Parafoveal Retinal Vessel Density Assessment by Optical Coherence Tomography Angiography in Healthy Eyes

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FINANCIAL DISCLOSURES:

Jay S. Duker receives research support from Carl Zeiss Meditec, Topcon, and OptoVue. Nadia K. Waheed is a consultant for Optovue, and receives research support from Carl Zeiss Meditec and Topcon. There are no conflicting relationships for any other author.
MY ROLE IN THIS RESEARCH:

- ✔ Conception and design of the work/project
- ✔ Acquisition of data
- ✔ Analysis and interpretation of data
- ✔ Creation and/or critical review of the presentation
Purpose

A) to assess the variability in vessel density (VD) measurements across three OCTA devices

B) to identify a method that offers the least amount of variation in VD

Optovue RTVue XR Avanti
Zeiss Cirrus
Zeiss Plex Elite 9000
Methodology

• Automatically segmented at the superficial capillary plexus, deep capillary plexus, and full retina

• Used an automatic thresholding algorithm in ImageJ to obtain binary and skeletonized images: Mean and Otsu methods

• Calculated Vessel Area Density (VAD) and Vessel Skeleton Density (VSD)
## Results: Example Output Across Devices

<table>
<thead>
<tr>
<th></th>
<th>Full retina original image</th>
<th>Binarized</th>
<th>Skeletonized</th>
<th>VAD (%)</th>
<th>VSD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Avanti</strong></td>
<td><img src="image1" alt="Full retina" /></td>
<td><img src="image2" alt="Binarized" /></td>
<td><img src="image3" alt="Skeletonized" /></td>
<td>44.09</td>
<td>19.19</td>
</tr>
<tr>
<td><strong>Cirrus</strong></td>
<td><img src="image4" alt="Full retina" /></td>
<td><img src="image5" alt="Binarized" /></td>
<td><img src="image6" alt="Skeletonized" /></td>
<td>45.72</td>
<td>13.35</td>
</tr>
<tr>
<td><strong>Plex</strong></td>
<td><img src="image7" alt="Full retina" /></td>
<td><img src="image8" alt="Binarized" /></td>
<td><img src="image9" alt="Skeletonized" /></td>
<td>46.85</td>
<td>6.89</td>
</tr>
</tbody>
</table>
Results - Coefficient of Repeatability Values

- Coefficient of Repeatability (CoR) was calculated to assess repeatability of measures on the same device.
- Lower CoR indicated a tighter dispersion and higher repeatability.
- The Mean and Otsu methods were compared and overall, the Mean method had lower CoR values.
- Mean VSD was more repeatable than Mean VAD.

### Comparison of Mean VAD (%) and Mean VSD (%) via CoR

<table>
<thead>
<tr>
<th></th>
<th>Full Retina</th>
<th>Superficial Layer</th>
<th>Deep Layer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean VAD</td>
<td>Mean VSD</td>
<td>Mean VAD</td>
</tr>
<tr>
<td>Avanti</td>
<td>2.23</td>
<td>2.02</td>
<td>2.33</td>
</tr>
<tr>
<td>Cirrus</td>
<td>3.32</td>
<td>1.49</td>
<td>2.86</td>
</tr>
<tr>
<td>Plex</td>
<td>1.63</td>
<td>0.45</td>
<td>1.64</td>
</tr>
</tbody>
</table>
Results – Mean VAD and VSD Across Devices

- Statistically significant differences were noted across all devices and layers for both methods.

- Differences were systematic for the Mean VSD method.

- Mean VAD might be a better method to compare across devices, while Mean VSD is better suited to follow on one device.
Results – Vessel Length Across Devices

Vessel length (mm) is a linear measure of the combined lengths of all the vessels that is not affected by differences in resolution of the devices.

<table>
<thead>
<tr>
<th>Device Comparison</th>
<th>Full Retina Significance Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avanti-Cirrus</td>
<td>ns (p=0.107)</td>
</tr>
<tr>
<td>Avanti-Plex</td>
<td>ns (p=0.244)</td>
</tr>
<tr>
<td>Cirrus-Plex</td>
<td>ns (p=1)</td>
</tr>
</tbody>
</table>

No difference was noted across devices using this quantitative parameter.
Results – Effect of Registration

• The three consecutive repeats for each eye were registered and averaged

• The same trend in significance and values was noted as before registration

• Bias was calculated to quantify the difference between original and registered images

• After the registration of images, mean VSD remained within 1% of the mean VSD value of a single scan

<table>
<thead>
<tr>
<th></th>
<th>Full Retina</th>
<th>Superficial Layer</th>
<th>Deep Layer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avanti</td>
<td>0.41</td>
<td>0.68</td>
<td>0.41</td>
</tr>
<tr>
<td>Cirrus</td>
<td>-0.69</td>
<td>-0.69</td>
<td>-0.51</td>
</tr>
<tr>
<td>Plex</td>
<td>-0.26</td>
<td>-0.17</td>
<td>-0.39</td>
</tr>
</tbody>
</table>
Conclusions

