Patch-based Convolutional Neural Network for Atherosclerotic Carotid Plaque Semantic Segmentation

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Abstract: ***Atherosclerotic plaque deposition within the coronary vessel wall leads to arterial stenosis and if not adequately treated, it may potentially have deteriorating consequences, such as a debilitating stroke, thus making early detection of the most importance. The manual plaque components annotation process is both time and resource consuming, therefore, an automatic and accurate segmentation tool is necessary. The main aim of this paper is to present the model for identification and segmentation of the atherosclerotic plaque components such as lipid core, fibrous and calcified tissue, by using Convolutional Neural Network on patch-based segments of ultrasound images. There was some research done on the topic of plaque components segmentation, but not in ultrasound imaging data. Due to the size of some plaque components being only a couple of millimeters, we argue that training a neural network on smaller image patches will perform better than a classifier based on the whole image. Besides the size of components, this decision is motivated by the observation that plaque components are not uniformly distributed throughout the whole carotid wall and that a locality-sensitive segmentation is likely to obtain better segmentation accuracy. Our model achieved good results in the segmentation of fibrous tissue but had difficulties in the segmentation of lipid and calcified tissue due to the quality of ultrasound images.***

Index Terms: ***carotid atherosclerotic plaque deposition, convolutional neural network, patch-based segmentation, plaque composition, ultrasound***

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1. *Introduction*

CORONARY artery stenosis (CAS) is one of the most occurring diseases that seriously threatens human health [1]. Early detection of this disease is very important, because if not adequately treated, it may potentially have deteriorating consequences, such as a debilitating stroke. Although this disease is often presented in the older population, there is an increasing number of young individuals that are at risk of premature CAS caused by poor life choices, obesity and other risk factors [2,3]. Many young people with early disease are at risk and consequently more patients are being treated at younger ages, requiring a direct assessment of treatment response [4].

The main cause of CAS is a deposition of atherosclerotic plaque within the coronary vessel that significantly reduces blood flow. Carotid atherosclerotic plaque deposition over time often leads to stroke and Transitional Ischemic Attack (TIA). Stroke represents the third leading cause of death in North America with a high mortality rate [5]. These serious accidents occur when atherosclerotic plaques in the arteries suddenly rupture, leading to the obstruction of the blood flow to the heart or the brain [6]. Although it was thought that evaluation of the Intima-Media Thickness (IMT) of the Common Carotid Artery (CCA) is the most useful tool for the investigation of preclinical atherosclerosis, it is now generally accepted that carotid plaque composition is a phenomenon distinct from IMT and has a stronger association with cardiovascular disease events [7]. The consensus is that rupture-prone vulnerable plaques are characterized by a thin or ruptured fibrous cap and a large lipid core, with a presence of some amounts of calcified tissue [8]. This is the reason that identification of lipid, fibrous, and calcification atherosclerotic plaque components are essential to pre-estimate the risk of cardiovascular disease and stratify patients as a high/low risk. This would allow patients to be treated in a preventive and adequate manner [9].

So far, most of the computational techniques for plaque tissue characterization have been developed for multi-contrast MRI. Besides MRI, computed tomography angiography (CTA), nuclear imaging and multi-detector computed tomography are used for detection. The problem with all of the mentioned imaging modalities is the high cost and scanning limitations that make its use in daily clinical practice limited. On the other hand, B-mode ultrasound (US) is widely used for the detection of artery stenosis due to its ease of use, availability and drastically lower cost. Because of mentioned advantages, the goal of this research was to develop a reliable tool for identification and segmentation of the atherosclerotic plaque components, by applying Deep Learning methods on US imaging data of carotid artery.

There are various works done on the topic of plaque segmentation that approach the problem in different ways on different imaging data. Athanasiou et al. [10] achieved 0.81 and 0.71 Jaccard similarity coefficients for calcification and lipid components, respectively. They used random forests algorithm for the classification of features that were extracted from Optical coherence tomography (OCT) imaging data. Rezaei et al. [11] proposed a set of algorithms for segmentation, feature extraction, and plaque type classification. A hybrid model using the fuzzy c-means (FCM) and k-nearest neighbor (KNN) algorithm was proposed to accurately segment the plaque area of intravascular ultrasound (IVUS) images. On MRI images, Clarke et al. [12] achieved respectable results using a minimum distance classifier algorithm. On the other hand, Hofman et al. [13] tested multiple supervised learning algorithms on MRI images, but low accuracy for calcification components has been found in every model.

