Three-Dimensional Ultrasonic Assessment of Atherosclerotic Plaques *

José Seabra[1], João Sanches[1], Luís M. Pedro[2], and J. Fernandes e Fernandes[2]

[1] Instituto Superior Técnico, Instituto de Sistemas e Robótica
[2] Faculdade de Medicina de Lisboa, Instituto Cardiovascular de Lisboa

Abstract. Carotid atherosclerosis is the most common life-threatening neurological disease and therefore an accurate assessment of atheromatous plaques is clinically important. Several studies were developed to characterize plaques from two-dimensional (2D) ultrasound images that are associated with high risk of stroke. However, 2D characterization may not be very accurate because it depends on the selection of a representative ultrasound image of the plaque by an experimented physician. In this paper we present a novel approach for diagnosis based on 3D ultrasound, which only requires a common ultrasound equipment without need of any additional and expensive devices like spatial locators. The semi-automatic algorithm uses medical guidance to obtain a 3D representation of the carotid artery and plaque and automatically generates measures to characterize the plaque in terms of dimensions and texture. A useful analysis tool is provided to allow the identification of vulnerable *foci* within the plaque.

1 Introduction

In the majority of western countries, atherosclerosis is the most prevalent and main cause of death. It is a disease of the large and medium size arteries, being characterized by plaque formation due to sub-endothelial accumulation of lipid, protein, and cholesterol esters. The most frequent location of the atherosclerotic lesion in the cerebrovascular sector is the common carotid bifurcation where plaque formation tends to produce stenosis which reduces the blood flow to the brain. Therefore, a significant effort has been done in the development of new techniques to assess the atherosclerosis state of the carotid artery.

Up to now the degree of stenosis has been targeted as the main indicator for plaque vulnerability and is the primary factor for deciding a surgical intervention [1]. This decision presents relevant clinical and financial consequences and therefore accurate diagnosis tools are needed. To increase the accuracy of the diagnosis, parameters aiming to identify vulnerable lesions have been studied using 2D B-mode ultrasound (US) imaging with computer-assisted analysis [2]. The ultrasound images are used to extract the carotid contours and measure the stenosis severity, to automatically or semi-automatically segment the intima-media layer thickness and to segment and classify the plaques with respect to

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their instability, based on intensity and texture [3]. However, 2D characterization is difficult and not very accurate because it depends on the selection of a representative ultrasound image of the plaque by an experimented physician. The classical methods do not allow a global visualization of the carotid anatomy nor the global extension and morphology of the plaques. For this reason an increasing amount of work has been published where 3D reconstructions of the carotid and plaques are used to better assess the risk of stroke.

Usually, in 3D ultrasound, a spatial locator is attached to the ultrasound probe to measure its position and orientation. The manipulation of the probe can be performed by mechanical devices or in a free-hand basis by the medical doctor. These devices are expensive and not usually provided with the traditional ultrasound equipment. Hence, 3D ultrasound algorithms usually require specialized experimental setup which is only available in academic laboratories or highly technological equipped medical centers. In this paper we propose an

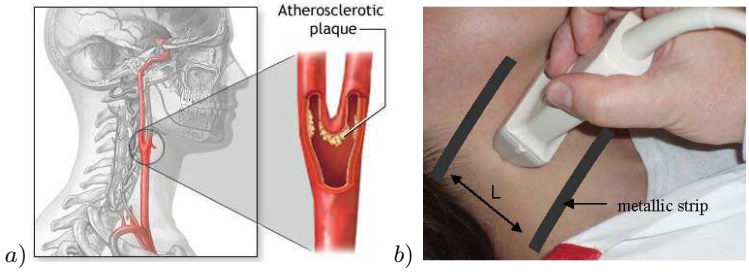

Fig. 1. a) Carotid anatomy. b) Acquisition protocol.

acquisition protocol that does not need spatial locators to obtain the 3D reconstruction. The anatomy and location of the carotid makes it possible to keep a uniform sweep velocity of the ultrasound probe allowing the acquisition of a set of nearly parallel cross sections. Furthermore, the paper proposes a volume based analysis algorithm of the atherosclerotic plaques in order to classify them with respect to its instability in a global and local basis. This new local approach analysis leads to significant and important improvements in the assessment of the atherosclerotic disease, primarly in concerning the risk of stroke.

