Automatic Assessment of Calcified Plaque and Nodule by Optical Coherence Tomography Adopting Deep Learning Mode

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Abstract

Purpose: Optical coherence tomography (OCT) has become the best imaging tool in assessment of calcified plaque and nodule. However, every OCT pullback has large number of images and artificial analysis need too much time and energy, so it is not suitable for clinical application. This study aimed to develop and validate an automatic assessment of calcified plaque and nodule by OCT using deep learning model.

Methods: The OCT images of calcified plaque and nodule were labeled by two expert readers based on the consensus. A deep learning model with a Multi-Scale and Multi-Task u-net network (MS-MT u-net) was developed. Then with the ground truth labeled by expert readers as reference, the diagnostic accuracy and agreement of the model would be validated.

Results: For the pixel-wise evaluation of calcified plaque, the model had a high performance with precision (93.95%), recall (88.95%) and F1 score (91.38%). For the lesion-level evaluation of calcified plaque, the quantitative metrics by the model correlated excellent with the ground truth (calcium score, $r=0.90$, $p<0.01$; calcified volume, $r=0.99$, $p\leq 0.01$). For calcified nodules, the model showed an excellent diagnostic performance of model including sensitivity (91.7%), specificity (89.3%) and accuracy (91.0%).

Conclusions: We developed a novel deep learning model for identifying attributes of calcified plaque and nodule. This model provides an excellent diagnostic accuracy and agreement with the ground truth, which reduces subjectivity of manual measurements and saves lots of time. These findings would help practitioners efficiently adopting appropriate therapeutic strategy in the treatment of calcified lesions.

Introduction

Calcification is prevalent in patients with coronary atherosclerotic plaques. Data from the ACUTY and HORIZONS-AMI study showed that moderate and severe calcified lesions were found in 32% of patients assessed by coronary angiography [1]. The high rigidity of calcified plaque constrains the delivery and expansion of stents, so moderate and severely calcified lesions are always associated with high percentage of complication like dissection, stent underexpansion, restenosis and thrombosis [2, 3]. In addition, calcified plaque also leads to thrombosis in the acute coronary syndromes (ACS). Although the major pathogenesis of ACS is plaque rupture, 2–7% of fatal thrombosis are caused by calcified nodules [4]. Calcified nodule is one type of calcified plaque, defined as a protruding calcification with rupture of fibrous cap and newly formed thrombosis.

Although intravascular ultrasound (IVUS) has a higher sensitivity and specificity than coronary angiography, it could not penetrate calcification to visualize its contour. Due to technology limitation, neither coronary angiography nor IVUS could accurately assess calcified nodules. While optical coherence tomography (OCT) has a higher resolution (10-20 μ m) than IVUS and could also penetrate superficial calcification, so it's an optimal imaging tool in quantitative assessment of calcified plaque and qualitative assessment of calcified nodules. A retrospective study developed an OCT-based calcium

scoring method in which calcified lesions with maximum angle $> 180^\circ$, maximum thickness $> 0.5\text{mm}$, and length $> 5\text{mm}$ may be independent risk factors for stent underexpansion [5]. Another study systematically investigated the morphological features of calcified nodule in vivo by OCT and found the similar incidence of calcified nodule in patients with ACS like pathology study [6]. Percutaneous coronary intervention (PCI) of calcified lesions guided by OCT may decrease the procedural complication and improve patients' long-term prognosis. However, it takes too much time and effort to analyze a large amount of OCT pullback data manually. Thus, an OCT-based deep learning algorithm to realize automatic assessment of calcified plaque and nodule was developed accordingly in this study.

Methods

Dataset and labeling

This was a single-center and retrospective study and all OCT pullbacks data were acquired with frequency-domain OCT system of Cornaris P80 (Vivolight Medical Device & Technology, Shenzhen, China). Exclusion criteria were pullbacks acquired after any stent implantation and uninterpretable OCT images due to residual blood, artifact or unclear lumen images. Because of the retrospective design, written informed consent for using anonymous patient data was obtained from the patients.

