

Deep learning-based intravascular ultrasound segmentation for the assessment of coronary artery disease☆

Takeshi Nishi^{a,b,*}, Rikiya Yamashita^c, Shinji Imura^a, Kazuya Tateishi^b, Hideki Kitahara^b, Yoshio Kobayashi^b, Paul G. Yock^a, Peter J. Fitzgerald^a, Yasuhiro Honda^{a,*}

^a Division of Cardiovascular Medicine, Stanford University School of Medicine and Stanford Cardiovascular Institute, Stanford, CA, USA

^b Department of Cardiovascular Medicine, Chiba University Graduate School of Medicine, Chiba, Chiba, Japan

^c Department of Biomedical Data Science, Stanford University School of Medicine, CA, USA

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ABSTRACT

Background: Accurate segmentation of the coronary arteries with intravascular ultrasound (IVUS) is important to optimize coronary stent implantation. Recently, deep learning (DL) methods have been proposed to develop automatic IVUS segmentation. However, most of those have been limited to segmenting the lumen and vessel (i.e. lumen-intima and media-adventitia borders), not applied to segmenting stent dimension. Hence, this study aimed to develop a DL method for automatic IVUS segmentation of stent area in addition to lumen and vessel area.

Methods: This study included a total of 45,449 images from 1576 IVUS pullback runs. The datasets were randomly split into training, validation, and test datasets (0.7:0.15:0.15). After developing the DL-based system to segment IVUS images using the training and validation datasets, we evaluated the performance through the independent test dataset.

Results: The DL-based segmentation correlated well with the expert-analyzed segmentation with a mean intersection over union ($\pm$ standard deviation) of 0.80 ± 0.20 , correlation coefficient of 0.98 (95% confidence intervals: 0.98 to 0.98), 0.96 (0.95 to 0.96), and 0.96 (0.96 to 0.96) for lumen, vessel, and stent area, and the mean difference ($\pm$ standard deviation) of 0.02 ± 0.57 , -0.44 ± 1.56 and -0.17 ± 0.74 mm² for lumen, vessel and stent area, respectively.

Conclusion: This automated DL-based IVUS segmentation of lumen, vessel and stent area showed an excellent agreement with manual segmentation by experts, supporting the feasibility of artificial intelligence-assisted IVUS assessment in patients undergoing coronary stent implantation.

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1. Introduction

Intravascular ultrasound (IVUS) is the most widely used intracoronary imaging modality which provides anatomic information in detail about vessel and lumen dimensions and atherosclerotic lesion characteristics including severity of stenosis, lesion length, and morphology which are poorly detected by conventional coronary angiography. A number of previous studies have shown that procedure guidance with IVUS improve health outcomes of patients with coronary artery disease (CAD) undergoing PCI by helping physicians optimize stent

implantation in multiple ways: guiding accurate lesion preparation, device sizing and procedure optimization [1,2].

Despite the advantages, IVUS remains underutilized in some settings in the US. The evaluation of IVUS requires a high level of expertise to obtain correct readings. The traditional manual segmentation of IVUS images is time-consuming, error-prone, and subject to intra- and inter-observer variability especially when assessed by an inexperienced analyzer. In addition, it is difficult to measure all cross-sections manually in the entire artery during the procedure due to limited time. These may limit adoption of IVUS in the cardiac catheterization laboratory and achievement of optimal PCI results even if IVUS is used during the PCI procedure.

Recent developments in artificial intelligence (AI) have paved the way for an automated, objective and quantitative approach to evaluate the vessel dimensions with IVUS [3]. Some DL methods have been proposed to develop automated IVUS segmentation. However, most of those have been constructed by using images from a relatively small number of subjects and limited to the lumen and vessel segmentation,

☆ These authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

* Corresponding authors at: Division of Cardiovascular Medicine, Stanford Cardiovascular Institute, Stanford University School of Medicine, 300 Pasteur Drive, Room H3554, Stanford, CA 94305-5637, USA.