Unfortunately, there isn't a lot of research done for plaque segmentation on ultrasound images of the carotid artery, due to their low image quality with incorporation of significant noise, artifacts etc. [14]. This is the reason why its role in vulnerable plaque assessment is overlooked, as most reviews focus on the limitations of Intima-Media thickness (IMT) [15-17]. Some research papers accomplished localization of plaque segments but were not able to classify plaque composition [18,19]. Lekadir et al. [20] presented a convolutional neural network (CNN) model for automatic classification of plaque composition that showed good accuracy. The problem with their approach is the inability of CNN model to work with US image of the whole carotid wall, but with a patch image of each plaque segment individually. This is inconvenient because it requires a lot of manual plaque segments extraction. Also, due to the fact that their model only performs classification and not segmentation, there is a lack of clear visual representation of the carotid wall plaque constitution. Nevertheless, this paper and numerous other researches showed that convolutional neural networks are the state-of-the-art in image segmentation.

In this paper, we describe the use of a deep learning CNN (U-net) for the identification of lipid, fibrous and calcification atherosclerotic plaque components on small patches of ultrasound images of the carotid artery wall, instead of working with the whole US image. These segmented patches are later reconnected in a way that shows plaque segmentation on an image as a whole. Reasons for using patch-based segmentation are great segmentation results on different imaging data that were achieved in some previous research papers [21,22]. This is especially true when the size of the imaging dataset is extremely small, which is often the case with biomedical images [23]. Although patch-based segmentation is usually used on high-resolution imaging data [24], due to the small size of some plaque components (some calcification components are just a couple of millimeters in size), we argue that doing segmentation of US image in smaller patches would result in better results than what would be achieved by segmenting image as a whole.

2. MATERIALS AND METHODS

A. Dataset

In order to develop and validate a tool for identification and segmentation of the atherosclerotic plaque components on US images, a dataset of original and annotated US images was needed. Imaging data were collected during TAXINOMISIS project, from Ethniko kai Kapodistriako Panepistimio Athinon, Greece and Faculty of Medicine, University of Belgrade [25]. The dataset consists of 108 patients who underwent the US examination. Each patient had captured the common carotid artery, the branches and carotid bifurcation in transversal and longitudinal projections. It should be noted that only CCA images in transversal projections were used in the dataset. The examination was performed in B mode and Color doppler mode, so the dataset contained these types of images. Also, all imaging data were anonymized respecting the data protection and safety.

During the preprocessing of the dataset, the US images were annotated together with the clinical experts, enabling efficient training, testing and validation of developed tools for detection and segmentation of atherosclerotic carotid artery. Two observers were participating in the image annotation. Image annotation has included labeling of atherosclerotic plaque components such as lipid core, fibrous and calcified tissue. All patients included in the dataset have fibrous plaque component as dominant one among other components.

B. Image Preprocessing

The image preprocessing module is composed of steps shown in Figure 1.

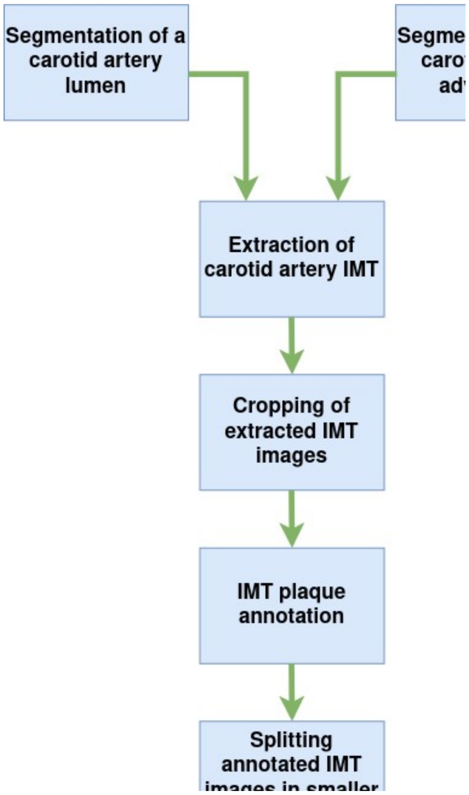
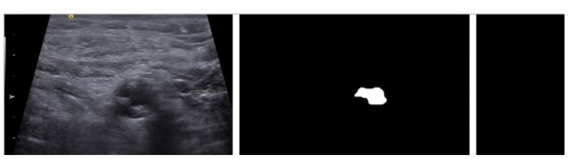


Figure 1:Ultrasound imaging data preparation process workflow of the image preprocessing module

We are only interested in a region of ultrasound image where deposition of plaque takes place, which is, in this case, Media of the carotid artery wall. This is the reason why it is important to remove tissue that is surrounding the carotid artery in the imaging data and only extract the wall of the carotid. To perform Media segmentation, two different CNN models were used to segment the lumen and adventitia of the carotid artery. As input data for these two models, observers manually annotated lumen and adventitia of the carotid artery. An example of an original ultrasound image with lumen and adventitia annotated images is shown in Figure 2.



a) b) c)

Figure 2: Original ultrasound image (a), annotated carotid lumen area (b), annotated carotid adventitia area (c)

After successful segmentation, outputs of these CNN models are combined in a way that would construct imaging data that only shows carotid Media and thus gives a clear view of plaque deposition within it.

