Imaging pulsatile retinal blood flow in human eye

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Abstract. A functional Fourier domain optical coherence
tomography instrument offering spectral Doppler imaging
of in vivo pulsatile human retinal blood flow was con-
structed. An improved phase-resolved algorithm was de-
veloped to correct bulk motion artifacts. Spectral Doppler
imaging provides complementary temporal flow informa-
tion to the spatially distributed flow information of the
color Doppler image by providing direct visualization of
the Doppler spectrum of the flow whose pattern can be
further quantified with various velocity envelope curves and
their corresponding flow indices. The coefficient of
repeatability on resistance index measurement was as-
essed by analyzing 14 measurements on two vessels
within two normal subjects. © 2008 Society of Photo-Optical In-
strumentation Engineers. [DOI: 10.1117/1.2967986]

Keywords: doppler; tomography; interferometry.

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Previous studies suggest that retinal haemodynamics play
an important role in glaucoma,1 diabetic retinopathy2 and
age-related macular degeneration.3 Therefore, it is desirable to
assess retinal blood flow in vivo in order to investigate their
role in major eye diseases. Although many flow measurement
technologies have been developed, they do not provide ade-
quate information for understanding the relationship between
retinal blood flow and important ocular diseases. Spectral
doppler optical coherence tomography (S-D OCT), a variation of
optical coherence tomography (OCT) that combines coherence
gating and laser Doppler effects, is an alternative that can
overcome some limitations of the technologies mentioned
above.4

Because of the unknown Doppler angle between the blood
flow and incident light beam and the absence of a quantifica-
tion method that can generate interpretable results for cli-
nicians, DOCT is not widely used in eye clinics. Conventional
DOCT only generates a snapshot of pulsatile ocular blood
flow that is projected along the light beam direction in a car-
diac cycle. Most recent developments in quantifying blood
flow information of the human eye utilizes 3-D vascular ori-
entation information to estimate Doppler angle and the abso-
olute flow velocity.5 On the other hand, it is noteworthy to
quantify the pulsatile flow pattern as an alternative method to
investigate retinal flow dynamics. A simple projected ocular
blood flow velocity (integration over the whole blood vessel
plot through a cardiac cycle was chosen by White to de-
monstrate the pulsatile flow property, although it is possible to
acquire much more hemodynamics information from the same
raw data. The M-mode scanning method has been used to
acquire temporal flow information in time-domain DOCT
systems.6 The short-time fast Fourier transformation method
from Doppler ultrasound was used to generate Dop-
pler spectrum wave forms but without further quantification,
which provides the most valuable information for clinicians.

The purpose of this paper is to implement the full concept of
spectral Doppler imaging, developed by scientists and cli-
nicians in ultrasound medicine, in a Fourier-domain DOCT sys-
tem and provide an alternative quantification method for an
ocular blood flow pattern that may be further investigated for
vascular related eye diseases.

“Spectral Doppler is a terminology from Doppler ultra-
sound and should not be related to spectral OCT that uses
spectral information as a contrast mechanism of OCT. Spect-
ral Doppler imaging of pulsatile retinal blood flow includes
Doppler spectrum visualization, using spectral Doppler wave
forms, and a method for quantifying the temporal properties
of flow, using various velocity envelopes and their corre-
ponding Doppler-angle-independent indices. Continuous
color Doppler data are acquired when the light beam performs
repeated dense scans over the region of interest. Spectral Dop-
pler analysis on the data shows how the velocity components
and longitudinally projected flow-volume-rate change over
time for scatters within the imaging volume with spectral
Doppler wave forms. Various velocity envelope curves can be
derived from spectral Doppler wave forms and used to extract
the corresponding pulsatility index (PI), resistance index (RI)
and several other indices that can provide interpretable
Doppler-angle-independent information needed to quantify
the pulsatile nature of ocular blood flow.

