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Christos Photiou, Evgenia Bousi, Ioanna Zouvani, Costas Pitris, "Measuring tissue dispersion using the cross-correlation of half-spectrum optical coherence tomography images," Proc. SPIE 10867, Optical Coherence Tomography and Coherence Domain Optical Methods in Biomedicine XXIII, 108670D (22 February 2019); doi: 10.1117/12.2510949

SPIE.

Event: SPIE BiOS, 2019, San Francisco, California, United States

Measuring Tissue Dispersion Using the Cross-correlation of Half-Spectrum Optical Coherence Tomography Images

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ABSTRACT

In Optical Coherence tomography (OCT), dispersion mismatches cause degradation of the image resolution and are, thus, compensated accordingly. However, dispersion is specific to the material that is causing the effect and can, therefore, carry useful information regarding the composition of the samples. In this summary, we propose a novel technique for estimating tissue dispersion by calculating the cross-correlation of images acquired at different center wavelengths to estimate the shift between their features, also known as walk-off, and use that to calculate the dispersion. Since a distinct reflector is not required, this method is applicable to any sample and can even be implemented *in vivo* and *in situ* in human tissues. The proposed technique was verified *ex vivo* resulting in Group Velocity Dispersion (GVD) values comparable to those obtained from estimating the walk-off from a mirror, as described in the literature. The applicability to cancer diagnosis was evaluated on a small set of gastrointestinal normal and cancer OCT images. Using the statistics of the GVD estimates, tissue classification resulted in 100% sensitivity and 81% specificity (92% correct classification rate). The success of these preliminary results indicates the potential of the proposed method, which should be further investigated to elucidate its advantages and limitations.

1. INTRODUCTION

The wavelength dependence of the index of refraction in many materials results in the phenomenon of dispersion which causes pulse-width broadening with detrimental effects in many applications ranging from communications to imaging. In Optical Coherence tomography (OCT), dispersion mismatch between the two arms of the interferometer causes point spread function (PSF) broadening and, therefore, a degradation of the resolution. In order to eliminate the dispersion effects, several techniques have been developed, ranging from inserting materials or a prism pair in one arm to fiber stretching or even computational compensation[1-6]. However, dispersion is specific to the material that is causing the effect and can therefore carry useful information regarding its composition and/or concentration[7]. In tissue, dispersion could be used, for example, to detect changes associated with early cancer and result in more accurate disease diagnosis. Three main methods are described in the literature by which the dispersion can be estimated from OCT images: (i) measuring the degradation of the PSF[8], (ii) measuring the shift (walk-off) between images taken at different center wavelengths[9-10], and (iii) calculating the second derivative of the phase of the spectrum[11-12]. However, these methods require that a strong reflector is present in the image, which might not always be the case in tissue. In addition, the presence of Mie scattering and speckle can be detrimental in the attempt to measure dispersion[13]. In this summary, we propose a new technique for estimating the dispersion in tissue, which uses the cross-correlation of two half-spectrum images to calculate the dispersion from the image walk-off, and it is, therefore, applicable to any tissue and can be implemented in vivo and in situ. The proposed method was verified ex vivo and its applicability to cancer diagnosis was evaluated on a small set of gastrointestinal normal and cancer images. The results were very encouraging supporting further evaluation.

2. METHODOLOGY

A. Estimating the GVD from the image walk-off

When dispersion is present, different wavelengths perceive varying path-lengths as they propagate through tissue. The result is an apparent shift in the structures of OCT images taken at different center wavelengths. This, so-called, walk-off can be measured from images formed by a splitting the interferometric signal in two halves (multiplied by a Hamming window to reduce artifacts) and creating two OCT images with half the source spectrum each. The GVD is, then, given by

$$GVD = \frac{\Delta z \lambda_0^2}{2\pi c^2 L \Delta\lambda},$$

where Δz is the differential walk-off, $\Delta\lambda$ the source bandwidth, λ_0 the center wavelength, and L the sample thickness.

