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Abstract. Measurements of the vessel lumen diameter are often used to determine the degree of atherosclerotic disease in carotid arteries. However, quantification results vary with imaging technique and acquisition settings. We aim at providing a tool that quantifies the lumen diameter on different image datasets and gives an estimate of quantification uncertainties, so that they can be taken into consideration when evaluating and comparing measurements. For the segmentation of the vessel lumen, we present an algorithm using ray-casting techniques and partial volume correction. We furthermore propose a scheme for the analysis and exploration of the lumen diameter. Finally, we present a clinically relevant application scenario, in which we explore agreement between lumen diameter estimations in corresponding computed tomography angiography, contrast-enhanced magnetic resonance angiography, time-of-flight, and subtraction images of carotid vessels with severe carotid atherosclerotic plaques. © 2018 Society of Photo-Optical Instrumentation Engineers (SPIE) [DOI: 10.1117/1.JMI.5.3.034003]

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1 Introduction

The carotid arteries constitute the major connection between the aorta and the brain (Fig. 1). Thus, they play a crucial role in oxygen supply, and stenoses as well as occlusions can lead to stroke. Vessels close to the carotid bifurcation are prone to develop atherosclerotic plaques. Measurements of the vessel geometry are an important tool for the assessment of pathologies and are used for monitoring the progress of the disease and therapy planning.

However, the measurements depend on imaging parameters, patient position, and quantification methods.¹ Uncertainty in lumen diameter may also have a large, nonlinear impact on hemodynamic analysis, so all further evaluations also heavily depend on the accuracy of the extraction of basic geometry.²

There is a variety of imaging techniques for carotid artery inspection that are used for the detection of vessel pathologies.³ To this date, digital subtraction angiography (DSA) is considered the gold standard, even though it is rather costly to acquire as it is more invasive than other imaging techniques.⁴ Widely available is computed tomography angiography (CTA), which provides three-dimensional (3-D) images based on contrast agent to enhance the vessels. Time-of-flight (TOF) and contrast-enhanced magnetic resonance angiography (CEMRA) are also often used in clinical practice. While CEMRA requires the injection of a contrast medium, TOFMRA visualizes the flow within a vessel without the need to administer contrast agent. Both can be acquired as 3-D volume or two-dimensional slices. Subtraction (SUB) images can be computed from the CEMRA images by subtracting an image taken before contrast administration. Structures that are present in both

images are suppressed and the vessels are displayed more clearly. On the downside, this technique can introduce motion artifacts, as there may already have been movement between the two image acquisitions.

All these imaging techniques capture different features (Fig. 2) and may result in different lumen quantifications.

We aim at providing a tool that not only performs lumen quantification but also gives an estimate of lumen detection uncertainties, so that they can be taken into consideration for follow-up examinations and therapy planning.

2 Related Work

Various techniques for accurately segmenting the vessel lumen have been proposed in literature.⁵ One such approach is region growing. It usually requires the user to specify seed points on the vessel lumen, from which the region is extended to cover the whole vessel structure. To reduce the sensitivity to noise and intensity inhomogeneities, several enhancements have been proposed, e.g., the wave propagation approach, which can prevent neighboring vessels from merging.⁶ Stochastic frameworks incorporate a vessel model and use high-level information, such as vessel geometry. They aim at finding a lumen segmentation that best explains the observation in the image while also agreeing to the vessel model.⁷ The underlying models can become very complex and usually require many parameters.

Instead of directly attempting to estimate the lumen region, it is also possible to extract the centerline first and then calculate the lumen boundary in a second step. This has the advantage that the segmentation can rely on the structure information provided by the centerline. One such algorithm is described by

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Fig. 1 Visualization of the CCA, ICA, and ECA in a volume rendering of CT image.

Wink et al.⁸ After semiautomatically estimating the centerline, ray-casting techniques are used to find the lumen border around the centerline points.

As carotid vessels and vessels with atherosclerotic plaques, in particular, can be very thin compared to the image resolution, quantification algorithms should also account for partial volume effects, which can introduce a significant bias in measurements.⁹ They occur if a voxel covers more than one type of tissue. Then the voxel intensity is a combination of the different tissue intensities. Especially, when dealing with image structures that are small compared to the voxel dimensions, this effect has to be accounted for.