2 Problem Formulation and acquisition protocol

The carotid is the major vessel which supplies the brain and face with blood. It is located in the lateral side of the neck, along its longitudinal axis and branches off in the external and internal carotids along the upward direction (see Fig.1a). This paper is focused on the bifurcation region where the plaque formation is more frequent. The goal is to acquire parallel cross-sections of the carotid to build a 3D mesh representing its anatomy. Since no spatial locators are being used the acquisition protocol is a critical process to guarantee the quality of the results. The ultrasound probe should be manipulated as uniformly as possible from the base of the neck up to the base of the skull keeping its orientation as static as possible. In a typical acquisition session, 60 images are acquired with a 5 to 12

MHz dynamic range linear transducer. Small variations on the orientation of the ultrasound probe are not critical because the algorithm performs the alignment of the images. This acquisition protocol is performed using two metallic strips (see Fig.1b), which come apart by a known distance, that are used as landmarks for signaling the limits of the probe course. Small variations on the sweep velocity, $V = V_0 + \Delta_V$ with $\Delta_V < 0.1V_0$ and $V_0 = 8cm/2sec = 4cm/sec$, leads to position errors $\leq 0.02cm$, which are small when compared with the total length of the probe course, $d = 8cm$ (for details see [4]).

3 Three-Dimensional Reconstruction

The reconstruction of the carotid and plaques is performed using a surface rendering approach where the contours of both structures are extracted from each image of the data sequence. To produce the final meshes these contours are regularized, linked, aligned and longitudinally smoothed. Since the spatial information inside the plaque is clinically relevant, volume rendering is also performed, only inside the plaques, to allow the assessment of its global and local instability. The overall mesh generating process is performed in the following steps:

1) Pre-processing. This step is used to attenuate the speckle noise present in the ultrasound images. The Bayesian denoising process is based on the *maximum a posteriori* (MAP) criterion and in the *total variation* (TV) edge preserving prior, being the optimization achieved by solving the Lyapounov equation [5] for which there are fast and efficient solvers described in the literature. Fig.2a-c displays an example of application of the pre-processing in a 346×440 pixel ultrasound noisy image (fig.2a), the filtered image using a combination of median and gaussian filters (fig.2b) and the filtered image using the MAP method (fig.2c). This image demonstrates the edge-preserving nature of this type of filter.

2) Contour extraction. The extraction of contours from the pre-processed images is done by using the active contours algorithm described in [6], based on the *Gradient Vector Flow* (GVF). The algorithm is used to automatically segment the anatomic objects under medical supervision. That is, under regular conditions the initialization of the GVF algorithm for a given image is obtained from the previous one, as displayed in fig.2d-f. However, the medical doctor may interfere with the process. He may change the initial contour or the default parameters, such as the internal and external energies of the contour. This functionality is useful when the algorithm wrongly converges due to bad initialization or, more important, when topological modifications arise. The need for accuracy and precision during the segmentation makes it necessary to use semi-automatic methods because the results are relevant for surgery taking decisions. Two situations need a special initialization: 1) the beginning of the bifurcation, where two contours must be merged into a single one. Both contours (fig.2d) intersect, after convergence, in the bifurcation plane (fig.2e). The new single contour results from these two contours by removing the intersection region; finally, the composed contour is used as initialization to segment the carotid in the bifurcation region (fig.2f); 2) in the first image containing the plaque, which must be manually defined (fig.2g). In the next images, the plaque segmentation

is made automatically. However, in order to force consistency of both contours, carotid and plaque, a post processing is needed. This procedure consists in the extraction of the plaque region from the intersection between the new contour defined for the plaque and the already existing one for the carotid, as well as, the correction of the carotid artery wall, by removing the region of the plaque.

