Using the Fourth Dimension to Distinguish Between Structures for Anisotropic Diffusion Filtering in 4D CT Perfusion Scans

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Abstract. High resolution 4D (3D+time) cerebral CT perfusion (CTP) scans can be used to create 3D arteriograms (showing only arteries) and venograms (only veins). However, due to the low X-ray radiation dose used for acquiring the CTP scans, they are inherently noisy. In this paper, we propose a time intensity profile similarity (TIPS) anisotropic diffusion method that uses the 4th dimension to distinguish between structures, for reducing noise and enhancing arteries and veins in 4D CTP scans. The method was evaluated on 20 patient CTP scans. An observer study was performed by two radiologists, assessing the arteries and veins in arteriograms and venograms derived from the filtered CTP data, compared to those derived from the original data. Results showed that arteriograms and venograms derived from the filtered CTP data showed more and better visualized small arteries and veins in the majority of the 20 evaluated CTP scans. In conclusion, arteries and veins are separately enhanced and noise is reduced by using the time-intensity profile similarity (fourth dimension) to distinguish between structures for anisotropic diffusion filtering in 4D CT perfusion scans.

1 Introduction

Cerebral CT perfusion (CTP) scans are acquired to detect areas of abnormal perfusion in patients with cerebrovascular diseases [1,2]. They consist of multiple sequential 3D CT scans over time, acquired after an injection of contrast material. Besides perfusion maps, vascular information can be derived from high resolution CTP scans [3–6]. In [4,5] we proposed a method to derive 3D arteriograms (showing only the arteries) and venograms (only veins) from 4D CTP scans. A limitation of CTP scans is, however, the low X-ray radiation dose that is used to acquire the multitude of sequential 3D CT scans over time. Therefore these scans are inherently noisy. Reducing the noise in these CTP scans has the potential to improve the quality of the CTP-derived arteriograms and

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venograms, if the filter is designed to enhance vascular structures. Several noise reduction methods [7–9] have been proposed in the literature for filtering 4D datasets. However, these methods are either based on non-local means or bilateral filtering, and they are not designed to enhance certain types of structures during filtering.

Anisotropic diffusion [10,11], on the other hand, can be designed to enhance certain types of structures. Montagnat [12] et al. proposed a 4D anisotropic diffusion filter for echocardiographic images. For each voxel in the 4D dataset, the 4D gradient is determined. If the gradient magnitude is larger than a certain threshold, diffusion is reduced (based on the diffusion function) in the direction of the gradient, but high in the directions orthogonal to the gradient. This method is an extension of edge-enhancing diffusion (EED) [11] to four dimensions. It is, however, insufficient for filtering the 4D CTP scans, in which the vessels show a large intensity change over time, due to the inflow and wash-out of contrast material. The gradient will therefore point in the direction of the temporal dimension (highest gray level fluctuation). Diffusion will be reduced in the direction of the gradient, but will be high in the directions orthogonal to the gradient, blurring the vessel edges, instead of enhancing them. Therefore, we propose to use a 3D diffusion tensor and filter each time volume separately. However, the eigenvectors and eigenvalues of the diffusion tensor are adjusted according to the difference between the time intensity profiles in the fourth dimension. Previous approaches [13,14] did propose to filter each time volume separately, but applied isotropic diffusion and therefore only adjusted the conductance parameter according to the fourth dimension. Our approach enables full anisotropic diffusion by determining the first order derivatives based on the difference between the time intensity profiles.

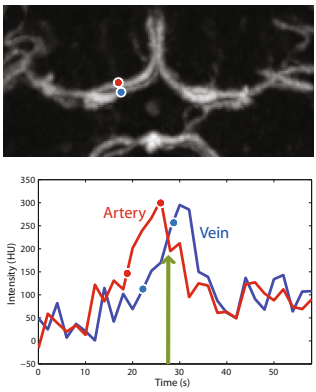

Fig. 1. Time-intensity profiles within a 4D CTP scan of voxels in an artery and a vein located close to each other as illustrated in the top image. If values would be averaged across the spatial and temporal dimension (i.e. red/blue dots) to reduce noise, the shape of the time-intensity profiles will change. However, for automatically separating the arteries and veins based on the time-intensity profiles, it is important that the shape of these profiles is preserved. The arrow indicates a point in time when the intensity value of the artery is similar to the intensity value of the vein.

