Automatic Segmentation and Visualization of Choroid in OCT with Knowledge Infused Deep Learning

Huihong Zhang, Jianlong Yang*, Kang Zhou, Liyang Fang, Fei Li, Yan Hu, Yitian Zhao, Xiulan Zhang, and Jiang Liu

Abstract—The choroid provides oxygen and nourishment to the outer retina thus is related to the pathology of various ocular diseases. Optical coherence tomography (OCT) is advantageous in visualizing and quantifying the choroid in vivo, because it does not suffer from the information contamination of the outer retina in fundus photography and scanning laser ophthalmoscopy. However, its application in the study of the choroid is still limited for two reasons. (1) The lower boundary of the choroid (choroid-sclera interface) in OCT is fuzzy, which makes the automatic segmentation difficult and inaccurate. (2) The visualization of the choroid is hindered by the vessel shadows from the superficial layers of the outer retina. In this paper, we propose to incorporate medical and imaging prior knowledge with deep learning to address these two problems. We propose a biomarker infused global-to-local network, for the choroid segmentation. It leverages the thickness of the choroid layer, which is a primary biomarker in clinic, as a constraint to improve the segmentation accuracy. We also design a global-to-local strategy in the choroid segmentation: a global module is used to segment all the retinal layers simultaneously for suppressing overfitting, then a local module is used to refine the segmentation with the biomarker infusion. The U-shape convolutional network is employed as the backbone in these modules. For eliminating the retinal vessel shadows, we propose a deep learning pipeline, which firstly use anatomical and OCT imaging knowledge to locate the shadows using their projection on the retinal pigment epithelium layer, then the contents of the choroidal vasculature at the shadow locations are predicted with an edge-to-texture two-stage generative adversarial inpainting network. The experiments shows the proposed method outperforms the existing methods on both the segmentation and shadow elimination tasks on a OCT dataset including 1280 labeled OCT B-scans and 136 OCT volumes. We further apply the proposed method in a clinical prospective study for understanding the pathology of glaucoma, which demonstrates its capacity in detecting the structure and vascular changes of the choroid related to the elevation of intraocular pressure.

Index Terms—choroid, optical coherence tomography, vasculature, glaucoma

I. INTRODUCTION

The choroid, lying between the retina and the sclera, is the vascular layer which provides oxygen and nourishment to the outer retina [1]. Because traditional imaging modalities like fundus photography and scanning laser ophthalmoscopy acquire 2D overlapping information of the outer retina and the choroid, the pathological changes of the choroid could not be precisely retrieved and evaluated. On the other hand, ocular ultrasound is able to do 3D imaging, but it needs to touch the eye and has a low spatial resolution.

Optical coherence tomography (OCT) is a high-resolution non-invasive 3D imaging modality that could precisely separate the information of the underlying choroid from the outer retina, thus has been becoming a powerful tool to understand the role of the choroid in various ocular diseases [2]. It has been shown that the thickness of the choroid layer extracted from OCT, is directly related to the incidence and severity of predominate ocular diseases, such as pathological myopia [3], diabetic retinopathy (DR) [4], age-related macular degeneration (AMD) [5], and glaucoma [6].

Besides, the choroidal vasculature has also been applied in the study and diagnosis of ocular diseases. Agrawal et al. found the choroidal vascularity index, which is extracted from binarized OCT B-scan, is related the vascular status of DR [7]. The choroidal vessel density (CVD), extracted from binarized en face choroid image, has been used in the...
evaluation of AMD [8] and central serous chorioretinopathy [9]. Wang et al. further introduced the choroidal vascular volume, which combines the CVD and the choroidal thickness, is more sensitive in detecting proliferative DR [10].

However, the application of the choroidal biomarkers in clinic is still quite limited, which may be attributed to two primary reasons. (1) The lower boundary of the choroid (choroid-sclera interface, CSI) in OCT is fuzzy, which makes the automatic segmentation difficult and inaccurate. (2) The visualization of the choroid is contaminated by the vessel shadows from the superficial layers of the outer retina.

