Fully Automated Calcium Detection Using Optical Coherence Tomography

Lambros S. Athanasiou, Christos V. Bourantas, George A. Rigas, Themis P. Exarchos, *Member, IEEE*, Antonis I. Sakellarios, Panagiotis K. Siogkas, Michail I. Papafaklis, Katerina K. Naka, Lampros K. Michalis, Francesco Prati and Dimitrios I. Fotiadis, *Senior Member, IEEE*

Abstract— Optical Coherence Tomography (OCT) is a new invasive technology for performing high-resolution crosssectional imaging of the coronary arteries. In OCT images only Calcified plaque (CA) components can be accurately depicted as light penetrates hard tissue. In this work we present an automated method for detecting CA in OCT images. The method is fully automated as no user intervention is needed and includes three steps. In the first step the region between the lumen and the maximum penetration depth of OCT from the lumen border is determined. In the second step the region is classified into 3 clusters using the K-means algorithm. CA is identified using the results of k-means. The method was validated using experts' annotations on 27 images. The sensitivity of the method is 83% with Positive predictive value (PVV) 74 %.

I. INTRODUCTION

Coronary optical coherence tomography [1,2] is a relatively new imaging modality which was introduced to overcome the limitation of previous coronary imaging techniques. In contrast to intravascular ultrasound (IVUS), that is based on tissue sound reflection, OCT is based on the analysis of the reflected light allowing visualization of intra-coronary features with a higher analysis [3,4].

However, light cannot penetrate tissue as sound does, therefore OCT has one drawback, its limited penetration depth (2-3.5mm) [5]. The OCT imaging ability is limited in

This research project has been co-financed by the European Union (European Regional Development Fund- ERDF) and Greek national funds through the Operational Program "THESSALY- MAINLAND GREECE AND EPIRUS-2007-2013" of the National Strategic Reference Framework (NSRF 2007-2013).

L. S. Athanasiou, P. K. Siogkas, A. I. Sakellarios and D. I. Fotiadis are with the Unit of Medical Technology and Intelligent Information Systems, Dept of Materials Science and Engineering, University of Ioannina, GR 45110 (email: <u>Imathanas@cc.uoi.gr</u>, <u>ansakel@cc.uoi.gr</u>, <u>psiogkas@cc.uoi.gr</u> corresponding author phone: +302651008803; fax: +302651008889; e-mail: <u>fotiadis@cs.uoi.gr</u>).

C. V. Bourantas is with the Dept. of Academic Cardiology, Castle Hill Hospital, Cottingham, HU 16 5JQ, East Yorkshire, UK (email: cbourantas@gmail.com).

M. I. Papafaklis is with the Harvard Medical School, Cardiovascular Division, Brigham and Women's Hospital, Boston, MA 02115, USA (e-mail: <u>m.papafaklis@yahoo.com</u>).

T. P. Exarchos and G. A. Rigas are with the institute of molecular biology and biotechnology, FORTH, Dept of Biomedical Research, GR 45110 Ioannina, Greece (email: <u>exarchos@cc.uoi.gr</u>, <u>rigas@cc.uoi.gr</u>).

K. K. Naka and L. K. Michalis are with the Michaelideion Cardiac Center, Dept. of Cardiology in Medical School, University of Ioannina, GR 45110 Ioannina, Greece (email: <u>anaka@cc.uoi.gr</u>, <u>lmihalis@cc.uoi.gr</u>).

F. Prati is with the Interventional Cardiology, San Giovanni Hospital, Via dell'Amba Aradam, 8, 00184 Rome, Italy (email: <u>fprati@hsangiovanni.roma.it</u>) depicting soft plaques as light cannot penetrate soft tissue. On the contrary, light penetrates calcium (CA) and in OCT CA is depicted with well-defined boundaries (Fig. 1 (b)). Additionally OCT has high sensitivity specificity in detecting CA [6] compared to other plaque types. Hence, the plaque type that an expert can accurately detect in OCT images is CA.

As manual plaque characterization is time consuming and is based on well trained readers, several studies attempted to correlate plaque types with backscattering and attenuation coefficients in order to produce automated plaque characterization methods. Xu *et al.* [7] correlated the backscattering and attenuation coefficients with CA, lipid pool and fibrous tissue, using histological findings. In an analogous attempt, van Soest *et al.* [8] correlated the attenuation coefficients with healthy vessel wall, intimal thickening, lipid pool and macrophage infiltration. They both correlated the coefficients with histological findings but they did not find any clear cutoff points between the different plaque types.