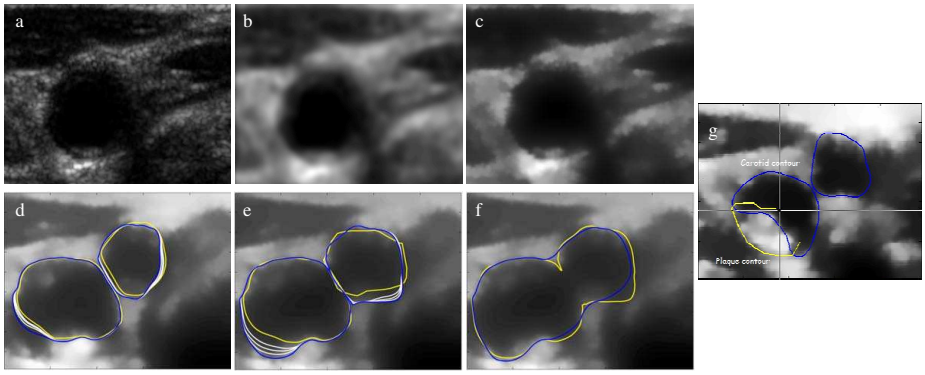

Fig. 2. a-c) Pre-processing. d-f) Segmentation of the carotid artery in the bifurcation. g) Manual detection of the plaque.

3) Contour re-sampling, smoothing and linking. The contours of the carotid and plaques are described by a set of control points not evenly spaced. These must be linked to build the 3D mesh representing the anatomy of the carotid and plaques. Therefore, a re-sampling is needed and smoothing is desirable. In this step a continuous vectorial function depending on scalar parameter s, describing each contour is estimated from the corresponding control points.

Let $c(s) = [x(s), y(s)]$ be the closed continuous contour where $0 \leq s \leq 1$. The control points describing this contour are $p_i = [x_i(s_i), y_i(s_i)]$ where s_i are the normalized positions of each point, along the contour, that is $s_0 = 0$ and $s_{M-1} = 1$. The M control points are considered noisy observations of the unknown curve, $c(s) = [\Phi(s)^T A, \Phi(s)^T B]$, where $\Phi(s) = [\phi_0, \phi_1, ..., \phi_{N-1}]^T$ is a column vector of the N basis functions, computed at position s, and $A = [a_0, ..., a_{N-1}]^T$ and $B = [b_0, ..., b_{N-1}]^N$ are vectors of coefficients to be estimated. The estimation of A (B is estimated in the same way) is performed by minimizing the following quadratic energy function,

$$E = (X - \Theta A)^T (X - \Theta A) + \alpha (\theta A)^T (\theta A) \tag{1}$$

with

$$\theta = \begin{pmatrix} 1 & 0 & 0 & ... & 0 & -1 \\ -1 & 1 & 0 & ... & ... & 0 \\ ... & ... & ... & ... & 1 & 0 \\ 0 & 0 & 0 & ... & -1 & 1 \end{pmatrix}, \Theta = \begin{pmatrix} \phi_0(s_0) & \phi_1(s_0) & ... & \phi_{N-1}(s_0) \\ \phi_0(s_1) & \phi_1(s_1) & ... & \phi_{N-1}(s_1) \\ ... & ... & ... & ... \\ \phi_0(s_{M-1}) & \phi_1(s_{M-1}) & ... & \phi_{N-1}(s_{M-1}) \end{pmatrix},$$

where θ is a difference operator and Θ is $M \times N$ matrix depending on the location of the control points. The vector $\hat{A}$ that minimizes (1) is

$$\hat{A} = (\Theta^T \Theta + \alpha \theta^T \theta)^{-1} \Theta^T X. \tag{2}$$

The vector $\hat{B}$ is obtained as $\hat{A}$ by replacing X by Y. From $\hat{A}$ and $\hat{B}$ the new evenly spaced control points are computed from

$$q_i = [\Phi(s_i)^T \hat{A}, \Phi(s_i)^T \hat{B}] \tag{3}$$

where $s_i = i/(L-1)$, $0 \leq i \leq L-1$ and L is the number of the new control points which will be used in the sequel of the segmentation process.

The re-sampled contours are linked in a pairwise basis, i.e. the contours on the second image are linked with the homologous in the first one, the contours on the third are linked with the homologous in the second one and successively, up to the last image. However, it is necessary to match them to allow a correct pairing of homologous control points. This is done by using the Iterative Closest Point (ICP) [7] algorithm which estimates a rigid transformation applied to the second set of points in order to minimize the distance between them. Once paired the linking of both set of points is possible.