2 Method

Anisotropic diffusion filtering as proposed by Weickert [10,11] uses the diffusion tensor to steer the filtering process, which allows for directional, anisotropic smoothing. The diffusion tensor is based on the structure tensor that uses first-order derivative information to describe structures in an image. The principal directions used for smoothing are thus based on the structure tensor [10]:

$$J_\rho(\nabla u_\sigma) = K_\rho * (\nabla u_\sigma \nabla u_\sigma^T) \tag{1}$$

where K is the Gaussian kernel with standard deviation ρ (integration scale), over which the orientation information is averaged, and ∇u_σ is the gradient of the image u at scale σ. Conventionally the structure tensor is based on the intensity information in a 2D or 3D image, with either two or three spatial dimensions. Pixels or voxels with similar intensity values located in close proximity to one another (low first-order derivative) are assumed to belong to the same structure, whereas high intensity variations (high first-order derivative), are considered as transitions from one structure to another. Four dimensional CT perfusion scans, however, consist of three spatial dimensions and one additional temporal dimension. Therefore, the fourth dimension [9] in CT perfusion scans can be used to distinguish between different types of tissues. Thus, instead of one intensity value per voxel, a range of intensity values (the time-intensity profile [9]) is available for each voxel in the 3D spatial domain. This is especially beneficial to differentiate between structures with contrast enhancement (e.g. arteries and veins, see Figure 1), due to the injection of contrast material prior to the CT perfusion scan acquisition. Similar time-intensity profiles are likely to belong to the same structure. In [9], the sum of squared differences (SSD) is used as a similarity measure:

$$\zeta(\xi, \mathbf{x}) = \frac{1}{T} \sum_{t=0}^{T-1} (I(\mathbf{x}(x, y, z, t)) - I(\xi(x, y, z, t)))^2 \tag{2}$$

where T is the size of the temporal dimension, $I(\mathbf{x}(x, y, z, t))$ is the intensity value of voxel $\mathbf{x}(x, y, z)$ at time point t and $I(\xi(x, y, z, t))$ is the intensity value of a neighboring voxel $\xi(x, y, z)$ at time point t. We propose to use the SSD similarity measure (2) between the time-intensity profiles to determine the first-order derivatives that are used to determine the structure tensor (1). The first-order derivatives can be approximated by using a finite differences scheme [11]. Instead of using the intensity values to determine the finite differences, the SSD values are used. In this way, the structure tensor is based on the structures described by the 4th dimension of the CT perfusion data. Principle axis transformation of the matrix with 4th dimension first-order derivative information provides the eigenvectors and eigenvalues of the 3D structure tensor $J_\rho(\nabla u_\sigma)$. The eigenvectors of this structure tensor are then used as the eigenvectors of the diffusion tensor. Consequently, the orientation of the diffusion tensor is based on the structures that are defined by the fourth dimension of the CT perfusion data.

The HDCS filter [15,16] can be used to filter noise from CT scans, while preserving as much structure as possible. This 3D anisotropic diffusion filter combines edge enhancing diffusion (EED) and coherence enhancing diffusion (CED) [17,18] proposed by Weickert [10,11] using a continuous switch. Since this filter enhances vessels (CED) and reduces noise (EED), we propose to extend this filter to 4D by integrating the fourth dimension into the finite difference scheme that determines the first-derivatives used to determine the structure tensor. Our approach consists of the following steps:

1. Perform 3D Gaussian smoothing with scale σ on each 3D sequential scan within the 4D CT perfusion data.
2. For each voxel $\mathbf{x}$ within the 3D spatial domain, determine:
   (a) $\zeta(\xi, \mathbf{x})$ using equation (2), for each neighboring voxel ξ within the discretization scheme.
   (b) the first-order derivatives $\delta u/\delta x$, $\delta u/\delta y$ and $\delta u/\delta z$, using a forward finite difference scheme.
   (c) the structure tensor elements and the gradient magnitude squared (used to determine the first eigenvalue (λ_{e_1}) of the EED diffusion tensor [15]).
3. Perform the conventional steps: smooth the structure tensor elements with scale ρ and determine the eigenvalues and eigenvectors of the structure tensor and the eigenvalues of the EED, CED and HDCS diffusion tensor [15].
4. Apply the HDCS diffusion filter of which the diffusion tensor is based on structures detected using information present in the 4th dimension, to each 3D sequential scan within the 4D CT perfusion scan.

