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Validation of parameter estimation methods for determining optical properties of atherosclerotic tissues in intravascular OCT

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Abstract

In this paper we present a new process for assessing optical properties of tissues from 3D pullbacks, the standard clinical acquisition method for iOCT data. Our method analyzes a volume of interest (VOI) consisting of about 100 A-lines spread across the angle of rotation (θ) and along the artery, z . The new 3D method uses catheter correction, baseline removal, speckle noise reduction, alignment of A-line sequences, and robust estimation. We compare results to those from a more standard, “gold standard” stationary acquisition where many image frames are averaged to reduce noise. To do these studies in a controlled fashion, we use a realistic optical artery phantom containing of multiple “tissue types.” Precision and accuracy for 3D pullback analysis are reported.

Our results indicate that when implementing the process on a stationary acquisition dataset, the uncertainty improves at each stage while the uncertainty is reduced. When comparing stationary acquisition dataset to pullback dataset, the values were as follows: calcium: $3.8 \pm 1.09 \text{ mm}^{-1}$ in stationary and $3.9 \pm 1.2 \text{ mm}^{-1}$ in a pullback; lipid: $11.025 \pm 0.417 \text{ mm}^{-1}$ in stationary and $11.27 \pm 0.25 \text{ mm}^{-1}$ in pullback; fibrous: $6.08 \pm 1.337 \text{ mm}^{-1}$ in stationary and $5.58 \pm 2.0 \text{ mm}^{-1}$. These results indicates that the process presented in this paper introduce minimal bias and only a small change in uncertainty when comparing a stationary and pullback dataset, thus paves the way to a highly accurate clinical plaque type discrimination, enabling automatic classification.

Keywords

OCT; Optical Coherence Tomography; iOCT; optical parameters; intravascular imaging

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1. INTRODUCTION

Intravascular optical coherence tomography (iOCT) is an invaluable tool for vascular assessments due to its high contrast and microscopic resolution. It has been shown that iOCT is able to distinguish between lipid, calcium, and fibrous plaques [1, 2], quantify microscopic features such as macrophage content [3], and aid in assessment of new coronary artery stent designs [4–6]. However, fast iOCT systems can produce 500+ image frames in a single 2.5s pullback scan, resulting in an explosion of image data which can be very difficult and labor intensive to analyze manually, thereby precluding measurements from every image frame. We are developing computational methods for automatically classifying tissue types in order to address many of the aforementioned challenges. Our methods employ both the physics of image formation and image analysis to compute features from 3D regions within the iOCT pullback volume, which will then be employed for an automated and highly precise tissue classification as a follow up study.

There have been previous studies relating to tissue identification and classification in OCT images [1, 7–9]. Yabushita et al. [1] published a qualitative plaque classification scheme where he describes fibrous plaques as characterized by homogeneous, signal-rich regions; calcium plaque by well-delineated, signal-poor regions with sharp borders; and lipid-rich plaques by signal-poor regions with diffuse borders. Kume et al. [7] have demonstrated *in vivo* evaluation of the different types of plaques with iOCT but argues that interpretation of OCT images based on qualitative criteria alone might be ambiguous. Xu et al [8] used transverse imaging of ex vivo arteries using a high-resolution OCT microscopic system. They imaged fixed tissue sections of coronary arteries and calculated attenuation and backscattering coefficients based on average of 400 –lines (over time). Using single scattering light model, they performed least squares fitting of log compressed data. They were able to discriminate numerically between the different plaque types. Using a catheter based system and a stationary acquisition, Van Soest et al [9] measured μ_t in both *in vivo* and *ex vivo* specimens. They corrected for the non-ideal imaging system, used a linear equation model on *log* compressed data and applied an elegant algorithm to determine regions in one dimension corresponding to a single, homogenous tissue type. They argued in favor of μ_t values as a function of depth within tissue.

In this study, we develop a method for assessing optical properties of tissue from 3D pullbacks, the standard clinical acquisition method for iOCT data. In this way, we can avoid the second injection of contrast agent to clear the lumen for a stationary acquisition. We operate on a volume of interest (VOI) consisting of about 100 A-lines spread across the angle of rotation (θ) and along the artery, z . This presents many challenges including eccentricity of the catheter relative to the lumen surface, catheter motion, etc. We meet this challenge using multiple processing steps including pixel shifting, noise reduction, and robust estimation. Results from the new pullback analysis method are statistically compared to those from a more traditional, “gold standard,” stationary acquisition. In order to do this in a controlled fashion, we use a realistic artery phantom containing multiple “tissue types”.

