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Title: Optical coherence tomography for coronary artery disease: analysis and applications
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Abstract — Intravascular optical coherence tomography (IVOCT) is a novel technique, which is used to analyze the underlying cause of cardiovascular disease. Because a catheter is used during imaging, the intensities can be affected by the catheter position. This work aims to analyze the effect of the catheter position on IVOCT image intensities and propose a compensation method to minimize this effect in order to improve the visualization and the automatic analysis of IVOCT images. In this paper, the effect of catheter position is modeled with respect to the distance between the catheter and the arterial wall (distance-dependent factor) and the incident angle onto the arterial wall (angle-dependent factor). A light transmission model incorporating both factors is introduced. On basis of this model, the interaction effect of both factors is estimated with a hierarchical multi-variant linear regression model. Statistical analysis shows that IVOCT intensities are significantly affected by both factors with $p < 0.001$, as either aspect increases the intensity tends to decrease. This effect differs for different pullbacks. The regression results were used to compensate for this effect. Experiments show that the proposed method can improve the performance of the detection of the bioresobable vascular scaffold struts.
2.1 Introduction

Cardiovascular disease (CVD) is a major cause of death worldwide [31]. One of the underlying processes that cause CVD is atherosclerosis, which is the long-term accumulation of plaque in the vessel wall. The extent and composition of atherosclerosis can be visualized in-vivo with intravascular optical coherence tomography (IVOCT) at a higher resolution of 10 to 20 µm [8, 32, 33] compared to other in-vivo imaging modalities, such as Intravascular Ultrasound (IVUS), Computed Tomography Angiography (CTA) or Magnetic Resonance Imaging (MRI).

IVOCT is an optical imaging modality using near-infrared (NIR) light as the imaging source. The images are acquired using a catheter which is inserted into the coronary artery. Images of arterial cross-sections are reconstructed from the echo time delay and the intensity of back-scattered light. Due to the high scattering of NIR light in blood caused by red blood cells, the artery is flushed with saline or a contrast medium to clear the blood inside the artery. The image intensity is assumed to be only tissue dependent, thus different types of tissue appear different [8].

In practice, however the signal magnitude may not only be dependent on the tissue type, but also on the position of the catheter with respect to the vessel wall, which causes non-tissue-related effects on the IVOCT image intensities [34, 35]. An example is given in Fig. 2.1. The average intensities are calculated within the thin superficial uniform layer of the IVOCT image of a non-pathological artery segment. Nevertheless, there is a clear variation in the profile of the average intensities (Fig. 2.1 b).

The importance of analyzing the effect on intensities caused by the position of the catheter has been well depicted in the field of IVUS. Courtney et al. showed that the IVUS image intensities are strongly related to the catheter position [36]. Their study concluded that when the distance or the angle towards the luminal wall increases, the intensity will decrease for both intima-media tissue and adventitia tissue. Earlier work [37, 38, 39] shows that the reflected ultrasound signal is critically dependent on the angle of incidence and varies for different types of arterial plaques.

In the literature of IVOCT image analysis, statistical values of the intensities are commonly used as key features for both automated detection algorithms and the quantitative studies. For example, mean intensity has been applied as one of the textural features for automated tissue characterization [40]. A recent stent strut detection algorithm has been proposed to train a supervised artificial neural network classifier with statistical features including the maximum, mean, median intensities, etc [41]. Furthermore, the percentiles values of the distribution are often used as thresholds. For example, the 5th percentile has been used as the threshold for noise removal [42, 43, 44, 45]. More percentiles were used as cutoff values to determine the trailing shadow [46, 44] for metal strut detection, and the black core regions [47] for the detection of the bioresorbable vascular scaffold (BVS) strut. With the assistance of the BVS strut detection, median values and peak values within the black core
2.1 Introduction

Figure 2.1: (a): An IVOCT image of a non-pathological artery wall: the artery has a regular and almost circular shape; three arterial layers, intima (I), media (M) and adventitia (A), are clearly visible (as shown in zoomed-in top-left corner). (b): Polar representation of the image in (a) sampled clockwise along radial A-lines from the catheter center shown as a bright line on the top of the image. For each A-scan, the average intensity within a superficial thin layer ($\approx 50\mu m$) is calculated and shown as the green profile. The white curve is the smoothed green profile.

region were quantitatively analyzed to track the variation of the BVS struts in post stenting and follow up IVOCT images at 6, 12, 24 and 36 month respectively.