The region of interest (ROI) was defined as regions with calcified plaque or nodule screened by OCT. And the datasets of calcified plaque and nodule were labeled respectively. Two expert analysts from the 2nd Affiliated Hospital of Harbin Medical University manually labeled the calcified plaque and nodule based on the consensus document [7, 8]. If labeling results of the two experts are quite different at the same region of the same frame, consensus must be reached together with an additional experienced interventional cardiologist. The calcification appears in an OCT cross-section view as a region of attenuated signal or heterogeneous area with sharply delineated border. When a calcified lesion was extremely thick and its border was vague due to signal attenuation, the maximum visible outline will be delineated. Calcified nodule, a particular type of calcified plaque, was defined as a protruding calcium with rupture of fibrous cap and newly formed thrombosis.

The data of 100 clinical OCT pullbacks was collected, and then expert readers were invited to screen out 201 ROIs. Based on the selected ROIs, the ground-truth of calcified plaque in each image were labeled. Finally, 4,254 OCT images containing calcified plaque were labeled. 3900 frames and 354 frames were divided into the training and testing datasets. For calcified nodules, a total of 50 clinical OCT pullback data were collected. Analogous to the process of selecting and labeling calcified plaque image, 470 calcified nodule images were labeled.

Data preprocessing

For deep learning model, data is usually enriched to improve the performance and robustness of the network. Considering Cartesian images are cross-sectional images of blood vessels, which in Cartesian images always have an approximately circular structure. Therefore, a more suitable data expansion

method is to rotate the image so as not to change the structural information of the blood vessel itself. In the end, we randomly selected 10 angles from 0 to 360 degrees for data rotation expansion. Specifically, the resolutions of polar image and cartesian image are 504x960 pixels and 704x704 pixels respectively.

Deep Learning Model

For the semantic segmentation tasks in the medical field, the u-net model has been widely used and achieved good accuracy. Based on the u-net model, this paper proposes a multi-scale, multi-task u-net network (MS-MT u-net), as shown in Figure 1. It is known that the calcified plaques are different in size & volume. In order to capture accurate information of calcium at various scales and improve the precision of calcified plaque measurement, this paper proposed the multi-scale model. Figure 2 shows the schematic diagram of the multi-scale model proposed in this article. For the input feature map, 4 different scale filter kernels forming the input feature map are used for features extraction under different receptive fields. The size of the filter kernels are 1x1, 3x3, 5x5 and 7x7. At last, the feature map obtained under different scale convolution kernels are directly added to the next layer of the network.

Furthermore, considering that the thickness and angle of calcification need to be calculated based on the identified calcified area, the accuracy of the edge recognition of the calcification contour is vital. First of all, based on the manually labeled calcification area, the calcification mask map will be generated (it is a 0-1 binary image, the pixel value in the calcification area is 1, and the pixel value of the remaining positions is 0). Then the canny operator will be used to extract the edge area of calcification. Finally, an expansion algorithm is applied to expand the edge, specifically using a disk filter of radius 12.

It can be seen that the acquisition of the edge mask will not increase the marking cost, and it can be obtained based on the gold standard extracted from marked calcification. In Figure 1, it can be seen that MS-MT u-net is a 5-layer encoding-decoding network. For each layer, a multi-scale module will firstly be used to extract features in different receptive fields, and then these features will be compared, added, and then connected to a nonlinear activation layer (ReLU). Down-sampling is 2x2 max pooling operation. In the up-sampling process of the decoding network, the convolution features are combined to perform up-sampling for the final segmentation result.

Loss Function

The loss functions in this paper consists of two parts - Negative Log Likelihood loss for calcification mask and edge mask. The formula of the total loss is given by

$$L_{\text{total}} = \lambda_1 L_{\text{calcification mask}} + \lambda_2 L_{\text{edge mask}} \quad (1)$$

where

$$L_{\text{calcification mask}} = \sum_x \log p_{\text{calcification mask}}(x; l_{\text{calcification mask}}(x)) \quad (2)$$

$$L_{\text{edge mask}} = \sum_x \log p_{\text{edge mask}}(x; l_{\text{edge mask}}(x)) \quad (3)$$

λ_1 and λ_2 are weight coefficients.

$L_{\text{calcification mask}}$ and $L_{\text{edge mask}}$ represent the pixel-wise classification error. The

x denotes the pixel position in image. $p_{\text{calcification mask}}(x; l_{\text{calcification mask}}(x))$ and

$p_{\text{edge mask}}(x; l_{\text{edge mask}}(x))$ are the predicted probability of x for ground-truth label

$l_{\text{calcification mask}}(x)$ and $l_{\text{edge mask}}(x)$ after softmax activation function.