2. METHODS

2.1 Image acquisition and selection of volumes of interest (VOIs)

Images were collected with the C7-XR system from St. Jude Medical Inc., MA. The swept source OCT system had a 1310nm center wavelength, 110 nm wavelength range, 50 kHz sweep rate, 20 mW output power, and ~12 mm coherence length. For pullbacks, the nominal speed was 20 mm/s over a length of 54 mm, resulting in a 100 fps frame rate and 271 frames per pullback. For stationary data acquisition, 121 frames were recorded over xx s with the catheter stationary at a predetermined location.

The optical tissue phantoms used in this experiment are described in detail in [10]. These phantoms were carefully fabricated with tightly controlled optical parameters allowing us to use them as gold standard while assessing clinically viable pullback data. Three phantoms were used in this experiment. Each phantom simulated one type of plaque (lipid, fibrous, and calcium) with known optical characteristics. For stationary imaging, the phantom was placed in a water bath and immobilized. The imaging catheter was moved along the lumen until the site of interest (containing phantom plaque) was identified. Then, the catheter sheath was held firmly on both sides to avoid any motion artifacts and five stationary acquisitions were obtained for each phantom. For pullback acquisitions, the same process as above was repeated except that we recorded 271 frames over a pullback length of 54mm (at 20mm/s) along the segment of phantom tissue. The protocol for *in vivo* imaging is described in [19].

The method used for identification of VOI's by an expert is detailed in [19]. The criteria used during human expert VOI identification is described in [1] (fibrous plaques were characterized by homogeneous, signal-rich regions; calcified regions by signal-poor regions with sharp borders; and lipid plaques by signal-poor regions with diffuse borders). TCFA was the most challenging type of plaque to identify [11]. The expert used the A-line intensity profile for each of the A-lines of the VOI while paying most attention to the separation between the lipid pool and the thin cap inside the signal-rich region described in [8].

In the stationary phantom acquisitions, there were 15 datasets in all (5 data sets for each plaque type). In these datasets, the expert marked between 5 and 20 VOIs depending on the plaque type and image quality. Markings were similarly done on the pullback data.

2.2 Image Analysis Algorithm

iOCT Pipeline—The processing pipeline for our iOCT image data analysis consisted of the following steps:

1. Pre-process in r- θ view: Correct for catheter optics
2. Remove Speckle noise using enhanced Lee filter [13, 14] on 2D r- θ images introducing minimum bias while preserving the sharp intensity level changes.
3. Determine and remove baseline.
4. Pixel-shift A-line within VOI's ensemble.

5. Log compress the data
6. Average across time to obtain an averaged image (stationary sequences)
7. Compute parameters using robust estimation approach as described by Gargsha et al [19] (pullback sequences)

This procedure is shown graphically in Figure 1.

Noise Characterization and Removal—Speckle in iOCT is a multiplicative noise and is a major challenge in analysis of optical properties [9][15][16]. To reduce speckle, we used the so-called enhanced Lee filter [13], which assumes multiplicative noise.

We first determine if noise in iOCT data is multiplicative in nature [17]. An observed pixel value z_i is related to the noise-free pixel, $x_{i,j}$

$$z_{i,j} = x_{i,j} v_{i,j} \quad (1)$$

where $v_{i,j}$ is a multiplicative noise with mean 1 and variance σ_v . We will analyze this relationship using methods described in [17]. Briefly, assume that the signal process x and the noise v are not correlated, the mean of z is $\bar{z} = \overline{xy} = \bar{x}$ And the variance of z is:

$$\text{var}(z) = E[(xv - \overline{xy})^2] = E[x^2] E[v^2] - \bar{x}^2 \bar{v}^2$$

If we examine an ensemble of pixel data or a flat region with fixed x value, $E[x^2] = \bar{x}^2$ and the variance reduces to

$$\text{var}(z) = x^2 (E[v^2] - \bar{v}^2) = \bar{x}^2 \sigma_v^2$$

From which we get

$$\sigma_v = \frac{\sqrt{\text{var}(z)}}{\bar{x}} = \frac{\sqrt{\text{var}(z)}}{\bar{z}} \quad (2)$$

In other words if the model described in equation (1) fits the iOCT data, then the standard deviation σ_v should equal the ratio of the standard deviation of z and the mean of z .

Speckle Noise Distribution: We computed a histogram from an average r - θ frame of an intralipid pullback (obtained by averaging across frames of the pullback) truncated to only include pixels to the right of the catheter line. Statistical analysis revealed that the distribution from water pullback. Then 3 additional VOIs were selected from different water pullbacks in order to confirm the initial findings. Since the data does not fit a normal distribution, a classical Lee filter [18] would introduce bias in our measurement. Therefore, we implemented the enhanced Lee described in [13, 14] that is more appropriate for data from a Rayleigh distribution.