Optical Coherence Tomography and Coherence Domain Optical Methods in Biomedicine XXIII
edited by James G. Fujimoto, Joseph A. Izatt, Proc. of SPIE Vol. 10867, 108670D

B. Ex vivo GVD measurement based on the walk-off of a reflector

A swept source OCT system was used to image samples of a collagen gel and porcine muscle and adipose tissue sections placed over a reflector which served as a reference for measuring the actual sample thickness and the resolution. Eight images were taken from different regions of each type of sample. Each interferogram was split into two halves (Fig. 1B) and two, half-spectrum, images were formed corresponding to different center wavelengths. To measure the walk-off, the shift of the reflector located behind the tissue was measured by locating its peaks in each image (Fig 1C, red and green lines). Using the location of the mirror, the actual thickness of the sample was also calculated as the distance between the top surface (Fig. 1A, green line) and the extension of the mirror line (Fig. 1A, blue line to the left). Based on these measurements, the GVD was estimated as the median of 250 measurements from individual A-Scans of each image. The standard deviation of the GVD of all images of each type was used as an estimate of the accuracy.

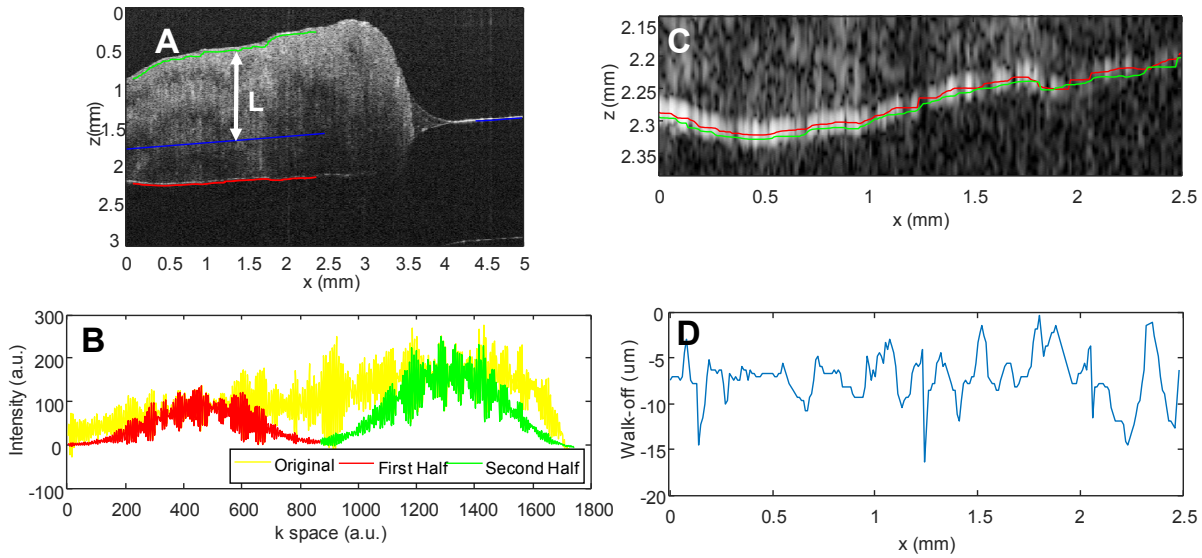

Figure 1. (A) OCT image of porcine muscle placed over a reflector (top surface: green, bottom surface: red, reflector: blue line). (B) A single interferogram (yellow) split into two halves (red and green). (C) The location of the bottom reflector from each half-spectrum image (red and green lines). (D) The walk-off between the two reflector locations

C. GVD measurement using the cross-correlation of corresponding A-Scans

Due to the absence of distinct reflectors in tissues, it is practically impossible to implement the technique described above *in vivo* and *in situ*. However, the walk-off between two images, acquired at different center wavelengths, can be estimated from the cross-correlation of A-Scans from corresponding regions of the two images. As described above, for Fourier Domain OCT images, each interferogram can be split into two halves forming two half-spectrum images at different center wavelengths. In the example of Fig. 2, corresponding regions (just above the bottom of the sample) are selected from each half-spectrum image of Figure 1 (Fig. 2 A&B). The cross-correlation of corresponding A-Scans is calculated and the first peak in the cross-correlation is detected. The walk-off is estimated from the distance of the peak from the zero-lag location (Fig. 2C) and the GVD is calculated using the equation of Section A. The walk-off estimation is more robust when there is enough speckle structure in the images to provide a better cross-correlation approximation. Fig. 2 D shows some typical cross-correlation curves with the arrow pointing to a miscalculation of the walk-off due to a weak cross correlation between A-Scans. This phenomenon is more common in clear samples such as the collagen gel used in the ex vivo experiments.