Training of deep learning model

The data preprocessing is implemented by matlab 2015b. The training & testing model is accomplished based on the pytorch framework with linux platform. And the GPU model of the computer is Titan Xp 12GB GPU.

Identification of Calcified plaque and nodule are trained separately, and the corresponding deep learning models for them are also carried out respectively. In the training process, the batch size is set to 2. Besides, we use the Adam algorithm with a starting learning rate of $\text{lr} = 10^{-3}$. In the follow-up process, the dynamic learning rate is used for training. And when the training loss on the verification set is stable, we reduce the learning rate to 1/5 of the previous one and set the maximum epoch to 200.

Performance evaluation

Calcified plaque pixel-wise qualitative evaluation of the deep learning model used traditional metrics as

below: (1) $\text{recall} = \frac{\text{TP}}{\text{TP} + \text{FN}}$, (2) $\text{precision} = \frac{\text{TP}}{\text{TP} + \text{FP}}$, (3) $\text{F1 score} = \frac{2 \times \text{precision} \times \text{recall}}{\text{precision} + \text{recall}}$ (TP is the number of true positives, FP is number of false positives, TN is the number of true positives and FN is the number of false negatives). The quantity evaluation metrics were the agreement or correlation including angle, thickness and area of calcified plaque in each frame. Besides, calcium scoring by Fujino and calcium volume were computed in the calcified lesion segment. The calcium score was defined as 2 points for maximum angle $>180^\circ$, 1 point for maximum thickness >0.5 mm, and 1 point for length >5 mm [5]. The calcium volume was defined as the sum of each calcium area multiplied by the cross-section interval

(0.2mm). Calcified nodule was evaluated in frame level and the diagnostic accuracy was defined that the overlapping portion between the deep learning model and ground truth was >80%.

Statistical analysis

Statistical analysis was performed using SPSS 22.0 (IBM, Armonk, NY). Continuous data are expressed as mean± standard deviation, or median (interquartile range) when appropriate. Categorical variables are presented as counts and percentages. Agreement between groups for continuous variables was assessed by means of Bland- Altman analysis, while the kappa coefficient was used for categorical variables. Correlation between ground truth and deep learning model predictions was evaluated using Pearson or Spearman correlation tests. A Pearson’s correlation coefficient of 0.70 or higher indicates strong positive relationship; an r value of 0.50 to 0.69 indicates moderate positive relationship, and an r value of 0.30 to 0.49 indicates weak positive relationship. For all analyses, two-sided *p* < 0.05 was considered statistically significant.

Results

For the pixel-wise evaluation of calcified plaque, the model had a high performance with precision (93.95%), recall (88.95%) and F1 score (91.38%) (Table 1)(Figure 4). The quantitative evaluation metrics are summarized in Table 2. For the lesion-level evaluation of calcified plaque, the quantitative evaluation metrics in the calcium score assessed by the model had a strong relationship with the ground truth (maximum angle, *r*=0.99, *p*< 0.01; maximum thickness, *r*=0.84, *p*< 0.01) (Figure 5). The Bland-Altman analysis also showed a strong agreement between model and the ground truth (maximum angle with a mean difference, 3.0±8.82; maximum thickness with a mean difference, 0.10±0.20) (Figure 5). As a result, the calcium score assessed by the model correlated excellent with the ground truth (*r*=0.90, *p*< 0.01). For the total volume of calcified lesion, the model also showed a significantly relationship (*r*=0.99, *p*< 0.01) and agreement (mean difference, 0.21±0.51) with the ground truth (Figure 6). In addition to high accuracy, the model was also high-efficiency to save time and energy of cardiologists. Our model cost 0.03 sec per frame and 12 sec per pullback compared with 15 sec per frame and 6000 sec per pullback by manually labeling.

Table 1
Qualitative evaluation of calcified plaque in pixel-wise
(n=354 frames)

	precision	recall	F1 score
Calcified plaque	93.95%	88.95%	91.38%
Values are number and percentage.			

Table 2
Quantitative evaluation of calcified plaque in lesion-level (n=31 segments)

	Deep learning model	Ground truth	r	p
Maximum angle (degree)	106.8±70.7	104.3±68.6	0.99	< 0.01
Maximum thickness (mm)	1.15±0.66	1.21±0.73	0.84	< 0.01
Calcium score	1.45±0.96	1.52±1.03	0.90	< 0.01
Calcium volume (mm ³)	4.96±4.70	4.73±4.30	0.99	< 0.01
Values are mean ± SD.				