A Fourier domain functional OCT system was developed
for retinal blood flow imaging. Briefly, low coherence light
with a center wavelength of 890 nm and FWHM bandwidth
of 150 nm was protected from optical feedback using a
broadband optical isolator before entering a 2 $\times$ 2 broadband
coupler-based interferometer. The light from the refer-
ence arm was focused onto a reference mirror with an optical
attenuator inserted into the optical path. The sample arm was
modified from the patient module of a Zeiss Stratus OCT
instrument. The detection arm was connected to a high-
performance spectrometer that allows the system bench-top
sensitivity of 100 dB with 650 μW light out of the sample
arm fiber and 50 μs CCD integration. A 9 dB of SNR roll-off
from zero imaging depth to 2 mm imaging depth was ob-
served. The system has an axial resolution of 3.5 μm. In this
study, the system speed was set at 16.7 K A-lines/s with its
CCD A-line integration time set at 50 μs and the line period
set at 60 μs. The maximum longitudinal velocity in retinal
tissue that corresponded to a phase difference of $\pi$ was deter-
mined to be 2.69 mm/s according to $V_{\text{max}} = \lambda/(4T),$ where
$T$ is the line period of the CCD camera. The measured phase
noise from a mirror was 2.66 mrad. The velocity measure-
ment error was determined to be <5% by imaging steady-

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noise from a mirror was 2.66 mrad. The velocity measure-
ment error was determined to be <5% by imaging steady-
state scattering flow (polystyrene bead solution with mean diameter of 0.3 μm and volume concentration of 0.26%) pumped at different velocities.

An improved phase-resolved algorithm that uses a Doppler variance image to select tissue pixels for histogram analysis of bulk phase was developed in this instrument to compensate for the axial eye movement. Most bulk motion presented in Fig. 1(a) has been corrected by the conventional histogram algorithm in Fig. 1(b). Additional motion artifacts resulting from bulk motion phase estimation error by normal histogram algorithm shown in Fig. 1(c) were corrected in Fig. 1(d) by the improved phase-resolved algorithm that eliminates the assumption that the vessel has to be small compared to the tissues in the same A-line.

For the scan protocol of spectral Doppler imaging, repeated color Doppler scans over the broken region of the red line shown in Fig. 1(e) for a short period of time were performed after a specific vessel was selected from the OCT fundus image generated from a 3-D scan immediately before spectral Doppler imaging. Spectral Doppler analysis was performed on the color Doppler images. In order to evaluate variation of measurements within one session, spectral Doppler imaging of 512 snapshots through eight cardiac cycles in 7.9 s was performed on one normal subject after the vessel was selected as shown in Fig. 1(e). Each snapshot used 256 A-lines on 132.5 μm tissue. The imaging speed of 65 snapshots per second is fast enough to capture the dynamic flow during a cardiac cycle. The structure image and velocity image for a typical snapshot are shown in Fig. 1(f). The longitudinal velocity sensitivity was 174 μm/s by fitting the velocity profile and calculating the standard deviation for the velocity image across the center of the vessel.

Before spectral Doppler analysis, a threshold was applied to the Doppler phase image and then some morphological operations were performed to get a vessel mask. The vessel center could then be easily determined from the peak positions after projecting the vessel mask to horizontal and vertical directions. A rectangular window centered at the estimated vessel center position can be applied to the velocity image in Fig. 1(f).

Next, the spectral Doppler wave forms in Fig. 1(g) could be generated after spectral Doppler analysis was performed for every velocity image snapshot that corresponded to one vertical line of the spectral Doppler wave forms. The velocity range was digitized into 256 velocity bins (υ0−υ255). An iteration of all the pixels within the window generates a function n(υi) that represents the number of pixels having velocity of υi. Because each pixel represents a vortex for the vessel lumen area, the product of the velocity of the velocity bin and the number of pixels that fall within the velocity bin produced gray scale amplitude, which is proportional to the longitudinal

