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# Constrained snake vs. conventional snake for carotid ultrasound automated IMT measurements on multi-center data sets

Filippo Molinari [a,*], Kristen M. Meiburger [a], Luca Saba [c], U. Rajendra Acharya [b], Mario Ledda [c], Andrew Nicolaides [d], Jasjit S. Suri [e,f,g]

[a] Biolab, Department of Electronics and Telecommunications, Politecnico di Torino, Torino, Italy
[b] Department of ECE, Ngee Ann Polytechnic, Singapore, Singapore
[c] Department of Radiology, A.U.O. Cagliari, Cagliari, Italy
[d] Vascular Diagnostic Center, Nicosia, Cyprus
[e] Fellow AIMBE, CTO, Global Biomedical Technologies, Inc. (GBTI), Roseville, CA, USA
[f] Biomedical Engineering Department, Idaho State University, Pocatello (Aff.), ID, USA
[g] AtheroPoint LLC, Roseville, CA, USA

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ABSTRACT

Accurate intima-media thickness (IMT) measurement of the carotid artery from minimal plaque ultrasound images is a relevant clinical need, since IMT increase is related to the progression of atherosclerosis.

In this paper, we describe a novel dual snake-based model for the high-performance carotid IMT measurement, called Carotid Measurement Using Dual Snakes (CMUDS). Snakes (which are deformable contours) adapt to the lumen-intima (LI) and media-adventitia (MA) interfaces, thus enabling the IMT computation as distance between the LI and MA snakes. However, traditional snakes might be unable to maintain a correct distance and in some spatial location along the artery, it might even collapse between them or diverge. The technical improvement of this work is the definition of a dual snake-based constrained system, which prevents the LI and MA snakes from collapsing or bleeding, thus optimizing the IMT estimation.

The CMUDS system consists of two parametric models automatically initialized using the far adventitia border which we automatically traced by using a previously developed multi-resolution approach. The dual snakes evolve simultaneously and are constrained by the distances between them, ensuring the regularization of LI/MA topology. We benchmarked our automated CMUDS with the previous conventional semi-automated snake system called Carotid Measurement Using Single Snake (CMUSS).

Two independent readers manually traced the LIMA boundaries of a multi-institutional, multi-ethnic, and multi-scanner database of 665 CCA longitudinal 2D images. We evaluated our system performance by comparing it with the gold standard as traced by clinical readers.

CMUDS and CMUSS correctly processed 100% of the 665 images. Comparing the performance with respect to the two readers, our automatically measured IMT was on average very close to that of the two readers (IMT measurement biases for CMUSS was equal to $-0.011 \pm 0.329$ mm and $-0.045 \pm 0.317$ mm, respectively, while for CMUDS, it was $0.030 \pm 0.284$ mm and $-0.004 \pm 0.273$ mm, respectively). The Figure-of-Merit of the system was 98.5% and 94.4% for CMUSS, while 96.0% and 99.6% for CMUDS, respectively. Results showed that the dual-snake system CMUDS reduced the IMT measurement error accuracy (Wilcoxon, $p < 0.02$) and the IMT error variability (Fisher, $p < 3 \times 10^{-2}$).

We propose the CMUDS technique for use in large multi-centric studies, where the need for a standard, accurate, and automated IMT measurement technique is required.



## 1. Introduction

This paper describes development of the clinically relevant approach allowing improved determination of intima-media thickness (IMT) of the carotid arteries.

Recently, the data from the World Health Organization [1] indicated that cardiovascular diseases account from one-third of all the global deaths in Western countries. The World Health Organization

*Abbreviations:* IMT, intima-media thickness; LI, lumen-intima; MA, media-adventitia; CMUDS, Carotid Measurement Using Dual Snake; CMUSS, Carotid Measurement Using Single Snake; LIMA, lumen-intima and media-adventita interfaces; $AD_F$, Far wall adventitia layer; ROI, region of interest; FOAM, First Order Absolute Moment; CF, conversion factor; FoM, Figure-of-Merit.

* Corresponding author. Address: BioLab – Department of Electronics and Telecommunications, Politecnico di Torino, Corso Duca degli Abruzzi 24, 10129 Torino, Italy. Tel.: +39 (0)11 564 4135; fax: +39 (0)11 564 4217.

*E-mail address:* filippo.molinari@polito.it (F. Molinari).

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also estimated that by 2040 the cardiovascular diseases would account for 50% of all global deaths, including also emerging countries and third world countries [1]. Atherosclerosis is the earliest manifestation of the onset of a cardiovascular disease. Atherosclerosis is defined as the degeneration of the arterial wall, with consequent deposition of lipids, calcium, and other blood-borne materials within the arterial wall itself. This process was documented in several studies about the genesis and progression of atherosclerosis [2–4].

In the multi-centric Rotterdam study, the intima-media thickness of the carotid arteries was found to be a predictor of cardiovascular risk [5]. Carotid IMT was also associated to the incidence of several cardiovascular diseases, as documented by other large clinical studies [6–10]. The accurate measurement of the IMT from ultrasound images is, therefore, clinically very important for the assessment of the risk factor of the patients and for screening purposes.