However, effected by the catheter position, the distributions of the intensities can appear different, which may increase the variation of those statistical numbers. The amount of the variation cause by the catheter position depends on the extent of its eccentricity. Further quantitative analysis of this effect can be helpful to develop a algorithm to compensated for it. To the best of our knowledge, only one study with respect to the effect of light incident position on OCT image intensities has been reported about that a non-perpendicular incident light cause a significant variance in the measurement of the articular cartilage [35]. In the followup studies of the bioresorption progress of the BVS strut, the bias in light intensity caused by the eccentric catheter was claimed to be minimized with normalization, yet involve more manual input and time consuming. On the other hand, results from IVUS cannot be applied directly to IVOCT, due to the differences in physical properties between both modalities.

The aim of this work is to analyze the effect of the catheter position, with regards to both the distance to the vessel wall and the incident angle of light, on IVOCT image intensities. Based on this analysis a compensation algorithm is proposed to reduce this effect. As an application of compensated images, images
with foam cells have been enhanced and compared with histological slides. Furthermore, the compensation algorithm is used in combination with an existing BVS detection algorithm.

The general structure of the paper is as follows. In 2.2.1, a light transmission model incorporating both distance-dependent and angle-dependent factors is introduced. In 2.2.2, a hierarchical multi-variant linear regression model is proposed to further investigate the relationship and estimate the both factors. The regression result is further used in 2.2.3 to propose a method to compensate images. Results are presented in Section 2.3. The compensated images were inspected comparing to the pathological images in 2.4.1. Furthermore, a BVS struts detection experiment with the compensated images was carried out in 2.4.2. All the experiments and results are discussed in Section 2.5 with limitations and the future works given as well. Conclusions are drawn in Section 2.6.

2.2 Materials and Methodology

Images of non-pathological segments from 9 IVOCT pullbacks recorded with a C7XR swept-source OCT system and a C7 Dragonfly Imaging Catheter (St. Jude Medical, Minnesota, USA) were used. The technical details are listed in Table 2.1 and Table 2.2.

Table 2.1: Technical details of the IVOCT system

<table>
<thead>
<tr>
<th>swept laser source</th>
<th>center wavelength</th>
<th>1310 nm</th>
<th>wavelength range</th>
<th>110 nm</th>
<th>sweep rate</th>
<th>50 kHz</th>
<th>output power</th>
<th>20 mW</th>
</tr>
</thead>
<tbody>
<tr>
<td>pullback frames</td>
<td>pullback speed</td>
<td>20 mm/s</td>
<td>pullback length</td>
<td>54 mm</td>
<td>image frames</td>
<td>271</td>
<td>frame rate</td>
<td>0.2 mm</td>
</tr>
</tbody>
</table>

Table 2.2: Number of selected frames in each pullback

<table>
<thead>
<tr>
<th>Pullback No.</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Frames</td>
<td>28</td>
<td>17</td>
<td>33</td>
<td>21</td>
<td>5</td>
<td>13</td>
<td>14</td>
<td>29</td>
<td>9</td>
<td>169</td>
</tr>
</tbody>
</table>

2.2.1 Distance and Incident Angle Extended Light Transmission Model

A schematic overview of light propagation for IVOCT imaging is shown in Fig. 2.2. The lights emitted from the catheter first travels through the flush medium before reaching the arterial wall with a distance denoted as \( x \). At the interface between the flush medium and the arterial wall, both reflection and refraction occur. \( \theta \) represents the incident angle of the light entering the arterial wall. \( \Delta x \) represents the light transmitting distance of the refracted
light beam inside the arterial tissue. For the convenience of explanation, we introduce $x = x_t + \Delta x$.

Figure 2.2: Light transmission. $x_t$ denotes the distance between the light source and the arterial wall, $\Delta x$ denotes the distance between the arterial wall and the detected position inside the arterial tissue, and $\theta$ is the incident angle of the light beam.