E-mail addresses: takeshi24@hotmail.co.jp (T. Nishi), yshonda@stanford.edu (Y. Honda).

not applied to segmenting stent dimension [4,5]. Hence, this study aimed to develop a DL method for IVUS segmentation to automatically delineate stent area in addition to lumen and vessel area based on large scale datasets.

2. Methods

2.1. Study dataset

To derive a segmentation model, we used a total of 45,529 images from 1576 IVUS runs collected to evaluate post-stent dimensions and cardiac allograft vasculopathy at Stanford University (Stanford, CA) between 2001 and 2015 and stored as a format of echoPlaque file (echoPlaque, Indec Systems, Santa Clara, California). IVUS was performed in a standard manner using an automated transducer pullback at 0.5 mm/s with a commercially available imaging system including 40-MHz IVUS (Boston Scientific Corporation [93.8%], Terumo Corporation [3.9%]) and 45-MHz IVUS (Volcano Corporation [2.3%]). The lumen, vessel (i.e. lumen-intima and media-adventitia borders), and stent leading edge in a target region (a stented segment plus proximal and distal reference segments or proximal 50 mm of the left anterior descending artery) were manually annotated typically at 1-mm intervals by cardiologists who were experts on IVUS image analysis using validated quantitative IVUS analysis software (echoPlaque, Indec Systems, Santa Clara, California). We did not analyze images with significant artifacts or large branches. In addition, we did not annotate media-adventitia border and did not analyze vessel area in the images in which acoustic shadowing due to calcification or attenuated signal plaque involves a large arc of $\geq 90^\circ$. The images will be converted to planar by transferring all the points from Cartesian coordinates to planar representation in Polar coordinates to simplify the calculations. As our IVUS datasets had various image sizes, we resized all datasets to 256×256 pixels to enable use in our network. The datasets were randomly split into training, validation, and test datasets (0.7: 0.15: 0.15 = 1103: 236: 237 runs [32,106: 6926: 6733 images]). To explore the applicability of the model to contemporary 60-MHz IVUS images, we gathered a separate validation group from an independent site (Chiba University, Chiba, Japan) which comprise 1000 images of consecutive 11 patients who underwent IVUS (AltaView, Terumo, Tokyo, Japan) for stent evaluation between January and March, images of which have adequate quality to analyze and did not include extensive (arc $\geq 90^\circ$) calcification or attenuated signal plaque. The Institutional Review Board of each site approved the study protocol.

2.2. Constructing a neural network model

We constructed a DL-based segmentation system using the training and validation datasets. The neural network architecture is designed based on a fully convolutional neural network (CNN) with encoder/decoder networks with the main body being DeepLabv3 [6–9]. The

pyramid pooling module is used to extract feature maps at multiple scales. We used the ResNet34 encoder and the Adam optimization algorithm as an optimizer [10]. The input for the model is a resized IVUS image, while the output of the model is the mask image, which indicates the vessel, lumen, and stent area in the IVUS image. We adapted cross entropy loss as the loss function for model training. The training batch size was set as 8, and epoch number was set as 20 with a learning rate being set as 0.001 for the first 10 epochs and then down to 0.0001 for the latter 10 epochs. After constructing the DL-based system to segment IVUS images using the training and validation datasets, we evaluated the performance through the independent test dataset.

2.3. Statistical analysis

The metrics used for the evaluation were the mean Intersection-Over-Union (IoU) and Dice similarity coefficient (DSC), common evaluation metrics for semantic image segmentation, which first compute the IoU and DSC for each semantic class and then compute the average over classes. IoU and DSC are defined as follows:

$$\text{IoU} = \text{true positives} / (\text{true positives} + \text{false positives} + \text{false negatives})$$

$$\text{DSC} = 2 \times \text{true positives} / (2 \times \text{true positives} + \text{false positives} + \text{false negatives})$$