Freiman et al.¹⁰ propose a machine-learning-based graph min-cut segmentation framework that accounts for partial volume effects. They show that the resulting lumen segmentation is better suited for further hemodynamic analysis.

There exist a number of studies that compare the agreement of measurements acquired with different imaging techniques or different algorithms. Most of them either rely on DSA images or expert input as reference. Kirişli et al.¹¹ present a framework for evaluation of different lumen segmentation and stenosis grading algorithms in coronary arteries. They use manual segmentations done by an expert as reference. They come to the conclusion that even though automatic lumen segmentations can have similar precision to the expert's one, none of the automatic stenosis

detection methods were reliable enough to replace an expert. Hameeteman et al.¹² provide a similar framework that is specifically tailored for comparing lumen segmentation and stenosis grading around the carotid bifurcation.

Often the minimal lumen diameter is used in literature and in clinical studies. This parameter can be defined in different ways. Traditionally, the lumen diameter is measured in projection images, which only measure the projection diameter at an assumingly optimal projection angle.¹³ Another approach takes into account the cross-sectional images.¹² The lumen diameter is defined as the shortest line that divides the lumen area into two equally sized areas.

3 Methods

We present an algorithm for the segmentation of the vessel lumen also taking partial volume effects into account (Sec. 3.1). Furthermore, we propose a framework for comparing measurements acquired from different image modalities (Sec. 3.2) to enable an assessment of the degree of uncertainty in the quantitative lumen measurement.

3.1 Vessel Segmentation

Our algorithm is composed of three major steps: (1) interactively generating the centerline for each vessel, (2) detecting the lumen boundary, and (3) performing the partial volume correction (PVC). All three steps are described in detail in the following sections.

3.1.1 Centerline

The centerline is generated interactively and requires a user to place markers in the image close to the assumed lumen center. As a preprocessing step, a cost image is computed, in which all voxels are assigned a value depending on the probability of belonging to a vessel (Fig. 3). The specific computation of the cost image depends on the image type. For CEMRA, TOFMRA, and SUB images, the vessels are clearly the brightest regions in the image, so first we compute thresholded images for both the original image as well as a Gaussian-smoothed image.

Fig. 2 Imaging modalities. (a) Axial slice of a 3-D CTA image. Bones are clearly visible as they have higher intensities than vessels. (b) Axial slice of TOF image. This imaging technique relies on the blood flow and can introduce artifacts in regions where the blood is flowing slowly. (c) Sagittal slice of CEMRA image. As well as CTA images, this acquisition technique uses contrast agent to enhance the visibility of vessels. (d) Sagittal slice of SUB image. Tissue surrounding the vessels is suppressed by subtracting a CEMRA image before contrast administration from an image with contrast agent, so only the vessels are visible.

Fig. 3 Shortest path estimation. (a) Coronal slice in CEMRA image and (b) shortest path connecting two points in the corresponding cost image.

These are additively combined to make sure that none of the vessels are missed. The exact thresholds depend on the image type and its intensity statistics. In the next step, the connected components of the resulting mask are computed and very small components are discarded. On the result, we use a skeletonization algorithm that uses successive erosion of border voxels.

From this, we can compute a cost image:

$$I_{\text{cost}} = \frac{1}{1 + \max(I_{\sigma}, I) \cdot (1 + I_{\text{skel}})}, \quad (1)$$

where I is the original image, I_{σ} a Gaussian-smoothed version of I , and I_{skel} is the smoothed skeletonization image. Voxels with low intensities in the cost image I_{cost} have a high probability of belonging to a vessel. As in CTA images, both bones and calcifications are brighter than the vessel lumen, it is necessary to suppress these structure in the preprocessing. This is done by a simple thresholding. The bright areas are replaced with background intensities so they are not mistaken for vessels. Afterward, the steps described above can be applied to CTA images as well.

The user can now select points in the image, which are supposed to be located on the centerline. The centerline is then computed as the shortest path between the points in the corresponding cost image (Fig. 3).

