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A REVIEW ON ARTERY WALL SEGMENTATION TECHNIQUES AND INTIMA-MEDIA THICKNESS MEASUREMENT FOR CAROTID ULTRASOUND IMAGES

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Stroke and heart attack, which could be led by a kind of cerebrovascular and cardiovascular disease named as atherosclerosis, would seriously cause human morbidity and mortality. It is important for the early stage diagnosis and monitoring medical intervention of the atherosclerosis. Carotid stenosis is a classical atherosclerotic lesion with vessel wall narrowing down and accumulating plaques burden. The carotid artery of intima-media thickness (IMT) is a key indicator to the disease. With the development of computer assisted diagnosis technology, the imaging techniques, segmentation algorithms, measurement methods, and evaluation tools have made considerable progress. Ultrasound imaging, being real-time, economic, reliable, and safe, now seems to become a standard in vascular assessment methodology especially for the measurement of IMT. This review firstly attempts to discuss the clinical relevance of measurements in clinical practice at first, and then followed by the challenges that one has to face when approaching the segmentation of ultrasound images. Secondly, the commonly used methods for the IMT segmentation and measurement are presented. Thirdly, discussion and

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evaluation of different segmentation techniques are performed. An overview of summary and future perspectives is given finally.

Keywords: Ultrasound (US) images; carotid artery; intima-media thickness (IMT); atherosclerosis; image segmentation; computer assisted diagnosis (CAD).

1. Introduction

According to a latest report by the World Health Organization (WHO), cardiovascular diseases (CVDs) represent the third leading cause of death in the world.[1] Therefore, the individuation of early prevention increased risk of CVDs is of uppermost importance in clinical practice. The earliest possible manifestation onset of a CVD is atherosclerosis. The atherosclerotic process refers to the arterial wall degeneration and lipids and other blood borne material deposition within the arterial wall of almost all vascular territories.[2–4]

Symptoms of cardiovascular diseases are associated with hypercholesterolemia, high blood cholesterol level, and atherosclerosis or build-up of plaques in the arterial walls.[5]

Early stage of atherosclerosis is initiated by the deposition of low density lipoprotein (LDL), infiltration of monocytes, and maturation of monocytes into macrophages in the intima. Advanced stage of atherosclerosis is associated with lipid-rich necrotic cores and calcium deposits in the thickened intima. Clinical manifestation of atherosclerosis comes from plaque rupture and thrombosis which could lead to myocardial infarction and stroke.[6]

The progression of atherosclerosis is both complex and lengthy. However, current imaging technologies are only capable of detecting advanced-stage lesions. Thus, early detection and prevention of atherosclerosis remains an attractive yet unrealized opportunity.[5]

Once left common carotid artery (CCA) born from the aortic arch and right CCA divided from brachiocephalic trunk, the CCAs follow the neck axis, at a depth of about 2–4 cm. In Fig. 1, it depicts the right CCA anatomy shape and position. It shows that CCA may course along the neck of a subject. Clinically, the B-mode ultrasonographic analysis of the CCA is the first routine examination for early diagnosis and follow-up[7] as shown in Fig. 2.

One of the most widely used indicator of cardiovascular and cerebrovascular risk is the CCA intima-media thickness (IMT).[8] Several studies

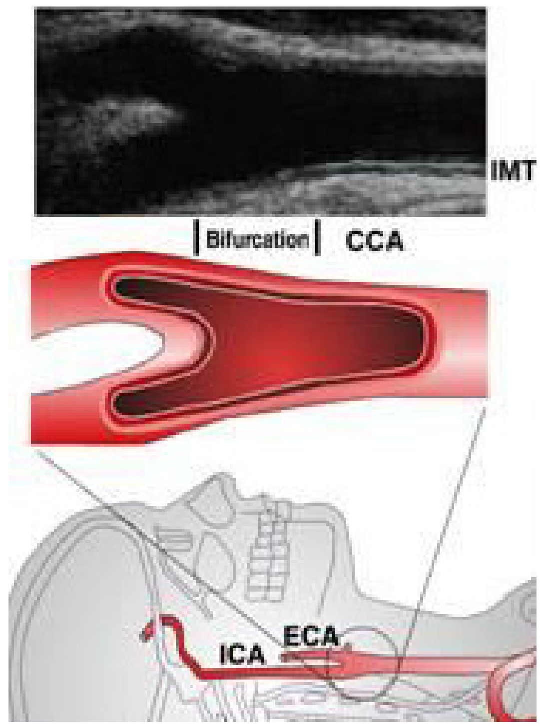


Fig. 1. From top to bottom: Demonstration of B-mode ultrasound CCA image; CCA anatomy shape; CCA anatomy position.

have showed that IMT had an important diagnostic and predictive value for incident myocardial infarction.[9,10] Ultrasound (US) is the most used diagnostic tools for assessing CVDs. US scanning could offer several paramount advantages in IMT clinical practice, such as: (1) real-time quick examination; (2) low-cost or economic; (3) repeatable and reliable; and (4) nonradiation and noninvasiveness.