To assess the practical validity, we calculated the actual lumen, vessel and stent area in mm^2 from the area in pixels using the calibration information. The agreement and correlation of the lumen, vessel and stent area between the DL-based segmentation and the expert-analyzed segmentation was assessed by Pearson correlation coefficient and mean difference and visualized by scatter plots and the Bland–Altman plots of randomly-selected 10% of the entire images. Continuous variables were expressed as mean $\pm$ standard deviations (SD) or 95% confidence intervals (CI). Two sets of continuous variables were compared with *t*-test. Correlation coefficients were z-transformed for the statistical comparison. Deep learning and statistical analysis were performed using Python version 3.6 programming language (Python Software Foundation, Beaverton, Oregon) with PyTorch library on a computer with a graphics processing unit (GeForce RTX2700 Super, NVIDIA, Santa Clara, California).

3. Results

In the whole dataset used for training/validation and test, the mean area of the lumen vessel and stent were $6.8 \pm 2.9 \text{ mm}^2$, $13.4 \pm 5.2 \text{ mm}^2$, and $7.3 \pm 2.5 \text{ mm}^2$, respectively. The diagnostic performance of the DL-based segmentation is summarized in Table 1. The DL-based segmentation correlated well with the expert-analyzed segmentation with a mean IoU ($\pm$ SD) of 0.80 ± 0.21 , correlation coefficient of 0.98 (95% CI: 0.98 to 0.98), 0.96 (95%CI: 0.95 to 0.96), and 0.96 (95%CI: 0.96 to

Table 1
Performance of the deep learning-based segmentation against expert analysis on the test dataset.

	Overall	Stent (+)	Stent (–)	P value
IoU	80 ± 21	76 ± 22	88 ± 12	<0.001
DSC	83 ± 20	80 ± 22	92 ± 12	<0.001
Correlation coefficient				
Vessel area	0.96 (95%CI: 0.95 to 0.96)	0.94 (95%CI: 0.94 to 0.95)	0.98 (95%CI: 0.98 to 0.98)	<0.001
Lumen area	0.98 (95% CI: 0.98 to 0.98)	0.98 (95%CI: 0.98 to 0.98)	0.98 (95%CI: 0.98 to 0.98)	0.68
Stent area	0.96 (95%CI: 0.96 to 0.96)	0.96 (95%CI: 0.96 to 0.96)	NA	NA
Mean difference				
Vessel area (mm^2)	-0.44 ± 1.56	-0.56 ± 1.73	-0.19 ± 1.04	<0.001
Lumen area (mm^2)	0.02 ± 0.57	0.03 ± 0.52	-0.005 ± 0.69	0.014
Stent area (mm^2)	0.17 ± 0.74	0.17 ± 0.74	NA	NA

Values are mean $\pm$ standard deviation or mean (95% confidence intervals). DSC indicates Dice similarity coefficient; IoU, Intersection-Over-Union; NA, not applicable.

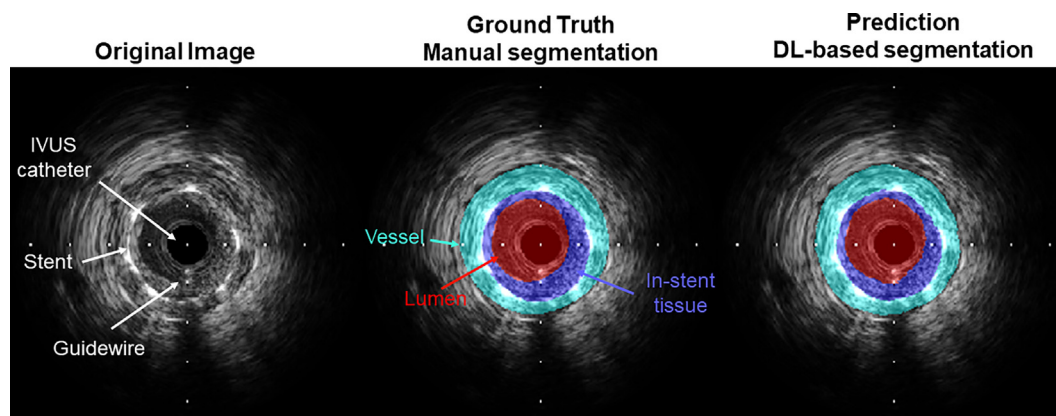


Fig. 1. An example IVUS image of original, ground truth, and prediction. Ground truth indicate manual segmentation delineated by experts; prediction indicates deep learning (DL)-based segmentation.