Athanasiou et al. [9] presented a semi-automated plaque method characterization based on OCT image characteristics. The user manually selected a region of interest (ROI) and the ROI was classified to CA, lipid pool, fibrous tissue and mixed plaque. The method's overall classification accuracy was 80.41%. Although this method was actually the first presented plaque characterization method in the literature, it had some major limitations: it was semi-automated and was based in experts' annotations for characterizing the plaque. Hence the method was time consuming and sensitive to experts' variability. Additionally when the selected ROI was out of OCT's penetration capability and the plaque could not be visualized the method classified the ROI as plaque (Fig. 1 (c)).

In this work, we present an automated method that addresses all the above limitations:

- it is fully automated as there is no user interruption in any step of the method,
- its characterization is not based on experts annotations as it uses k-means clustering method to detect CA,
- CA which can be penetrated by light and is well defined by OCT is detected.

The method is validated using experts CA annotations over the OCT images and sensitivity 83% is reported.



Figure 1. An OCT image: (a) The initial image. (b) The image with experts' annotations. Calcium is marked with white. Soft tissue is marked with red and its upper border cannot be defined due to the limited penetration of light. (c) Soft tissue detection using Athanasiou *et al.* [9] method. (d) Calcium detection using Athanasiou *et al.* [9] method.

II. MATERIALS AND METHODS

A. Penetration Area detection

The first step of the proposed method is to detect the Penetration Area (PA) in each OCT frame. As PA we denote the region which is located between the lumen border and the maximum penetration depth of OCT from the lumen border (1.5 mm).

Lumen Detection

In order to detect automatically the lumen border in each frame we apply the following procedure (Fig. 2):

- i. transform the OCT image (I) to polar coordinates (I_p) and apply a Gaussian filter on initial image, I_p ,
- ii. perform Otsu's [10] automatic thresholding method in order binary objects to be revealed and remove the catheter pixels,
- iii. remove the non-zero objects with length less than 1/length(I) and mean intensity greater than 200. These objects corresponds to artefacts (catheter artifact, etc),
- iv. scan each column of the image from top to bottom and save the 1st non-zero pixel of the column in order to find the lumen contour,
- v. transform the image from polar to cartesian coordinates.

Lumen Border Expansion

To detect the PA region, the lumen border must be expanded up to 1.5 mm. The radial center in the Cartesian image I is the catheter center. As the distance from the

center of catheter to the lumen points varies, a set radial expansion using the current radial center is not possible. Thus the radial center is transferred from the catheter center to lumen centroid and the lumen points are expanded to 1.5 mm.

The centroid $CN(C_x, C_y)$ of each lumen border for the *n* pixels of the border is defined as:

$$C_{x} = \frac{1}{6A} \sum_{q=1}^{n-1} (x_{q} + x_{q+1}) (x_{q} y_{q+1} - x_{q+1} y_{q}), \qquad (1)$$

$$C_{y} = \frac{1}{6A} \sum_{q=1}^{n-1} (y_{q} + y_{q+1}) (x_{q} y_{q+1} - x_{q+1} y_{q}), \qquad (2)$$

where A is the lumen area defined as:

$$A = \frac{1}{2} \sum_{q=1}^{n-1} (x_q y_{q+1} - x_{q+1} y_q).$$
(3)



Figure 2. Lumen detection procedure: (a) The initial image is transformed to polar coordinates, (b) The catheter pixels and the catheter artifact, (c) The lumen border in the polar image, (d) The lumen border in Cartesian coordinates.

B. K-means clustering

K-means [11] is an unsupervised learning algorithm that classifies a given dataset $N \{x_1, ..., x_N\}$, where $x_i \in \mathbb{R}^D$, through a fixed number of *K* clusters. The goal is the *N* data to be classified to *K* clusters such as in each cluster the squared Euclidean distance of the points from their cluster center, μ_i , to be minimized:

$$J = \sum_{l=1}^{N} \sum_{i=1}^{K} o_{l,i} \left\| x_l - \mu_i \right\|^2, \qquad (4)$$

where $o_{l,i}$ is a binary variable indicating the given cluster to the point. If x_l is given to cluster j then $o_{l,i} = 1$ and $o_{l,i} = 0$ for $m \neq j$. The pixels corresponding to PA region are the given dataset N and classified to K = 3 clusters (K = 2, 3 and 4 clusters were tested).

C. Calcium detection

The OCT image is segmented into 3 regions using *K*-means method as shown in Figure 3 (b). In order to find the calcium we scan each radial form the lumen centroid to the end of PA. The radial part between two different colors which has the same color as the area below the catheter artefact is considered as calcium. The above procedure is shown in Fig. 3.



Figure 3. (a) Initial image: (b) Segmented image using the *K*-means clustering method, (c) Calcium detected over the initial image.

