Segmentation of Arteries and Veins on 4D CT Perfusion Scans for Constructing Arteriograms and Venograms

Adriënne Mendrik, Evert-jan Vonken, Annet Waaijer, Ewoud Smit,
Mathias Prokop and Bram van Ginneken

Image Sciences Institute, University Medical Center Utrecht,
Heidelberglaan 100, 3584 CX Utrecht, The Netherlands

ABSTRACT

3D CT Angiography (CTA) scans are currently used to assess the cerebral arteries. An additional 4D CT Perfusion (CTP) scan is often acquired to determine perfusion parameters in the cerebral parenchyma. We propose a method to extract a three dimensional volume showing either the arteries (arteriogram) or the veins (venogram) from the 4D CTP scan. This would allow cerebrovascular assessment using the CTP scan and obviate the need for acquiring an additional CTA scan. Preprocessing steps consist of registration of the time volumes of the CTP scan using rigid registration and masking out extracranial structures, bone and air. Next a 3D volume is extracted containing the vessels (vascular volume) by using the absolute area under the first derivative curve in time. To segment the arteries and veins we use the time to peak of the contrast enhancement curve combined with region growing within a rough vessel segmentation. Finally the artery/vein segmentation is used to suppress either the veins or the arteries in the vascular volume to construct the arteriogram and venogram. To evaluate the method, 11 arteriograms and venograms were visually inspected by an expert observer, with special attention to the important cerebral arteries (Circle of Willis) and veins (straight and transverse sinus). Results show that the proposed method is effective in extracting the major cerebral arteries and veins from CTP scans.

Keywords: segmentation, 4D, CT, arteries, veins, CT perfusion

1. INTRODUCTION

In clinical practice 3D CT Angiography (CTA) scans are used to assess the cerebral arteries. These scans are acquired by injecting contrast material and, after a suitable delay, scanning the volume of interest. An additional 4D CT Perfusion (CTP) scan is often acquired by injecting contrast material and then scanning several 3D volumes over time. These CTP scans are currently used to evaluate the cerebral perfusion using maps of the Cerebral Blood Volume (CBV), Mean Transit Time (MTT) and Cerebral Blood Flow (CBF = CBV/MTT),[1] in patients with cerebrovascular diseases, such as acute stroke,[2] subarachnoid hemorrhage (SAH)[3] and carotid occlusion.[4]

We anticipate to extend the diagnostic yield of these CTP scans to also include CT Angiographic information. For this purpose, the CTP scans were reconstructed with 0.625mm thick slices, instead of the usual 5mm thick slices used for generating the perfusion parameter maps. Since CTP scans image the contrast bolus over time, the time to peak of the contrast bolus can be used to separate the arteries from the veins. Blood flows from the heart, to the arteries into the narrower arterioles and even narrower capillaries, perfusing the tissue. After this, the blood returns through the wider venules and even wider veins. If the blood-brain barrier is intact, the contrast material will pass through the capillary network, but remains completely intravascular.[5]

When the cerebral arteries need to be assessed, the aim is to acquire the CTA scan, such that contrast material is present in the arteries. Unfortunately CTA scans usually suffer from venous overprojection, when contrast material is not only present in the arteries, but also partly in the veins at the time of scanning, obscuring the view on the arteries (Figure 1).

Further author information: Send correspondence to Adriënne Mendrik (adrienne@isi.uu.nl)

Medical Imaging 2009: Image Processing, edited by Josien P. W. Pluim, Benoit M. Dawant,
Proc. of SPIE Vol. 7259, 72590Z · © 2009 SPIE
CCC code: 1605-7422/09/$18 · doi: 10.1117/12.812135