### 2.2.1.1 Light Transmission Model

As the light propagates inside the arterial wall, the intensity of an OCT signal is typically modeled as the first order scattering function of $x$ and $\Delta x$ as [48]:

$$I_b(x) \cong \frac{1}{2} I_{in} \mu_b T(x) \cdot e^{-2\mu_t \Delta x}, \quad (2.1)$$

where $I_{in}$ denotes the light intensity upon entering the arterial wall. $I_b(x)$ denotes the back-scattered light intensity from the distance $x$. $\mu_b$ represents the back-scattering coefficient, and $\mu_t$ is the total attenuation coefficient (summation of scatter and absorption). $T(x)$ is the confocal function which is defined as [28]:

$$T(x) = \left[ \left( \frac{x - z_0}{z_R} \right)^2 + 1 \right]^{-1}. \quad (2.2)$$

where $z_0$ and $z_R$ are the beam waist and the Rayleigh length, respectively.

The intensity entering the luminal wall is affected by two factors: the attenuation in the flush medium region (FMR), and the reflection and refraction at the interface of flush medium and the arterial wall. In a well-flushed artery, the FMR region can be regarded as homogeneous, non-scattering and weakly attenuating, obeying the Lambert-Beer law [49]. With a constant attenuation, $\mu_f$, the light decay is determined by the distance from the catheter to the lumen wall, $x_t$. 
The interaction of the light is more complex at the interface between FMR and the lumen tissue due to the relative irregular surface of the arterial wall. To analyze the effect of the incident angle on image intensities, the total effect of the incident angle is normalized into 0 to 1 by using a term similar to the Fresnel transmission ratio. Thus $I_{in}$ is modeled as:

$$I_{in} \sim I_0 \cdot Tr(\theta, n_i, n_t)\beta_2 \cdot e^{-\mu f x_t}.$$  

(2.3)

where $\beta_2$ is the parameter to be estimated. $Tr(\theta, n_i, n_t)$ is the Fresnel like function which is calculated with the incident angle $\theta$, index of refraction of the incident medium $n_i$ and transmission medium $n_t$, respectively [49]. With Eq. 2.3 substituted in Eq. 2.1 and taking the logarithm from both sides results in:

$$\ln I_b(x) \cong -\mu f x_t + \beta \ln Tr(\theta, n_i, n_t) + \ln T(x_t + \Delta x) - 2\mu f \Delta x + C(I_0, \mu_b).$$

(2.4)

where $C(I_0, \mu_b) \cong \ln(I_0 \cdot \mu_b)$ is a constant term.

### 2.2.2 Parameter estimation of the linear model with Hierarchical linear regression

#### 2.2.2.1 Hierarchical linear regression

Hierarchical linear models are specifically utilized for data with hierarchical structures [50]. Here, a hierarchical linear model is designed to analyze the potential relationship between OCT image intensities and three factors; distance: ($x$), angle: $\ln Tr(\theta, n_i, n_t)$ and the constant term $C(I_0, \mu_b)$. The linear model for regression is:

$$\ln I_b(x) = \beta_0 + \beta_1 \cdot x + \beta_2 \cdot \ln Tr(\theta, n_i, n_t).$$

(2.5)

In order to keep the consistency of the notations, the parameters were denoted as $\beta_0$, $\beta_1$ and $\beta_2$. The A-lines can be hierarchized into different frames, which in turn can be hierarchized into different pullbacks. Based on this observation, a three-level linear model is considered for this study (see Fig. 2.3).

![Figure 2.3: Multi-level linear model](image)
2.2.2 Implementation

The lumen border in the Cartesian images was used to estimate the incident angle. To compensate for the polar to Cartesian transformation, the lumen border points were resampled with respect to the depth. The angle was calculated in a window of 9 points.

The index of refraction of the flush solution is 1.449 mm (read from the stored data). The refraction index of intima is about 1.358 mm \cite{51}. Therefore the incident angle is the only variable during the calculation of the transmission ratio for each point.

Intensities of only a thin inner layer of the arterial wall are used for the statistical analysis, then $\Delta x \approx 0$, and thus $x = x_t + \Delta x \approx x_t$. The general trend of the signal regards to the distance $x_t$ is decreasing due to both the attenuation of the flush medium and the confocal function. Approximating this term as linear, the object model for hierarchical linear regression can be written as:

$$\ln I_b(x) = C(I_0, \mu_b) + \beta_1 \cdot x_t + \beta_2 \ln Tr(\theta). \quad (2.6)$$

This can be equalized to the hierarchical linear regression model if we denote $\beta_0 = C(I_0, \mu_b)$, thus the linear regression can be used to investigate the linear relationship regarding the distance and the incident angle.

2.2.3 Compensation

The linear model which describes the effect of the catheter position can also be used for the compensation of this effect.