III. DATASET

For validation of proposed the the plaque characterization method we used OCT examinations from 10 patients. The data were provided by the San Giovanni Hospital of Rome. All participants provided informed consent, while the study was approved by the local ethical committee. The images were acquired using a Frequency Domain (FD - OCT) OCT equipment (LightLab Imaging, Inc) with a 6 Fr FD-OCT catheter (C7 Dragonfly). Automated contrast injection was performed to optimize the best image quality in all pullbacks.

Two experts examined independently the OCT images and detected all the CA plaques. Microcalcifications and disagreements between experts' annotations were not included in the study. Totally 27 annotated images were selected in order to validate the proposed method. These images were annotated as containing one or more CA plaques. Finally the images were characterized using the proposed method. Microcalcifictions detected by the proposed method were also excluded from the validation process.

IV. RESULTS

In order to validate the proposed method we computed the following validation metrics: Pearson Correlation, Sensitivity and Positive predictive value (PPV). Additionally Bland-Altman analysis was performed. As true positive values we denote the common plaque area (overlapping area) characterized by the method and annotated by the experts. As false positive values we denote the area detected by the method and not by the experts and as false negative the area annotated as plaque but not detected by the method. The Pearson Correlation, Sensitivity and PPV of the method was 0.434, 83% and 74%, respectively. Fig. 4shows the Correlation graph between the CA plaques annotated by the experts and detected by the proposed method. Fig. 5 shows the plot of Bland-Altman analysis and in Fig. 6 some application examples are presented.



Figure 4. Correlation graph between the CA plaques annotated by the experts and detected by the proposed method.



Figure 5. Bland-Altman analysis plot between for the CA plaques annotated by the experts and those detected by the proposed method.

V. DISCUSSION

In this work, a fully automated plaque characterization method, for detecting CA plaques in OCT images, is presented. The method detects automatically the lumen border and expands the border to the maximum penetration depth of OCT catheter. The *K*-means clustering method is used to classify the pixels of the PA area to 3 clusters and by scanning the radials of the classified image CA plaques are automatically detected. The method sensitivity in detecting CA is 83%.

Methods described in the literature either tried to correlate the back scattered light signal with plaque components [7,8] or presented a semi-automated and time consuming method [9]. As only CA plaque borders in OCT can be fully imaged and experts can accurately detect CA we presented a fully automated CA detection method. The presented method can detect accurately the lumen and CA plaques in all images of an OCT pullback. The time complexity of the method is relative low as it requires about 5 seconds to characterize one frame using a core i7 desktop computer with 8 GB of RAM. Additionally, as CA is the plaque type with high clinical interest [12,13] and manual detection is time consuming the proposed method can be used for clinical purposes.



Figure 6. Application examples of the proposed method: (a) initial image, (b) experts annotations, and (c) CA plaque detected by the proposed method are marked with white. PA region boundaries are marked with red.

VI. CONCLUSIONS

Characterization of the atherosclerotic plaque is important for diagnosing and treating Coronary Artery Disease (CAD). We presented a fully automated method for detecting the lumen border and characterizing CA plaques in OCT images. The method processes the OCT images and classifies the plaque with 83% sensitivity. Further research will focus on the validation of the lumen border and the automatic detection of other plaque components. Such an approach could be valuable, as the border of the other plaques cannot be fully detected by the experts.

REFERENCES

- [1] L. Athanasiou, N. Bruining, F. Prati, and D. Koutsouris, "Optical Coherence Tomography: Basic Principles of Image Acquisition," in *Intravascular Imaging: Current Applications and Research Developments*, ed: IGI Global, 2011, pp. 180-194.
- [2] F. Prati, G. Guagliumi, G. S. Mintz, M. Costa, E. Regar, T. Akasaka, P. Barlis, G. J. Tearney, I. K. Jang, E. Arbustini, H. G. Bezerra, Y. Ozaki, N. Bruining, D. Dudek, M. Radu, A. Erglis, P. Motreff, F. Alfonso, K. Toutouzas, N. Gonzalo, C. Tamburino, T. Adriaenssens,

F. Pinto, P. W. Serruys, and C. Di Mario, "Expert review document part 2: methodology, terminology and clinical applications of optical coherence tomography for the assessment of interventional procedures," *European Heart Journal*, May 31 2012.