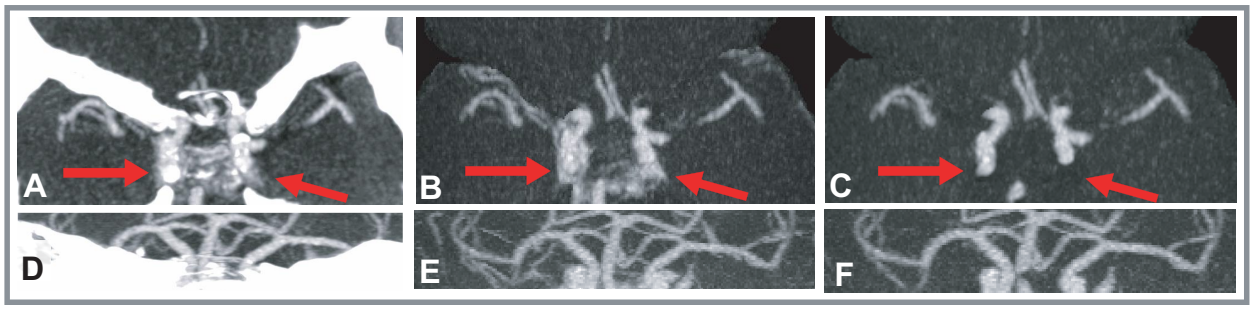


Figure 1. Illustration of venous overprojection (arrows) near the skull base. Figures A-C show an axial Maximum Intensity Projection (MIP) of 11mm and figures D-F show a coronal MIP of 77mm. (A,D) Venous overprojection in the CT Angiography scan indicated by the arrows. (B,E) Vascular volume from the CT Perfusion scan showing both arteries and veins. (C,F) Arteriogram from the CT Perfusion scan suppressing the veins increases visibility of the arteries.

In this paper we propose a method for constructing a 3D arteriogram (containing the cerebral arteries) and venogram (containing the cerebral veins) from the 4D CTP data. The advantage is two-fold, constructing an arteriogram and venogram from the CTP data will solve the problem of venous overprojection and acquisition of an additional CTA scan next to the CTP scan will be redundant, reducing cost and radiation dose to the patient.

2. METHOD

Our method to obtain the 3D arteriogram and venogram from the 4D CTP data consists of several steps. First, a short outline of the algorithm steps is given, before they are described more extensively in the paragraphs below:

1. Preprocessing
   (a) Register the time volumes using rigid registration (with a skull mask)
   (b) Get intracranial structures: Mask out bone, air and everything outside the skull
2. Construct a 3D image showing the vessels (vascular volume)
   (a) Determine the first derivative in time (di/dt) for each voxel in the CTP volume
   (b) Construct the vascular volume: Fill each voxel in the vascular volume with the absolute area under the (di/dt) curve
3. Segment arteries and veins
   (a) Segment the vessels: Set a threshold on the vascular volume (based on the histogram) to roughly segment the vessels
   (b) Create a zero crossing volume: For every voxel within the vessel segmentation, determine the zero crossing of the (di/dt) curve
   (c) Determine the histogram of the zero crossing volume (eroded version, to get more stable estimate)
   (d) Detect the 2 highest peaks in the histogram of the zero crossing volume (first = artery peak, second = vein peak)
   (e) Define the artery (zero crossing $<$ artery peak) and vein (zero crossing $>$ vein peak) seeds
   (f) Perform region growing within vessel segmentation by propagating 2 (artery and vein) region growing fronts
4. Construct the arteriogram and venogram by multiplying a smoothed version of the inverted artery and vein segmentation masks with the vascular volume.