2. Method

2.1. *Review methodology*

The PubMed database was searched for clinical studies evaluation and measurement of the IMT. The search terms used were: "Ultrasound," "carotid artery," "intima-media thickness (IMT)," "atherosclerosis" in

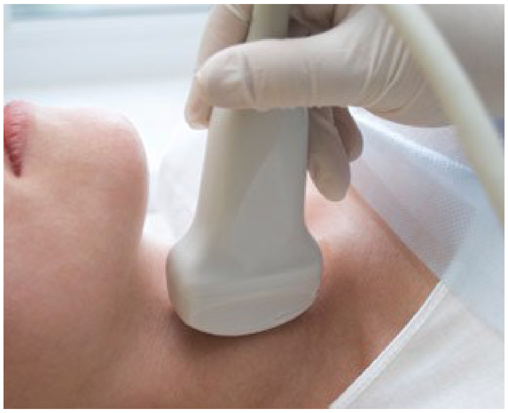


Fig. 2. Demonstration of the CCA routine scan by physicians.

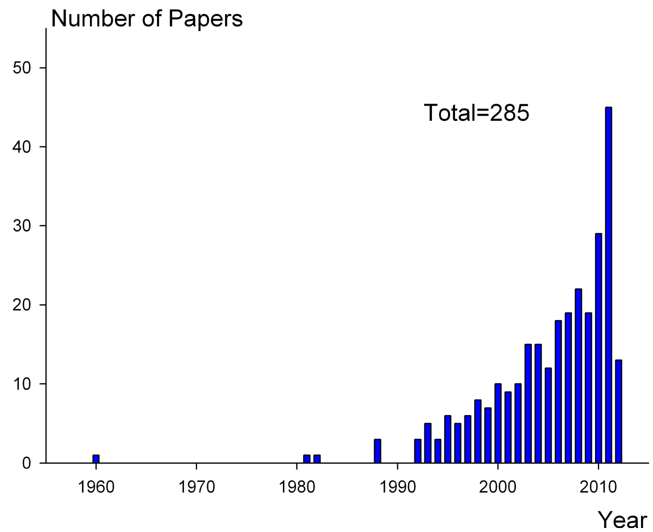


Fig. 3. Chart of articles published trend per year.

various combinations. Two independent reviewers, Wanji He and Kaitong Li, performed the literature search and data mining. All clinical studies which reported results on the IMT segmentation and evaluation were retrieved. Case report studies were excluded from our analysis. Animal or *in vitro* studies were also excluded. There was no time or nation limit to our analysis. The end of this search was 15th of August 2011. Finally, 285 papers were retrieved, including some early access papers to be published in 2012. The publication amount versus year chart is shown in Fig. 3.

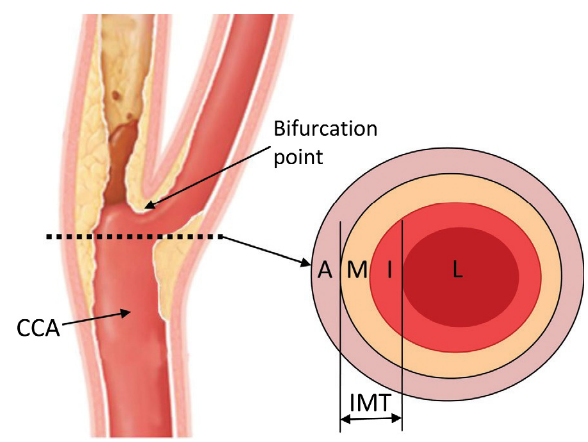
3. Clinical Significance of IMT Measurement

3.1. *CCA anatomical structure*

The CCA wall consists of three different layers namely *intima* (internal tunica), *media* (thick layer of transversal muscular tissues), and *adventitia* (external and more connective) respectively as shown in Fig. 4.

The IMT is correlated with an enlarged risk of severe pathologies. Hence, CCA layer analysis is significant for an effective evaluation to a patient. Although both near and far walls could be visualized on B-mode US scanning, far wall has better reflections because of relatively higher intensity. This is due to the acoustics impedance sequence of the lumen−intima−media−adventitia (LIMA) interface. Therefore, the measurement of far wall IMT is the distance between lumen−intima (LI) and media−adventitia (MA) boundaries. Figure 5 shows a normal carotid artery image and its schematic illustration of echo zones (Z1−Z7) and relevant vessel interface of the near wall (I2, I3) and far wall (I5, I6). IMT is defined as the distance between the leading edge of lumen−intima interface (the first echogenic line) and media−adventitia interface (the second echogenic line) of the arterial wall.[11] When the clinical examination aims at measuring the IMT, the longitudinal view is required. Lumen diameter (LD) is the distance between I3 and I5.

Figure 6 shows a sagittal cross section of a CCA with manually annotated boundaries overlaid. Figure 7 shows the manual segmentations of inner



(a) (b)

Fig. 4. (a) Schematic sagittal cross section of a carotid artery showing the bifurcation point and the CCA; (b) transverse cross section of a carotid artery showing the adventitia (A), media (M), intima (I), and lumen (L), as well as the IMT measurement (images adapted from Ref. 12).