- [3] H. G. Bezerra, M. A. Costa, G. Guagliumi, A. M. Rollins, and D. I. Simon, "Intracoronary Optical Coherence Tomography: A Comprehensive Review Clinical and Research Applications," *Jacc-Cardiovascular Interventions*, vol. 2, pp. 1035-1046, Nov 2009.
- [4] F. Prati, E. Regar, G. S. Mintz, E. Arbustini, C. Di Mario, I. K. Jang, T. Akasaka, M. Costa, G. Guagliumi, E. Grube, Y. Ozaki, F. Pinto, P. W. J. Serruys, and E. s. O. R. Document, "Expert review document on methodology, terminology, and clinical applications of optical coherence tomography: physical principles, methodology of image acquisition, and clinical application for assessment of coronary arteries and atherosclerosis," *European Heart Journal*, vol. 31, pp. 401-415, Feb 2010.
- G. J. Tearney, E. Regar, T. Akasaka, T. Adriaenssens, P. Barlis, H. G. [5] Bezerra, B. Bouma, N. Bruining, J. M. Cho, S. Chowdhary, M. A. Costa, R. de Silva, J. Dijkstra, C. Di Mario, D. Dudek, E. Falk, M. D. Feldman, P. Fitzgerald, H. M. Garcia-Garcia, N. Gonzalo, J. F. Granada, G. Guagliumi, N. R. Holm, Y. Honda, F. Ikeno, M. Kawasaki, J. Kochman, L. Koltowski, T. Kubo, T. Kume, H. Kyono, C. C. Lam, G. Lamouche, D. P. Lee, M. B. Leon, A. Maehara, O. Manfrini, G. S. Mintz, K. Mizuno, M. A. Morel, S. Nadkarni, H. Okura, H. Otake, A. Pietrasik, F. Prati, L. Raber, M. D. Radu, J. Rieber, M. Riga, A. Rollins, M. Rosenberg, V. Sirbu, P. W. Serruys, K. Shimada, T. Shinke, J. Shite, E. Siegel, S. Sonoda, M. Suter, S. Takarada, A. Tanaka, M. Terashima, T. Thim, S. Uemura, G. J. Ughi, H. M. van Beusekom, A. F. van der Steen, G. A. van Es, G. van Soest, R. Virmani, S. Waxman, N. J. Weissman, and G. Weisz, "Consensus standards for acquisition, measurement, and reporting of intravascular optical coherence tomography studies: a report from the International Working Group for Intravascular Optical Coherence Tomography Standardization and Validation," Journal of the American College of Cardiology, vol. 59, pp. 1058-72, Mar 20 2012.
- [6] H. Yabushita, B. E. Bouma, S. L. Houser, H. T. Aretz, I. K. Jang, K. H. Schlendorf, C. R. Kauffman, M. Shishkov, D. H. Kang, E. F. Halpern, and G. J. Tearney, "Characterization of human atherosclerosis by optical coherence tomography," *Circulation*, vol. 106, pp. 1640-5, Sep 24 2002.
- [7] C. Y. Xu, J. M. Schmitt, S. G. Carlier, and R. Virmani, "Characterization of atherosclerosis plaques by measuring both backscattering and attenuation coefficients in optical coherence tomography," *Journal of Biomedical Optics*, vol. 13, pp. -, May-Jun 2008.
- [8] G. van Soest, T. Goderie, E. Regar, S. Koljenovic, G. L. J. H. van Leenders, N. Gonzalo, S. van Noorden, T. Okamura, B. E. Bouma, G. J. Tearney, J. W. Oosterhuis, P. W. Serruys, and A. F. W. van der Steen, "Atherosclerotic tissue characterization in vivo by optical coherence tomography attenuation imaging," *Journal of Biomedical Optics*, vol. 15, pp. -, Jan-Feb 2010.
- [9] L. S. Athanasiou, T. P. Exarchos, K. K. Naka, L. K. Michalis, F. Prati, and D. I. Fotiadis, "Atherosclerotic plaque characterization in Optical Coherence Tomography images," *Conf Proc IEEE Eng Med Biol Soc*, vol. 2011, pp. 4485-8, 2011.
- [10] N. Otsu, "Threshold Selection Method from Gray-Level Histograms," *Ieee Transactions on Systems Man and Cybernetics*, vol. 9, pp. 62-66, 1979.
- [11] C. M. Bishop, *Neural networks for pattern recognition*. Oxford New York: Clarendon Press; Oxford University Press, 1995.
- [12] C. von Birgelen, G. S. Mintz, D. Bose, D. Baumgart, M. Haude, H. Wieneke, T. Neumann, J. Brinkhoff, M. Jasper, and R. Erbel, "Impact of moderate lesion calcium on mechanisms of coronary stenting as assessed with three-dimensional intravascular ultrasound in vivo," *American Journal of Cardiology*, vol. 92, pp. 5-10, Jul 1 2003.
- [13] R. Virmani, A. P. Burke, F. D. Kolodgie, and A. Farb, "Vulnerable plaque: the pathology of unstable coronary lesions," *J Interv Cardiol*, vol. 15, pp. 439-46, Dec 2002.