Methodology for micro-CT data inflation using Intravascular Ultrasound images

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***Abstract*— In this paper, a framework for the inflation of micro-CT data using intravascular ultrasound (IVUS) images, is presented. The proposed methodology consists of four steps. In the first step a centerline is extracted from the micro-CT images. In the second step the micro CT images are segmented automatically using the k-means algorithm. In the third step IVUS- micro-CT images are co-registered based on fiducial markers selected manually by the experts. Finally, the images are inflated by applying a transformation method on each image. The transformation method is based on the IVUS and micro-CT contour difference. The proposed methodology for inflating micro-CT images could increase the reliability of correct plaque labeling process as well to enhance the accuracy of the produced training dataset from the micro-CT images.**

I. Introduction

The mechanisms of coronary artery disease (CAD initiation and progression [1] have been studied for many years in the past decades [2]. Imaging methods have been developed through years, both invasive and non-invasive [3, 4], which provide cardiologists with reliable tools able to identify flow-limiting atherosclerotic plaques, which are major determinant of clinical outcome [5], and provide the appropriate interventions.

Intravascular ultrasound (IVUS) [6] is an invasive imaging modality which provides high resolution cross-sectional images of the coronary arteries. IVUS permits detailed evaluation of the lumen, media-adventitia wall and evaluation of plaque composition. Several methodologies have been proposed in the literature which allow automated processing of the IVUS in order to segment and characterize the plaque region [7-9]. These methods were validated using either expert annotation [8, 10] or histological data [9, 11].

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Although histology is considered as the gold standard for atherosclerotic plaque characterization an accurate correspondence between the histology and IVUS images is needed. Therefore, anatomical landmarks such as surrounding tissue layout, side branches etc, are detected and matched in both IVUS and histological images. However tissue fixation at unphysiological intraluminal pressure as well as dehydration for paraffin embedding leads to artery wall shrinkage and coartation which is evident as gross deformations in cross-sectional histological images [12]. To address this problem, experts are studying the histological images and annotate both IVUS and histology in order to find an additional correspondence between the plaques regions. This procedure was followed to validate the Vitual Histology (VH-IVUS) plaque characterization method [11] which is widely used in the clinical and research arena nowadays. However, deformation of arterial cross sections at histology, combined with expert annotations over these images, makes the validation of IVUS methods histology observer-dependent and time-consuming.

Micro-CT is a powerful imaging technique providing high resolution images of small specimens. The feasibility of micro-CT for the analysis of the coronary artery wall has already been evaluated [13]. It provides high quality images able to visualize the 3D shape and size of the plaque precisely, even though it can't be used in large animals *in-vivo*. Due to its excellent spatial resolution, Micro-CT has been shown able to detect small early lesions at submillimetric scale and to be well correlated with histology. Although, a detailed plaque characterization is an advantage of histology as is considered the current gold standard for visualizing plaque components, it remains time-consuming and lab intensive [14]. However both micro-CT and histology produce distorted images, due to the lack of blood pressure. Hence, both techniques require expert's intervention in order to be used for plaque characterization. To overcome this limitation an artery inflation method is needed.

We propose a micro-CT inflation methodology using IVUS images. The methodology is based on two main assumptions:

1. Lumen is deformed and compressed due to the lack of blood pressure; however the translation of center of gravity is negligible.
2. Outer wall and plaque lesions are not compressed by the gravity force, or the compression is negligible.

The methodology, consists of four main steps: a) micro-CT centerline extraction, b) micro CT Image segmentation, c) IVUS- micro-CT image registration and d) estimation and application of a transformation on each micro-CT image. The proposed methodology for inflating micro-CT images increases the reliability of correct plaque labeling process as well as enhances the accuracy of the produced training dataset from the micro-CT images.

II. Materials And Methods

The methodology for micro-CT inflation for each frame includes the following steps:

A. *Micro-CT centerline extraction*. The center of vessel in micro-CT is detected using image segmentation

B. *IVUS/Micro-CT Lumen detection*. Micro-CT Lumen contour S_1 as well as IVUS Lumen borders S_2 are detected.

C. *IVUS/Micro-CT contour registration.* Contours S_1 and S_2 are co-aligned based on user provided landmarks.

D. *Micro-CT image transformation*. Transformations X and Y are created based on the contour difference $S_2 - S_1$ used for image interpolation, resulting in the inflated micro-CT image.

The above steps are presented in Figure 1. The method for vessel inflation estimates the deformation of the inner wall and applies an inverse transformation to create an image as close as possible to the uncompressed vessel.

