Pulsed illumination spectral-domain optical coherence tomography for human retinal imaging

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Abstract: We present pulsed illumination spectral-domain optical coherence tomography (SD-OCT) for in vivo human retinal imaging. We analyze the signal-to-noise (SNR) for continuous wave (CW) and pulsed illumination SD-OCT. The lateral beam scan motion is responsible for a SNR drop due to lateral scanning induced interference fringe washout. Pulsed illumination can reduce the SNR drop by shorter sample illumination time during the integration time of a camera. First, we demonstrate the SNR benefit of pulsed illumination over CW as function of lateral scan speed for a paper sample. Finally, we show better SNR in retinal images of a normal subject with pulsed illumination SD-OCT over CW at high lateral scanning speed.

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1. Introduction

OCT has emerged as a promising technology [1, 2] for in-vivo imaging in a wide range of medical applications. Current ophthalmic applications of OCT have included diseases such as age-related macular degeneration, [3, 4] diabetic retinopathy, [5, 6] macular holes, [7, 8] intraocular tumors, [9] and glaucoma. [10-12] In particular, glaucoma is the third leading cause of worldwide blindness, after cataract and trachoma. [13] The evolution from time-domain [1] to spectral-domain [14] and optical frequency domain imaging (OFDI), [15, 16] has made simultaneous improvement in sensitivity [17-19], high speed, [20, 21] and axial resolution feasible in many applications, such as retinal imaging. [22-24]

As OCT utilizes lateral point-scanning, motion of the sample or scanning beam during the measurement causes SNR reduction and image degradation in SD-OCT and OFDI. [25] Yun et al. theoretically investigated axial and lateral motion artifacts in CW SD-OCT and swept-source OFDI, and experimentally demonstrated reduced axial and lateral motion artifacts using a pulsed source and a swept source in endoscopic imaging of biological tissue. [25, 26] Stroboscopic illumination in full field OCT was demonstrated, resulting in reduced motion artifacts for in-vivo measurement. [27] In ophthalmic applications of SD-OCT, SNR reduction caused by high speed lateral scanning of the beam over the retina may be dominant over axial patient motion. Using pulsed illumination can reduce lateral motion artifacts. We analyzed the SNR benefit of pulsed-illumination over CW SD-OCT, demonstrating that pulsed illumination provides a better SNR for in-vivo high speed human retinal imaging.

The structure of the paper is as follows: the SNR benefit of pulsed-source over CW SD-OCT theoretically analyzed for different lateral scanning speeds. Then, a paper sample was measured to show the validity of the theory. Finally, the SNR for in-vivo human retinal imaging with pulsed-illumination and CW SD-OCT was analyzed and compared with the theory.

2. Benefits of pulsed illumination SD-OCT

2.1. Theory

Yun et al. [25] derived the equations for the SNR decrease due to lateral motion in CW SD-OCT. For a CW source, the SNR decrease is given by,

$$\text{SNR decrease} = -5 \log_{10} \left( 1 + 0.5 \frac{\Delta x^2}{w_o^2} \right),$$

(1)

where $\Delta x$ is the scanning distance during the camera integration time and $w_o$ denotes full-width-half-maximum (FWHM) of the beam profile. The normalized displacement is defined as $\Delta x/w_o$. For pulsed illumination, $\Delta x$ is replaced by $(\tau_{\text{pulse}}/\tau_{\text{camera}}) \Delta x$, where $\tau_{\text{pulse}}$ is the pulse width in time and $\tau_{\text{camera}}$ is the integration time of the camera for a single A-line. As can be seen in Fig. 1, pulsed-illumination SD-OCT has a significant SNR benefit over CW SD-OCT when the displacement $\Delta x$ is larger than the FWHM $w_o$ of the beam profile under the same average power. For example, at a normalized displacement of 4, a 20% duty cycle pulsed illumination has a 4.2 dB better SNR than CW illumination.

Figure 1 also shows that for CW illumination, a normalized displacement of 1 gives 1 dB decrease in SNR. At a source center wavelength of 841 nm, an axial motion of 50 nm per A-line would also result in a 1 dB SNR reduction. [25] At an A-line rate of 29.3 kHz, this corresponds to an axial velocity of about 1.5 mm/s, which for retinal imaging is, in general, much higher than encountered in practice.
2.2. Experimental setup

