \left[ W_p \cdot T_0 \cdot S \cdot \omega \right],
\]

\[
\text{Metric}_1 = \frac{H_p}{\left[ W_p \cdot T_0 \cdot S \cdot \omega \right]},
\]

\[
\text{Metric}_2 = \frac{H_p}{\omega^2},
\]

where $H_p$, $W_p$, $T_0$, $S$ are peak height, peak width, take-off time, initial slope respectively. $\omega$ is a penalty function related to the distance of a voxel from the center of the image volume. Example maps for each metric are shown below. The highest scoring pixels are shown in white. Recall that only one slice of an entire volume is shown.

4. ARTERIAL LIKELIHOOD MAPS - CHOOSE TOP VOXELS
Arterial maps for each metric are constructed by averaging the time courses associated with the voxels having the highest values of the respective map metrics. The maps are explained above. Notice that the Metric 2 curve peaks latest. Red curves are the respective arterial time-courses; blue curves shown in each panel are the same mean tissue curve. White marker indicates peak time of mean curve.

ALGORITHM DESIGN

Our interest is in designing an algorithm for finding AIFs that is fast and robust. Therefore we restrict ourselves to those methods that:

- Do not require curve-fitting (or other iterative procedures) at each voxel.
- Do not fail in the presence of very noisy data.

ALGORITHM EVALUATION

We evaluate our automated AIF algorithm both visually and by its impact downstream on the perfusion maps. That is, we want to locate arterial voxels but we are primarily concerned with whether or not the resultant CBF and CBV images made automatically are distinguishable from those made by selecting arterial voxels manually. Specifically, we ask:

- What is the correlation (r) between auto- and manual images?
- What is the difference ($\chi^2$) between auto- and manual images?

METHODS

PRE-CONDITIONING OF IMAGE VOLUMES

1. MOTION CORRECTION - OPTIONAL
Any algorithm that processes pixels across time is sensitive to subject movement. The greatest effect occurs at the edges of the image.

2. MASKING - REQUIRED
Masking is needed to remove non-brain voxels which can interfere with the automated AIF algorithm. It can also be used to trim the images of edge pixels that are corrupted by motion artifacts. The mask is made from a mean image which is thresholded to remove the background and filtered via morphological opening to eliminate non-brain clusters.

3. ARTERIAL ALGORITHM FOR ARTERIAL CURVES

3.1. ARTERIAL LIKELIHOOD METRICS
Each voxel in the image is evaluated for its “arterial-ness”. Three Arterial Maps are made — one for each map metric based on one or more characteristics of the concentration-time curve at each voxel.

\[
\text{Metric}_0 = \frac{1}{\omega} \left[ W_p \cdot T_0 \cdot S \cdot \omega \right],
\]

\[
\text{Metric}_1 = \frac{H_p}{\left[ W_p \cdot T_0 \cdot S \cdot \omega \right]},
\]

\[
\text{Metric}_2 = \frac{H_p}{\omega^2},
\]

where $H_p$, $W_p$, $T_0$, $S$ are peak height, peak width, take-off time, initial slope respectively. $\omega$ is a penalty function related to the distance of a voxel from the center of the image volume. Example maps for each metric are shown below. The highest scoring pixels are shown in white. Recall that only one slice of an entire volume is shown.

4. ARTERIAL LIKELIHOOD MAPS - CHOOSE TOP VOXELS
Arterial maps for each map are constructed by averaging the time courses associated with the voxels having the highest values of the respective map metrics. The maps are explained above. Notice that theMetric 2 curve peaks latest. Red curves are the respective arterial time-courses; blue curves shown in each panel are the same mean tissue curve. White marker indicates peak time of mean curve.

5. ARTERIAL CURVES - CALCULATE MOMENTS
The shapes of the three candidate curves shown below, are characterized by evaluating four parameters related to the moments of their distributions. The area, mean-time, variance-in-time and skew of the curves are related to the first four moments of the curves. The highest scoring curve based on a weighted scoring system is chosen as the arterial input data. Points awarded for the best and next best curves as follows:

- Large area under curve: 4, 2 points.
- Early center of gravity: 4, 2 points.
- Low variance in time: 2, 1 points.
- Large positive skew: 2, 1 points.

For the curves shown above, the scores are $M_0(9) > M_0(7) > M_0(2)$.

6. CURVE-FITTING
Arterial curve data are fitted to a (linearized) gamma-variate. Points used for fitting lie between $T_0$ and the beginning of recirculation.

MANUAL SELECTION OF ARTERIAL VoxELS

7. USE OF PEAK HEIGHT (METRIC 2)
In manual generation of the AIF, an operator must visually identify arterial voxels. We have found that the peak height of the concentration curve (coupled with knowledge of anatomy) is quite useful for identifying arterial voxels. Generally the easiest voxels to locate are part of the Circle of Willis and middle cerebral arteries (see figure.) Note: in order to make a fair comparison between automated and manual methods, the number of arterial voxels contributing to the AIF was held constant.