Figure 1 is a demonstration of the CSI and the retinal vessels and their projection on the underlying layers. The position above the orange dashed line shows the fuzzy CSI in a B-scan. The anisotropy of the red blood cells inside the vessels cause strong forward attenuation of the probe light, thus bring shadow-like dark tails to the underneath layers extending to the choroid and the sclera (white arrow). The center part of Fig. 1 is a segmented OCT volume, which could further be used to generate the en face images of each layer in the right side. The ganglion cell layer (GCL) possesses the retinal vessels (black arrows) and has high light reflectance (green box). The depth-projected vessel shadows (black arrows) turn dark on the vessel-absent retinal pigment epithelium (RPE) layer (pink box) and the choroid layer (orange box). It is evident that the shadows bring difficulties to the extraction of the choroidal vasculature.

Due to their clinical significance, the automatic segmentation and visualization of the choroid have drawn numerous research interests recently [11]–[17]. However, the majority of the choroid segmentation methods are based on graph search [18], which is restricted by the choice of a suitable graph-edge weight model [15]. The inferior choice of the edge weight or the variation of OCT image features would cause inaccuracy in the choroid segmentation [19], so tedious manual inspection and correction are still required for clinical usage [20]. The existing methods for eliminating the vessel shadows are based on the compensation of vessel-induced light attenuation [21], [22], but the effectiveness of this kind of A-line based method is limited to small vessels and capillaries in OCT retinal imaging. The large vessel shadows still have residue on the choroid [23].

To address these two problems, and inspired by the recent success of deep learning in medical image processing [24], [25], we propose an automatic segmentation and visualization method for the choroid in OCT via knowledge infused deep learning. The main contributions of our work include:

- We propose a biomarker infused global-to-local network, for the choroid segmentation. It leverages the thickness of the choroid layer, which is a primary biomarker in clinic, as a constraint to improve the segmentation accuracy.
- We design a global-to-local strategy in the choroid segmentation: a global module is used to segment all the retinal layers simultaneously for suppressing overfitting, then a local module is used to refine the segmentation with the biomarker infusion.
- For eliminating the retinal vessel shadows, we propose a deep learning pipeline, which firstly locate the shadows using their projection on the retinal pigment epithelium layer, then the contents of the choroidal vasculature at the shadow locations are predicted with an edge-to-texture generative adversarial inpainting network.
- The experiments shows the proposed method outperforms the existing methods on both the segmentation and shadow elimination tasks on a OCT dataset including 1280 labeled OCT B-scans and 136 OCT volumes.
- We further apply the proposed method in a clinical prospective study for understanding the pathology of glaucoma, which demonstrates its capacity in detecting the structure and vascular changes of the choroid related to the elevation of intra-ocular pressure (IOP).

The remainders of the paper are organized as follows. We review the existing techniques related to the proposed method in Section II. The methodology of the proposed method is presented in Section III. To validate the effectiveness and clinical significance of the proposed method, we conduct extensive experiments in Section IV. We analyse and discuss the details of the proposed method in Section V, and draw our conclusion in Section VI.

II. RELATED WORKS

1) Automatic Choroid Segmentation: The segmentation of the retinal layers in OCT has been explored since the commercialization of spectral domain (SD) OCT [26]–[28], but the segmentation of the choroid layer was usually not included in these studies, which may be attributed to the fuzzy CSI (as a comparison, the outer retinal layers usually have sharp and smooth boundary as shown in Fig. 1). Hu et al. adapted the graph search algorithm to semi-automatically identify the choroidal layer in SD-OCT [11]. Tian et al. segmented the CSI by finding the shortest path of the graph formed by valley pixels using Dijkstras algorithm [12]. Alonso et al. developed an algorithm that detected the CSI based on OCT image enhancement and a dual brightness probability gradient [13]. Chen et al. generated a gradual intensity distance image. Then an improved 2-D graph search method with curve smooth constraints was used to obtain the CSI segmentation [14].

Deep learning techniques have also been used in the segmentation of the choroid. Sui et al. combined the graph search with convolutional neural network (CNN) by using the CNN to decide the edge weights in the graph search [15]. Masood et al. converted the segmentation tasks into a binary classification task, which extracted the choroid part of OCT images into patches with or without the CSI [16]. The U-shape convolutional network (U-Net) may be the most successful architecture for medical image segmentation to date [29]. Cheng et al. proposed an improved U-Net with refinement residual block and channel attention block for the choroid segmentation [17].