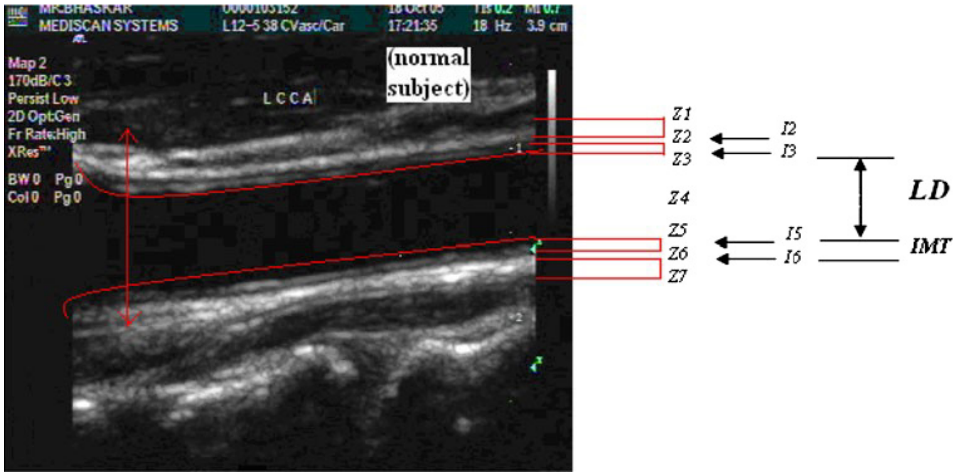


Fig. 5. Sample of echographic appearance of a normal CCA in longitudinal projection of US image. Depth increases from top to bottom. Usually, the intima layer cannot be distinguished by the media. The IMT is calculated as the distance between the lumen–intima (LI, I5) interface and the media–adventitia (MA, I6) interface (image adapted from Ref. 13).

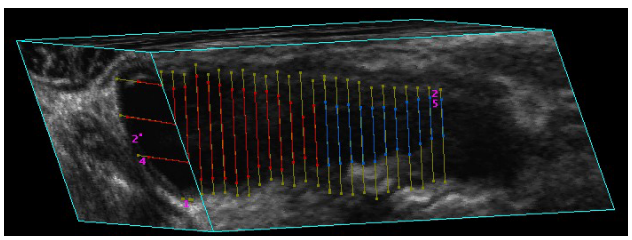


Fig. 6. Sagittal cross section of a CCA in a 3D US image. The contours on the image show the manual delineations done by the physician [Robarts Research Institute (RRI), University of Western Ontario (UWO), London, Ontario, Canada].

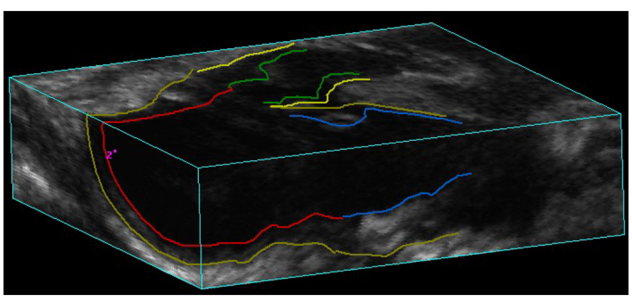


Fig. 7. Long axis view of a 3D US image of carotid artery. [Robarts Research Institute (RRI), University of Western Ontario (UWO), London, Ontario, Canada].

and outer walls overlaid on a 3D US image. And the scholars found that the segmentation accuracy is high distal to the bifurcation (BF) and decreases proximal to the BF.[12] It also revealed that the standard deviation of the segmentation error is higher near the BF. Therefore, most of IMT measurement researches were on special CCA region, which is within 20 mm extension from far wall BF.[14]

3.2. *Clinical significance of IMT measurement*

Both CCA wall segmentation and IMT measurement are the most important two steps in computer-aided clinical applications. IMT measurement is the key to perform measurements of further clinical usage.

The relationship between the IMT and the increased CVD risk is presented in several reported studies from different regions (refer to: Europe,[15] Latin American Cities,[16] Asia/Africa and Middle East,[17] Japan,[18] United States,[19,20] and China[21]). The studies confirmed that increased IMT value is often related to the arterial wall properties change, thus exposing the patients to increased CVD risks. There is a high correlation between CVD and IMT value, therefore, it is important to measure and monitor vessels IMT with a progression or regression plaque on the wall.

This review will focus on the techniques that have been developed to perform CCA wall segmentation and IMT measurement in 2D B-mode ultrasound longitudinal images.

4. Challenges in IMT Measurement

Although the individuation of ultrasound imaging has its own characters in clinical practice, unfortunately, ultrasound is operator-dependent. And ultrasound images also have a lower signal-to-noise ratio (SNR) than other imaging modalities (such as, MRI and CT).

4.1. *Noises*

Ultrasound images suffer from artifacts such as image speckle, shadowing, and poor definition of the artery boundaries. These artifacts make it hard to distinguish the interest object and background.