3.1.2 Lumen boundary detection

The boundary detection is based on the analysis of cross-sectional image planes that are placed perpendicular to the local centerline direction. Similar to other algorithms in this area, we define a set of rays within each plane pointing outward from the centerline point (Fig. 4).^{5,14}

For each ray v , we extract the intensity and gradient profiles $I_{v,r}$ and $G_{v,r}$, respectively, from the original image in the direction of the ray using trilinear resampling, where r is the radial distance from the center. First, the intensity profile is analyzed to get a reference value for the vessel and tissue intensities in this cross section. We set

$$I_{\text{vessel}} = \max_{v,r} I_{v,r} \quad \text{and} \quad I_{\text{tissue}} = \frac{1}{|R|} \sum_v \left(\min_r I_{v,r} \right), \quad (2)$$

defining the vessel intensity I_{vessel} as the maximum intensity over all ray samples in the cross section. For the tissue intensity

Fig. 4 (a) Maximum intensity projection of a CEMRA image. The detected centerline has been marked orange and one cross section that is perpendicular to the centerline is represented by the blue rectangle. (b) Corresponding cross section with radial rays and sample points used for the lumen contour detection.

I_{tissue} , we find the lowest intensity for each ray and then calculate the average over all those values. To get an estimate for the vessel radius, we compute a score function for all rings around the centerline point (Fig. 5):

$$\text{score}_r = \frac{\bar{G}_r}{(a + |\bar{I}_r - 0.5 \cdot I_{\text{vessel}}|) \cdot r},$$

where $\bar{I}_r$ and $\bar{G}_r$ are the mean intensity and gradient, respectively, for a ring with radius r around the center. The parameter a scales the impact of the radius. This score favors high gradients close to the center and intensities near half the vessel intensity. The radius with the maximum score is used as a rough radius estimate r_e , which is only used to limit the boundary search space. For the true radius estimation, we assume that the real radius is no larger than θ_{tight} , which is a constant that was determined empirically (Sec. 4). We calculate for each ray the radius $r_{\text{tight}} < \theta_{\text{tight}}$, for which the intensity first drops below the tissue threshold $\theta = (I_{\text{vessel}} + I_{\text{tissue}})/2$ (Fig. 5). In case there is no such radius $r_{\text{tight}} < \theta_{\text{tight}}$ within the search space, we choose the next larger radius, for which the intensity has a local minimum instead. This gives us one radius estimation for each ray, from which we get a boundary point on each ray. From these, we can interpolate the complete boundary. However, in some cases,

Fig. 5 Lumen boundary detection in cross sections. (a) Overlaid over the cross section are the initial radius estimate r_e and the derived tight and loose search areas. (b) Top: the score function for one ray in a cross section showing a clear peak at the supposed lumen boundary. Bottom: the curve shows the radial intensity profile of one ray as well as the tissue threshold. The intersection is the outer lumen border.

the true boundary does not lie within the search area. This may for instance happen when the lumen does not take a circular shape but is partially obstructed by atherosclerotic plaque. Then the radii on different rays can differ strongly, while the first estimation assumes a roughly circular shape and thus similar radii in all directions. To account for those special cases, we calculate a second radius estimate $r_{loose} < \theta_{loose}$ for each ray, which is calculated the same way as r_{tight} , except that it can have a larger range (Fig. 5). For both boundaries, we calculate the center and the variation of distances from all boundary points to the center. The boundary corresponding to r_{loose} is chosen instead of the boundary corresponding to r_{tight} , if the variation of r_{loose} is significantly smaller than the variation of r_{tight} . This is based on the assumption that a large variation indicates faulty estimations.

To make the border calculation more robust to small changes in the centerline, we recompute the centerline points by setting them to the gravity centers of the lumen and then repeat the whole calculation with the new centerline.

3.1.3 Partial volume correction

As the algorithm described above estimates vessel intensities separately for each cross section, it will generally overestimate the lumen diameter if the lumen cross section is only covered by a few voxels. In this case, we apply a PVC by taking into account the overall vessel intensity estimate I_{ref} . For each cross section, we compute

$$\text{correction factor} = \sqrt{\frac{I_{vessel} - I_{tissue}}{I_{ref} - I_{tissue}}}, \quad (3)$$

where I_{ref} is the maximum intensity across the whole vessel. The lumen radius on each ray is then corrected by multiplying with the correction factor. Figure 6 demonstrates the effect.