Enhanced Lee Filter: The enhanced Lee filter as described in [14] reduces speckle while preserving texture information. It is an adaptation of the Lee filter and similarly uses local statistics (coefficient of variation) within individual filter windows. Each pixel is put into one of three classes, which are treated as follows:

- Homogeneous region: The pixel value is replaced by the average of the filter window.
- Heterogeneous region: The pixel value is replaced by a weighted average.
- Point “pixel”: The pixel value is not changed.

Baseline Analysis—To measure the baseline (noise floor) intensity level we took two different approaches. In both, we employed the model described in [9], which is repeated here for convenience.

$$I_d(r) = I_0 T(r) S(r) \exp(-\mu_t r) + I_{\text{offset}} \quad (3)$$

Taking the natural log of both sides of equation (3) yields:

$$\ln \left[\frac{(I_d(r) - I_{\text{offset}}(r))}{(T(r; z_0, z_R) S(r))} \right] = \ln(I_0) - \mu_t r \quad (4)$$

For the stationary phantom images, we applied the speckle removal algorithm described above to all 121 frames and averaged them. From the average r - θ frame, we computed a horizontal profile (i.e. along r) and identified a region within the vessel wall where the signal fell off to a minimum level, giving us the required offset to use in the model. For the pullback, however, we used pullback dataset, where, rather than measure the noise along r , we selected an angle of an A-line, then we created an image across the pullback direction composed of all of the A-lines having the same angle in each of the pullback r - θ frame. The average of this image gave us the desired baseline.

Pixel Shift Correction—In an ideal pullback, the catheter would be fixed at the center of the lumen and would, therefore, appear as a straight line in r - θ view (assuming that the vessel is perfectly circular.). In addition, the A-line's shape would look ideal as described by equation (3). However, typically, the catheter moves during a pullback and therefore its distance from the vessel wall is continuously changing. If an image is “corrected” by “sliding” the A-lines such that the lumen border is a straight line in an r - θ frame, it would weight equally any two points that are at the same depth within the vessel. Also, all of the A-lines within an expert-marked VOI would be at the same distance from the catheter. We call this process “pixel shift correction”.

Steps in pixel shift correction are (i) compute lumen border (using dynamic programming), and (ii) shift pixels of each A-line in an r - θ frame such that the vessel wall becomes a straight line. The red peaks in Figure 2 represent the reference point from which the exponential attenuation occurs for each A-line (i.e. where the intensity is I_0) and the blue

illustrates the lowest point. The flat blue is the baseline level after baseline offset correction as described above.

3. RESULTS

Results of the baseline analysis for stationary acquisition were such that an intensity level of approximately 6.7 (mean) was considered as baseline so that images were corrected by subtracting the baseline, dividing each A-line by the imaging system model and any negative values were truncated to zero. For the pullback, we received roughly the same values; however, we expect that in a clinical pullback, results will be different since there the fluids will contain a lot more scatterers than in water (blood/saline mixture).

Next, we analyzed the noise characteristics. The noise distribution is found to be a Rayleigh distribution with noise variance σ_v being constant and it is equal to 0.14994. Figure 3 shows an example of what an image looks like before and after speckle noise removal.

Table 1 shows a comparison of results of parameter estimation on 15 stationary phantom data sets of all three plaque types as a function of the processing steps in the pipeline. ~20 VOIs were used for each plaque type. We first analyze calcium plaques. Without any processing, μ_t for calcium has a large uncertainty (expressed as larger standard deviation). After enhanced Lee filtering application, the uncertainty of μ_t is greatly reduced with insignificant bias. When we pixel-shifted and averaged the A-lines, we observed that no additional bias was introduced, and uncertainty is significantly reduced (i.e. lower standard deviation, lower cv). Next, we studied lipid plaques. With no processing, we see a large uncertainty in μ_t but with a much lower cv . When we processed the frame using the same steps as before, we observe a progressively reducing cv . In fact, cv is much lower than that for calcium, indicating very high precision of μ_t . Last, we will analyze fibrous plaques. Here we see that due to noise removal and other steps, cv is significantly lowered indicating very high precision of μ_t . The data of Table 1 is shown graphically in Figure 4 for all plaque types.

We now compare our results so far with phantom pullbacks. Looking at Figure 5 we observed that the average μ_t 's were very similar to those for the stationary, however the uncertainty was higher. Pullbacks introduce other sources of noise such as motion, speed variations and other machine related disturbances during measurements. However, the nice thing is that the average value of the μ_t for each of the tissue types remain relatively constant, thus confirming that the robust estimation method used to calculate the optical values for the pullback, yielded the same results as the stationary acquisition where the more traditional method (averaging across the pullback and then across Θ) was used.