Speckle noise is the most important noise source in ultrasound imaging. Some researchers, such as Loizou *et al.*[22] presented a very detailed review on speckle noise in carotid longitudinal images and an overview of detailed discussion is reported in 2005.[23] One of the most used method to reduce the speckle noise is nonlinear filtering, using speck reducing anisotropic diffusion method (SRAD).[24]

4.2. *Biological variability*

In carotid ultrasound images, the contrast is lower at boundaries parallel to the ultrasound beam, compared to boundaries orthogonal to the ultrasound beam. Usually, CCA would be represented horizontally in an image frame. The ideally spatial position between ultrasound transducer and CCA ensures the possibility of good artery visualization in US images. However, the horizontal anatomical section is not always feasible because of patients' variability. Lucev *et al.*[25] gave a relatively complete discussion on possible carotids anatomical variations, such as, curved or tackled CCA. And he found that the great blood vessels of the neck had numerous variations. 40 carotid arterial systems were investigated for the appearance variability. In 20 cases (50%) the level of the bifurcation corresponded to the superior border of the thyroid cartilage. At the level of the inferior border of the hyoid bone, carotid bifurcation occurred in 10 cases (25%). A higher level opposite the superior border of the hyoid bone was found in five cases (12.5%). Also, bifurcation appeared at the level of the inferior border of the thyroid cartilage in five cases (12.5%).

That means the CCAs show great biological variability, and during surgery or ultrasound or radiologic examination, physicians must be cautious and take all possibilities into consideration.

4.3. *Operator dependent*

There are some specific requirements in order to perform a correct and effective computer-based IMT measurement [9]. The image should be acquired by a trained physician using a high-frequency linear probe and insonating the common tract of the CCA. The optimal location of IMT measurement is within 1 cm from the bifurcation point. Both antero-lateral and postero-lateral longitudinal views should be acquired. Optimal imaging techniques and performing computer algorithms enable fast and accurate artery wall evaluation and IMT measurement.

The mechanical US system in Ref. 12 and 26 studies acquired images by translating a linear ultrasound transducer (L12-5, Philips, Bothell, WA, USA) with an 8.5 MHz central frequency using a motorized linear device along the neck of each subject at a uniform speed of 3 mm/s for about 4 cm without cardiac gating.[27] 3D images were constructed from the 2D frames received from the US machine (ATL HDI 5000, Philips, Bothell, WA, USA) and displayed using multi-planar reformatting.[28] The voxel size in the 3D data was $\approx 0.1 \times 0.1 \times 0.15\,\text{mm}^3$.

5. Segmentation Techniques and IMT Measurement Methods

The manual segmentation method was described by Egger *et al.*[29] and is summarized here. Prior to contouring, the expert first located the BF and defined an approximate medial axis of the carotid artery by choosing two points on the axis. The multiplanar 3D viewing software presented 2D images of the artery by slicing through the 3D image orthogonally to the medial axis, in the inferior direction from the BF, with an interslice distance (ISD) of 1 mm. The expert then performed contouring of arteries on each of these images. Figure 6 shows a sagittal cross section of a CCA with manually annotated boundaries overlaid. An expert outlined the vessel boundaries five times repeatedly within a single day between repetitions on transverse 2D slices extracted from 3D US images. The images were randomized and the operator was blinded to the image order during each repetition to reduce memory bias.[12] However, this method still suffered from the potential errors and variabilities because of the variable interactions among inter-observers and intra-observers.

In order to reduce segmentation bias, several US segmentation algorithms had been reviewed in a survey by Noble.[30] Here, we are primarily interested in reporting on recent algorithms that were used for the segmentation of the intima and media layer in US images.

The majority of the existing literatures on carotid vessel wall segmentation focuses on obtaining IMT measurements from 2D US images that are parallel to the approximate central axis of the artery (henceforth referred to as longitudinally oriented images). These studies on carotid artery boundaries segmentation included the application of dynamic programming,[31] deformable snakes,[32] Hough transforms,[33] and classification approaches[34] to detect the carotid boundaries on longitudinally oriented images.

The first approach to perform carotid wall segmentation was based on edge detection.[35,36] Pignoli and Longo[35] were first to introduce computer methods with the aim of measuring IMT. The same structure was adopted by Touboul *et al.*[36] in 1992, who also used an IMT measurement technique based on edge detection in his followed clinical study.[9,15,17,36] In 1997, Wendelhag *et al.*[37] tried dynamic programming method to segment the vessel walls and gained promised results — manually and algorithm method of IMT values (mean $\pm$ SD) — 0.88 ± 0.25 (mm) and 0.92 ± 0.25 (mm), respectively.

The computer-based method had hugely developed since then. In 2000, Liang *et al.*[31] proposed a dynamic programming technique based on the thought of the evolution of the previous one by Wendelhag *et al.*,[37] but introduced multi-scale analysis. Dynamic programming was applied in an iterative progress, starting from the image in a coarse representation and then slowly applying step-by-step refinement iteration. Hence, the global position of the artery in the image was estimated on a coarse scale, while precise position of the wall layers was estimated in a fine scale. Therefore, the dynamic programming method could balance reducing computational cost and ensuring accurate performance. Cheng *et al.*[38] proposed a snake-based technique for CCA segmentation in 2002. They improved the traditional snakes by modifying the external energy to overcome the poor segmentation performance in the region comprised between the intima and the adventitia layers. In 2005, Stein *et al.*[39] proposed a gradient-based methodology for measuring the IMT of the carotid distal wall. In 2007, Delsanto *et al.*[40,41] proposed a combined approach of classification and snake-based segmentation to perform IMT measurement. The aim was to form a completely user-independent segmentation strategy. Completely user-independent layer extraction based on signal analysis (CULEXsa)[40,41] is an algorithm for extracting the layers of the artery wall. Briefly, the fundamental steps of the algorithm are the following three steps: (1) ROI Identification; (2) Gradient-based initial segmentation; and (3) Segmentation refinement through active contour.