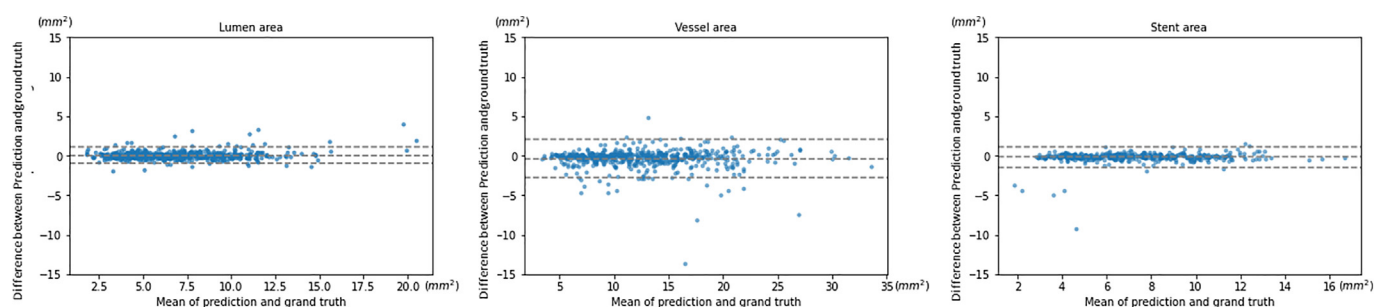


Fig. 2. Bland–Altman plot between prediction and ground truth of lumen, stent, and vessel area values. Ground truth indicate manual segmentation delineated by experts; prediction indicates deep learning (DL)-based segmentation. Mean difference between ground truth and prediction is shown in solid line and 95% limits of agreement (LOA) are shown in dotted lines.

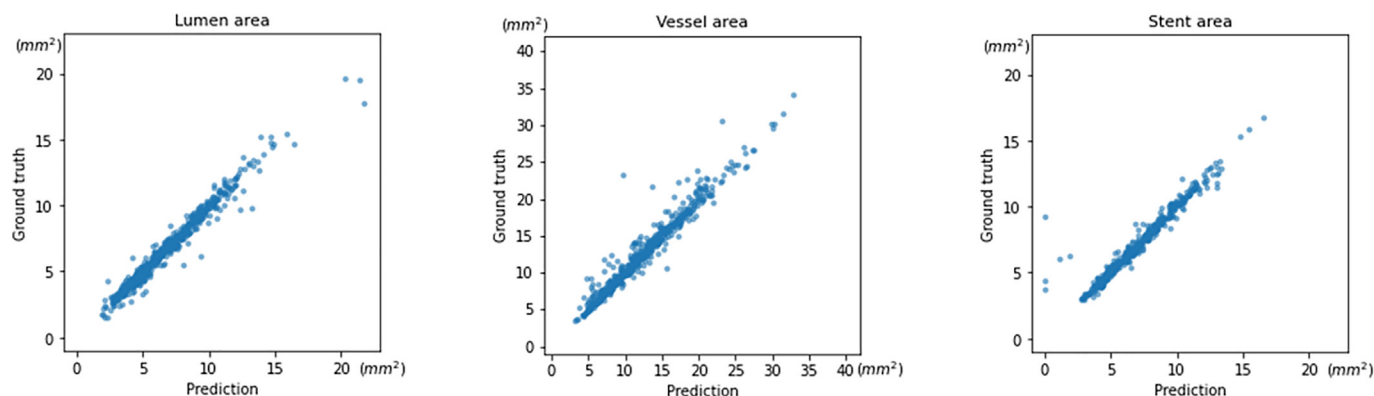


Fig. 3. Correlation between prediction and ground truth of lumen, stent, and vessel area values. Ground truth indicate manual segmentation delineated by experts; prediction indicates deep learning (DL)-based segmentation.