In clinical practice, the IMT is usually measured by expert sonographers on longitudinal B-Mode images. By means of the scanner caliper, the sonographer places two markers in correspondence of the lumen-intima (LI) and of the media-adventitia (MA) interfaces. The distance between the two markers is the estimation of the IMT. This process introduces variability in the results, which is linked to the sonographers experience. In a recent study, Polak et al. showed [11] that when different trained sonographers manually measured the IMT, a difference of 0.21 mm was observed (since the average value of the IMT of atherosclerotic patients is about 0.9 mm, the difference was about 23% of the nominal value). This inter-reader variability could lead to an incorrect assessment of the patients' risk assessment. Hence, computer methods aiding the IMT measurement find their utility in order to reduce the measurement variability while maintaining the measurement precision.

Touboul et al., were the first to propose a computer method to aid the IMT measurement [12] and used it in the epidemiological PARC study [13], which was focused on the assessment of carotid IMT measurement reproducibility. The results of the PARC study revealed the need for a computer system capable of measuring the IMT with a low error (compared to manual tracings by experts). Touboul et al. obtained an IMT measurement error equal to 0.0185 mm. This study was one of the first proposing a computer system for the IMT measurement in multi-centric studies (*i.e.*, in studies where images are collected by different physicians in different Institutions, which usually capture images using different ultrasound equipment).

Hence, computer methods aiding the IMT measurement find their utility in order to reduce the measurement variability while maintaining the measurement precision. When the LI and MA interfaces are traced by an image processing algorithm, the process is called "segmentation". In 2010, Molinari et al. [14] revised all the most used computer techniques for the carotid wall segmentation and IMT measurement. In this work, we benchmarked our innovative Dual Snake paradigm for the carotid LIMA automated segmentation and IMT measurement. We called this novel system as CMUDS (Carotid Measurement Using Dual Snake, a patented technology by Global Biomedical Technologies, CA, USA under the class of AtheroEdge™ systems). To fully appreciate the rationale of our choice and innovation, we would like to briefly revise the previously proposed solutions for computer-based IMT measurement. The most used image processing techniques for LIMA tracings and IMT measurement can be subdivided into:

1. edge-based and gradient-based methods [15–19];
2. dynamic programming and modeling methods [20–24];
3. analysis techniques based on specific distributions (*e.g.*, Nakagami, Hough) [25–27];
4. parametric deformable models (*i.e.*, snakes) [28–30].

The principal advantage of standalone edge-based methods is the fast computation. In fact, edge detection can be performed by simple operations such as the high pass filtering of the image. These operations are very effective and the overall time required to high pass filter a B-Mode image is less than 0.5 ms. The principal drawback of edge-based methods is their sensitivity to noise because they are based on image differentiation. In fact, since edge detectors search for intensity variations, noise can lead to false edge detections and false edges.

The dynamic programming techniques are based on the minimization of a cost function, which derives from the image features. Cost terms and cost functions (in some algorithms up to 20 among terms and functions were defined [21]) are related to physical characteristics of the image such as the pixel density. Since in ultrasounds the image characteristics depend on the scanner and on the settings, dynamic programming techniques are difficult to use in a multi-centric scenario, where images might come from different Institutions and different equipment.

The segmentation methods that model the carotid wall boundaries usually consider predetermined intensity features or shapes. Among all the intensity distributions, the Nakagami distribution [25] models the sequence of low intensity (*i.e.*, the carotid lumen), medium intensity (*i.e.*, the intima and media layers), and the high intensity (*i.e.*, the adventitia layer). The model can be accurate only if the overall intensities associated to layers do not change. Thus, the methods based on intensity distributions could not recognize the layers' intensities correctly if different scanners are adapted in acquisition protocol. The image transforms, such as the Hough transform [26], are used to detect specific shapes in an image. For example, Golemati et al. [26] used the Hough transform to detect the lines associated to the LI and MA interfaces. However, this method can only process images where the LIMA interfaces are straight horizontal lines and therefore, this is a limitation. This strategy poses a challenge to curved arteries or inclined arteries.

The snake-based techniques have two major advantages:

- They are versatile because they can adapt to almost any carotid morphology. Since snakes are deformable curves, they can assume different shapes, and so they can correctly recognize the interfaces of straight, inclined, and curved carotids.
- They maintain a smooth shape of the LIMA profiles. This is clinically important, because, from a physiological point of view, the profiles of the wall layers are always regular and not disconnected.

Snakes, however, suffers also from two major drawbacks:

- *Need for initialization*: Snakes are dynamic contours, which evolve (or change) from an initial shape and converge (settle down at the correct stable position) over time. Therefore, the contour has to be created (initialized) before convergence happens. It has been shown that the initialization influences the final segmentation [31]. This happens because, once initialized, the snakes evolve while following the intensity changes in the image. Hence, clearly, the location of the snake initialization is important for the final result.
- *Sensitivity to noise*: This is because the snake is attracted by image discontinuities. As we have already discussed, intensity discontinuities are usually measured by using gradients. However, as mentioned above, gradients are noise sensitive. In carotid ultrasound images, there are different noise sources, the principal are: blood rouleaux and hypoechoic appearance of the LIMA interfaces due to lack of gel on the skin or incorrect insonation angle.

In the last years, many snake-based techniques have been proposed for the IMT measurement of the carotid arteries. Delsanto