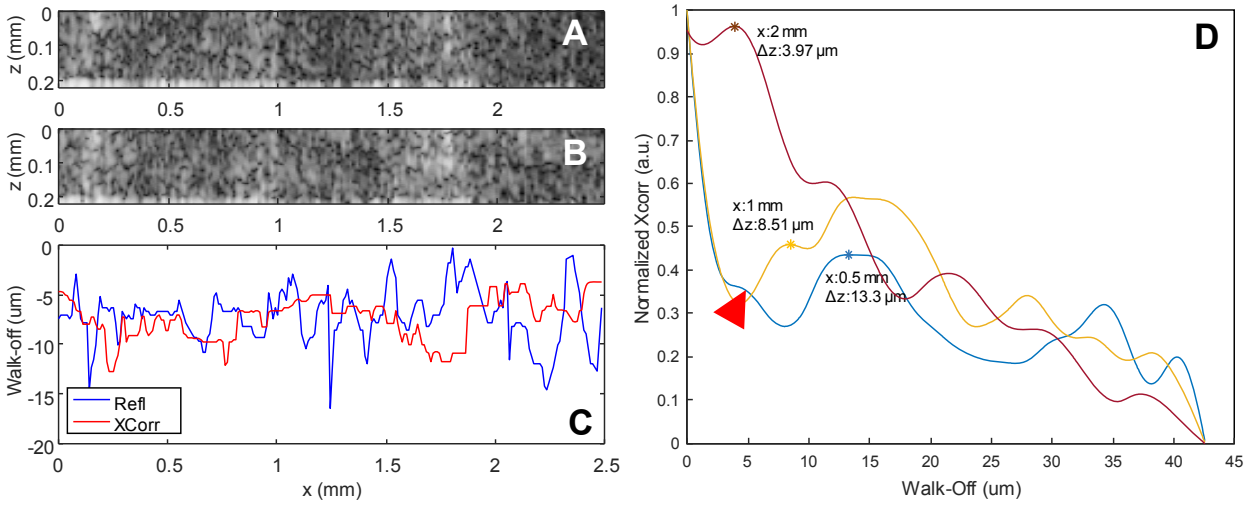

Figure 2. (A) Portion of the first half-spectrum OCT image from just above the bottom surface of the sample. (B) Similar portion from the second half-spectrum OCT image. (C) The walk-off of for the 250 A-Scans in A & B calculated from the cross-correlation. The blue line is the walk-off from Fig. 1D. (D) Three indicative cross-correlation curves. The red arrow points to a missed maximum.

D. Application of the cross-correlation dispersion measurement method to GI images

To demonstrate the applicability of the novel cross-correlation method to human tissues, the technique was applied to images from normal and cancerous colon obtained from patients who were scheduled for surgical excision. Eleven normal and 14 abnormal images were included in this preliminary study. Since the actual tissue thickness could not be measured, it was estimated from the distance measured by OCT in air divided by an average index of refraction of 1.45 (error < 5%). The GVD was estimated up to a depth of approximately 0.5 mm (as measured in air) for 500 A-Scans per image (Fig. 3). Using the statistics of these GVD measurements (such as mean, standard deviation, etc.) the samples were classified as normal or abnormal using Linear Discriminant Analysis (LDA) and leave-one-out-cross-validation (LOOCV).

3. EXPERIMENTAL RESULTS

Table 1 summarizes the results of the GVD measurements using the standard walk-off method from the literature (Section A) and the cross-correlation technique (Section C) described above. The values agree within one standard deviation (10-20 %) experimentally verifying the validity of the proposed technique. The proposed method accurate even for highly scattering tissues (less inter-sample variation) such as the adipose sample used here. The GVD measurements from the normal and abnormal GI tissues exhibit statistically significant differences (Fig. 4A & B). Combining the GVD distribution statistics using MANOVA results in perfect separation of the samples. Using the standard deviation of the GVD values, with LDA and LOOCV, the samples were classified with 100% sensitivity and 82 % specificity (92% correct classification). One example of the classification scatter plot is shown in the Fig. 4 C).