3.2 Quantification and Exploration

Given the centerline and lumen segmentation, the lumen diameter can now be extracted. We define the diameter as the radius corresponding to the circle that has the same area as the lumen cross section. This way it directly corresponds to the amount of blood that could theoretically flow through this cross section. To get comparable measurements for different images of the same patient, we need to establish correspondences between the images. Instead of registering the images, we extract measurements only at specific planes that are defined with respect to the flow diverter, so their computation is based on the vessel geometry and independent of imaging parameters. In this way, corresponding planes of the same vessel in different image types can be compared without actually having to register the images and change the data by applying a transformation that requires resampling with interpolations.

Our region of interest is defined as a sphere with radius 2 cm around the flow diverter point and covers the common carotid artery (CCA), internal carotid artery (ICA), and external carotid artery (ECA) in close proximity of the bifurcation. We place one plane directly within the bifurcation bulbous 4 mm below the flow diverter. The other planes are positioned equidistant with a fixed step size along the centerline within the whole region of interest (Fig. 7). Furthermore, we add one plane 3 cm below the flow diverter, which is needed for estimating the stenosis using the carotid stenosis index (CSI) method¹⁵ and one plane at the location of minimum diameter in the ICA stenosis. All planes are oriented perpendicular to the centerline.

In addition to the lumen diameter, distances between cross-sectional gravity center and lumen wall are calculated for 12 sectors in each plane (Sec. 4.2). We also estimate the grade of ICA stenosis using the NASCET method¹⁶ and the CSI.¹⁵ Both methods use the formula $\frac{n-d}{n} \times 100\%$, where d is the smallest diameter in the ICA and n is the normal ICA diameter, which would be present without the stenosis. The NASCET method

Fig. 6 Effect of the PVC on the segmentation. (a) Curved planar reconstruction of a CEMRA image along the centerline. The vessel contains a stenosis. The blue line marks the cross section for analysis. (b) Lumen diameters along the vessel shown in (a). The upper line denotes the diameter before PVC while the lower line reflects the correction. (c) Lumen segmentation for the cross section with stenosis marked in (a) and (b) before (outer ring) and after (inner ring) PVC. The resulting diameter after PVC is considerably smaller.

Fig. 7 Sample positions and orientations for the measurement planes. They are placed perpendicular to the centerline around the carotid bifurcation. The lumen diameter is estimated in each cross section.

measures n at a reference position in the distal ICA, while CSI uses the diameter of the proximal CCA and assumes the correlation $n = 1.2 \times \text{CCA diameter}$.

4 Experiments

For our experiments, we placed the reference planes according to the scheme described in Sec. 3.2 with a distance of 4 mm

along the centerline within a sphere of radius 2 cm. This results in five planes in each vessel segment in addition to the plane in the bifurcation bulb.

Furthermore, we set $a = 50$, $\theta_{\text{tight}} = 1.6 \cdot r_e$, and $\theta_{\text{loose}} = 3.0 \cdot r_e$. These values turned out to perform well for our test data, which are described below.

4.1 Data

CEMRA, SUB images, and TOFMRA were performed in eight patients with severe carotid atherosclerotic plaques. All MRI images were acquired on a Siemens 3T scanner. The CEMRA and SUB images have voxel dimensions of $0.6 \times 0.6 \times 0.7 \text{ mm}^3$, while the TOF images were acquired with voxel dimension $0.5 \times 0.5 \times 1.0 \text{ mm}^3$. The patient group consisted of seven males and one female patient with a median age of 68.5 years (range 55 to 79). CTA was only available for four patients with voxel dimensions $0.4 \times 0.4 \times 1.0 \text{ mm}^3$ (Table 1).

Table 1 Dataset used for evaluation.