With Media extracted, pictures were left with a large number of background pixels. This is extremely unfavorable, because it leads to a highly imbalanced dataset. For this reason, the excess background was cropped out, leaving only Media in the picture as shown in Figure 3b.

With Media of carotid artery wall extracted, images were sent back to observers who annotated different plaque components. Images with plaque annotated are shown in Figure 3c.

a) b) c)

Figure 3: Original ultrasound image (a), extracted carotid artery Media (b), annotated plaque (c)

Unfortunately, due to the process of plaque components annotation being so time-consuming and high criteria for the selection of good samples, the dataset consists of only 67 annotated images. This was one of the reasons for using a patch-based segmentation approach with U-net as a convolutional neural network model of choice. Images and corresponding masks were split into patches of size 16x16 pixels resulting in a dataset of 9998 total patches. It should be noted that we tried to work with larger patches of size 32x32 pixels, but this didn't show any improvement in segmentation results. The total dataset was split into two subsets: 90% of samples were part of the training dataset, while the remaining 10% represented the test dataset.

C. Methods

Multi-class image segmentation (or pixel labeling) aims to label every pixel in an image with one of a number of classes. In this project, the problem of atherosclerotic plaque components segmentation is defined as a multiclass segmentation model, where four classes should be detected in images: background (area outside the segmented Media showed in Figure 3c), fibrous, calcified, and lipid atherosclerotic plaque components.

Image input size was 16x16 pixels. Pixel map for the model was defined as follows:

- background (0) is annotated with dark blue color,
- fibrous plaque (1) is annotated with light blue color,
- lipid plaque (2) is annotated with yellow color,
- calcified plaque (3) is annotated with red color.

We used U-net architecture in the plaque components segmentation model as many previous reports showed that U-net achieves great results for the segmentation task on biomedical imaging data [26]. The original U-net model described by Ronnerberger et al. [26] was modified in a way that gives the best result on our dataset. The U-net model consists of an encoder to extract image features and a decoder to upsample feature maps to their original size.

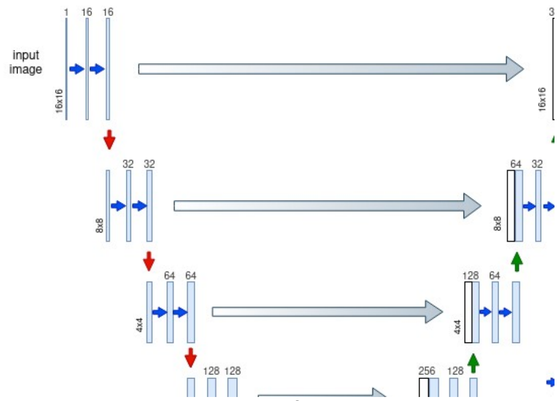


Figure 4: U-net model used for plaque components segmentation task

As seen in Figure 4, our U-net model is simpler than the original U-net model. The left branch is the encoder with five blocks, where each block contains two convolutional layers with a kernel of size 3x3 pixels followed by a 2x2 max-pooling layer. Encoder blocks use convolutional layers with 16, 32, 64, 128 and 256 filters respectively. The right branch shows a decoder with a structure symmetric to the encoder path. In each decoder block, 2×2 upconvolution and skip connection are followed by two more convolutional layers with 3×3 filters, and the last decoder block produces the segmentation mask with 1×1 convolution and sigmoid activation function. For each convolutional layer activation function of choice is a rectified linear unit (ReLU). All convolutional layers are padded so that the resulting segmentation map preserves the same height and width. In this way, the resulting segmentation map has the same resolution as the input image. Also, every other convolutional layer was followed by a dropout layer as a way of overfitting prevention.

For the training phase, we performed 100 epochs, with batch size 16. Optimizers SGD, Adam and RMSprop were tested, but the results were fairly similar, so Adam was used in the final model. On the other hand, the choice of a loss function had a big impact on results. Categorical cross-entropy loss, which is often used in both multiclass classification and segmentation problems, had trouble with this dataset due to highly imbalanced classes. This imbalance is shown in Figure 5 where background and fibrous tissue constitute more than 95% of the image.