Our measurement system has been previously described by Nassif et al. [28]. For the measurements presented here, the light source was a high power SLD (SLD-371-HP3, Superlum, Russia) with a spectral bandwidth of 48.8 nm FWHM at a center wavelength of $\lambda_o=843.1$ nm. The current driver to the source could be operated in CW, and pulsed mode triggered by a signal from the computer. The maximum output power of the SLD was 23 mW and the measured axial resolution was 7.9 µm in air. The maximum average output power of the SLD in pulsed mode was determined by the pulse width and the pulse repetition rate. The pulse repetition rate was the same as the spectrometer triggering frequency, i.e. 29.3 kHz. The pulse width was set to 7 µs (~20% duty cycle), giving 400 µW in the sample arm after the slit lamp. For CW operation, a neutral density filter was inserted in the source arm to adjust the average power to the same value as in pulsed operation, such that the SNR decrease for pulsed and CW illumination could be compared directly. The collimated beam exiting the slit lamp was focused by a 30 mm focal length biconvex lens on a paper sample placed in the focal plane of the lens as illustrated in Fig. 2.

The FWHM beam diameter $w_o$ was calculated as 8.2 µm, and the lateral scanning range was 16 mm as measured on the sample. To control the normalized displacement, the lateral scan range remained unchanged but the number of A-lines per one complete lateral scan was decreased, resulting in increased lateral scan velocity. The scan range, the number of A-lines and the spot size were used to calculate the normalized displacement $\Delta x/w_o$. The paper sample was measured in two different configurations: parallel to the focal plane, and at a 4.1° tilt as illustrated at the top of Fig. 3. The number of A-lines per image was reduced from 1000 to 300 in 100 A-line decrements. The SNR was measured in each image with CW and pulsed illumination.
2.3. Results and discussion

For pulsed source illumination, the pulse width was set to 7 µs (20% duty cycle), which is equivalent to changing $\Delta x$ to $0.2\Delta x$ in Eq. (1). The average power incident on the paper sample was kept constant for CW and pulsed illumination. The SNR was calculated from the average of the maximum signal in each A-line near the center of each image. 80% and 20% of the A-lines near the center in each image were considered to calculate SNR for horizontal and slanted flat paper, respectively. The SNR from experiment and theory for pulsed and CW illumination are presented in Fig. 3.

Fig. 3. SNR decrease for the flat paper sample parallel to the focal plane (left) and with 4.1° tilt (right) for CW and pulsed illumination compared with theory. 1000 and 500 A-lines are equivalent to 2.3 and 4.3 normalized displacements, respectively.
The best fit for \( w_0 \) was 7 \( \mu \)m, in good agreement with the calculated value of 8.2 \( \mu \)m. The data was normalized to give 0 dB SNR at the smallest normalized displacement of the pulsed illumination. Figure 3 shows a significantly reduced SNR decrease for pulsed illumination. The equal SNR decrease between horizontal and slanted surfaces shows that a stationary slanted surface does not generate a further SNR decrease, despite that at a 4.1° slant, a scan length of 16 mm and 1000 A-lines per scan, the path length to the sample surface increases by 1.1 \( \mu \)m per A-line. For retinal imaging, this implies that the retinal curvature in an image is not expected to contribute to a SNR decrease. The experimental data agrees very well with the theory and demonstrates that the SNR for pulsed illumination is higher than for CW.

3. Application to human retinal imaging

3.1. Experimental setup

We applied, for the first time to our knowledge, pulsed illumination to human retinal imaging. We analyzed the SNR by changing the normalized displacement, and we compared SNR with CW illumination. The pulse width was 8 \( \mu \)s and the pulse repetition rate was 29.3 KHz, synchronized with the integration time of the high-speed line scan camera. The voltage input for horizontal scan was the same as in the paper sample experiment, ± 2.5 V, however the actual scan range was 8.6 mm on the retina, which is about half the scan range on the paper sample. This is due to the higher refractive power of the eye as compared to that of the 30 mm bi-convex lens, which also will result in a smaller spot size on the retina.

The normalized displacement was adjusted based on the actual scan range on the retina. According to the ANSI standard for safe use of lasers, the maximum permissible exposure expressed as the average power of a pulse train increases with the pulse repetition rate up to a frequency of 55 kHz, where the limit to continuous wave exposure is reached. The \( MPE_{sp} \) for a single pulse between 1 ns to 18 \( \mu \)s is given by,

\[
MPE_{sp} = 5.0 \cdot C_A \cdot 10^{-7} \text{ [J/cm}^2\text{]} \tag{2}
\]

with \( C_A = 1.66 \) for 810 nm. The MPE of a pulse in the pulse train is given by the single pulse MPE, multiplied by a correction factor determined by the number of pulses \( n \) during a time interval of at most 10 seconds for small source ocular exposure. The maximum average power into the eye is then given by this MPE of a pulse in the pulse train, multiplied by the repetition frequency \( f_{rep} \) and the limiting aperture of 0.385 cm\(^2\).