4) Vertical alignment and smoothing. In order to compensate the small lateral displacements of the ultrasound probe during the acquisition process an alignment procedure of the contours is needed. In this step, the contours are aligned with the homologous ones in the previous image. After the alignment, a smoothing operation is applied to the vertical lines to attenuate discontinuities in the final mesh. This procedure is similar to the one applied to the contours in step 3. The alignment of two consecutive images is achieved by minimizing an energy function involving translation vectors associated with each image, i.e.

$$E_i = \sum_{k=0}^{L-1} \left[p_i(k) - p_{i-1}(k) - t_i \right]^2 \tag{4}$$

where $p_\tau(k)$ is the k-th control point of the i-th contour and t_i is the compensation vector related to the i-th image. Using matrix notation leads to

$$E_i = (P_i - P_{i-1} - \theta t_i)^T (P_i - P_{i-1} - \theta t_i) \tag{5}$$

with $P_\tau = [p_{\tau x}(0), p_{\tau y}(0), ..., p_{\tau x}(L-1), p_{\tau y}(L-1)]^T$, $t_i = [t_{ix}, t_{iy}]^T$ and $\theta = \begin{pmatrix} 1\,0\,1\,...\,0\,1 \\ 0\,1\,0\,...\,1\,0 \end{pmatrix}^T$. The vector that minimizes (5) is

$$t_i = (\theta^T \theta)^{-1} \theta^T (P_i - P_{i-1}) \tag{6}$$

5) VRML generation. The final step of the reconstruction algorithm consists in the creation of a finite-element mesh, by applying different luminescence and transparency codes to the defined elements in order to facilitate the anatomy inspection. This information and criteria are used to create 3D virtual reality models of both carotid artery and atherosclerotic plaque, like shown in Fig.4.

4 Plaque Classification

The morphology and texture of the plaques have prognostic relevance [8]. For instance, a smooth surface and a homogenous texture indicates a stable plaque, while an irregular surface and a heterogeneous texture are typical in unstable plaques. Studies comparing plaque histology with ultrasonography have suggested that echolucent (darker) plaques have more lipid and hemorrhage, which indicates inflammatory activity and therefore instability. Conversely, echogenic (brighter) plaques are associated with the presence of more calcium and fibrous tissue, which are stable components. Therefore, a method is proposed for compu-

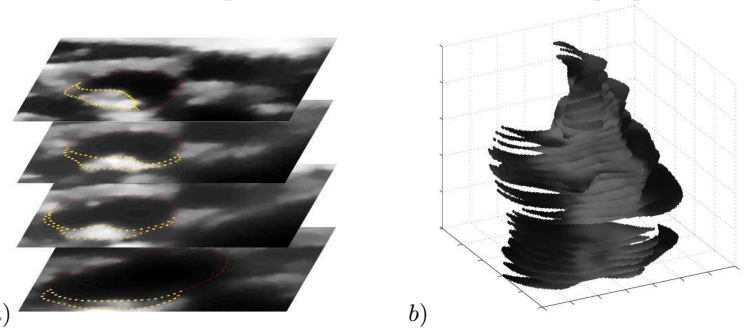

Fig. 3. a) Extraction of plaque US information. b) 3D US reconstruction.

tational analysis of atherosclerotic disease, either based on global or local data. In the former approach, plaque volume and extension, level of stenosis, grayscale median (GSM) and percentage of echolucent pixels (PEP) are used. In the local analysis, statistical measures, such as mean, median, variance, standard deviation, skewness and curtosis, are computed for each location inside the plaque. Global measures characterize heterogeneity and echogenicity of plaques and local statistics allow the identification of possible active and unstable *foci* whithin the plaque. This new local analysis methodology improves the diagnosis based only on global characterization of the plaque. Fig.3a shows the plaque segmentation results. Fig.3b displays a 3D view of an entire reconstructed plaque which may be inspected using opaque or semi-transparent visualization techniques.

5 Experimental Results

In this section examples of reconstructions using real data from two clinical studies are presented. Fig.4 shows 3D views of a healthy (a) and a diseased carotid (b) where the plaque is well observed. In this framework is easy and fast to evaluate the geometry and extension of the plaques and its precise localization inside the carotid. The local assessment of plaque severity is also available by using the program interface, as shown in Fig. 5. The results for plaque characterization are based on a third clinical study. Besides the carotid anatomy, the program also gives important global information. The example presents a diseased carotid containing a moderately echogenic plaque (GSM of 37), with a considerable level of stenosis (61% at most and 51% in average), PEP of 53% and a smooth surface.