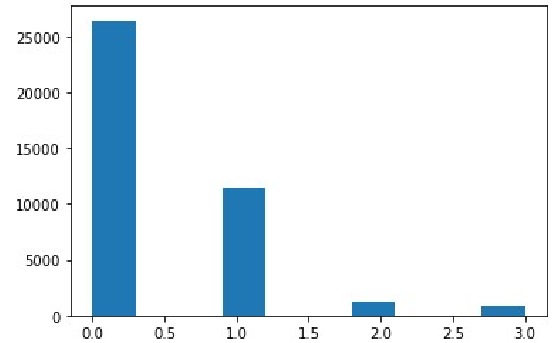


Figure 5: Number of pixels for each class present on one image sample

To handle this imbalanced data, a custom weighted loss function that combines categorical focal and dice losses was used. Weights for each class that gave best results are: [0.37 0.93 6.30 7.41]. Weights were estimated according to the number of pixels for each class, resulting in classes 2 and 3 having larger weights values due to a lower number of pixels belonging to these two classes.

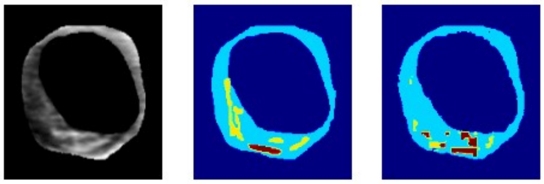
3. *Results and Discussion*

For evaluation of the model, Jaccard similarity coefficient (JSC) is used, as is the case in segmentation tasks. JSC is computed as Intersection over Union between segmentation mask of one sample predicted by the U-net model and annotated image (ground truth) of the same sample. JSC values are shown in Table 1.

Table 1. Mean and class-wise JSC scores

	TEST DATASET
Mean JSC	53.75%
Background class JSC	95.94%
Fibrous plaque class JSC	67.34%
Lipid plaque class JSC	25.17%
Calcified plaque class JSC	26.54%

As seen from the results, it was clear that the U-net model struggled to correctly segment lipid and calcified plaque components, while the fibrous component was mostly correctly segmented. This is due to previously mentioned imbalanced classes. Looking at the complete image created by connecting segmented patches presented in Figure 6c, another problem can be spotted. Instead of a couple of large segments of different plaque components (as seen on the annotated image in Figure 6b), the predicted segmented mask is filled with a lot of smaller segments. This is likely due to the small size of patches. It seems that splitting an image into patches also causes the loss of important features in the process. Larger patches of size 32x32 pixels were tested as well, but results did not improve.



a) b) c)

Figure 6: Original ultrasound Media (a), annotated plaque components (b), U-net segmentation mask (c)

Since there isn't other research done on the topic of plaque components segmentation in ultrasound imaging data, it is hard to compare results, but looking at JSC scores and segmented masks, it was clear that with the current ultrasound dataset, patch-based segmentation was not the right approach. It should be noted that some of the previously discussed works achieved better results but on different imaging data (MRI, OCT) with much larger datasets.

4. Conclusion

We developed a deep learning method for the segmentation of different plaque components of the carotid artery in ultrasound imaging data. Instead of using the whole image as input data, a developed U-net model was implemented to work on smaller patches that were then reconnected to display the segmentation mask of the whole ultrasound image. Unfortunately, it was shown that by splitting images into patches that are too small, deeper features of the image were lost along the way. This results in segmentation masks that are not accurate enough. There are strong indications that, with ultrasound images of higher resolution, bigger patches, that still contain enough features, should be extracted.

Further research will focus on developing a method that would segment ultrasound images as a whole, instead of splitting them into patches. This way, important features would not be lost. The limitations of a small dataset will be handled in further research as well.

References

[1] Virani, S., Alonso, A., "Heart Disease and Stroke Statistics-2021 Update: A Report from the American Heart Association", Circulation, 2021, pp. e478-e498.

[2] Bonow, R., Smaha, L.,"World Heart Day 2002: The international burden of cardiovascular disease: Responding to the emerging global epidemic", Circulation, 2002, pp. 1602- 1605.

[3] Yach, D., Hawkes, C., "The global burden of chronic diseases—Overcoming impediments to prevention and control", JAMA, 2004, pp. 2616-2622.

[4] Niu, L., Zhang, Y., "Standard deviation of carotid Young's modulus and presence or absence of plaque improves prediction of coronary heart disease risk", Clin Physiol Funct Imaging, 2017, pp. 682–687.