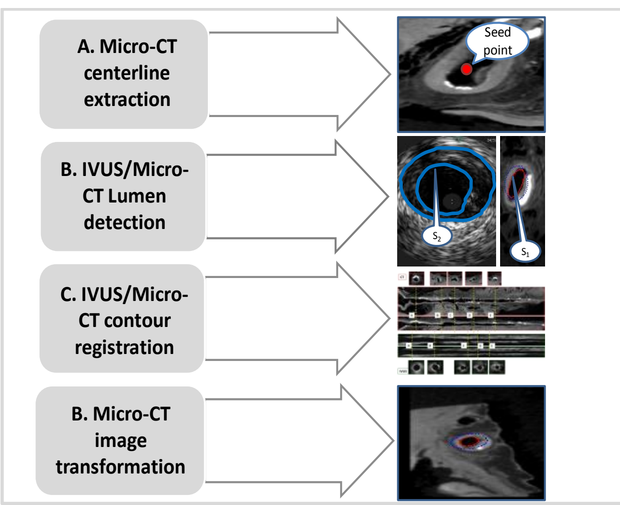


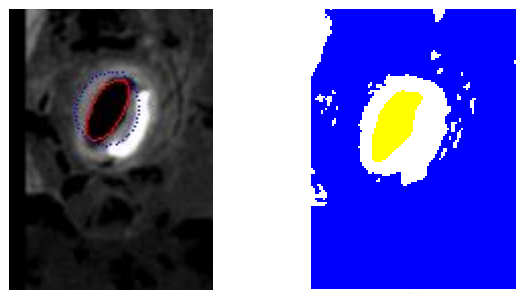
Figure 1: Schematic presentation of the proposed methodology.

A. Micro-CT centerline extraction

The first step in our methodology is the extraction of the artery centerline from the micro-CT images. The centerline is required for the estimation of the artery borders and used as point of reference for the inflation process. For the experiments performed in the following sections, the centerline of the artery in the micro-CT images were semi-automated extracted, using a seed point provided by the expert. The lumen area has low intensity compared to the artery border. Therefore a threshold is initially applied on the image to detect areas with low intensity. Then the detected areas are connected using image labeling. The area containing the seed point is considered as the lumen area and the centerline point is calculated as the center of gravity of the specific area. The centerline of frame k is used as seed point for frame $k+1$. Towards a fully automated method there are several limitations, mainly regarding the non-standardized protocols used for micro-CT multi-planar reformation (MPR). For the IVUS case the corresponding reference point for each frame is the catheter location (image center).

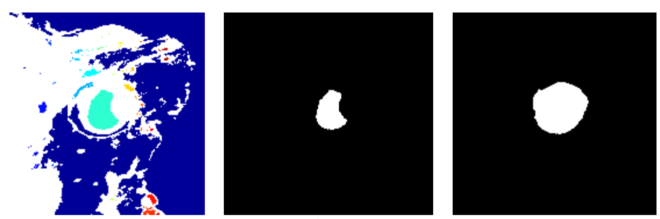
B. IVUS/Micro-CT Lumen detection

The micro-CT image is clustered in 2 classes using the K-means algorithm [15]. Experiments demonstrated the 2 classes are sufficient to separate lumen from outer wall which is required for this step of the algorithm. Figure 2 presents the cluster results in micro-CT images and their corresponding initial images. Afterwards the image regions with the same label are detected and the region which includes the center of the vessel detected in the previous step is regarded as the lumen area (Figure 3-a). The inner wall region is depicted in Figure 3-b. The outer-wall detection is based on thresholding and the distance from the lumen area. The outer wall region is depicted in Figure 3-c. To detect lumen and outer wall in IVUS, we used the method proposed by Plissiti *et al.* [16]. This method is based on deformable models. The approach entails an initial contour of the lumen border and the media adventitia border (outer wall) to be provided at the first frame of the IVUS series.



(a) (b)

Figure 2: a) Initial images, b) Clustered images.



(a) (b) (c)

Figure 3: a) Clustered image. b) Inner wall and b) outer wall regions from classified micro-CT Image

C. Micro-CT/IVUS contour registration

Medical experts selected manually paired frames of micro-CT and IVUS, on corresponding segments of the artery along the entire vessel. Fiducial points such as side branches and calcified plaques are used as landmarks. By measuring the distance between branches the same artery segments are detected on both micro-CT and IVUS. An example of Micro-CT and IVUS registration is shown in Figure 4 where five different landmarks were identified on both IVUS and micro-CT cross sections, by the experts.