4. DISCUSSION

Characterization of atherosclerotic plaques is extremely important for determining the risk of a cardiovascular event. However, manually analyzing 100's of frames of iOCT image data and accurately making clinical decisions needs a high level of expertise and an inordinate amount of time. An automated approach will be a great step in the right direction; however, discrimination of atherosclerotic plaques using a computer algorithm is still not accurate

enough for use in a clinical setting as a support system for decision making. Our results indicate an improved accuracy and precision as compared to previously reported approaches for optical parameter estimation. Furthermore, this study may enable us to determine morphological features of coronary plaques that are at risk of rupture. In this study, phantoms were employed to obtain a "gold standard" against which to compare clinical results. Phantoms have also proved useful for establishing the best set of processing steps needed for a fully automated iOCT data analysis. We applied the widely used sigma (Lee) filter to be useful for iOCT image analysis. No consistent bias was observed in any of the pipeline stages, which is encouraging. Our results have indicated an improvement in image quality, robustness in estimation, improved visualization of hard-to-analyze data, and an improved feature space clustering that would aid in unsupervised learning.

For stationary phantom data, calcified and lipid plaques exhibit roughly the same average intensity (signal poor regions), however, the high attenuation of the lipid and the low attenuation of the calcium help us to distinguish between the two. The homogeneity of fibrous plaque is expressed by a low attenuation coefficient, while a high value of the average intensity indicates that it is signal rich. When we compared stationary phantoms with pullback phantoms, we observed that estimates were numerically comparable however the spread (standard deviation) for pullbacks was slightly higher due to motion artifacts during pullback.

Next, we acknowledge some of the limitations in our approach. The results highly depend on the quality of the expert marking. In fact, Kume et al [7] show that when using iOCT, evaluation of the different types of plaques could be possible *in vivo*, however, they also argue that interpretation of OCT images based on qualitative criteria alone might be prone to errors and ambiguities. In this study, computation efficiency was not considered. Using parallel processing and GPU might make a significant difference in compute times; this is reserved for a future study. Fibrous plaques thinner than 25 μ m were not marked. Many artifacts such as catheter uniformity, polarization effect, and blood clearance may influence the reproducibility of optical parameters estimation. In addition, we would also like to note that although we performed the noise analysis in an intralipid bath, this will not be representative of a clinical pullback noise since when performing a clinical pullback, the characteristics of the contrast agent (or the saline) which may be mixed with blood, might be different. Therefore, the same analysis will be performed on a clinical data as well.

We developed a framework for plaque characterization using three distinctive features, the attenuation coefficient, the average intensity and the incident intensity of VOI. We used expert-marked VOIs from stationary phantom data, estimated optical parameters, and compared with pullback data. We introduced the concept of iOCT image pipeline analysis and applied an enhanced Lee filter to remove speckle noise. Results suggest that the aforementioned features are suitable for highly accurate plaque type discrimination, enabling automatic classification. Machine learning algorithms can further exploit regional image features from iOCT images such as texture and shape-based features.

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Figure 1. graphical illustration of (r,θ) pipeline processing. The green indicates human operation while the rest is performed by our software.

(a)

(b)

Figure 2.
A VOI before (a) pixel shift and after (b). Indices along the axes are index numbers

Figure 3.
Illustration of an r - θ frames before (left) and after (right) speckle removal.

Figure 4.

μ_t estimates as a function of processing steps in the processing pipeline for different tissue types using stationary acquisition. Going from left to right we see calcium, lipid and fibrous.

Figure 5.

Stationary vs. pullback: μ_t uncertainty (right y-axis) and coefficient of variation (left y-axis).

Calcium is shown in (a), Lipid in (b) and Fibrous in (c). The bottom bars represent the coefficient of variation (std/mean)

Attenuation coefficient (μ_t) results of stationary dataset numerical analysis in the different pipeline stages (σ is the standard deviation and cv is the coefficient of variation where $cv = \sigma/mean$)

Table 1

	Raw			Extended Lee Filter			Pixel-shift & Averaging		
	μ_t	σ	cv	μ_t	σ	cv	μ_t	σ	cv
Calcium	3.882	2.022	0.521	3.805	1.570	0.413	3.800	1.094	0.288
Lipid	10.842	0.515	0.048	11.218	0.507	0.045	11.025	0.417	0.038
Fibrous	7.083	2.199	0.310	5.980	1.818	0.304	6.080	1.337	0.220