Table 3
The diagnostic validation of calcified nodule

		Ground truth		Total (n)
		+	-	
Model	+	66	3	60
	-	6	25	31
Total (n)		72	28	100
Values are number. Positive (+), Negative (-)				

For the validation of calcified nodule, 100 frames were selected randomly in the test set. We observed an excellent diagnostic performance of model including sensitivity (91.7%, 95%CI 82.7%-96.9%), specificity (89.3%, 95%CI 71.8%-97.7%) and accuracy (91.0%, 95%CI 83%-95%) (Figure 3).

Discussion

The important findings of our study were summarized as follows. (1) The calcification attributes could be identified automatically by the novel deep learning algorithm with a high performance and fast computation speed. (2) The novel deep learning algorithm provides a tool to quantitatively evaluate common metrics of calcified plaque in clinical practice including angle, thickness, volume and calcium score. (3) Calcified nodule as a unique type of calcified lesion, automatically assessed by the model with an excellent diagnostic accuracy.

Facing a large number of images, it takes too much time to manually identify the coronary lesions for clinical expertise. Besides, the manual method could not solve the subjective difference and provide a good reproducibility [9]. Many previous studies have applied artificial intelligence to automatically identify the plaque characteristics in OCT images [10–13]. The deep learning is a necessary way to achieve artificial intelligence. The common deep learning algorithm methods include U-net, Deeplab v3+ and SegNet [14]. Ughi et al. firstly used the automatic algorithm to identify the characteristics of

atherosclerotic plaques by textural features and optical attenuation coefficient [10]. The overall pixel-wise diagnostic accuracy was 81.5%. Lee et al. developed a two-step deep learning method combined with 3D convolutional neural network and SegNet. The sensitivity, precision and F1 score of the model were 86.2%, 75.8% and 78.1% [14]. Our study proposed a Multi-Scale and Multi-Task u-net network (MS-MT u-net) based on the u-net model. For the task of calcification segmentation, the size of calcification is not fixed and diverse. In order to capture calcification information at various scales and improve the accuracy of calcification, we proposed a multi-scale module. For each feature map, we empty four filter kernels to extract features in different receptive fields. The sizes of the four filter kernels are as follows 1x1, 3x3, 5x5 and 7x7. Finally, the feature maps obtained from the four filter kernels are added and input into the next layer. In our study, the model had a better performance with precision (93.95%), recall (88.95%) and F1 score (91.38%) in pixel-wise evaluation of calcified plaque.

Although the morphological characteristics of identified calcified lesions is important, what's more vital are the quantity evaluation including angle, thickness, length, area, volume and a comprehensive calcium scoring directly predicting stent underexpansion. It will affect the whole therapeutic strategy prior to stent implantation. Fujino et al reported that aggressive plaque pre-modification should be considered such as cutting balloon or rotational/orbital atherectomy when the calcium score reaches 4 [5]. Previous study reported that the automated assessments of deep learning model had a strong correlation with the ground truth. The mean value of agreement was -0.13mm (95% CI, -0.52 to 0.25mm) and -7 degree (95% CI, 52 degree to 37 degree) for calcified plaque thickness and angle respectively [15]. There were only five calcified lesions taking into analysis and automatically obtained scores were right in four out of five lesions. The sample size was very small. In our study 31 lesions were included and the results showed that the mean value of agreement was 0.10mm (95% CI, -0.30 to 0.49mm) and 3.0 degree (95% CI, -14.3 to 20.3 degree) for maximum calcified plaque thickness and maximum calcification angle. The calcium score computed by the model correlated excellent with the ground truth ($r=0.90$, $p<0.01$) with accuracy of 93.5% (29/31). Compared with previous studies, we not only take into consideration of the quantity metrics in a single-section (maximum angle and thickness), but also the total volume of calcified lesion. Our deep learning model also showed a significant correlation ($r=0.99$, $p<0.01$) and agreement with the ground truth.