Table 1. GVD measured with the PSF degradation and speckle-PSF methods and mean index of refraction measurements

	Walk-Off (Reflector)			Walk-Off Cross-Correlation		
	Median (fs^2/mm)	Inter-Sample Std (fs^2/mm)	Intra-Sample Std (fs^2/mm)	Median (fs^2/mm)	Inter-Sample Std (fs^2/mm)	Intra-Sample Std (fs^2/mm)
Collagen	-135.18	15.14	5.37	-155.92	30.36	15.67
Muscle	-135.26	73.61	21.76	-139.96	34.72	23.48
Adipose	-247.02	240.15	60.64	-247.86	81.50	49.52

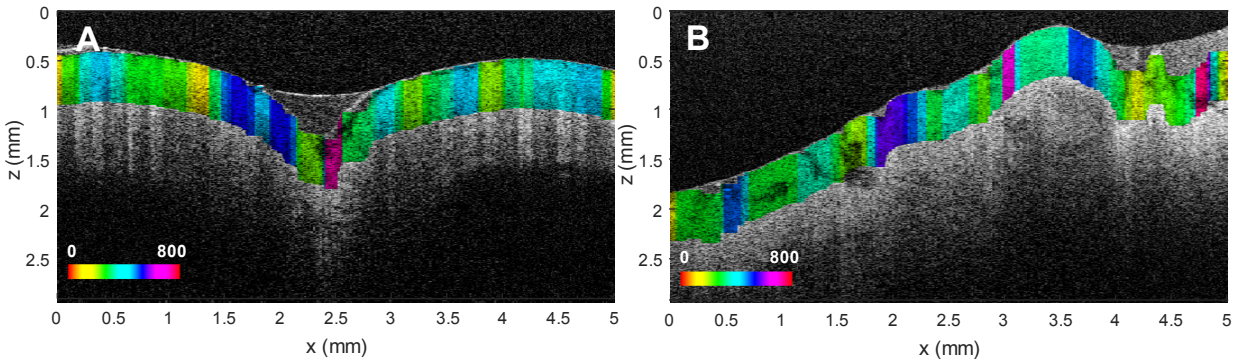

Figure 3. Overlay of OCT image (gray scale) and GVD (pseudocolor hue) for each A-Scan for normal (A) and adenocarcinoma (B).

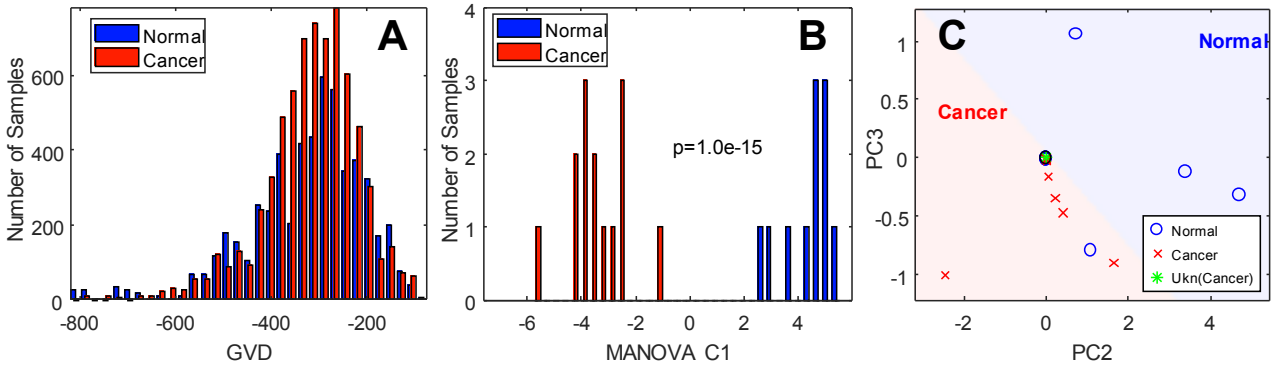

Figure 4. (A) Distribution of GVD measured from normal and abnormal colon tissue. (B) Distribution of the combined statistics (using MANOVA) for each sample. (C) LDA/LOOCV classification results. An unknown sample (cancer) was correctly classified.

4. CONCLUSIONS

Given the results presented above, the GVD can be effectively estimated from the walk-off, using cross-correlation, a technique not requiring distinct reflectors and, thus, applicable to any type of tissue *in vivo* and *in situ*. Such information could also be useful in the detection of tissue changes and could prove diagnostically useful. The success of these preliminary results indicates that further investigation is warranted, which should include both *ex vivo* and *in vivo* validation on a wider range of samples, to further elucidate the advantages and limitations of the proposed technique.

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