2) Vessel Shadow Elimination in OCT: In 2011, Girard et al. developed an attenuation compensation (AC) algorithm to remove the OCT vessel shadows and enhance the contrast
of optic nerve head [21]. This algorithm was then employed in the calculation of the attenuation coefficients of retinal tissue [30], enhancing the visibility of lamina cribrosa [31], and improving the contrast of the choroid vasculature and the visibility of the sclera-choroid interface [32], [33].

Very recently, Mao et al. analysed the energy profile in each A-line and automatically compensated the pixel intensity of locations underneath the detected blood vessel [22]. However, both of these methods perform well for the removal of small vessel shadows but unable to handle the large vessel shadows, which would lead to shadow residue on the choroid [23].

3) Inpainting/Object Removal: After locating the vessel shadows, we propose to use inpainting techniques, which is also referred as object removal. Here the object to be removed is the vessel shadows. Inpainting techniques have been extensively studied and applied in various computer vision and pattern recognition related fields (see [34], [35] and the references therein). Early inpainting techniques primarily filled the targeted area with information from similar or closest image parts, such as exemplar-based inpainting (EBI) [36], or used higher-order partial differential equations to propagate the information of surrounding areas into the targeted area, such as coherence transport inpainting (CTI) [37].

Deep learning, especially generative adversarial network (GAN) [38], is a powerful tool for image synthesis [39], which has also shown its superiority in image inpainting [40]–[42]. Yeh et al. used a GAN model to search for the closest encoding of the corrupted image in the latent image manifold using context and prior losses, then passed the encoding through the GAN model to infer the missing content [40]. Yu et al. utilized contextual attention on surrounding image features as references during GAN training to make better predictions [41]. Nazeri et al. proposed a two-stage GAN inpainting method, which comprises of an edge generator followed by an image completion network. The edge generator hallucinates edges of the missing region of the image, and the image completion network fills in the missing regions using hallucinated edges as a priori [42].

III. METHODOLOGY

Figure 2 is an illustration of the framework of our method, which primarily includes the choroid segmentation using the proposed Bio-Net, en face projection, and the shadow localization and elimination pipeline. We use the U-Net for shadow location mask generation and the Deshadow-Net for shadow elimination. The Deshadow-Net follows the architecture of the two-stage inpainting GAN in [42]. The choroid layer of a OCT volume is firstly segmented by the Bio-Net. We also can get the RPE layer by moving the upper boundary of the choroid 20 µm upward. Then the OCT volume is projected into the 2D en face plane with the mean value projection along the axial direction, for generating the en face RPE and choroid images. The vessel shadows in the RPE image is segmented with the U-Net to locate their positions. Finally, the shadow location mask in combination with the en face choroid image are inputted into the Deshadow-Net for the shadow elimination.

A. Bio-Net for Choroid Segmentation

As shown in Fig. 3, the Bio-Net is a cascade of biomarker prediction network, global multi-layers segmentation module, and local choroid segmentation module. Firstly, the biomarker prediction network is trained to predict the biomarker, and its parameters are fixed after that. Then, we follow the anatomical hierarchy of the retinal OCT and employ the global multi-layers segmentation module to segment the OCT image into 12 layers. Finally, the global multi-layered result and the original OCT image are concatenated and fed into the local choroid segmentation module to segment the choroid region, where the biomarker information is infused and applied as a regularization.

1) Biomarker Prediction Network: We employ the choroidal thickness as a prior knowledge, which has been found to be related to various ocular diseases as mentioned in the Introduction, to assist the segmentation. The choroidal thickness denotes the average distance between the upper boundary (Brueses membrane, BM) and the lower boundary (CSI). The biomarker prediction network trained a thickness
image structure information of the retinal OCT. We employ the U-Net [29] as the biomarker prediction network outputs a vector $\mathbf{B}_{\text{bio,reg}}$ of the global multi-layers segmentation module, where the biomarker, and the parameters are fixed after that. The biomarker prediction network is trained to predict the biomarker, and its parameters are fixed after that. Then, we follows the anatomical hierarchy of the retinal OCT and employ the global multi-layers segmentation module to segment the OCT image into 12 layers. Finally, the global multi-layered result and the original OCT image are concatenated and fed into the local choroid segmentation module to segment the choroid region, where the biomarker information is infused and applied as a regularization.