\[
MPE = \left( n^{-0.25} \right) MPE_{sp} f_{rep} 0.385 \text{cm}^2
\]

\[
= MPE_{sp} \cdot 10^{-0.25} \cdot f_{rep}^{0.75} \cdot 0.385 \text{ cm}^2 [\mu W] \tag{3}
\]

Figure 4 shows the maximum permissible average power in the pulse train as a function of repetition frequency, and the maximum permissible power of CW illumination (which cannot be exceeded). Although the maximum average power increases up to a frequency of 55 kHz, the energy in a single pulse, which ultimately determines the SNR or sensitivity of a single A-line, decreases. The optimal sensitivity would be achieved for a single pulse every 10 sec, which is incompatible with high-speed imaging. The maximum permissible exposure (MPE) for human retinal imaging at a wavelength of 810 nm is 423.5 \( \mu \)W for pulsed illumination with 29.3 kHz repetition rate and 8 \( \mu \)s pulse length, and 640 \( \mu \)W for CW illumination. [29]
Fig. 4. Maximum permissible exposure expressed as average power into the eye, according to the ANSI standards for CW and pulsed illumination. Red line: CW power limitation. Black line: Pulsed source power limitation calculated from Eq. (3) as a function of pulse repetition frequency. The smaller MPE of CW and pulsed illumination at specific frequency determines the power limitation to the retina.

Fig. 5. Integrated reflectance images of in-vivo human retina centered on the optic nerve head for two kinds of illumination (CW and pulsed) at two different lateral scanning speeds. (a) CW, 1000 A-lines (b) pulsed, 1000 A-lines (c) CW, 500 A-lines (d) pulsed, 500 A-lines. Four regions of interest are indicated (zones A to D), where the SNR was analyzed in each image. Some discontinuities in (a) and (b) were caused by eye motion during the two times longer measurement time as compared to (c) and (d). The lateral scan angle of 30° in the experiment results in 8.6 mm lateral scan range. Vertical scan range is 5.2 mm on the retina.

The sample arm power after the slit lamp of CW and pulsed illumination was set to 600 µW and 385 µW respectively. The 385 µW average power for pulsed illumination will cause a 1.9 dB smaller SNR compared to the 600 µW for CW. This has been accounted for in the SNR analysis comparing pulsed and CW illumination. As shown in Fig. 5, integrated reflectance images of the retina [30, 31] of a healthy volunteer at two different lateral scanning speeds characterized by 1000 and 500 A-lines per image for CW and pulsed illumination were measured. We can see some discontinuities in the 1000 A-line images because of the two times longer measurement time relative to the 500 A-line images.
3.2. Results and discussion

The SNR in each measurement was calculated and analyzed as follows. First, we selected 4 regions of interest based on the integrated reflectance image as shown in Fig. 5 to compare the SNR in the same region of the retina for CW and pulsed illumination. Zone A is comprised of 5 frames and the other zones contain 9 frames. Even if we selected the same regions of the retina based on Fig. 5, the depth location of the retina in each frame was slightly different for the pulsed and CW case. The sensitivity of SD-OCT decreases with depth [17, 32], and the normalized sensitivity decay was measured in our previous work. [28] Each original A-line was divided by the normalized sensitivity of the system as a weighting factor to correct for the depth dependent sensitivity. Since the depth dependent sensitivity has the smallest roll-off close to the zero-delay position of the reference arm, the regions of interest were selected to the left side of the optical nerve head (ONH) because they are closest to the zero-delay position of the reference arm, as shown in Fig. 6.

![Fig. 6. ONH images from zone C in Fig 4(a) ~ 4(d) at the same location, gray scale coded over the same dynamic range. The ONH is in axially different locations. SNR was compared after correcting for the depth dependent sensitivity decrease. The horizontal dimension is 8.6 mm and vertical dimension is 1.7 mm.](image)

The highest signal in each A-line was detected and averaged over the region of interest (ROI) in each image and the SNR of each image was averaged again in each zone. Table 1 shows the SNR of each zone for different experimental conditions.