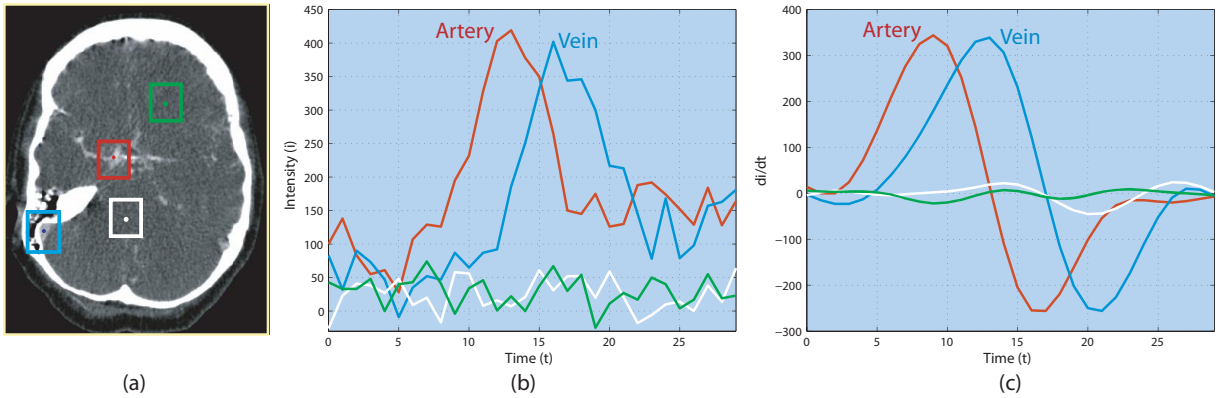


Figure 2. Illustration of the intensity change per voxel over time in a 4D CT Perfusion (CTP) scan. (a) One slice of the 4D CTP scan, in which the location of the 4 example voxels is marked: vein (blue), artery (red) and 2 parenchyma voxels (white and green). (b) Graph showing the intensity over time. (c) Graph showing the first derivative of the time/intensity curves.

2.1 Preprocessing

For temporal analysis, registering the volumes of the CTP scan over time is essential. For each volume a skull mask is created, by thresholding the volume at a value of 600 Hounsfield Units (HU) and selecting the largest connected component. Each volume is registered to the first time volume using the skull mask. Since non-rigid movement of the intracranial structures over time is neglectable, rigid registration is used. Sum of squared differences is used as a similarity measure and gradient descent to solve the optimization problem (using elastix, a registration package freely available at http://elastix.isi.uu.nl/).

Since we are interested in the intracranial vessels, the skull mask is used to discard all structures outside the skull. Other structures that are easy to mask out based on their HU are bone and air. To also include the partial volume voxels in the skull base, a mask is created by setting the bone threshold at 200 HU in the first time volume (in which no contrast material is present). The air threshold is set at -200 HU (to also include partial volume voxels with bone). Because the volumes are registered, this mask can be used in all volumes over time.

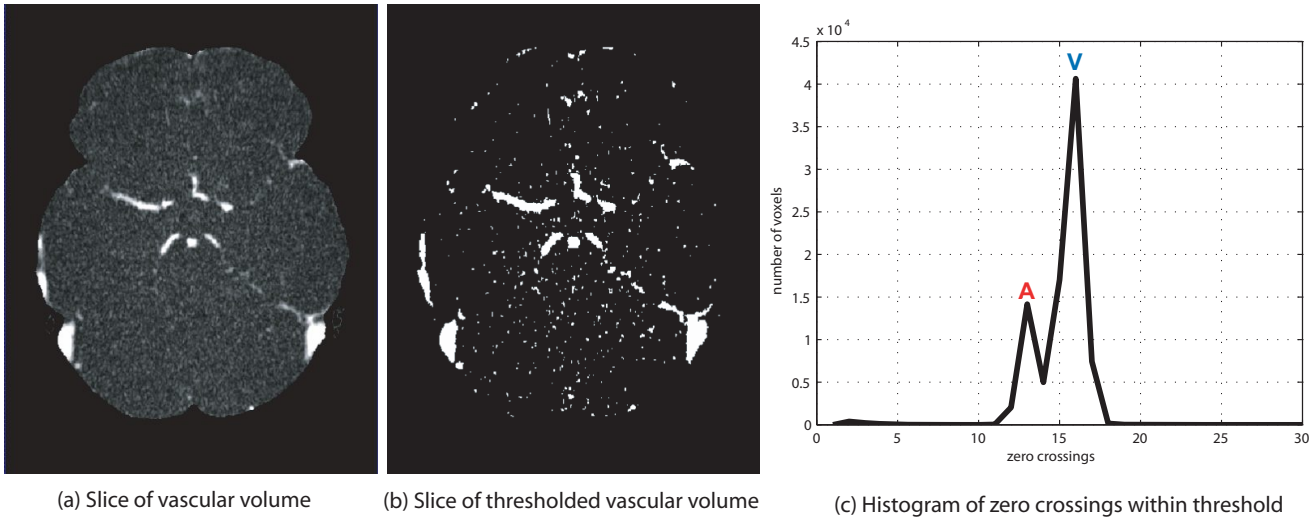
2.2 Constructing a 3D vascular image from the 4D CTP scan

The next step is to construct a 3D image, from the 4D CTP data, which shows the intracranial vessels in which contrast material is present. Figure 2(b) shows an example of the voxel intensities over time of an artery voxel, a vein voxel and two cerebral parenchyma voxels. Due to the injection of contrast material, both the artery and vein voxels show a large intensity change over time (contrast enhancement curve). Therefore we take the first derivative in time for every voxel within the volume, as shown in Figure 2(c). This is done using Gaussian derivatives at scale $\sigma = 3$ (≈ 6 sec.). To construct the vascular volume, the absolute area under the first derivative curve is determined for every voxel in the volume. A scale of 3 was chosen based on experiments to result in the highest vessel signal. A Maximum Intensity Projection (MIP) of part of a vascular volume is shown in Figure 4(A).