The landmarks identified in the two image sources are used for frame alignment, and border registration. The slice index of two landmark points is used for frame alignment, and the location of the landmark in the image is used to rotate the IVUS borders accordingly in order to be aligned with the corresponding micro-CT frames.

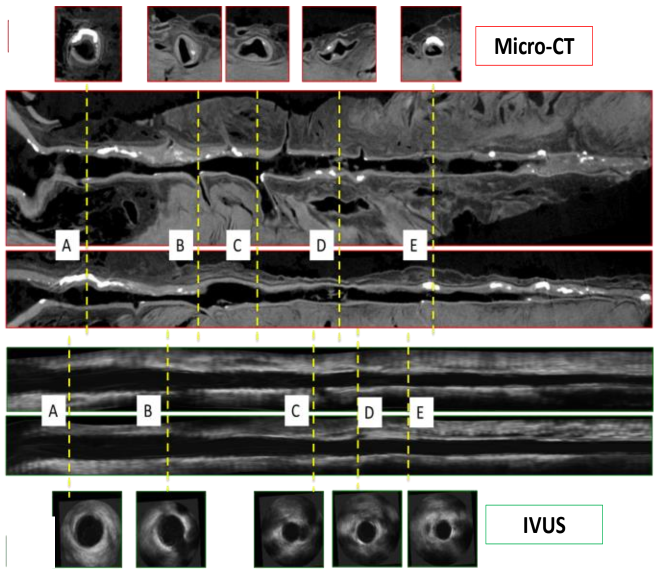


Figure 4: Micro-CT and IVUS registration. Five different landmarks were identified on both IVUS and micro-CT cross section, by the experts.

D. *Micro-CT image transformation*

After frame alignment and border registration a translation map is created for each frame. The translation map consists of two images, one representing the translation of each pixel in the X axis and one with the corresponding translation on the Y axis. In order to construct the translation map, both the original inner wall curve (extracted from micro-CT), let S_1, and the new curve (extracted from IVUS and aligned with micro-CT image), let S_2, are interpolated in $[-\pi, \pi]$. Then the function giving the curve distance over an angle is considered as:

$$F(\theta) = D_{s_2}(\theta) - D_{s_1}(\theta), \quad (1)$$

where $D_{s_2}(\theta), D_{s_1}(\theta)$ the distance of the curve points S_2, S_1 respectively, corresponding to angle θ from the curve's center of gravity.

Then the polar images P_X and P_Y for X and Y translations respectively, are produced with the following formula:

$$P_X(\theta, r) = \begin{cases} \sin(\theta) F(\theta) & r \geq D_{S_1}(\theta) \\ r & r < D_{S_1}(\theta) \end{cases}.$$
$$P_Y(\theta, r) = \begin{cases} \cos(\theta) F(\theta) & r \geq D_{S_1}(\theta) \\ r & r < D_{S_1}(\theta) \end{cases}. \quad (2)$$

The Cartesian images are then created from the corresponding Polar images. Examples of Polar and Cartesian translation images for X are given in Figure 5.

The inflated image I is produced by 2D interpolation of the initial image using the Cartesian translation maps for X and Y axes.

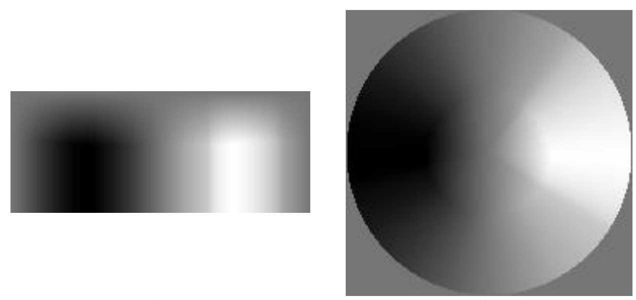
III. Dataset

micro-CT

An in-house developed micro-CT scanner installed at IFC-CNR, Pisa, was used [17]. All the tomographic acquisitions were made with 720 projections over 360 degrees, for a total scan time of 54 min and a total exposure of 2268 mAs. For each sample, we have obtained a reconstructed volume of 512x512x1400 isotropic voxels of size of 57.4^3 μm^3. ImageJ (NIH, Bathesda, USA, ver. 1.47b, http://rsbweb.nih.gov/ij/) was used to crop the image to the minimum volume of interest. OsiriX (ver. 5.0.1 32 bit, http://www.osirix-viewer.com) was used to perform 3D curved MPR of the coronary artery, image segmentation and 3D volume rendering (VR).