**3) Local Choroid Segmentation Module**: The local choroid segmentation module takes the concatenated OCT image and multi-layered result $\mathbf{C}_{\text{input}}$ as input and predict the choroid region $\mathbf{C}_{\text{pred}}$ via another segmentation block $\mathbf{U}_c$. $\mathbf{C}_{\text{pred}} = \mathbf{U}_c(\mathbf{C}_{\text{input}})$. It is trained with $L_{\text{seg,choroid}}$. When $\mathbf{C}_{\text{pred}}$ is feed into the biomarker prediction network, it is compared with $\mathbf{B}_{\text{pred}}$, then another loss termed $L_{\text{bio,choroid}}$ is produced.

$$L_{\text{seg,choroid}} = \frac{1}{N} \sum_{i=0}^{11} |\mathbf{B}_{\text{pred}} \ln(\mathbf{G}_{\text{pred}}) - (1 - \mathbf{B}_{\text{pred}}) \ln(1 - \mathbf{G}_{\text{pred}})|$$

Finally, the Bio-Net is trained by minimizing the total loss.

$$L_{\text{total}} = \lambda_{\text{seg,multi-layers}} L_{\text{seg,multi-layers}} + \lambda_{\text{seg,choroid}} L_{\text{seg,choroid}} + \lambda_{\text{bio,choroid}} L_{\text{bio,choroid}}$$

where $\lambda_{\text{seg,multi-layers}}$, $\lambda_{\text{seg,choroid}}$, $\lambda_{\text{bio,choroid}}$ denote hyper-parameters.

### B. Shadow Elimination Pipeline

Different from the previous shadow elimination methods that could not eliminate the shadows from large vessel [21], [22], we propose a novel method that is able to remove the shadow without the limitation in vessel caliber. It firstly locates the vessel shadows then uses image inpainting techniques to repair the shadow-contaminated areas. As shown in Fig. 4, we segment the retinal vessel shadows from the en face RPE image with the U-Net [29]. The generated shadow mask could be used to locate the shadows in a OCT volume. Then the shadow mask in combination with the en face choroid image are fed into the shadow elimination module, namely the Deshadow-Net, to get a shadow-free choroid image.

#### 1) Shadow Localization: The idea of using RPE to locate the vessel shadows is inspired by two medical and imaging knowledge. (1) The retinal layers below the outer plexiform layer and above the BM are avascular [43], so any vessel-like structure appears on these layers are the projected shadows. (2) As shown in Fig. 5, the RPE layer has the highest OCT light reflectance and best shadow contrast compared with other avascular layers including outer nuclear layer (ONL) and photoreceptor layer (PRL).

To fully locate the shadow mask on the en face choroid, we further enhance the U-Net segmentation results with morphological manipulation including dilation and erosion.
PyTorch library in the Ubuntu 16.04 operating system and shadow elimination performance. Have been used for achieving superior segmentation method. For using it in the scenarios that the OCT systems domain discrepancy caused by manufacturers in the proposed Topcon OCT systems, so we did not consider to remedy the test set, each contains 640 B-scans. B-scan images were randomly divided into a train set and a test set, each contains 640 B-scans.

A. Automatic Choroid Segmentation

2) Shadow Elimination: As demonstrated in Fig. 4 the Deshadow-Net is a cascade of two GANs. Each GAN has a pair of generator and discriminator. The generators follow the architecture in [44] and the discriminators use a 70 x 70 PatchGAN architecture [45]. The inputs of the Deshadow-Net are the shadow-contaminated choroid image and the shadow location mask. Before entering the first GAN, the structure feature of the en face choroid is extracted with the Canny edge detector [46]. The first GAN is employed to generate the structure (edge) information in the shadow mask areas. The second GAN uses the edges of the choroidal vasculature generated in the first GAN as a prior, to fill the texture information of the choroid. Then we could get the shadow-free choroid from the output of the second GAN.

IV. EXPERIMENTS

A. Automatic Choroid Segmentation

1) Dataset: For the training and testing of the BioNet, we use a dataset named AROD with 256 x 20 B-scans [47]. Each B-scan has 512 A-lines with 992 pixels in each A-scan. Since the B-scans in the same volume have high similarity, Cheng et al. [48] annotates the boundary information for 1/4 of the B-scans, thus 256/4 x 20 = 1280 B-scans are used. The 1280 B-scan images were randomly divided into a train set and a test set, each contains 640 B-scans.