Completely automatic layer extraction based on integrated approach (CALEXia)[42] consists of feature extraction, line fitting, and classification that enables the automated tracing of the carotid adventitial walls. CALEXia consists of two parts: (1) A module that automatically locates the CCA in the image; (2) a segmentation procedure that automatically traces the LI and the MA contours of the distal wall once CCA has been localized.

The CULEX and CALEX approaches are based on completely different strategies. CULEXsa exploits the local statistics of the image pixels to automatically discriminate between lumen pixels and tissue pixels. The segmentation process is based on a combination of gradient and snake paradigms. While the CALEXia strategy is based on an integrated approach of feature extraction, line fitting, and classification. The feature extraction procedure is needed to select what we called seed points. These points constitute the basis of both the automated CCA localization and of the segmentation. By connecting the seed points and classifying the resulting line segments, the adventitia layers of the CCA can be easily traced. The segmentation of the LI and MA boundaries is relying on a fuzzy K-means classifier. Although they are both completely user-independent techniques, CULEXsa and CALEXia exploit totally different image features.

Comparing the performance of the two approaches, CALEXia showed limited performance in segmenting LI interface, but outperformed CULEXsa in MA interface. Meanwhile CULEXsa suffered from the problem of noise and image artifacts. Finally, the major advantage of CALEXia with respect to CULEXsa is the computational cost.

An active contour segmentation technique and dynamic programming method for extracting the intima–media layer of the CCA ultrasound images employing semiautomatic region of interest identification and speckle reduction techniques is presented by Santhiyakumari *et al.*[13]

Table 1. Common carotid wall segmentation techniques and IMT measurements methods.

Year	Author	Method	Manual (mm)	Algorithm (mm)
2000	Liang[31]	DP	0.88 ± 0.24	0.93 ± 0.25
2002	Cheng[38]	Snake	—	0.65 ± 0.16
2005	Stein[39]	ED	0.67 ± 0.15	0.67 ± 0.12
2007	Delsanto[40,41]	Snake+FCM	0.77 ± 0.22	0.71 ± 0.16
2010	Molinari[34]	IA	0.92 ± 0.30	0.75 ± 0.39
2011	Santhiyakumari[13]	AC	—	0.59 ± 0.02
		DP	—	0.69 ± 0.016

DP: Dynamic Programming; ED: Edge Detection; FCM: Fuzzy C-means Method; IA: Integrated Approach; AC: Active Contour.

Table 1 summarizes various computerized methods that have been developed for ultrasound segmentation of the IMT.

When processing large sets of ultrasound images, the user always has two sets of IMT measurements values: the proposed algorithm measured IMT value and the manual IMT value. *Boundary distance-based* metrics and *region-based* metrics are mostly used to evaluate the algorithm compared with manual results. The mean absolute distance (MAD) and maximum absolute distance (MAXD) were used as boundary distance-based metrics. Dice coefficient as a region-based measurement to compare the two segmentations boundaries on a slice-by-slice basis.

The IMT values ($IMT_{mean \pm SD}$ (mm)) for manual (IMT_M) and algorithm (IMT_A) quoted in Table 1 reflect the accuracy of the method described in related papers. The data indicate that the listed methods are not statistically significantly different from the manual results. And the IMT measurements results could conclude that the magnitudes of the IMT values have been used to explore the rate of prediction of blockage existing in the cerebrovascular and cardiovascular pathologies and also hypertension and atherosclerosis.

In the above, we described the most performing techniques for carotid wall segmentation and IMT measurement in US imaging. For each methodology, we only describe basic principles and black IMT measurement performance.

6. Discussion

Several investigations have been reported that rely on an expert observer to manually outline the carotid walls.[43,44] Although the manual segmentation method used in IMT measurements may make a larger clinical trial laborious, until a semiautomatic or fully automatic segmentation technique is validated and generally accepted. Furthermore, manual techniques must still be used, in fact, are being used in reviewed clinical trials.[28,44,45]

In any case, validation of new segmentation algorithm will require manual segmentation results. However, manual segmentation of these boundaries is labor intensive and time-consuming.[44] There are several studies that report on semi-automated segmentation methods for delineating carotid walls on 2D US images.[46]

The coefficients of variation of the algorithm in Ref. 12 (5.1%) and manual methods (3.9%) are not significantly different, but the average time is saved using the algorithm. Operator time of 8.3 ± 1.5 min is required by an expert to manually delineate the inner and outer contours for a single 3D US image (11 2D carotid images). However, the algorithm takes 2.8 min in all of whole schedule (1.6 ± 0.3 min of preprocessing and 1.2 ± 0.2 min of execution) on a single core of a PC with processor speed of 2.5 GHz. It provides a way to reduce operator time and interaction, and with necessary required precision.

Accurate and fast carotid wall segmentation in US imaging is the key to perform a precise IMT measurement and evaluation. From a practical point of view, the segmentation strategies and measurement methods that have been proposed so far essentially are divided into three emerging studies.

