Automatic Reference Selection Method for Unsupervised Artery/Vein Separation in Time-Resolved Contrast-Enhanced Magnetic Resonance Angiography

F. Santini[1], S. G. Wetzel[2], and K. Scheffler[1]

[1]MR-Physics - Department of Medical Radiology, University of Basel, Basel, Switzerland, [2]Department of Medical Radiology, University of Basel, Basel, Switzerland

Introduction. Time-resolved contrast-enhanced Magnetic Resonance Angiography (CE-MRA) allows the visualization of the passage of a contrast agent bolus from the arterial to the arterio-venous phase, thus giving diagnostically-effective information in all vascular diseases, ranging from arterio-venous malformations to stenosis and occlusions. For an appropriate diagnosis, it is necessary to suppress the background structures and remove venous overlay from the arteriogram and arterial overlay from the venogram, which is usually done with post-processing techniques. The most effective methods for this task rely on the analysis of time courses of the brightness of each voxel in the dataset, which are compared to arterial and venous reference time courses using some measure of similarity (Cross-Correlation [1], Double-Reference Correlation [2], and more). All these methods require manual selection of the references, thus increasing the time needed to apply the technique, and decreasing the reproducibility of the results because a new element of variability is introduced. In this work, an algorithm based on a modified *k-means* cluster analysis that automatically identifies reference time courses is presented. This algorithm was specifically optimized to work with Double Reference Correlation Analysis.

Materials and Methods. 3D datasets of the head with a time resolution of 1.5 seconds were acquired during the first pass of a contrast agent (Gadolinium-DOTA) bolus with a T1-weighted Radio-Frequency spoiled Fast Low-Angle SHot (FLASH) sequence (TR=1.74ms, TE=0.64ms, flip angle α=15°, Matrix = 128x128x56, field-of-view = 255x255x123.2mm^3, resolution = 2.0x2.0x2.2 mm^3), on a 1.5T scanner (Magnetom Avanto, Siemens, Erlangen, Germany), and then transferred to a separate personal computer for data post-processing using Matlab (The Matworks, Natick, MA). The basic assumption of our technique is that the voxels of a dataset can be separated into three sets: arterial, venous and background set. Each set has a characteristic time course which differentiates it from the other two sets, because they are affected by the passage of the contrast agent bolus in different ways. Voxels belonging to background structures represent around 90% of the image, and are characterized by a small variance in the signal because they are virtually not affected by the bolus. They are therefore removed from further calculations by applying a threshold on the signal variance. Considering each time point as a different coordinate in a multi dimensional vector space, the remaining time courses form separate clouds and can be divided into clusters through a modified version of the *k-means* clustering algorithm. This algorithm also allows the identification of the center points of the clusters (centroids), which will be used as references. Instead of minimizing a Minkowski-type distance (Eq. 1, where x_i and c_i are the ith coordinates of the test point and of the centroid respectively, N is the number of dimensions of the space and p is an arbitrary number), which is the usual method for the *k-means* algorithm, our approach uses the inner product between every vector and the unit vector in the direction of the centroid (which geometrically is the projection of the vector along the centroid's direction, Eq. 2, where $\overline{C_i}$ is the ith coordinate of the unit vector in the direction of the centroid) as inverse measure of distance. This permits the identification of references that are optimized for correlation-based algorithms, because inner product and correlation have the same mathematical formulation. The *k-means* algorithm also needs to know *a priori* the number of clusters to identify. In this case it was chosen to be k=3, to allow the identification of voxels that might receive feeding from both arteries and veins (e.g. in fistulae) as a separate cluster. The desired reference centroids were selected by choosing the two that minimized the mutual dot product.

$$d = \sqrt[p]{\sum_{i=1}^{N} | x_i - c_i |^p} \quad \text{(Eq. 1)}$$

$$d' = \sum_{i=1}^{N} x_i \overline{c_i} \quad \text{(Eq. 2)}$$

Results. The algorithm was successfully applied for the identification of references in all the cases considered, and the artery/vein separation algorithm subsequently applied was able to correctly identify the vessels. Figure 1 shows the reference time courses in two cases, in which the contrast agent bolus had different dynamics (arterial reference is in green and venous reference is blue). Figure 2 shows the results of the double-reference correlation algorithm applied to the dataset of a normal subject (on the left) and of a subject suffering from dural fistula (on the right). Veins are depicted in blue and arteries in red; in the case of the fistula patient the arterialization of the left transverse sinus can be appreciated as well as the retrograde arterial flow in the right transverse sinus and jugular vein (depicted in purple).

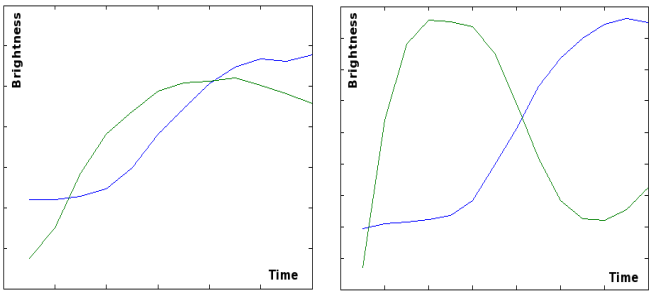

Figure 1 – Automatically identified reference time courses.

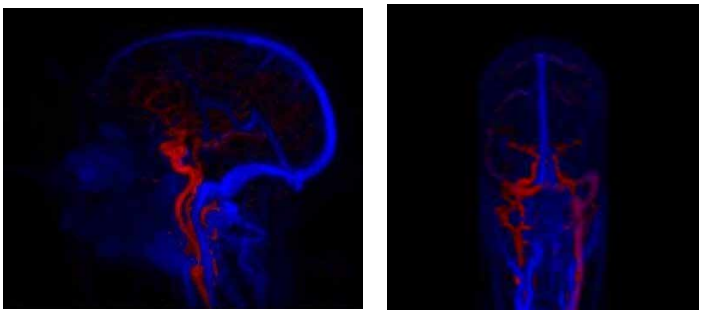

Figure 2 – Angiography performed using Double-Reference Correlation Analysis.

Discussion. The method here presented overcomes the most time-consuming step of the currently known artery/vein separation algorithms based on the analysis of time resolved datasets. Without this method, qualified operator intervention for reference selection is necessary, because correct identification of references is crucial for the algorithm performance and for reproducibility of the results. Eliminating the need of operator intervention drastically reduces the time required to obtain the final result, thus increasing productivity. Furthermore, the use of centroids of the identified clusters as references guarantees that the references have highest similarity with voxels in the set to which they belong, thus allowing the subsequent separation algorithm to have optimal performance.

References

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