IVUS

The dimensions of each frame was $384x384$ pixels and the system used was the Volcano Therapeutics, Rancho Cordova, CA. The catheter was the Eagle Eye Gold, Volcano Therapeutics with 2.9-F and 20-MHz diameter and frequency, respectively.



(a) (b)

Figure 5: a) the Polar translation map and b) the corresponding Cartesian translation map.

The methodology proposed was tested in four datasets of micro-CT and IVUS images of pig coronary arteries, acquired using the methods discussed above, each consisting of more than 1000 slices.

IV. Results

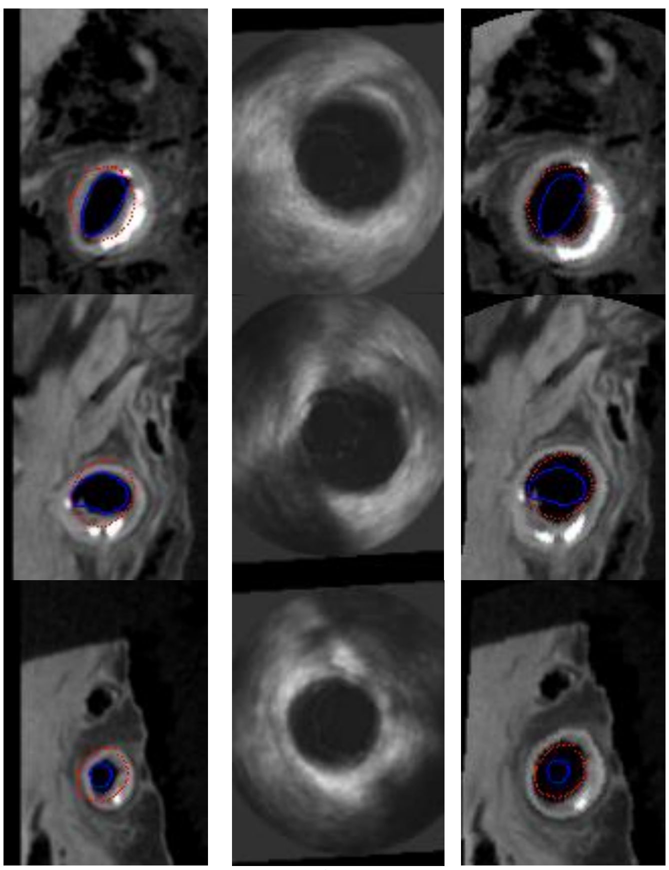
Using the X and Y translation maps the inflated image is created using 2D interpolation of the original image. Examples of the original images, the corresponding IVUS and the resulting inflated images is given in Figure 6. It can be observed that the inner wall in the inflated image and the IVUS based inner wall curve are similar. Additionally the thickness of the wall and plaque lesions are preserved.

V. Discussion

In this work, we present a methodology for image registration and inflation using micro-CT images. The methodology uses IVUS to inflate the micro-CT images which is deformed and compressed due the lack of intraluminal blood pressure.

The proposed method was applied in four different datasets of micro-CT and IVUS images on pig coronary arteries. The qualitative results indicated that the method has provided with excellent results, especially in cases where the border of the micro-CT inner wall was close to convex, which ensure a better estimation of $F(\theta)$ in Eq. (1).

Although by applying the proposed artery inflation method we overcome the experts intervention step over the micro-CT images, intervention is needed in order to identify fiducial markers. The corresponding starting and ending frames should be detected in both micro-CT and IVUS images. Moreover, the relative angle between IVUS and micro-CT is necessary and should be extracted by finding bifurcations on both micro-CT and IVUS. The relative angle should be detected at least at two frames and for the rest of the frames could be extracted using interpolation, considering a slow changing relative angle. In addition, a realistic validation should be performed using IVUS plaque characteristics. By comparing the area of the different plaque types in micro-CT images and their corresponding IVUS images the proposed inflation methodology will be calculated.



(a) (b)

Figure 6: a) micro-CT initial image, b) corresponding IVUS images c) micro-CT inflated image. The blue curve corresponds to the inner wall of the initial micro-CT image and red one to the IVUS inner wall for the corresponding frame.

VI. CONCLUSIONS

Both micro-CT and histology produce images corresponding to deformed vessels. This deformed images are due to the lack of blood pressure. Currently, using the proposed micro-CT inflation methodology we can overcome this limitations. Although, the presented methodology is applied to micro-CT images, its application could be used for inflating histological images also. However a detailed and realistic validation should be performed when the methodology is applied to both micro-CT and histological images.

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