Patient	1	2	3	4	5	6	7	8
Age	70	58	67	73	79	73	64	55
Sex	m	w	m	m	m	m	m	m
TOF	x	x	x	x	x	x	x	x
CEMRA	x	x	x	x	x	x	x	x
SUB	—	x	x	x	x	x	x	x
CTA	—	x	x	x	x	—	—	—

Fig. 8 (a) Rendering of the vessel volume extracted from the TOF image and from the CEMRA image as half transparent overlay and color-coding for case 7. Red means TOF diameter is smaller, blue means CEMRA diameter is smaller, and white means the difference is close to zero. The diameter right before the stenosis is smaller for the TOF estimation than for the CEMRA estimations as there is likely to be reduced blood flow. The images have been rigidly registered so the diameters were not affected by the registration. (b) Visualization of differences between lumen diameter estimated from TOF and CEMRA images on an idealized geometry. (c)–(g) Further examples of diameter differences between TOF and CEMRA for patients 2 to 6.

4.2 Results and Discussion

For each image type, the lumen was segmented automatically using the intensity-based segmentation with PVC. The segmentation was guided by an interactively generated centerline. The quantification scheme described above was used to extract the lumen diameter at certain reference positions in the vessel. Finally, the results are visualized and can be explored based on color-coded rendering (Fig. 8) curves or bulls-eye plots (Fig. 9). The latter are displayed either isolated or embedded

into a 3-D visualization. In the 3-D visualization, the bulls-eye plots are placed perpendicular to the centerline in the respective cross sections.

Figure 10 shows the quantification result for one patient. Differences can be observed between the four modalities that were available. To test reproducibility of the measurements, we re-evaluated the data again for seven of the patients and compared the results. The user guides the generation of the centerline, chooses the flow diverter point on the vessel segmentation

Fig. 9 Detailed comparison of differences between the segmentation of a TOF cross section and a CEMRA cross section. (a) Lumen contour in a TOF cross section. (b) Bulls-eye plot for the TOF cross section representing the diameter (inner ring) and disagreement (outer ring) with the corresponding CEMRA cross-section. (c) Lumen contour in the CEMRA cross section corresponding to (a).

Fig. 10 Quantification result for patient 2. (a) Visualization of the placement of the reference planes in the centerline extracted from the TOF image. Pink lines represent the position and orientation of a cross section. (b) Lumen diameters and stenosis grading result for patient 2 for all reference planes along the CCA and ICA as shown in (a) in all four modalities.

Table 2 Absolute differences [mean $\pm$ standard deviation (mm)].

	Total	CCA	ICA	ECA	Bifurcation	Minimum diameter
TOF	0.22 $\pm$ 0.29	0.13 $\pm$ 0.16	0.28 $\pm$ 0.38	0.18 $\pm$ 0.20	0.48 $\pm$ 0.56	0.04 $\pm$ 0.06
CEMRA	0.31 $\pm$ 0.59	0.12 $\pm$ 0.20	0.41 $\pm$ 0.51	0.12 $\pm$ 0.18	0.50 $\pm$ 0.61	0.04 $\pm$ 0.04
All	0.28 $\pm$ 0.27	0.12 $\pm$ 0.19	0.33 $\pm$ 0.46	0.15 $\pm$ 0.19	0.50 $\pm$ 0.57	0.04 $\pm$ 0.05

surface, and sets the reference plane in the distal ICA for the NASCET stenosis index, so these are the parameters that may be different in the re-evaluation. Table 2 shows the absolute differences between the two independent measurements. The best agreement is achieved for the minimum diameter in the stenosis, which does not rely on plane correlation. Measurement differences on ICA, where the stenosis is located, are slightly higher than on the CCA and ECA. Worst agreement

is achieved for the plane in the bifurcation. Overall, the results show a good reproducibility with an average error below the image pixel dimension.

Table 3 summarizes the quantification of the diameter differences between the four image types available in our dataset as well as the differences between the stenosis rating. Even though the dataset was very small, it already gives some insight into how the image type impacts the diameter measurement.

Table 3 Mean differences and standard deviation in millimeters for the diameter measurements in different image types for the corresponding planes. The last two columns show the mean difference between the stenosis degree.