2.3 Segmentation of the arteries and veins

Blood flows from the arteries to the veins, therefore the artery contrast enhancement curve has an earlier time-to-peak than the vein curve (Figure 2(b)). To separate the arteries from the veins, the zero crossings of the first derivative curves are used, which correspond to the time-to-peak of the contrast enhancement curves at scale 3 (Figure 2(c)).

First the vessels in the vascular volume are roughly segmented by setting a threshold on the vascular volume. Based on the assumption that the first part of the histogram of the vascular volume is background noise, which has a Gaussian distribution, the peak of the histogram is detected and a Gaussian is fitted on the histogram, at



(a) Slice of vascular volume (b) Slice of thresholded vascular volume (c) Histogram of zero crossings within threshold

Figure 3. (a) Illustration of one slice of the vascular volume extracted from the CTP scan. (b) Rough vessel segmentation on the vascular volume. (c) Histogram of the zero crossing volume (eroded), used to determine the typical artery (A) and vein (V) zerocrossings for the region growing seeds. The zero crossing volume shows for each voxel within the vessel segmentation, the zero crossings of the first derivative contrast enhancement curve.

the left site of the peak. The threshold is taken to be three times the standard deviation at the right site of the histogram peak. An example of a thresholded slice is shown in Figure 3(b). Acquiring a rough vessel segmentation (oversegmentation) enables us to better suppress all artery and vein voxels (including partial volume voxels) for constructing the arteriogram and venogram in step 4.

After this, a zero crossing volume is constructed, in which every voxel within the vessel segmentation is filled with the time (t) of the zero crossing of the first derivative curve. To determine the typical artery and vein zero crossing, the zero crossing volume is eroded using a sphere with a radius of 1 voxel (to get rid of the background noise). In the histogram of this volume the two highest peaks are detected, the first corresponding to a typical artery zero crossing and the second to a typical vein zero crossing (Figure 3(c)).

These zero crossings are then used to determine the artery and vein seeds used for region growing. All voxels with a zero crossing below the typical artery zero crossing are used as artery seeds and all voxels with a zero crossing above the typical vein zero crossing are used as vein seeds. To segment the arteries and veins, region growing is performed propagating two region growing fronts within the vessel segmentation, one using the artery seeds and one using the vein seeds. Voxels with a zero crossing value between the typical artery and vein zero crossings are assigned to either one of the fronts based on connectivity to the artery or vein seeds.

2.4 Construct arteriogram and venogram

The final step in this algorithm is to construct the arteriogram and venogram. The artery and vein segmentation masks are inverted and gaussian smoothing ($\sigma = 1$) is applied. The vein segmentation mask is multiplied with the vascular volume to suppress the veins and construct the arteriogram. The artery segmentation mask is multiplied with the vascular volume to suppress the arteries and construct the venogram. Figures 4(B,C) show examples of a Maximum Intensity Projection of a venogram and arteriogram.

3. EXPERIMENTS

Eleven cerebral CTP scans of patients with various cerebrovascular diseases (acute stroke/subarachnoid hemorrhage/carotid occlusion) were processed. The scans (5.3 mGy/slice) were acquired on a 64-slice CT scanner (64P Brilliance, Philips Medical Systems) during injection of 40 ml of (300 mg I/L) contrast material at 5ml per second. The resolution of each volume in the CTP scan is $0.43\times0.43\times0.625$mm. Volumes were scanned every 2 seconds during 1 minute, resulting in 4D datasets of $512\times512\times64\times30$ voxels.