6.1. *3D studies and segmentation*

US imaging measurements for quantifying carotid atherosclerosis, not only including IMT[47] we discussed here, but also having total plaque area

(TPA),[48] total plaque volume (TPV),[27,49] and vessel wall volume (VWV).[29,50] The use of 3D techniques has primarily focused on measuring volume changes through time to monitor disease progression. And VWV would be more efficient than IMT measurement.[50]

6.2. *Plaque segmentation and stenosis evaluation*

The risk of stroke increases with the severity of carotid stenosis and is reduced after carotid endarterectomy. The degree of internal carotid stenosis is the only well-established measurement which is used to assess the risk of stroke. Therefore, the need of accurate atherosclerotic carotid plague segmentation in US imaging for assessment stenosis degree is an important task. There are several recent methods for segmenting carotid plaques in Ref. 51.

6.3. *Motion correction*

Most motion studies are aimed at the use of 2D ultrasound. But some pioneer had some researches on $3D/4D$ US motion estimation.[52]

7. Conclusion

In the past decades, Computer Assisted Diagnosis (CAD) algorithms for carotid US images processing have continuously grown in both number and performance. Active contours, dynamic programming, and integrated approaches have been presented to segment the carotid walls and trace the boundaries of the LI and MA interfaces. The techniques have been developed and are now available to perform user-independent ultrasound images segmentation from simple architecture to complex approaches.

Major challenges that will be faced in near future would be the urgent demand between accurate/fast measurement performance and intelligent automation. Characterization and validation studies will be required in order to carefully assess the effect of such variability on segmentation performance.

All the efforts made on CAD would reduce the examination time, increase IMT measurement accuracy, and in the end, promote the human being healthy. Such capability would advance the opportunity for early clinical detection and prevention of atherosclerosis.

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References

1. World Health Organization, "Cardiovascular disease," (2007).
2. J. J. Badimon, B. Ibanez and G. Cimmino, "Genesis and dynamics of atherosclerotic lesions: Implications for early detection," *Cerebrovasc. Dis.* **27**(1), 38–47 (2009).
3. M. Walter, "Interrelationships among hdl metabolism, aging, and atherosclerosis," *Arterioscler. Thromb. Vasc. Biol.* **29**(9), 1244–1250 (2009).
4. A. M. Kampoli, D. Tousoulis, C. Antoniades, G. Siasos and C. Stefanadis, "Biomarkers of premature atherosclerosis," *Trends Mol. Med.* **15**(7), 323–332 (2009).
5. T. T. Le and J.-X. Cheng, "Non-linear optical imaging of obesity-related health risks: Review," *J. Innovative Opt. Health Sci.* **2**(1), 9–25 (2009).
6. A. J. Lusis, Atherosclerosis, *Nature* **407**(6801), 233–241 (2000).
7. F. Mao, J. Gill, D. Downey and A. Fenster, "Segmentation of carotid artery in ultrasound images: Method development and evaluation technique," *Med. Phys.* **27**, 1961–1970 (2000).
8. A. Simon, J. Gariepy, G. Chironi, J. L. Megnien and J. Levenson, "Intima-media thickness: A new tool for diagnosis and treatment of cardiovascular risk," *J. Hypertens.* **20**(2), 159–169 (2002).
9. P. J. Touboul, M. G. Hennerici, S. Meairs, H. Adams, P. Amarenco, M. Desvarieux, S. Ebrahim, M. Fatar, R. Hernandez Hernandez and S. Kownator, "Mannheim intima-media thickness consensus," *Cerebrovasc. Dis.* **18**(4), 346–349 (2004).
10. I. M. Van der Meer, M. L. Bots, A. Hofman, A. I. del Sol, D. A. M. van der Kuip and J. C. M. Witteman, "Predictive value of noninvasive measures