Based on the linear regression model, the primary goal for the compensation is to normalize the IVOCT image intensities within the superficial layer of the non-pathological artery. This can be achieved with the following equation involving the regression result:

$$I_{\text{compensated}}(y) = \frac{I_{\text{original}}(y) \cdot e^{\beta_0}}{I_b(x)}. \quad (2.7)$$

As defined, $I_{\text{original}}(y)$ and $I_{\text{compensated}}(y)$ denote the original and the compensated IVOCT signals at the depth $y$. $\beta_0$ is the estimated constant term in the regression model. With a thin layer with thickness $\Delta x$ selected, $I_b(x)$ is the average intensity within the superficial thin layer:

$$I_b(x) = \int_{y=x_t}^{x_t+\Delta x} I_{\text{original}}(y) / \Delta x. \quad (2.8)$$

Noting the following mathematical equation holds,

$$I_b(x) \sim \beta_1 \cdot \int_x^\infty I_b(t) \, dt, \quad (2.9)$$
where $\hat{\beta}_1$ is the estimated parameter. The intensities can be normalized as follows:

$$I_{\text{compensated}}(y) = \frac{I_{\text{original}}(y) \cdot e^{\hat{\beta}_0}}{\hat{\beta}_1 \cdot \int_{x}^{\infty} I_b(t) \, dt} \approx \frac{I_{\text{original}}(y) \cdot e^{\hat{\beta}_0}}{\hat{\beta}_1 \cdot \sum_{x}^{M} I_b(t)}.$$  \tag{2.10}

Here $M$ is a large depth selected far enough away from the lumen border. Noting that:

$$\sum_{y=x}^{M} I_{\text{compensated}} = \frac{e^{\hat{\beta}_0}}{\hat{\beta}_1} = \text{constant},$$  \tag{2.11}

the principle of this compensation method is to normalize the summation of intensities behind the lumen border. Since arterial tissues are strong scattering and weak absorbing, the summation of the IVOCT intensities should be approximately constant (linearly related to the total emitting energy from the catheter) for most arterial tissue types, thus this method is not limited to only compensate the IVOCT images of non-pathological arteries.

### 2.3 Results

#### 2.3.1 Hierarchical linear regression

The hierarchical linear regression considers three fixed effects and two random effects. The F-tests result for each of the fixed effects specified in the model indicate that all three effects contribute to the model statistically significantly with $p < 0.001$.

Table 2.3: Estimates of Fixed Effects$^a$

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate</th>
<th>Std.Error</th>
<th>df</th>
<th>t</th>
<th>Sig.</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lower Bound</td>
</tr>
<tr>
<td>$\beta_0$</td>
<td>6.512</td>
<td>0.162</td>
<td>8.013</td>
<td>40.318</td>
<td>0.000</td>
<td>6.140</td>
</tr>
<tr>
<td>$\beta_1$</td>
<td>$-0.00227$</td>
<td>0.000</td>
<td>79838</td>
<td>$-279.2$</td>
<td>0.000</td>
<td>$-0.00229$</td>
</tr>
<tr>
<td>$\beta_2$</td>
<td>2.818</td>
<td>0.073</td>
<td>80041</td>
<td>38.848</td>
<td>0.000</td>
<td>2.676</td>
</tr>
</tbody>
</table>

$^a$ Dependent Variable: Natural logarithm of Intensities.

Table 2.3 shows the results of the fixed model. It was found that the constant related to light source ($\beta_0 = 6.5121, SE = 0.1615, p < 0.001$), the distance between catheter and artery wall ($\beta_1 = -0.0023, SE = 0.0000, p < 0.001$) and the logarithm of 'Fresnel' transmission ratio ($\beta_2 = 2.8178, SE = 0.0725, p < 0.001$) – all were significant predictors.

Table 2.4 shows the results for the two random factors and residual covariance matrices. Results indicate that both of the defined random effects - the frame number ($N_a = 0.0060, SE = 0.0007, p < 0.001$) and pull-back number ($N_a = 0.2542, SE = 0.1173, p < 0.05$) – contribute to the covariance statistically.
2.3 Results

Figure 2.4: A and C are the images before compensation and on the right side B and D are the compensated images. The image in A is a clear example of the effects caused by the eccentric position of the catheter, the compensated image B shows more evenly distributed intensities around the artery wall. In the second example C, the light intensities are more or less homogeneous but there is information missing at 1 o'clock. After compensation, the shadow region is removed (D).

significantly with almost two thirds of the total variance. However, the influence of the frame number is relatively very small (∼1.6%) compared to the other contributors. Based on this observation, this random effect can be ignored during modeling.