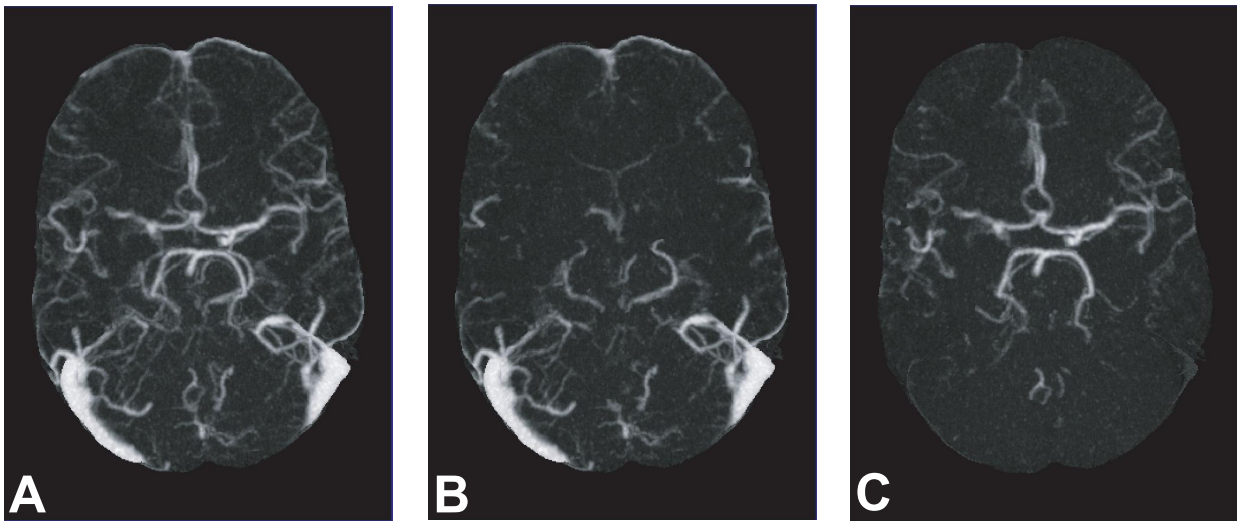


Figure 4. A: Maximum Intensity Projection of 29mm of a vascular volume extracted from a CTP scan showing both arteries and veins. B: MIP of corresponding venogram constructed by suppressing the arteries using the artery segmentation. C: MIP of corresponding arteriogram constructed by suppressing the veins using the vein segmentation.

After processing the CTP scans using our algorithm, an expert observer visually inspected 11 of the resulting arteriograms and venograms. During evaluation, the observer focused on the arteries and veins that are most important for diagnosing cerebrovascular diseases. These are the arteries within the Circle of Willis (CoW) and the straight and transverse sinus (veins). The completeness of the arteries and veins was scored from 0-100% compared to the vascular volume, which contains all vessels, extracted from the CTP scan. For the remaining (smaller) arteries and veins a score from 0-100% (5% steps) was given to the percentage of arteries and veins visible in the arteriogram and venogram respectively. If not visible in the arteriogram or venogram, the observer was asked to categorize the size of these arteries and veins (small, medium, or large).

4. RESULTS

The results are shown in Table 1. The CoW was scored complete in the majority of the arteriograms and most of the remaining arteries were visible. There were no scores below 80% visible in the arteriograms. The straight and transverse sinus were also complete in the majority of the venograms and most of the remaining veins were visible. In 3 cases the straight sinus was not present in the scanned CTP volume. There were no scores below 70% visible in the venograms.

Figure 1 illustrates that venous overprojection (indicated by the arrows) is reduced in the arteriogram extracted from the CTP scan compared to the CTA scan and the vascular volume from the CTP scan.

Table 1. Results observer study. The numbers represent the number of arteriograms/venograms in which the percentage was scored. The size of the misclassified arteries was small in 6 cases and medium in 3 cases. The size of the misclassified veins was small in 8 cases and medium in 3 cases.

Type of vessel	**100% visible**	**90-99% visible**	**80-89% visible**	**70-79% visible**
Circle of Willis	9	1	1	0
Remaining arteries	2	8	1	0
Straight sinus	7	1	0	0
Transverse sinus	9	1	0	1
Remaining veins	0	7	2	2

5. DISCUSSION

In this paper an automatic method for constructing a 3D arteriogram and venogram from a 4D CT Perfusion scan was presented. The method was applied to eleven CTP scans. Results show that constructing arteriograms and venograms from CTP data and separating the arteries and veins using time information and spatial connectivity is feasible. This is especially true for the larger arteries and veins, which are separated well. Medium and smaller arteries and veins are separated well in most cases. Separating the arteries and veins, results in a better view on both type of vessels and has the potential to improve diagnostic accuracy of cerebrovascular disease. Another advantage of the arteriogram and venogram is that bone is suppressed. Bone removal in CTA scans is problematic, since vessel and bone intensities overlap and some vessels are in proximity to bone (Figure 1). A second unenhanced (no contrast material) CT scan could then be acquired to be able to segment the bone.[6] This unenhanced CT is similar to the first time volume of the CTP scan, when contrast material has not yet entered the arteries.