Calcified nodule as a unique type of calcification is also responsible for ACS in 1/20 [16]. Calcified nodule is a plaque with protruding calcification through a disrupted fibrous cap and newly formed thrombi in pathology definition. OCT is the most suitable intravascular imaging tool for the diagnosis of it. In addition to the above morphological features, the most distinctive point in identifying calcified nodules is the presence of severe calcification proximal or distal to the lesion. Hence, our novel deep learning algorithm takes adjacent frame information of calcified nodule into analysis, which could greatly improve the diagnostic accuracy (Figure 7). To the best of our knowledge, this is the pioneer study to utilize the deep learning algorithm to automatically recognize calcified nodules. Our study result showed an excellent diagnostic performance of the new model in the perspective of sensitivity (91.7%, 95%CI 82.7%-96.9%), specificity (89.3%, 95%CI 71.8%-97.7%) and accuracy (91.0%, 95%CI 83%-95%).

In addition to high accuracy of qualitative and quantitative evaluation, the calculation time duration is a key factor in clinical application of the deep learning algorithm. Lee et al. reported that their deep learning model analysis took 0.3 sec per frame [14]. Assuming there are 400 frames in a single pullback, the automatic analysis would take around 120 sec compared with 0.5-2 hours by cardiologist' experience. In our study, in order to improve the operation efficiency, we analyzed and optimized the network in the time consumption of computation. In particular, in effort to reduce the running time of the whole network, the new model replaced the Central Processing Unit (CPU) processing part with Graphics Processing Unit (GPU) processing. This novel deep learning algorithm only takes 0.03 sec per frame and 12 sec each pullback. The high-new model would enhance the working efficiency in real-world clinical application.

Limitations

There are also limitations in this study. Firstly, the ground truth was labeled by two experts and there may be many mislabeled images according to histology. In this study, the two expert analysts must reach an agreement on all labeling result according to the expert consensus. Besides, OCT has a high sensitivity and specificity in recognizing the calcification which had been verified in histological controlled trials. Secondly, the sample size of calcified nodules was small in this study. Previous study reported that only 2-7% of Acute Coronary Syndromes (ACS) was due to calcified nodules, so it is difficult to collect cases with calcified nodule cases in the clinical practice. Thirdly, the performance of the novel deep learning algorithm needs more real-world data to verify.

Conclusion

We developed a novel deep learning model for recognizing attributes of calcified plaque and nodule, automatic computation of calcium score and calcified volume. This model provides an excellent diagnostic accuracy and the result agrees with the ground truth, which also reduces subjectivity of manual measurements and saves lots of time. These findings would help practitioners efficiently adopting appropriate therapeutic strategy in the treatment of calcified lesions.

Declarations

Conflict of interest

There are no conflicts of interest.

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Figures

Figure 1

The framework of MS-MT u-net. MS-MT u-net is an encoder-decoder network with five layers. For each layer, multi-scale modules are used to extract features in different receptive fields, then these features are added which is followed by a nonlinear activation layer (ReLU). The 2x2 max pooling operation was used

for down-sampling layer. In the decoder process, upsampling will be carried out by combining convolution features to obtain the final segmentation result.

Figure 2

Multi-scale module (MS). For the input feature map, 4 different scale filter kernels forming the input feature map are used for features extraction under different receptive fields. The size of the filter kernels are 1×1 , 3×3 , 5×5 and 7×7 . At last, the feature map obtained under different scale convolution kernels are directly added to the next layer of the network.

Calcification

100 OCT pullbacks

screen out region of interest
(ROI) and label each frame

Calcified nodules

50 OCT pullbacks

screen out region of interest
(ROI) and label each frame

Figure 3

Study flow chart. The utility of the different datasets for calcification (left column) and calcified nodule (right column) is indicated.

Figure 4

Predicted calcification by model shows good correlation with the ground truth. Images are: OCT image (a), labeled image (b), automatic segmentation (c).

Figure 5

The relationship and agreement of maximum angle/thickness between the deep learning model and the ground truth. Correlation of maximum calcification angle (a), Bland-Altman analysis of maximum calcification angle (b), Correlation of maximum calcification thickness (c), Bland-Altman analysis of maximum calcification thickness (d)

Figure 6

The relationship and agreement of maximum volume between the deep learning model and the ground truth. Correlation of maximum calcification volume (a), Bland-Altman analysis of maximum calcification volume (b).

Figure 7

The case shows that the current frame is identified as calcified nodules according to the presence of calcification proximal or distal to the lesion.