[5] Benjamin, E., Muntner, P., "Heart Disease and Stroke Statistics-2019 Update: A Report from the American Heart Association", Circulation, 2019, pp. e281-e327.

[6] Petty, G., Brown, Jr. R., "Ischemic stroke subtypes: A population-based study of incidence and risk factors", Stroke, vol. 30, no. 12, 1999, pp. 2513–2516.

[7] Vancraeynest, D., Pasquet, A., "Imaging the vulnerable plaque", Journal of the American College of Cardiology, 2011, pp. 1961-1979.

[8] Kwee, R., "Systematic review on the association between calcification in carotid plaques and clinical ischemic symptoms", J. Vasc. Surg., vol. 51, no. 4, 2010, pp. 1015–1025.

[9] Ricotta, J., Aburahma, A., "Updated society for vascular surgery guidelines for management of extracranial carotid disease", J. Vasc. Surg., vol. 54, no. 3, 2011, pp. e1–e31.

[10] Athanasiou, L., Bourantas, C., "Methodology for fully automated segmentation and plaque characterization in intracoronary optical coherence tomography images", Journal of Biomedical Optics, vol. 19, no. 2, 2014, pp. 026009.

[11] Rezaei, Z., Selamat, A., "Automatic plaque segmentation based on hybrid fuzzy clustering and k nearest neighborhood using virtual histology intravascular ultrasound images", Applied Soft Computing, vol. 53, no. 39, 2017, pp. 380-395.

[12] Clarke, S., Hammond, R., "Quantitative assessment of carotid plaque composition using multicontrast MRI and registered histology", Magn Reson Med, vol. 50, no. 6, 2003, pp. 1199–1208.

[13] Hofman, J, Branderhorst, W., "Quantification of atherosclerotic plaque components using in vivo MRI and supervised classifiers", Magnetic Resonance in Medicine, vol. 55, 2006, pp. 790–799.

[14] Hashimoto B., "Pitfalls in carotid ultrasound diagnosis", Ultrasound Clinics 6.4, 2011, pp. 463-476.

[15] Loizou, C., Pattichis, C., "Snakes based segmentation of the common carotid artery intima media", Med. Biol. Eng. Comput., vol. 45, no. 1, 2007, pp. 35-49.

[16] Golemati, S., Stoitsis, J., "Using the Hough Transform to Segment Ultrasound Images of Longitudinal and Transverse Sections of the Carotid Artery", Ultrasound Med. Biol., vol. 33, no. 12, 2007, pp. 1918-1932.

[17] Cheng, J., Li, H., "Fully Automatic Plaque Segmentation in 3-D Carotid Ultrasound Images", Ultrasound Med. Biol., vol. 39, no. 12, 2013, pp. 2431-2446.

[18] Zhou, R., Azarpazhooh, M., "Deep Learning-Based Carotid Plaque Segmentation from B-Mode Ultrasound Images", Ultrasound in medicine & biology, vol. 47, no. 9, 2021, pp. 2723–2733.

[19] Jain, P., Sharma, N., "Hybrid deep learning segmentation models for atherosclerotic plaque in internal carotid artery B-mode ultrasound", Computers in biology and medicine, 136, 2021, pp. 104721.

[20] Lekadir, K., Galimzianova, A., "A Convolutional Neural Network for Automatic Characterization of Plaque Composition in Carotid Ultrasound,", IEEE, IEEE journal of biomedical and health informatics, vol. 21, no. 1, 2017, pp. 48–55.

[21] Mechrez, R., Goldberger, J., "Patch-Based Segmentation with Spatial Consistency: Application to MS Lesions in Brain MRI", International Journal of Biomedical Imaging, 2016, pp. 1–13.

[22] Selvan, R., Dam, E., "Patch-based medical image segmentation using Quantum Tensor Networks", arXiv preprint arXiv:2109.07138, 2021

[23] Sekou, T., Hidane, M., "From Patch to Image Segmentation using Fully Convolutional Networks - Application to Retinal Images", ArXiv, abs/1904.03892., 2019

[24] Hou, L., Samaras, D., "Patch-based convolutional neural network for whole slide tissue image classification",

Proceedings of the IEEE conference on computer vision and pattern recognition, 2016, pp. 2424-2433.
[25] TAXINOMISIS Project, Accessed: 24.12.2021, Available: https://taxinomisis-project.eu/
[26] Ronneberger, O., Fischer, P., “U-net: Convolutional networks for biomedical image segmentation”, International Conference on Medical image computing and computer-assisted intervention, 2015, pp. 234-241.