A limitation of the CTP data is that the scan coverage is limited to the detector width of the scanner. The 64 slice scanner that was used for scanning the patients has a 4cm coverage. CT Angiography scans have a much larger coverage (usually shoulders to top of the head). However, new generation scanners[7] are able to acquire CTP scans with whole brain coverage, solving this drawback.

Another point of attention is the fact that analysis of the CTP data relies heavily on precise registration of the time volumes. Since the scan coverage is limited to 4cm, it can occur (although not often) that, due to patient motion, the volume of interest in the head moves outside the scan coverage between two consecutive time volumes. When this occurs, the registration algorithm will not be able to correct for this. Increased scan coverage will decrease this problem.

The method described in this paper for separating the arteries and veins uses the time information (zero crossings of the first derivative contrast enhancement curve) solely to extract the seeds for region growing. Therefore all remaining voxels within the vessel segmentation are assigned to either the artery or vein class based on connectivity to the seeds. One could think of extending this by using the time information of the remaining voxels as an additional weight in the region growing process. Arteries and veins which lie in proximity to each other would benefit from this approach.

In conclusion, a new automatic method for extracting arteries and veins from 4D cerebral CT Perfusion data was proposed. The observer study showed that arteries (Circle of Willis) and veins (straight and transverse sinus) important for diagnoses of cerebrovascular disease are separated well. Extracting an arteriogram and venogram from the CTP data will obviate the need for an additional CTA scan, when scan coverage of the CTP scan is increased, and will result in increased visibility of the arteries and veins compared to CTA. Further research is necessary to investigate the diagnostic accuracy of the arteriogram and venogram from CTP.

ACKNOWLEDGMENTS

This work was supported by a research grant from Philips Medical Systems.

REFERENCES

[1] Hoeffner, E. G., Case, I., Jain, R., Gujar, S. K., Shah, G. V., Deveikis, J. P., Carlos, R. C., Thompson, B. G., Harrigan, M. R., and Mukherji, S. K., "Cerebral perfusion CT: Technique and clinical applications," *Radiology* **231**, 632–644 (2004).

[2] Wintermark, M., Reichhart, M., Thiran, J.-P., Maeder, P., Chalaron, M., Schnyder, P., Bogousslavsky, J., and Meuli, R., "Prognostic accuracy of cerebral blood flow measurement by perfusion computed tomography, at the time of emergency room admission, in acute stroke patients," *Annals of Neurology* **51**, 417–432 (2002).

[3] Nabavi, D. G., LeBlanc, L. M., Baxter, B., Lee, D. H., Fox, A. J., Lownie, S. P., Ferguson, G. G., Craen, R. A., Gelb, A. W., and Lee, T. Y., "Monitoring cerebral perfusion after subarachnoid hemorrhage using CT," *Neuroradiology* **43**, 7–16 (2001).

[4] Jain, R., Hoeffner, E. G., Deveikis, J. P., Harrigan, M. R., Thompson, B. G., and Mukherji, S. K., "Carotid perfusion CT with balloon occlusion and acetazolamide challenge test: Feasibility," *Radiology* **231**, 906–913 (2004).

[5] Cianfoni, A., Colosimo, C., Basile, M., Wintermark, M., and Bonomo, L., "Brain perfusion CT: Principles, technique and clinical applications," *Radiol. Med.* **112**, 1225–1243 (2007).

[6] Manniesing, R., Viergever, M. A., and Niessen, W. J., "Vessel enhancing diffusion a scale space representation of vessel structures," *Medical Image Analysis* **10**, 815–825 (2006).

[7] Klingebiel, R., Siebert, E., Diekmann, S., Wiener, E., Masuhr, F., Wagner, M., Bauknecht, H.-C., Dewey, M., and Bohner, G., "4-D imaging in cerebrovascular disorders by using 320-slice CT: Feasibility and preliminary clinical experience," *Academic Radiology* **16**, 123–129 (2009).