Note that the data throughout this paper was collected from Topcon OCT systems, so we did not consider to remedy the domain discrepancy caused by manufacturers in the proposed method. For using it in the scenarios that the OCT systems are from different manufacturers, domain adaptation methods [49], [50] have been used for achieving superior segmentation and shadow elimination performance.

2) Implementation: Our Bio-Net is implemented by using PyTorch library [51] in the Ubuntu 16.04 operating system and the training was performed with NVIDIA GeForce GTX 1080 Ti GPU. We first train the Biomarker Prediction Net to predict the thickness of the B-scan choroid. The backbone is a ResNet18 [52] and it is trained with Adam optimizer with the learning rate of 0.01 and a batch size of 8. The parameters are fixed after that. Then we train the rest of the Bio-Net end-to-end. We utilize flipping and rotation to augment the data. The batch size is 4 and the optimizer is Adam [53]. The initial value of the learning rate is 0.01, and then the learning rate is reduced to 1/10 of the original when the number of iterations is 40, 80, 160, and 240, respectively. We set the hyper-parameter \( \lambda_{\text{seg, multi-layers}} = 1 \), \( \lambda_{\text{seg, choroid}} = 1 \), \( \lambda_{\text{bio, choroid}} = 0 \). It took about 4 hours for each training of the Bio-Net.

3) Evaluation Metrics: We employ dice index (DI), intersection-over-union (IOU), average-unsigned-surface-detection-error (AUSDE), accuracy (Acc), and sensitivity (Sen) to quantitatively evaluate the performance of the Bio-Net. The DI and IOU show the proportion of the overlap between the segmented choroid region and the ground truth (larger is better). The AUSDE [54] represents the pixel-wise mismatch between the segmented choroid boundary and the ground truth (smaller is better). Acc and Sen represent the accuracy and sensitivity of the segmentation compared with the ground truth (larger is better).

4) Results: We compare the BioNet with the existing choroid segmentation methods based on graph search and deep learning. The graph search method use the open source algorithm in [55] and its Matlab implementation [56]. The deep learning methods include the U-Net [29], which is the backbone of our Bio-Net, and the improved U-Net in [17].

Figure 6 shows the visual examples of the choroid segmentation. From left to right are the input OCT B-scans, ground truth, and the segmentation results using the graph search, U-Net, improved U-Net, and our Bio-Net, respectively. As demonstrated in the figure, all of the methods have better performance in the segmentation of the upper choroid bound (the BM) then the lower boundary (the CSI), which may be attributed to the clearer BM in this side. The deep learning methods generally perform better in the CSI segmentation than the graph search. But the U-Net and improved U-Net have local segmentation errors and
discontinuity in both the BM and CSI. The performance degradation in the BM segmentation may suggest the graph search method has better robustness and generalization capacity. On the other hand, because of adding the biomarker knowledge constraint, the proposed method has better consistency in the segmentation of both the CSI and BM and is very close to the ground truth.

Their quantitative comparison is listed in Table I. The performance of deep learning methods is better than the graph search method with the IOU increased by nearly 40%, AUSDE decreased by over 40 pixels, DI increased by nearly 30%, and Sen increased by over 40%. Our Bio-Net outperforms other methods listed in the table with 90.77% DI, 83.10% IOU, 6.23 pixels AUSDE, and 97.14% Acc, which may suggest the infusion of the biomarker prior and the global-to-local strategy contribute to the improvement of the segmentation. We further analyse the quantitative contribution of each innovation in the Discussion Section below.

B. Shadow Localization and Elimination

1) Dataset: We employ 30 OCT volumes for the training and testing of the shadow localization and elimination pipeline. Each volume has $992 \times 512 \times 256$ voxels. They cover a field of view (FOV) of $6 \times 6$ mm$^2$ region and a imaging depth of around 2 mm. We randomly divided these volumes into 25 testing sets and 5 evaluation sets. The choroid and RPE layers of these volumes were segmented with the Bio-Net. Then the en face RPE images were manually annotated by two medical experts with pixel-level precision.