The estimated plaque volume of $1,352mm^3$ is also important, but its relevance depends on the plaque extension. Even more important than the volume itself is the respective evolution along the time. This application is particularly suitable for this type of prospective clinical approach, allowing the comparison of the atherosclerotic plaque volume and extension at different stages of the disease.

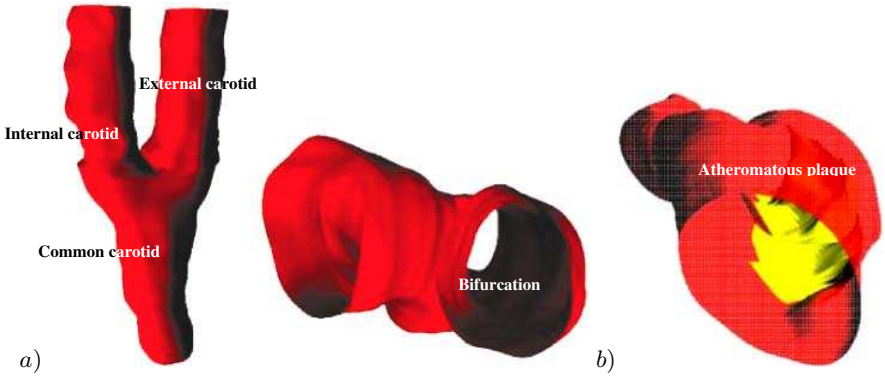

Fig. 4. 3D realistic models of normal (a) and diseased (b) carotid arteries.

The plaque echogenic analysis, in particular the GSM, determines whether (or not) the plaque is stable, considering the consensual threshold given in the literature ($GSM = 32$). This binary classification is however very simplist because it does not take into account if the GSM is closer to the threshold and, even worst, it does not give any information about the extension of the unstable regions inside the plaque.

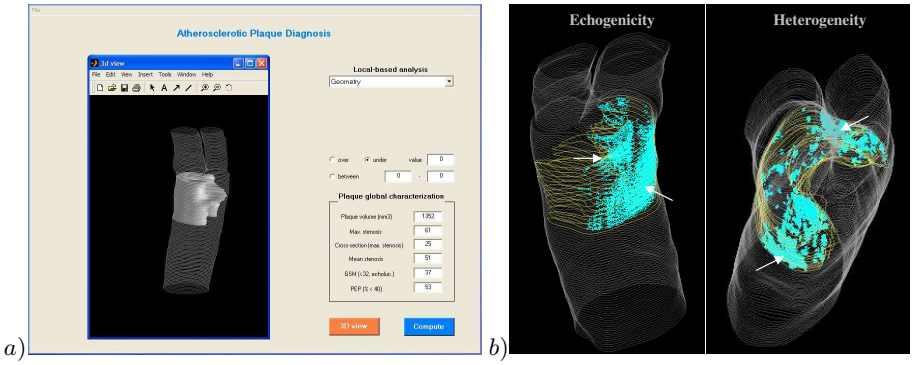

Fig. 5. a) User-interface for plaque classification. b) Local detection of unstable regions within the plaque.

Local assessment is needed to obtain information not provided by the global measurements. Fig. 5b shows the local analysis of the plaque using two different criteria to identify the unstable regions: first, the most echolucent regions at the central core (on the left), where the median values are below 20, and the most

heterogeneous regions (on the right), where the standard deviation is above 20, mainly in the peripheral locations of the plaque.

6 Conclusions

This project proposes a new computer-based tool for plaque characterization, involving the reconstruction of a 3D mesh of the carotid and plaque and a volume based classification method of the plaques. This is important for the identification of individuals at high risk of stroke, making easier the clinical decision of surgical intervention. This classification is much more accurate than those based only on 2D images, since it considers the entire information from the plaque. Furthermore, the heterogeneity and echogenicity of the plaque is also analyzed in a local basis, in order to identify possible unstable locations inside the plaque.

The application presents a user-friendly interface which allows a complete medical exam in about one hour, including image acquisition. Furthermore, the acquisition process only needs a common ultrasound equipment without need of additional expensive equipment such as spatial locators or mechanical scanners. Automatic global and local evaluation of textural parameters in conjunction with its 3D integration in the carotid artery anatomy, leads to significant improvements of the current state-of-the-art atherosclerosis diagnosis tools.

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