• Statistically significant variability exists among VD between the Avanti, Cirrus, and Plex Elite for a single normal imaged patient

• Mean VAD was more comparable across devices, while Mean VSD was more repeatable, but less comparable across devices

• The swept-source device demonstrated the greatest intra-session repeatability

• Less than 1% difference in VD existed between registered and unregistered images, which was statistically significantly different

• Perhaps, a conversion factor may be able to account for the systematic differences between devices
Acknowledgements

Dr. Jay S Duker’s lab at the New England Eye Center

Dr. Nadia K. Waheed,
New England Eye Center

Malvika Arya BS, A. Yasin Alibhai MD, Carl B. Rebhun BA, Xuejing Chen MD, Elias Reichel MD, Caroline R. Baumal MD, Andre J. Witkin MD, Jay S. Duker MD, Nadia K. Waheed MD MPH
Appendix
Results: Example Output Segments

<table>
<thead>
<tr>
<th></th>
<th>Plex original image</th>
<th>Binarized</th>
<th>Skeletonized</th>
<th>VAD (%)</th>
<th>VSD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCP</td>
<td>A1</td>
<td>A2</td>
<td>A3</td>
<td>45.5954</td>
<td>6.6569</td>
</tr>
<tr>
<td>DCP</td>
<td>B1</td>
<td>B2</td>
<td>B3</td>
<td>43.2459</td>
<td>6.0038</td>
</tr>
<tr>
<td>Full Retina</td>
<td>C1</td>
<td>C2</td>
<td>C3</td>
<td>46.8531</td>
<td>6.8945</td>
</tr>
</tbody>
</table>
**Mean VSD for Full Retina on the Plex**

- CoR calculation representative (0.45)

**Mean VSD of Plex Original Repeats and Registered for Full Retina**

- Bias calculation representative (-0.26)
Coefficient of Repeatability (CoR) was calculated to assess repeatability.

### Coefficient of Repeatability (CoR)

<table>
<thead>
<tr>
<th></th>
<th>Otsu VAD</th>
<th></th>
<th>Otsu VSD</th>
<th></th>
<th>Mean VAD</th>
<th></th>
<th>Mean VSD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Avanti</td>
<td>Cirrus</td>
<td>Plex</td>
<td>Avanti</td>
<td>Cirrus</td>
<td>Plex</td>
<td>Avanti</td>
</tr>
<tr>
<td>SCP</td>
<td>5.55</td>
<td>4.40</td>
<td>6.66</td>
<td>2.84</td>
<td>1.79</td>
<td>3.11</td>
<td>2.33</td>
</tr>
<tr>
<td>DCP</td>
<td>4.83</td>
<td>8.00</td>
<td>3.19</td>
<td>2.28</td>
<td>1.41</td>
<td>2.68</td>
<td>2.86</td>
</tr>
<tr>
<td>Full</td>
<td>7.14</td>
<td>8.00</td>
<td>3.19</td>
<td>2.68</td>
<td>1.41</td>
<td>2.68</td>
<td>2.86</td>
</tr>
</tbody>
</table>

Mean VSD for Full Retina on the Plex: 0.46

Difference of Repeat 1 - Repeat 2:

-0.5, 0, 0.5, 1

Mean of Repeat 1 and Repeat 2:

-0.44, 0.01
## Results-Ranges

### Otsu VAD

<table>
<thead>
<tr>
<th></th>
<th>Avanti</th>
<th>Cirrus</th>
<th>Plex</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCP</td>
<td>DCP</td>
<td>Full</td>
<td>SCP</td>
</tr>
<tr>
<td>7.73</td>
<td>4.27</td>
<td>9.74</td>
<td>6.09</td>
</tr>
</tbody>
</table>

### Otsu VSD

<table>
<thead>
<tr>
<th></th>
<th>Avanti</th>
<th>Cirrus</th>
<th>Plex</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCP</td>
<td>DCP</td>
<td>Full</td>
<td>SCP</td>
</tr>
<tr>
<td>3.72</td>
<td>1.90</td>
<td>4.56</td>
<td>2.22</td>
</tr>
</tbody>
</table>

### Mean VAD

<table>
<thead>
<tr>
<th></th>
<th>Avanti</th>
<th>Cirrus</th>
<th>Plex</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCP</td>
<td>DCP</td>
<td>Full</td>
<td>SCP</td>
</tr>
<tr>
<td>3.65</td>
<td>1.64</td>
<td>3.87</td>
<td>2.14</td>
</tr>
</tbody>
</table>