<table>
<thead>
<tr>
<th>SNR (dB)</th>
<th>CW, 1000 A-line</th>
<th>pulsed, 1000 A-line</th>
<th>CW, 500 A-line</th>
<th>pulsed, 500 A-line</th>
</tr>
</thead>
<tbody>
<tr>
<td>zone A</td>
<td>29.0</td>
<td>28.7</td>
<td>25.1</td>
<td>28.1</td>
</tr>
<tr>
<td>zone B</td>
<td>29.8</td>
<td>29.4</td>
<td>26.8</td>
<td>28.9</td>
</tr>
<tr>
<td>zone C</td>
<td>31.3</td>
<td>30.6</td>
<td>28.9</td>
<td>30.3</td>
</tr>
<tr>
<td>zone D</td>
<td>31.1</td>
<td>30.5</td>
<td>28.0</td>
<td>30.2</td>
</tr>
</tbody>
</table>
The data was fitted to the theory in the following way: since the reflectivity of a particular location on the retina varies, SNR values in the 4 zones could not be compared directly. However, SNR values for pulsed and CW illumination within the same zone could be compared directly. The same offset was subtracted from the SNR values within a zone. The offset varied by zone, and was determined by a fit to the theory. The beam diameter \( w_0 \) in each zone was also determined by a fit to the theory, giving 3.8, 4.6, 5.7, and 4.7 \( \mu m \) for zones A to D, respectively. The smallest RMS spot size on the retina layer can be simulated with Zemax as \( \sim 3 \mu m \) with Navarro’s model [33] and \( \sim 5 \mu m \) with Gullstrand Schematic Eye No.1 [34]. The normalized displacement is slightly different in each zone due to the variation of \( w_0 \). The SNR values in each zone and the theory are shown in Fig. 7.

The 1.9 dB better relative SNR for CW illumination over pulsed illumination at zero normalized displacement in Fig. 7 reflects the higher average power permitted under the ANSI standards. We can see that the SNR was almost the same at 1000 A-lines per image with CW and pulsed illumination but it was 1.4 to 3.0 dB higher with pulsed illumination for larger normalized displacement. The variation in beam diameter is attributed to a difference in curvature between the retina and the focal plane of the imaging system, where the best overlap between retina and focal plane was realized in zone A, good overlap was realized in zone B and D, and the worst overlap was realized in zone C.

One consideration that should be taken into account is that shortening the pulse length while maintaining average power and pulse repetition rate will decrease the lateral motion artifact but also increases the ratio of RIN over shot noise. For a shot noise limited system, this ratio needs to be smaller than 1. Using Eq. (2) in ref [20] and replacing \( P_{ref} \) with \( J_p/\tau_i \), with \( J_p \) the energy of the pulse and \( \tau_i \) the pulse duration, gives,

\[
\sigma_{noise}^2 = \sigma_{noise}^2 + \frac{\eta e^2 J_p}{E_v} + \left( \frac{\eta e J_p}{E_v} \right)^2 \tau_i \tau_{coh} \left[ e^2 \right]
\]

\( \eta \) is the quantum efficiency, \( e \) the charge of an electron, and \( \tau_{coh} \) is the coherence time of the laser. The coherence time \( \tau_{coh} \) is related to the pulse duration \( \tau_i \) by

\[
\tau_{coh} = \frac{\tau_i}{\ln(2)}
\]
The reference arm pulse energy $J_p$ to saturate the spectrometer to 90% of the full well capacity is independent of pulse length. The pulse energy for which the shot noise still dominates over RIN noise is given by $J_p < \frac{E_r \tau_r}{\eta \tau_{coh}}$, which shows that reducing the pulse length also reduces this pulse energy. In our case of an 8 μs pulse length, the pulse energy is still more than a factor of two below the value where RIN noise is equal to shot noise. [20]

4. Conclusions

We examined the SNR decrease due to lateral motion for CW and pulsed illumination and demonstrated good correlation between experimental data and theory for two different samples: a) paper, and b) in-vivo human retina. With equal incident power, depending on the normalized displacement of the beam across a paper sample, a ~3 to ~6 dB better SNR was found for pulsed over CW illumination. In ophthalmic applications, lateral motion from high speed beam scanning can be regarded as a dominant factor contributing to SNR decrease. As mentioned in section 3.1, according to the ANSI standards, the MPE for pulsed illumination in our setup is 423.5 μW, as compared to 640 μW for CW. Therefore, based on the MPE, CW should have a 1.8 dB better SNR over pulsed illumination. However, due to the SNR decrease resulting from fast lateral scanning, the SNR was almost the same between CW and pulsed illumination with 1000 A-lines per image over an 8.2 mm scan range. The measured SNR for pulsed illumination was 1.4 to 3.0 dB higher than for the CW source at a two times larger normalized displacement and agreed well with the theory. In conclusion, with CW illumination under our experimental conditions we have demonstrated that doubling the scan speed or normalized displacement resulted in up to 2.5 dB of SNR reduction. With pulsed illumination the lateral scan speed could be doubled at a cost of up to 0.5 dB SNR reduction. Pulsed illumination permits higher scan speeds and reduced scan times for large area retinal scans at a much smaller SNR penalty than CW illumination.

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