3 Experiments and Results

The proposed time-intensity profile similarity (TIPS) anisotropic diffusion filter was applied to 20 patient cerebral CTP scans (scanned every 2 s during 60 s at 80 kVp and 150 mAs), acquired on a Philips Brilliance 64-slice CT scanner during injection of 40 ml of (300 mg I/ ml) contrast agent at 5 ml/s, and reconstructed with 0.625 mm thick sections. The filter parameters were set as follows. The σ and ρ were set to 0.5 and 1.0 respectively for all patient scans, to preserve small vessels. The time step size (τ) was set to 0.03 based on the voxel size (0.43x0.43x0.625 mm) as described in [15]. The regularization parameter α and the contrast parameter for the CED diffusion tensor (λ_c) were set as described in [15] to be 0.001 and 15.0. The contrast parameters of the EED (λ_e) and HDCS (λ_h) diffusion tensors varied for each of the patient CTP scans and are dependent on the sum of squared difference between the time-intensity profiles. They were determined within a region of interest in the white matter, selected on the temporal average image of the CTP data. The average first eigenvalue of the structure tensor (μ_1) and the average gradient magnitude were determined within the ROI and used to set λ_h and λ_e respectively. The number of iterations (η) was set to be 30 for all patient CTP scans.

Arteriograms and venograms were derived from the original and filtered CTP scans using the method proposed in [4]. To assess the performance of the TIPS

anisotropic diffusion filter we performed an observer study. The quality of the arteriograms and venograms derived from the filtered data were compared to the original arteriograms and venograms, by two expert observers (radiologists). Maximum intensity projections (MIPs) of 40 mm were presented to the observers in pairs (unfiltered versus filtered) with two different window level settings: a window level (W/L: 380/220) for the assessment of large vessels (> 1.5 mm) and a window level (W/L: 200/120) for the assessment of small vessels (< 1.5 mm). Observers were asked to score the quality (on a 5-point scale) of the large and small arteries in the arteriogram and large and small veins in the venogram and to specify whether more arteries and veins were visible in the arteriograms and venograms derived from the filtered CTP data. Table 1 shows the results of the observer study. In general the quality of the small vessels was scored to be improved and the quality of the large vessels was scored equal in the majority of the cases. Observer agreement [19] was very good (κ: 0.81) for the large veins, and good for the large arteries (κ: 0.66) and small arteries and veins (κ: 0.61). In the majority of the cases, the observers specified that more small arteries (Obs.1: 70 %, Obs.2: 75 % with κ: 0.95) and veins (Obs.1: 60 %, Obs.2: 80 % with κ: 0.80) were visible in the arteriogram and venogram derived from the filtered CTP data. Figure 2 shows two examples of cases in which the observers scored that more small arteries and veins were visible in the arteriogram and venogram derived from the filtered CTP data.

Table 1. Results of quality assessment (5-point scale) scores of the arteries and veins in arteriograms and venograms derived from the filtered CTP data compared to those derived from the original CTP data. Percentages indicate in how many percent of the 20 cases the corresponding score was assigned by the observer.

Quality assessment	**Large**	**Small**	**Large**	**Small**
Expert observer 1	**Arteries**	**Arteries**	**Veins**	**Veins**
Much worse	0 %	0 %	0 %	0 %
Worse	0 %	0 %	0 %	0 %
Equal	65 %	30 %	85 %	20 %
Better	30 %	60 %	15 %	80 %
Much better	5 %	10 %	0 %	0 %
Expert observer 2				
Much worse	0 %	0 %	0 %	0 %
Worse	5 %	0 %	0 %	15 %
Equal	75 %	15 %	100 %	15 %
Better	20 %	75 %	0 %	65 %
Much better	0 %	10 %	0 %	5 %

To determine the signal to noise ratio (SNR) in the original and filtered CTP data, regions of interest (ROIs) were placed in large and small arteries in the

arterial phase and large and small veins in the venous phase of the 4D CTP data as well as in the background. The SNR was determine for large and small vessels by subtracting the background mean from the vessel mean and dividing by the standard deviation of the background. The average SNR over all 20 CTP scans increased significantly ($p < 2.8 \cdot 10^{-4}$ paired two-tailed T-test) from 14.6 (σ:4.1) to 29.5 (σ:9.4) for large vessels ($> 1.5mm$) and from 3.6 (σ:1.1) to 6.8 (σ:3.0) for small vessels ($< 1.5mm$).