of atherosclerosis for incident myocardial infarction: The rotterdam study," *Circulation* **109**(9), 1089–1094 (2004).
11. J. T. Salonen and R. Salonen, "Ultrasound b-mode imaging in observational studies of atherosclerotic progression," *Circulation* **87**(3 suppl), II56–II65 (1993).
12. E. Ukwatta, J. Awad, A. D. Ward, D. Buchanan, J. Samarabandu, G. Parraga and A. Fenster, "Three-dimensional ultrasound of carotid atherosclerosis: Semiautomated segmentation using a level set-based method," *Med. Phys.* **38**, 2479–2493 (2011).
13. N. Santhiyakumari, P. Rajendran *et al.*, "Detection of the intima and media layer thickness of ultrasound common carotid artery image using efficient active contour segmentation technique," *Med. Biol. Eng. Comput.* **49**(11), 1299–1310 (2011).
14. K. Hameeteman, M. Freiman, M. Zuluaga, L. Joskowicz, S. Rozie, M. Van Gils, L. Van den Borne, J. Sosna, P. Berman and N. Cohen, "Carotid lumen segmentation and stenosis grading challenge," *Carotid Lumen Segmentation and Stenosis Grading Challenge, Part of the 3rd "3D Segmentation in the Clinic: A Grand Challenge" Workshop at the MICCAI 2009* (2009).
15. P. J. Touboul, M. G. Hennerici, S. Meairs, H. Adams, P. Amarenco, N. Bornstein, L. Csiba, M. Desvarieux, S. Ebrahim and M. Fatar, "Mannheim carotid intima media thickness consensus (2004–2006)," *Cerebrovasc. Dis.* **23**(1), 75–80 (2006).
16. H. Schargrodsky, R. Hernandez-Hernandez, B. M. Champagne, H. Silva, R. Vinueza, L. C. Silva Aycaguer, P. J. Touboul, C. P. Boissonnet, J. Escobedo, F. Pellegrini, A. Macchia and E. Wilson, "Carmela: Assessment of cardiovascular risk in seven latin American cities," *Am. J. Med.* **121**(1), 58–65 (2008).
17. P. J. Touboul, R. Hernandez Hernandez, S. Kucukoglu, K. S. Woo, E. Vicaut, J. Labreuche *et al.*, "Carotid artery intima media thickness, plaque and framingham cardiovascular score in asia, Africa/middle east and latin America: The parc-aala study," *Int. J. Cardiovas. Imaging* **23**(5), 557–567 (2007).
18. H. Watanabe, K. Yamane, G. Egusa and N. Kohno, "Influence of westernization of lifestyle on the progression of imt in Japanese," *J. Atheroscler. Thromb.* **11**(6), 330–334 (2004).
19. M. J. Roman, T. Z. Naqvi, J. M. Gardin, M. Gerhard-Herman *et al.*, "American society of echocardiography report: Clinical application of noninvasive vascular ultrasound in cardiovascular risk stratification: A report from the American society of echocardiography and the society for vascular medicine and biology," *Vasc. Med.* **11**(3), 201–211 (2006).
20. A. R. Bhuiyan, S. R. Srinivasan, W. Chen, T. K. Paul and G. S. Berenson, "Correlates of vascular structure and function measures in asymptomatic young adults: The bogalusa heart study," *Atherosclerosis* **189**(1), 1–7 (2006).
21. L. Liu, F. Zhao, Y. Yang, L. T. Qi, B. W. Zhang, F. Chen, D. Ciren, B. Zheng, S. Y. Wang and Y. Huo, "The clinical significance of carotid intima-media thickness in cardiovascular diseases: A survey in Beijing," *J. Hum. Hypertens.* **22**(4), 259–265 (2007).
22. C. P. Loizou, C. S. Pattichis, M. Pantziaris, T. Tyllis and A. Nicolaides, "Quality evaluation of ultrasound imaging in the carotid artery based on normalization and speckle reduction filtering," *Med. Biol. Eng. Comput.* **44**(5), 414–426 (2006).
23. C. P. Loizou, C. S. Pattichis, C. I. Christodoulou, R. S. H. Istepanian, M. Pantziaris and A. Nicolaides, "Comparative evaluation of despeckle filtering in ultrasound imaging of the carotid artery," *IEEE Trans. Ultrason., Ferroelectr., Freq. Control.* **52**(10), 1653–1669 (2005).
24. Y. Yongjian and S. T. Acton, "Speckle reducing anisotropic diffusion," *IEEE Trans. Image Process.* **11**(11), 1260–1270 (2002).
25. N. Lucev, D. Bobinac, I. Maric and I. Drescik, "Variations of the great arteries in the carotid triangle," *Otolaryngol. Head Neck Surg.* **122**(4), 590–591 (2000).
26. J. Awad, A. Krasinski, G. Parraga and A. Fenster, "Texture analysis of carotid artery atherosclerosis from three-dimensional ultrasound images," *Med. Phys.* **37**, 1382–1391 (2010).
27. C. D. Ainsworth, C. C. Blake, A. Tamayo, V. Beletsky, A. Fenster and J. D. Spence, "3D ultrasound measurement of change in carotid plaque volume: A tool for rapid evaluation of new therapies," *Stroke* **36**(9), 1904–1909 (2005).
28. A. Fenster, D. B. Downey and H. N. Cardinal, "Three-dimensional ultrasound imaging," *Phys. Med. Biol.* **46**, R67–R99 (2001).
29. M. Egger, J. D. Spence, A. Fenster and G. Parraga, "Validation of 3D ultrasound vessel wall volume: An imaging phenotype of carotid atherosclerosis," *Ultrasound Med. Biol.* **33**(6), 905–914 (2007).
30. J. A. Noble and D. Boukerroui, "Ultrasound image segmentation: A survey," *IEEE Trans. Med. Imag.* **25**(8), 987–1010 (2006).
31. Q. Liang, I. Wendelhag, J. Wikstrand and T. Gustavsson, "A multiscale dynamic programming procedure for boundary detection in ultrasonic artery images," *IEEE Trans. Med. Imag.* **19**(2), 127–142 (2000).