The histogram of the residual (Epsilon = 0.1276, SE = 0.0006, p < 0.0001) is distributed symmetrically around zero with a mean value of -2.01E-11 and a standard deviation of 0.3568, thus indicating the model can fit the data well.

2.3.2 Compensation

With the results of the linear regression, images can be compensated using Eq 2.10 proposed in Section 2.2.3. Figure 2.4 demonstrates the compensation of IVOCT images of non-pathological arteries. The non-uniform image intensities behind the lumen border and even a small shadow artifact on the lumen wall were compensated. The non-uniform image intensities and even a small
Analysis on Position of Catheter

Table 2.4: Baseline patient characteristics (n = 30)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate</th>
<th>Std.</th>
<th>Wald Z</th>
<th>Stg.</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lower Bound</td>
</tr>
<tr>
<td>Residual</td>
<td>0.128</td>
<td>0.001</td>
<td>199.864</td>
<td>0.000</td>
<td>0.126</td>
</tr>
<tr>
<td>Intercept[Frame] Variance</td>
<td>0.006</td>
<td>0.001</td>
<td>8.541</td>
<td>0.000</td>
<td>0.005</td>
</tr>
<tr>
<td>Intercept[Pull-back] Variance</td>
<td>0.234</td>
<td>0.117</td>
<td>1.997</td>
<td>0.046</td>
<td>0.088</td>
</tr>
</tbody>
</table>

a. Dependent Variable: Natural logarithm of Intensities.

unusual shadow on the lumen wall were compensated.

2.4 Application of the compensated images

2.4.1 Pathological images with foam cells

The performance of compensated algorithm is compared with histological cross sections. Selected frames from two ex-vivo OCT pullbacks on explanted hearts [52] were used. OCT imaging was performed with the Ilumien PCI Optimisation system and a C7 Dragonfly Imaging Catheter of LightLab Imaging, St. Jude Medical, Minnesota, USA. The proximal 5 cm of the vessels were cut out and standard paraffin embedding was performed. For every 200 \( \mu m \), 3 \( \mu m \)-thick sections were cut and stained with haematoxylin-eosin. These slices were annotated by a pathologist and matched with the corresponding OCT frames based on anatomical landmarks.

Two examples with bright spots are given in Fig. 2.5. In Fig 2.5 A-C, the image intensities marked with red arrows were darkened due to the residual of blood within lumen. In the compensated image, the darkened regions were compensated and the edges between the calcified region and the fibrous region are more clear. In Fig 2.5 E-F, the image regions near side branches were darkened due to the eccentric catheter position. The foam cells, marked with the red arrows, are more accentuated in the compensated image than in the original image.

2.4.2 BVS strut detection

In order to examine the performance of the compensation algorithm for automated image segmentation, it is tested combining with the BVS detection proposed by Wang et al [47]. For this purpose, 8 post-stenting follow-up pullbacks were used which were acquired with a C7-XR imaging system and C7 imaging catheter (St. Jude Medical Inc., St. Paul, MN, USA) at 6-12 months. All the stent struts are the ABSORB 1.1 BVS (Abbott Vascular, Santa Clara, CA, USA). The ground truth (GT) data contains 7933 black cores in total.
2.5 Discussions

The aim of this work is to investigate the influence of the position of the catheter on IVOCT intensities and to use this knowledge to compensate for it. Two aspects of the catheter’s position were analyzed, the distance between the catheter and

For a impartial comparison, the compensated pullbacks were rescaled linearly by aligning the 99.5 percentile value of the histogram to that of the original pullbacks, thus the same parameters can be applied. The results were evaluated by counting the true positive (TP), the false positive (FP), false negative (FN), and the F-score was calculated as the measurement of the detecting performance [53].

With the described data and experimental settings, the compensated images were used for automatic BVS strut detection. The detection results can be seen in Table 2.5 where the outperformed F-score is marked with bold font. An example of improved BVS detection image can be seen in Fig 2.6.