**Table 1 Intrasession coefficient of variation of Doppler flow indices for one measurement.**

<table>
<thead>
<tr>
<th>Cycle</th>
<th>PI</th>
<th>RI</th>
<th>SD</th>
<th>DA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.0753</td>
<td>0.62559</td>
<td>2.6709</td>
<td>0.64352</td>
</tr>
<tr>
<td>3</td>
<td>1.0551</td>
<td>0.621</td>
<td>2.6386</td>
<td>0.64393</td>
</tr>
<tr>
<td>4</td>
<td>1.1869</td>
<td>0.6805</td>
<td>3.1299</td>
<td>0.55727</td>
</tr>
<tr>
<td>5</td>
<td>1.1362</td>
<td>0.65217</td>
<td>2.875</td>
<td>0.606</td>
</tr>
<tr>
<td>6</td>
<td>1.4098</td>
<td>0.7561</td>
<td>4.1</td>
<td>0.45478</td>
</tr>
<tr>
<td>7</td>
<td>1.0667</td>
<td>0.61789</td>
<td>2.617</td>
<td>0.65965</td>
</tr>
<tr>
<td>8</td>
<td>1.0539</td>
<td>0.64</td>
<td>2.7778</td>
<td>0.59284</td>
</tr>
<tr>
<td>Mean</td>
<td>1.140557</td>
<td>0.656179</td>
<td>2.972743</td>
<td>0.593999</td>
</tr>
<tr>
<td>Std. Dev.</td>
<td>0.128572</td>
<td>0.049147</td>
<td>0.527933</td>
<td>0.070866</td>
</tr>
<tr>
<td>Coe. Var.</td>
<td>0.112727</td>
<td>0.0749</td>
<td>0.177591</td>
<td>0.119303</td>
</tr>
</tbody>
</table>


projection of the flow-volume-rate contributed by each velocity bin. The summation of the gray scale amplitude along the y-axis gives the total longitudinal projection of flow-volume-rate of a vessel at a given time point. The summation of the gray scale amplitude along the y- and x-axes for one cardiac cycle provides the longitudinal projection of total flow volume within that cardiac cycle. Note that spectral Doppler wave forms with other gray scale intensity definitions can be defined according to other physical meanings, such as particle numbers or particle energies. Different color channels may be introduced to represent multiple flow-related parameters in a color-coded plot of spectral Doppler wave forms.

In order to obtain more quantitative, interpretable results, different Doppler velocity envelopes, such as maximum velocity envelope, mean velocity envelope, and flow-volume-rate envelope, can be derived from the spectral Doppler waveforms accordingly. Figure 1(h) shows an example of the maximum velocity envelope derived from the spectral Doppler waveforms in Fig. 1(g). For each cardiac cycle in Fig. 1(h), symbol S represents the peak systolic maximum velocity, symbol D represents the end diastolic maximum velocity and symbol A represents the temporal average of maximum velocity. The PI and RI are defined as follows to characterize the curve and remove the dependence on Doppler angle:

\[
PI = \frac{(S - D)}{A}, \quad RI = \frac{(S - D)}{S}.
\]

(1)

Similar Doppler indices, such as the S/D ratio and D/A ratio, can be defined accordingly. Cycle 2 was excluded for statistical calculation due to eye motion. Table 1 summarizes the flow indices measured for other cardiac cycles, their average values, standard deviation values, and coefficients of variance for the maximum velocity envelope curve. The quantitative indices indicated above can be derived accordingly for other envelope curve definitions.

The intersession repeatability\(^2\) of RI measurement was assessed from multiple pairs of measurements. One measurement pair was defined as two separate measurements on the same vessel site. We measured two retinal vessels from two normal subjects. Each vessel was measured seven times in the same day. There were 21 independent measurement pairs out of seven repeated measurements on each vessel. The intersession coefficient of repeatability (CoR) of 0.08336 was calculated from the 42 pairs of measurement on two vessels (see Table 2) according to the formula: CoR = 1.96 \* \sqrt{(\sum(d_i - \bar{d})^2)/(n-1)}.

In summary, we have developed a functional Fourier domain optical coherence tomography instrument that allows spectral Doppler flow imaging of in vivo human retinal flow. An improved phase-resolved algorithm was developed to correct the bulk motion artifacts. The CoR was assessed for RI measurements using 14 measurements of two vessels within two normal subjects. This method provides an alternative way to quantify retinal blood flow with Doppler-angle-independent flow indices that may provide insight on the retinal flow in many vascular related eye diseases.

**Acknowledgment**

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**References**