32. C. P. Loizou, C. S. Pattichis, M. Pantziaris, T. Tyllis and A. Nicolaides, "Snakes based segmentation of the common carotid artery intima media," *Med. Biol. Eng. Comput.* **45**(1), 35–49 (2007).
33. S. Golemati, J. Stoitsis, E. G. Sifakis, T. Balkizas and K. S. Nikita, "Using the hough transform to segment ultrasound images of longitudinal and transverse sections of the carotid artery," *Ultrasound Med. Biol.* **33**(12), 1918–1932 (2007).
34. F. Molinari, G. Zeng and J. S. Suri, "An integrated approach to computer-based automated tracing and its validation for 200 common carotid arterial wall ultrasound images," *J. Ultrasound Med.* **29**(3), 399–418 (2010).
35. P. Pignoli and T. Longo, "Evaluation of atherosclerosis with b-mode ultrasound imaging," *J. Nucl. Med. Allied Sci.* **32**(3), 166–173 (1988).
36. P. J. Touboul, P. Prati, P. Y. Scarabin, V. Adrai, E. Thibout and P. Ducimetire, "Use of monitoring software to improve the measurement of carotid wall thickness by b-mode imaging," *J. Hypertens.*, **10**, S37–S42 (1992).
37. I. Wendelhag, Q. Liang, T. Gustavsson and J. Wikstrand, "A new automated computerized analyzing system simplifies readings and reduces the variability in ultrasound measurement of intima-media thickness," *Stroke* **28**(11), 2195–2200 (1997).
38. D. Cheng, A. Schmidt-Trucksass, K. Cheng and H. Burkhardt, "Using snakes to detect the intimal and adventitial layers of the common carotid artery wall in sonographic images," *Comput. Met. Programs Biomed.* **67**(1), 27–37 (2002).
39. J. H. Stein, C. E. Korcarz, M. E. Mays, P. S. Douglas, M. Palta, H. Zhang, T. LeCaire, D. Paine, D. Gustafson and L. Fan, "A semiautomated ultrasound border detection program that facilitates clinical measurement of ultrasound carotid intima-media thickness," *J. Am. Soc. Echocardiogr.* **18**(3), 244–251 (2005).
40. S. Delsanto, F. Molinari, P. Giustetto, W. Liboni and S. Badalamenti, "Culex: Completely user-independent layers extraction: Ultrasonic carotid artery images segmentation," *IEEE Conf. of the 27th Annual Int. Engineering in Medicine and Biology Society (IEEE-EMBS 2005)*, pp. 6468–6471 (2005).
41. S. Delsanto, F. Molinari, P. Giustetto, W. Liboni, S. Badalamenti and J. S. Suri, "Characterization of a completely user-independent algorithm for carotid artery segmentation in 2-d ultrasound images," *IEEE Trans. Instrum. Meas.* **56**(4), 1265–1274 (2007).
42. F. Molinari, G. Zeng and J. S. Suri, "Intima-media thickness: Setting a standard for a completely automated method of ultrasound measurement," *IEEE Trans. Ultrason., Ferroelectr., Freq., Control.* **57**(5), 1112–1124 (2010).
43. I. Shai, J. D. Spence, D. Schwarzfuchs, Y. Henkin, G. Parraga, A. Rudich, A. Fenster, C. Mallett, N. Liel-Cohen and A. Tirosh, "Dietary intervention to reverse carotid atherosclerosis," *Circulation* **121**(10), 1200–1208 (2010).
44. B. Chiu, M. Egger, J. D. Spence, G. Parraga and A. Fenster, "Quantification of carotid vessel wall and plaque thickness change using 3D ultrasound images," *Med. Phys.* **35**, 3691–3700 (2008).
45. P. A. Barnett, J. D. Spence, S. B. Manuck and J. R. Jennings, "Psychological stress and the progression of carotid artery disease," *J. Hypertens.* **15**(1), 49–55 (1997).
46. P. Abolmaesumi, M. R. Sirouspour and S. E. Salcudean, "Real-time extraction of carotid artery contours from ultrasound images," *IEEE Symp. on 13th Computer-Based Medical Systems (CBMS2000) Proc.*, pp. 181–186 (2000).
47. M. L. Bots, A. W. Hoes, P. J. Koudstaal, A. Hofman and D. E. Grobbee, "Common carotid intima-media thickness and risk of stroke and myocardial infarction: The rotterdam study," *Circulation* **96**(5), 1432–1437 (1997).
48. J. D. Spence, M. Eliasziw, M. DiCicco, D. G. Hackam, R. Galil and T. Lohmann, "Carotid plaque area," *Stroke* **33**(12), 2916–2922 (2002).
49. A. Landry, J. D. Spence and A. Fenster, "Measurement of carotid plaque volume by 3-dimensional ultrasound," *Stroke* **35**(4), 864–869 (2004).
50. A. Krasinski, B. Chiu, J. D. Spence, A. Fenster, and G. Parraga, "Three-dimensional ultrasound quantification of intensive statin treatment of carotid atherosclerosis," *Ultrasound Med. Biol.* **35**(11), 1763–1772 (2009).
51. C. P. Loizou, C. S. Pattichis, M. Pantziaris and A. Nicolaides, "An integrated system for the segmentation of atherosclerotic carotid plaque," *IEEE Trans. Inf. Technol. Biomed.* **11**(6), 661–667 (2007).
52. S. Meairs and M. Hennerici, "Four-dimensional ultrasonographic characterization of plaque surface motion in patients with symptomatic and asymptomatic carotid artery stenosis," *Stroke* **30**(9), 1807–1813 (1999).