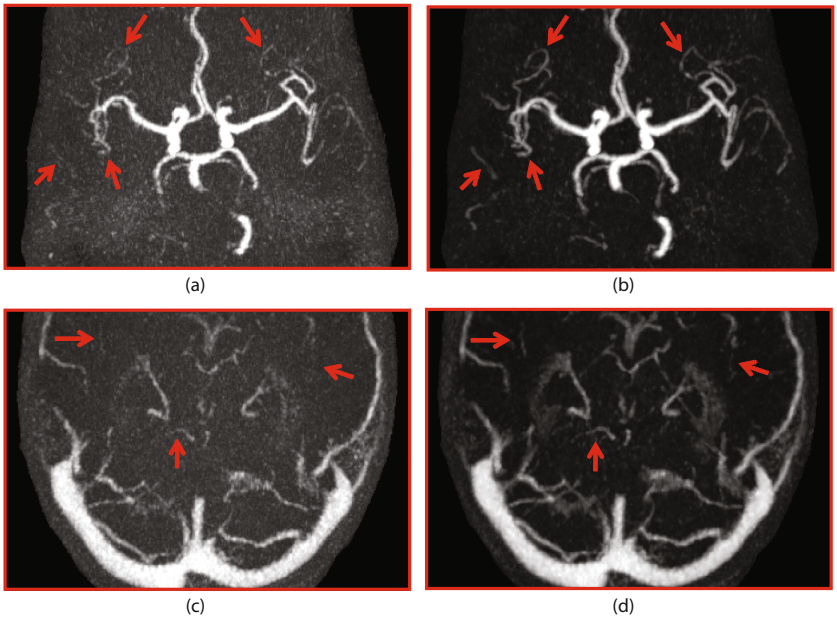

Fig. 2. Subimages of maximum intensity projections of an arteriogram and venogram (W/L 320/160) from two different patients used in the evaluation. The arrows indicate locations where visualization of smaller vessels improved due to filtering. (a) Arteriogram derived from the original CTP data. (b) Arteriogram derived from the CTP data filtered with the TIPS anisotropic diffusion filter. (c) Venogram derived from the original CTP data. (d) Venogram derived from the CTP data filtered with the TIPS anisotropic diffusion filter.

4 Discussion and Conclusion

In this paper a TIPS anisotropic diffusion method was proposed for enhancing vessels and reducing noise in 4D CT perfusion (CTP) data, to improve the quality of arteriograms and venograms derived from this data. The proposed filter uses the 4th dimension to distinguish between structures after which diffusion is performed on each 3D sequential scan in the 4D dataset. Therefore, intensity values are not mixed over time, preserving the time-intensity profiles. Even when

the intensity value of the arteries and veins is similar at a certain point in time (arrow in Figure 1), the structure tensor of the TIPS anisotropic diffusion filter will not be disturbed. Since the similarity between the time-intensity profiles (fourth dimension) is used to distinguish between structures, both the arteries and veins will be detected as separate tubular like structures and diffusion will be performed accordingly.

The use of this principle is not limited to the HDCS filter, but can be used for all diffusion based filtering techniques, such as plain EED [10] or CED [17]. It could even be used for other derivative based methods, such as VED [20] or the vesselness filter [21], if the 1st-order derivatives would be substituted by 2nd-order derivatives and the structure tensor by the Hessian. Another way of extending anisotropic diffusion methods to four dimensions, is by adding another dimension to the structure and diffusion tensor, like Montagnat [12] proposed for 4D cylindrical echocardiographic images. However, most of these filters would then lose the very properties that made them successful in the first place. The key to our approach is that we provide a way to exploit the additional information (fourth dimension) present in the 4D CTP data, and still profit from the benefits of the various anisotropic diffusion filters or vesselness filters. The similarity measure between the time-intensity profiles is also not limited to the sum of squared difference (SSD) used in this paper, but the SSD typically increases the contrast between similar and non-similar profiles.

A limitation of our study was that we did not compare our approach to for example the TIPS bilateral filter [9]. Bilateral filters and non-local mean filters have been proven to work very well, and have the advantage of being less time consuming. However these methods lack the property of directional smoothing that anisotropic diffusion based methods do have. This is illustrated by Weickert in his fingerprint example (Figure 2 in [17]), in which he illustrates that CED is able to connect the interrupted lines in a fingerprint image. CED was incorporated in the HDCS filter [9] that was evaluated in this paper, to be able to connect small vessels that were interrupted by noise. Therefore, our hypothesis was that the TIPS HDCS filter would increase the visibility of small arteries and veins without degrading the larger arteries and veins. The observer study confirmed our hypothesis. The results showed that the signal to noise ratio in the CTP data improved significantly. The effect of filtering was most pronounced in the small arteries and veins that were lost in the noise in the original data. The observers indicated in the majority of the cases that more small arteries and veins were visible after filtering and the quality was better. Future work consists of comparing TIPS anisotropic diffusion to the TIPS bilateral filter to confirm our hypothesis that the anisotropic diffusion filter is better able to filter the small vessels than the bilateral filter.

In conclusion, in this paper we have shown that arteries and veins can be enhanced and noise reduced, by using the similarity between the time-intensity profiles (fourth dimension) to distinguish between structures for anisotropic hybrid diffusion in 4D CT perfusion scans.

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