0.96) and the mean difference ($\pm$ SD) of 0.02 ± 0.57 , -0.44 ± 1.56 and -0.17 ± 0.74 mm² for lumen, vessel and stent area, respectively (Figs. 1, 2 and 3).

We explored the model performance in images with stent ($n = 4883$) and those without stent ($n = 1850$) separately. The mean IoU ($\pm$ SD) was higher in the images without stent than that with stent (0.88 ± 0.12 vs 0.76 ± 0.21 , $p < 0.001$). The agreement and correlation of the vessel area between the DL-model and the expert analysis were better in images without stent than in the images with stent (correlation coefficient: 0.98 [95%CI: 0.98 to 0.98] vs. 0.94 [95%CI: 0.94 to 0.95], $P < 0.001$; -0.19 ± 1.04 vs. -0.56 ± 1.73 , $P < 0.001$). The mean

difference between the DL-model and the expert analysis was slightly smaller in images without stents than those with stents (-0.005 ± 0.69 vs 0.03 ± 0.52 , $P = 0.014$), while the correlation coefficient of the lumen area did not significantly differ (correlation coefficient: 0.98 [95%CI: 0.98 to 0.98] vs. 0.98 [95%CI: 0.98 to 0.98], $P = 0.68$).

In the external dataset with 60-MHz IVUS images, where the mean area of the vessel, lumen and stent were 6.4 ± 2.2 mm², 11.2 ± 4.1 mm², and 6.0 ± 1.5 mm², respectively, the correlation coefficient and the mean difference between the DL-based and the expert-analyzed segmentations were 0.99 (95% CI: 0.98 to 0.99) and 0.15 ± 0.38 mm² for lumen area, 0.99 (95%CI: 0.98 to 0.99) and -0.63 ± 0.74 mm² for

vessel area, and 0.99 (95%CI: 0.99 to 0.99) and $0.05 \pm 0.20 \text{ mm}^2$ for stent area. It took 37 s for the DL model to perform the segmentation of the 1000 IVUS images although the expert spent around 30 h to perform the analysis for the IVUS images.

4. Discussion

By training and evaluating on large-scale IVUS image datasets, we constructed a CNN model to segment lumen, vessel, and stent structures on IVUS and demonstrated that the proposed DL-based method provided excellent segmentation performance as compared with human experts.

Automated quantitative IVUS analysis has been long-hoped-for to improve the objectivity of IVUS image analysis and to allow this analysis to be done in a timely manner. Before the deep-learning era, several image segmentation methods were proposed to automatically delineate the boundary of a coronary artery structures on IVUS, utilizing a number of computational approaches such as simple edge detection based on setting a pixel intensity threshold, active counter control, and the methods that utilize radiofrequency signal data [11–13]. Despite those past efforts, the automated IVUS analysis has not been widely employed in real practice, likely due to inadequate segmentation accuracy and limited availability requiring software from a specific vendor and radiofrequency signal data. Machine learning algorithms, especially deep neural networks, have demonstrated great potential, achieving or surpassing human performance in several visual tasks. Recently, neural networks have been explored for IVUS image analysis, showing promising performance in segmenting the vessel and lumen architectures [3–5]. Recent studies have shown that the fully CNN models achieved high performance for segmentation of the vessel and lumen [4,5]. Yang et al. used a publicly available IVUS dataset where the train and test sets consist of 109 and 326 20-MHz IVUS frames from 10 patients to develop a CNN model and showed the model achieved IoU of 0.86 and 0.90 for the vessel and lumen in the test dataset. Kim et al. developed a CNN model based on 38,625 40-MHz IVUS frames from 35 patients with coronary artery disease acquired from a single hospital and showed that the model achieved IoU of 0.73 and 0.86 for the vessel and lumen. Those previous models lacked stent segmentation and were constructed based on limited number of subjects. We developed the CNN model to delineate stent as well as vessel and lumen structures using the largest dataset which contained a broad range of images with regards to variety of subjects and IVUS vendors, demonstrating excellent agreement of image segmentation between the DL-based model vs. expert analysis.