Figure 2.5: Demonstration of the effect of compensation. From right to left are histology images, original IVOCT images and compensated images. In the histology images, red arrow indicates the location with form cells, and stars mark the calcified lesions as landmarks. The original and the compensated images are displayed at the same contrast and brightness level, and the red arrows mark noticeable regions for comparison.
Table 2.5: The stent struts detection results

<table>
<thead>
<tr>
<th>Data set</th>
<th>No. of GT</th>
<th>Original Pullback (%)</th>
<th>Compensated Pullback (%)</th>
<th>F-score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>TP</td>
<td>FP</td>
<td>FN</td>
</tr>
<tr>
<td>1</td>
<td>776</td>
<td>86.5</td>
<td>21.4</td>
<td>13.5</td>
</tr>
<tr>
<td>2</td>
<td>891</td>
<td>94.2</td>
<td>8.5</td>
<td>5.8</td>
</tr>
<tr>
<td>3</td>
<td>1158</td>
<td>82.6</td>
<td>2.7</td>
<td>17.4</td>
</tr>
<tr>
<td>4</td>
<td>910</td>
<td>78.2</td>
<td>1.4</td>
<td>21.8</td>
</tr>
<tr>
<td>5</td>
<td>1389</td>
<td>91.9</td>
<td>8.9</td>
<td>8.1</td>
</tr>
<tr>
<td>6</td>
<td>847</td>
<td>85.0</td>
<td>22.8</td>
<td>15.0</td>
</tr>
<tr>
<td>7</td>
<td>1059</td>
<td>81.7</td>
<td>17.2</td>
<td>3.6</td>
</tr>
<tr>
<td>8</td>
<td>903</td>
<td>96.6</td>
<td>4.3</td>
<td>3.4</td>
</tr>
<tr>
<td>Total</td>
<td>7933</td>
<td>87.2</td>
<td>10.4</td>
<td>10.9</td>
</tr>
</tbody>
</table>

GT: ground truth; TP: true positive; FP: false positive; FN: false negative

\[ F\text{-score} = \frac{2TP}{2TP+(FN+FP)} \]

the arterial wall, and the angle of incidence of the light penetrating the arterial wall.

2.5.1 Hierarchical linear regression

The statistic analysis focuses on intima-media regions on the artery wall, thus the tissue-dependent effects were minimized in the study. Similar region selection criteria have been used by Courtney on IVUS images [36]. The statistical results show that the amount of light that enters the artery wall is significantly related to the catheter position. In the linear model, an angle related transmission ratio has been used to model the trend. The trend of this transmission ratio is conforming to empirical observations.

As the angle of incidence increases, the IVOCT intensities decrease accordingly. The more the angle of incidence approaches to a critical angle, the faster the IVOCT intensities decrease. When the angle of incidence approaches this critical angle, light propagation into the tissue in the artery wall is limited. This can explain the ‘signal dropout’ reported by van Soest et al [34]. When the incident angle becomes equal or even larger than the critical angle, there is no light entering the artery wall, and thus the transmission ratio will be zero. This results in the appearance of disconnecting tissue along the arterial wall, which has been reported as dissection artifacts in an IVUS study by Mario et al [39].

As random variables, the pullback number and frame number contribute to the hierarchical linear model significantly in terms of covariance. The covariance contribution of frame number is relatively small enough to be ignored. The covariance of the pullback number occupies almost two thirds of the total covariance. Since the same flush medium was used, this suggests that the distance-dependency can differ between IVOCT imaging catheters. This confirms the statement of van Soest et al., that the parameters of catheters differ from each other [28].
2.5 Discussions

Figure 2.6: An example of image with improved BVS detection. **A.** The cross section with ground truth BVS delineated with cyan color. **B.** Detection results with the original image delineated with white color. **D.** Detection results with the compensated image delineated with white color. Within each black core of the ground truth, the percentile of both original and compensated image can be seen in **C.**

2.5.2 Compensation

The compensation of the intensities in the OCT images can enhance the visualization of arterial tissues in IVOCT images. An eccentric position of the catheter or the residual blood inside the lumen can result in inhomogeneous intensity in homogeneous tissue, which requires the contrast and brightness levels to be constantly adjusted during visual inspection. Our proposed compensation algorithm improves the visualization by balancing the signal levels within each pullback, which can be seen in both in-vivo (Fig. 2.4) and ex-vivo images (Fig. 2.5).