2) Implementation: The shadow localization and elimination pipeline is also implemented using the PyTorch library. For training the U-Net in the shadow localization, we employ the Adam optimizer for training. The initial learning rate is set to 0.0001. Then we gradually decrease the learning rate with a momentum of 0.9. We further enhance the segmentation result of the U-Net with six iterations of dilation and erosion.

For the shadow elimination, the Deshadow-Net is pre-trained with the neutral scene datasets in then fine-tuned with our choroid datasets. The training of the model is divided into three stages: the edge model, the inpainting model, and the joint model, as suggested in the original implementation.

3) Evaluation Metrics: We employ the IOU, Acc, Sen and area under the curve (AUC) to evaluate the segmentation performance of the U-Net. Because no ground truth is available for the shadow elimination task, we employ the vessel density (VD) in the evaluation, which is an indirect but clinically useful metrics. We follow the calculation of the VD in as

$$VD = \frac{\int_A V \, dA}{\int_A dA},$$

(6)

Where $A$ is the region of interest (ROI). Here it refers to the $6 \times 6$ mm$^2$ centered on fovea. $V$ is the binarized vessel
map. For an arbitrary pixel, if it belongs to a vessel, $V = 1$, otherwise $V = 0$.

4) Results: Figure 7 demonstrates an example of using the U-Net in the segmentation of the retinal vessel shadows on the RPE image. The U-Net output is further processed to retrieve the shadow mask using dilation and erosion. The U-Net achieves superior performance on the vessel shadow segmentation with an Acc of 0.969, an AUC of 0.938, an IoU of 0.901, and a Sen of 0.967. After the dilation and erosion, the vessel caliber is around 5 pixels wider than that of the original shadow, which makes sure the shadow could be completely removed by the Deshadow-Net.

Ronneberger et al. have demonstrated the U-Net was capable of achieving excellent segmentation performance with tens of training samples [29]. Here we found the U-Net could be efficient with less training samples. Figure 8 demonstrates the AUC and Acc values as functions of the number of training samples for the RPE shadow segmentation. As shown in the figure, the AUC and Acc values are close to 0.9 with a single training sample. The two metrics trend to be stable when the number of training images is larger than 5, which might be related to the high uniformity of the morphological patterns of the RPE vessel shadows among different OCT volumes.

We compare the proposed shadow elimination pipeline with the A-line based AC algorithm [21] and our previous implementation of this shadow localization and elimination pipeline, which used the CTI as the inpainting algorithm [23]. Figure 9 demonstrates the visual examples of the shadow elimination. From left to right: the original en face choroid image, the shadow mask, and the shadow elimination results using different methods. The second and third rows are the zoom-in views inside the blue and yellow boxes in the first row, respectively. The last row are the corresponding vessel maps.

As shown in the figure, the original choroidal vasculature is conterminated by the retinal vessel shadows at the locations shown in the shadow mask. Inside the zoom-in views, the AC could enhance the contrast of the choroidal vessels and minimize small vessel shadows but could not get rid of the large vessel. Using the localization and elimination strategy, both the large and small vessel shadows could be thoroughly eliminated, but as shown in the zoom-in views, the CTI introduces unnatural artefacts compared with the proposed method.

The vessel shadows could be treated as the real vessels in clinical assessment, which would cause the overestimation of the VD. The calculated VD values of the vessel maps in the last row of Fig. 9 are: 0.510 for the original choroid, 0.504 for the AC, 0.501 for the CTI, and 0.500 for the proposed method. We also calculate a VD of 0.499 without including the shadow areas. The results are in accordance with the overestimation assumption, in which the original image has the highest VD. The AC method could eliminate part of the shadows thus lower the VD. The CTI and proposed method could further lower the VD because they remove the shadows completely. Besides, their VDs are very close to that of the masked vessel map, which indicate the effectiveness of this shadow localization and elimination pipeline. We checked the VDs of other testing datasets, which follow the exactly same trend. However, because the variation of the VDs among different eyes are much larger than that of the shadow elimination, we did not include their average values and standard deviations here.

C. Application in a Clinical Prospective Study

Primary angle-closure glaucoma (PACG) is prevailing not only in East Asia but also in overseas Chinese and Eskimos [57]. The patients with PACG were found to have higher IOP and thicker choroids than normal controls [58]. Previous studies showed the changes of the choroid thickness and blood flow might be associated with the PACG [6], but the
initial mechanism underlying angle closure has not been fully understood. Here we applied the proposed method in a clinical prospective study, which quantitatively detected the changes of the choroid in response to IOP elevation [20].