When comparing the segmentation performance of our DL-based model between images with stents and those without, the segmentation performance was better in images without a stent than in images with a stent, especially in segmenting vessel area. In stented segments, there are more reflection and absorption of the US wave than in non-stented segments because there are stent struts and atherosclerotic plaques which are reflective and/or absorb the US waves from the transducer and therefore more likely cause ambiguous media-adventitia borders behind them. In the aspect of the mean IoU calculation, the difficulty to obtain high mean IoU value usually increases with increasing the number of segmentation classes as in the case of the present study. These possibly explain the lower segmentation performance in images with a stent than those without. Nonetheless, the lumen and vessel area in the stented segments derived from the DL-based segmentation still showed excellent correlation and agreement with the expert analysis, supporting its applicability in real practice even in the setting of coronary stent implantation.

4.1. Clinical implication

Although there is increasing evidence that IVUS-guided PCI improves clinical outcomes, the adoption rate is still low in the United

States and elsewhere. The additional procedural time and operator expertise are reported main reasons for the reluctance use of IVUS [14]. Automated analyses are of key-importance to avoid additional time and encourage operators, who are even not much experienced in IVUS analysis, to use IVUS. Our DL model can produce comprehensive segmentation of stent area as well as vessel and lumen area based on the largest dataset, showing excellent agreement with expert analysis. Of note, the DL-based analysis required much less time segmenting IVUS images compared with the analysis done by the cardiologists (37 s vs 30 h) with excellent performance in the present study. The speed of analysis (segmenting 100 frames in 4 s in our case) can overcome the time intensive limitations associated with the current IVUS analysis routine. This improves the efficiency of the IVUS analysis and make the clinical practice and research smoother and more effectively. In addition, this method does not require a radiofrequency signal and is not restricted to IVUS images from a specific vendor, therefore can be widely applicable. The DL-based automated segmentation will facilitate the uptake of IVUS-based clinical decisions, likely leading to improve quality of treatment and health outcomes of patients with CAD undergoing PCI. Furthermore, this work will serve as a basis for future AI research in the field of intracoronary imaging and will promote broad adoption of AI-assisted IVUS evaluation in the clinical and research settings.

4.2. Limitation

Some limitations of the present study should be considered. First, we included only images that were considered analyzable into the datasets. Therefore, the segmentation performance of this DL-based models may not be reproducible when image quality is poor due to artifacts which can occur in real clinical practice. Second, the manual IVUS segmentation was done by the experts at one site; further validation across multi-institutions would be needed to establish the robustness of this DL-based segmentation. Third, we included only 40- or 45-MHz IVUS images; the constructed DL-method is therefore not directly applied to IVUS images obtained with higher- or lower-frequency ultrasound signals (i.e., 20- and 60-MHz). We explored the performance of the current DL-model in the 60-MHz IVUS and demonstrated that good correlation and agreement with expert analysis, suggesting the possible applicability of the DL model developed with 40 MHz IVUS images to the 60-MHz IVUS segmentation. Nonetheless, future work is needed to improve and sophisticate the DL models for 40- and 60-MHz IVUS segmentation with more images and annotated data being accumulated. Fourth, the DL model in the present study is dedicated to just the segmentation of lumen, vessel and stent structures and does not function for the purpose of qualitative assessment such as detecting dissection, thrombotic material, stent expansion and apposition, and calcified regions, which is also important IVUS assessment and of help in real practice. Both automatic quantitative and qualitative IVUS analyses (i.e., segmentation and detection/classification) should be integrated in the future IVUS software.

5. Conclusions

The proposed automated DL-based IVUS segmentation of lumen, vessel, and stent area showed excellent agreement with manual segmentation by experts, supporting the feasibility of AI-assisted IVUS assessment in patients undergoing coronary stent implantation.

Disclosure

All authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Declaration of Competing Interest

None.

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