Mean difference	CCA	ICA	ECA	Bifurcation	Min ICA	Total	NASCET	CSI
ITOF–CEMRAI	0.54	0.80	0.35	0.79	0.63	0.56	0.24	0.11
ICTA–CEMRAI	0.32	0.54	0.27	0.47	0.41	0.38	0.12	0.05
ITOF–CTAI	0.48	0.93	0.34	0.57	0.56	0.58	0.26	0.09
ISUB–CEMRAI	0.21	0.33	0.17	0.58	0.32	0.24	0.10	0.05
TOF–CEMRA	–0.39	–0.07	–0.14	–0.29	0.00	–0.19	–0.08	–0.01
CTA–CEMRA	–0.05	–0.19	–0.25	–0.07	–0.34	–0.17	0.04	0.04
TOF–CTA	–0.31	0.22	0.20	–0.45	0.23	0.05	–0.04	–0.03
SUB–CEMRA	–0.09	–0.11	–0.12	–0.35	–0.19	–0.11	0.00	0.02

Table 4 Average diameters for each vessel computed across the whole dataset.

Average diameters (mm)	TOF	CEMRA	SUB	CTA
ICA	4.51 (± 0.99)	4.40 (± 1.32)	4.32 (± 1.24)	4.29 (± 1.77)
ECA	4.38 (± 1.06)	4.42 (± 1.16)	4.29 (± 1.24)	4.07 (± 1.19)
CCA	6.60 (± 0.96)	6.88 (± 0.95)	6.77 (± 0.96)	6.41 (± 1.19)

The SUB and CEMRA images have the largest agreement, which is only to be expected, since they have been derived from the same image sequence. TOF images seem to slightly underestimate the lumen diameter compared to CEMRA images. For TOF imaging, this can be explained by the acquisition method. While TOF images only detect regions in which there is blood flow, the contrast agent applied for CEMRA imaging can also diffuse into regions with reduced blood flow. This observation is supported when comparing the lumen extracted from different images of one patient directly (Fig. 8). The representation via accurate vessel volume rendering is not optimal for comparing vessel diameters, as the vessels are not perfectly aligned, since registering them would also influence the lumen geometry. Figure 8(b) shows the color-coded differences between the TOF and CEMRA estimations for the same patient as Fig. 8(a), indicating increased uncertainty toward the bifurcation and around the stenosis. This can be explained by the fact that plane orientations have a huge impact on correct lumen diameter extraction. If a plane is tilted, the corresponding diameter will be overestimated. Especially, in areas where the centerline is strongly bent (e.g., around the bifurcation or stenoses), small changes in the positioning of the plane can thus affect the diameter estimation and increase uncertainties.

Uncertainties in diameter estimations also impact the result of the stenosis quantification. We compared results for the NASCET stenosis rating and the CSI (Table 3). The CSI was more reliable in our test cases, which uses a reference value from the CCA instead of the ICA. This is in accordance with the observation that the CCA can be quantified more reliably.

We also computed average diameters for all vessels as well as differences between measurements from different image types (Table 4). The average diameters are in accordance previously given in literature¹⁷ considering that the carotid vessels in our dataset all contain pathological changes.

5 Conclusion and Outlook

We have presented a method for the quantitative and visual analysis of angiography-based lumen assessment of the carotid arteries that also helps to identify differences in quantifications in different modalities. In the application to TOF, CTA, CEMRA, and SUB images, we observed that the average absolute error between the lumen estimates for the different modalities is in the range of the actual spatial resolution. The disagreement could be explained by differences in image orientation, resolution, and imaging techniques. Another source of uncertainty is the placement of planes, since they are oriented perpendicular to the centerline, their orientation and thus potentially also the diameter will vary, if the centerline is curved differently.

We have seen that there are regions that are prone to inaccuracies, as for example the bifurcation, and that image acquisition method has an impact on geometry measurements. Furthermore, the definition of the lumen diameter and the orientation of cross sections play an important role in extracting accurate diameter estimates. All these factors that can create uncertainties should be considered when dealing with lumen geometry extraction, especially when the geometry is used for further analysis, e.g., stenosis detection and grading.

In future work, we plan to further analyze different frameworks for the comparison of carotid vessel geometry in terms of accuracy, robustness, and clinical meaningfulness. Furthermore, we want to include black-blood sequences in our comparison, which are also suitable for investigating vessel wall thickness and plaque components.

Disclosures

The authors state no conflicts of interest and have nothing to disclose.

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