1) Data Collection: We recruited 34 healthy volunteers with the ages ranging from 18 to 30 years old, with no
previous history of IOP exceeding 21 mm Hg. The participants were volunteers recruited mainly from the Zhongshan Ophthalmic Center at Sun Yat-sen University Medical School, and nearby communities in Guangzhou, China. The study was approved by the Ethical Review Committee of the Zhongshan Ophthalmic Center and was conducted in accordance with the Declaration of Helsinki for research involving human subjects.

A swept-source OCT system with the A-line rate of 100 kHz (DRI OCT-1 Atlantis, Topcon, Japan) was employed to collect data from both of their eyes. We used the $6 \times 6 \text{mm}^2$ FOV volumetric scan protocol centered on fovea. Each of the volumes contains 256 B-scans and each of the B-scans has 512 A-lines. Each A-line contains 992 data points uniformly distributed in a depth range of $\sim 3$ mm.

To simulate the state of high IOP, after taking the baseline scans in a normal sitting position, each of the volunteers was asked to take scans in upside-down position. The average IOP was increased to $34.48 \pm 5.35$ mm Hg because of the upside-down, compared with the average IOP of $15.84 \pm 1.99$ mm Hg at the normal position. A total of 136 OCT volumes were acquired (34 volunteers, 68 eyes, normal and high IOP).

2) Results: With the proposed knowledge infused deep learning method, we processed this clinical dataset to retrieve the thickness of the choroid and the VD in normal and upside-down states. The choroid thickness is the average value of the $6 \times 6 \text{mm}^2$ FOV. We summarize their statical averages and standard deviations in Table II.

| IOP (mm Hg) | CT ($\mu$m) | VD |
|-------------|-------------|----|
| Normal      | $15.84 \pm 1.99$ | $226.39 \pm 52.44$ | $0.511 \pm 0.171$ |
| Upside-Down | $34.48 \pm 5.35$ | $238.34 \pm 54.84$ | $0.488 \pm 0.164$ |

* CT: choroid thickness.

shallowing of the anterior chamber, which may be of relevance for the pathogenesis of the PACG.

Figure 10 demonstrates the vessel maps of 5 study cases from the clinical dataset in normal (top) and high IOP states (bottom). In OCT imaging, the change on the vessel map is related to the change in blood flow. On these vessel maps, we could observe the reduction in blood flow in the high IOP state.

V. DISCUSSIONS

We further analyse and discuss the details of the proposed method in this section, including the ablation study of the Bio-Net and the comparison of different inpainting methods.

A. Ablation Study of Bio-Net

To evaluate the effectiveness of the global multi-layers segmentation module and the biomarker prediction Net, we combine them with the U-Net respectively.

Table III and Fig. 11 illustrate the effectiveness of the biomarker prediction network and the global multi-layers segmentation module. In the experiment, we take the U-Net as a baseline, the table demonstrates that the infusion of the biomarker prediction network can lead to an improvement on the choroid segmentation task, as the DI increases from

![Fig. 11. Ablation study of the Bio-Net. From left to right: the input OCT B-scans, ground truth, the segmentation results using the global multi-layers segmentation module (GMS), the U-Net baseline (base) and the GMS, the baseline and the biomarker constraint (Bio), and our Bio-Net, respectively.](image-url)
and elimination pipeline. The widely-used image similarity measures are not directly implemented. Thus we created artificial retinal imagings, which quantitatively detected the changes of the choroid in response to IOP elevation. The results show it is able to detect the structure and vascular changes of the choroid efficiently.

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TABLE IV

|               | Masked | EBI [36] | CTI [37] | GAN [42] |
|---------------|--------|----------|----------|----------|
| SSIM          | 0.778 ± 0.085 | 0.901 ± 0.043 | 0.931 ± 0.015 | 0.946 ± 0.013 |
| PSNR          | 11.851 ± 2.605 | 25.988 ± 3.117 | 29.352 ± 3.712 | 30.615 ± 3.824 |
| MSE (×10^3)   | 3.464 ± 1.895 | 0.165 ± 0.092 | 0.109 ± 0.082 | 0.091 ± 0.071 |

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