Noting in Fig. 2.5 C and D, a shadow artifacts caused by the residual blood in the protective sheath were compensated as well. This is because our compensation algorithm compensates the total energy behind the lumen border for each A-line. The shadow artifacts caused by factors within the lumen, eg. residual blood, thromobosis etc., may cause a sudden drop of the total energy comparing to A-lines in the neighborhood. Therefore, normalizing the total energy can compensate such local shadow artifacts as well. The principle of the
algorithm is that for each pixel at the lumen boundary, the same amount of light enters the tissue, such that further analysis can be carried out without the bias caused by the catheter position. It is designed to overall enhance the absolute intensities for each A-line rather than changing the relative trend. Therefore, it will not affect the parameters like attenuation and backscatter. This is why the proposed algorithm preserves the dark trend within regions with weak backscattering (calcified lesion, dark square inside BVS stent struts, etc) or behind tissue with high attenuation (macrophages, foam cells, etc). Because of the total reflection, the tangential signal dropout cannot be compensated.

The compensation algorithm improves the BVS struts detection for 6 out of 8 pullbacks by 0.8-6.4 percent in F-score. In general, the overall result indicates that the compensation algorithm can potentially improve the performance of the BVS struts detection. A example can be seen in Fig 2.6. From the box-and-whisker plot of the percentile values within the black cores, we can observe that the percentiles in the compensated image are lower than that in the original images. Furthermore, it is worth noting that the lower percentiles over all the black cores are more condensed distributed. This can be the main reason that the proposed algorithm improves detection, since the lower percentile is used as a threshold in the BVS strut detection [47].

Meanwhile, in the results of the other two pullbacks with lower performances, the FP ratio tends to be higher in the detected results with compensated images. A FP example can be seen in Fig 2.6 D between the catheter and the guidewire. This is because our algorithm is designed to compensate the tissue region, which may cause structures with certain black-core-like appearance inside the lumen to be enhanced and detected, thus the FP ratio was increased. The method as described by Wang was not adjusted for the compensation experiment. Further optimization might improve the performance for the two case.

2.5.3 Limitations

The range of the estimated incident angles in the experiment is relatively small due to the elliptical shape of the artery wall, which is an inevitable issue of in-vivo IVOCT data. Since the angle related term is between 0 and 1, the logarithm operation can enlarge the range of the transmission term in the linear model. Another potential issue related to the angle estimation is that the angle of incidence has been estimated with 2-D IVOCT images: the best estimation that can be achieved at present. The estimation can approximate the spatial angle well because the imaging catheter has elasticity to resists over-bending, and can thus be assumed parallel to the longitudinal direction of the artery. Nevertheless, it would be interesting to measure the angle of incidence in 3-D in a future study.

There are two catheter related terms for modeling the IVOCT signal. One is the confocal function, the other is the spectral coherence term. Both terms can be different for different catheters. This can be the reason for the variation which lies in the estimated intercept for the hierarchical regression results. So
the compensation factor can be different as well. This can be solved by using statistical analysis of non-pathological images typically present in each pullback. Normalizing the signal to noise ratio (SNR) can be another solution to incorporate the differences [54].

With a long distance between the catheter and the lumen wall, the light was assumed to be attenuated mainly by the flush medium. The confocal function can be another potential reason. Limited by the linear regression purpose, the logarithm of the confocal function has been incorporated into the model with a fitted linear function.

2.5.4 Future work

In this paper, the compensation algorithm shows its potential to be as a preprocessing step for automatic BVS stent struts detection. For further incorporating the algorithm into the standard BVS detection workflow, more validation studies are needed, thus the parameters can be further optimized with the compensated images. Meanwhile, it is interesting to see if the compensation algorithm can improve the automatic detection of metal stent struts [ref] as well. Further experiments will be carried out for the metal stent strut detection in the future.

Additionally, for the statistical analysis, a more complex model can be used by involving higher power multivariate regression for example, then the higher power approximation of the confocal function can be used.

2.6 Conclusions

Both aspects regarding to the catheter position, the distance from the catheter to the artery wall and the angle of light incident upon the artery wall, significantly affect IVOCT image intensities. The hierarchical linear regression result shows that, as either aspect increases the intensity decreases. Using the hierarchical linear regression result, the proposed mathematical solution can compensate both pathological and non-pathological images. Results show that the proposed compensation algorithm potentially improves the visualization of IVOCT images, and allows a improved performance for the BVS struts detection.