### Mean VSD

<table>
<thead>
<tr>
<th></th>
<th>Avanti</th>
<th>Cirrus</th>
<th>Plex</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCP</td>
<td>DCP</td>
<td>Full</td>
<td>SCP</td>
</tr>
<tr>
<td>2.45</td>
<td>1.43</td>
<td>2.48</td>
<td>1.24</td>
</tr>
</tbody>
</table>
## All Bias Values (Average difference between registered and unregistered)

<table>
<thead>
<tr>
<th></th>
<th>Avanti</th>
<th>Cirrus</th>
<th>Plex</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Otsu VAD</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SCP</td>
<td>2.632</td>
<td>-1.169</td>
<td>SCP</td>
</tr>
<tr>
<td>DCP</td>
<td>4.451</td>
<td>4.057</td>
<td>SCP</td>
</tr>
<tr>
<td>Full</td>
<td>2.761</td>
<td>1.344</td>
<td>DCP</td>
</tr>
<tr>
<td>SCP DCP Full</td>
<td>0.858</td>
<td>1.767</td>
<td>Full</td>
</tr>
<tr>
<td><strong>Otsu VSD</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SCP</td>
<td>1.101</td>
<td>-1.098</td>
<td>SCP</td>
</tr>
<tr>
<td>DCP</td>
<td>1.097</td>
<td>0.275</td>
<td>SCP</td>
</tr>
<tr>
<td>Full</td>
<td>0.822</td>
<td>-0.64</td>
<td>DCP</td>
</tr>
<tr>
<td>SCP DCP Full</td>
<td>-1.098</td>
<td>-0.228</td>
<td>Full</td>
</tr>
<tr>
<td><strong>Mean VAD</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SCP</td>
<td>1.512</td>
<td>1.536</td>
<td>SCP</td>
</tr>
<tr>
<td>DCP</td>
<td>2.588</td>
<td>2.416</td>
<td>SCP</td>
</tr>
<tr>
<td>Full</td>
<td>2.362</td>
<td>1.297</td>
<td>DCP</td>
</tr>
<tr>
<td>SCP DCP Full</td>
<td>1.536</td>
<td>1.411</td>
<td>Full</td>
</tr>
<tr>
<td><strong>Mean VSD</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SCP</td>
<td>0.679</td>
<td>-0.689</td>
<td>SCP</td>
</tr>
<tr>
<td>DCP</td>
<td>0.405</td>
<td>-0.511</td>
<td>SCP</td>
</tr>
<tr>
<td>Full</td>
<td>0.41</td>
<td>-0.686</td>
<td>DCP</td>
</tr>
<tr>
<td>SCP DCP Full</td>
<td>-0.689</td>
<td>-0.167</td>
<td>Full</td>
</tr>
</tbody>
</table>
Trends for All Layers for Mean VAD and Mean VSD Unregistered

SCP Mean VAD

DCP Mean VAD

Full Mean VAD

SCP Mean VSD

DCP Mean VSD

Full Mean VSD

Avanti  Cirrus  Plex

Avanti  Cirrus  Plex

Avanti  Cirrus  Plex

Avanti  Cirrus  Plex

Avanti  Cirrus  Plex

Avanti  Cirrus  Plex
Values and Comparisons after Registration

Mean VAD

- **Registered SCP**
  - Avanti: 43.34
  - Cirrus: 45.46
  - Plex: 47.19

- **Registered DCP**
  - Avanti: 44.20
  - Cirrus: 42.54
  - Plex: 43.19

- **Registered Full Retina**
  - Avanti: 45.96
  - Cirrus: 46.60
  - Plex: 48.83

Mean VSD

- **Registered SCP**
  - Avanti: 17.52
  - Cirrus: 12.05
  - Plex: 6.61

- **Registered DCP**
  - Avanti: 18.32
  - Cirrus: 10.97
  - Plex: 5.73

- **Registered Full Retina**
  - Avanti: 18.72
  - Cirrus: 12.45
  - Plex: 7.03
Unregistered vs Registered Mean VSD

** SCP Mean VSD unreg vs reg **

17.24 17.52 12.51 12.05 6.75 6.61
Avanti unreg Avanti reg Cirrus unreg Cirrus reg Plex unreg Plex reg

18.14 18.32 11.38 10.97 6.08 5.73
Avanti unreg Avanti reg Cirrus unreg Cirrus reg Plex unreg Plex reg

** DCP Mean VSD unreg vs reg **

18.57 18.72 13.07 12.45 7.29 7.03
Avanti unreg Avanti reg Cirrus unreg Cirrus reg Plex unreg Plex reg

ns

Full Mean VSD unreg vs reg

18.57 18.72 13.07 12.45 7.29 7.03
Avanti unreg Avanti reg Cirrus unreg Cirrus reg Plex unreg Plex reg
Similarity between Mean VSD and Otsu VSD

Mean VSD

Otsu VSD

Full Retina  | Superficial Layer  | Deep Layer
Avanti  |
Cirrus  |
Plex
Vessel Length (mm) Device Comparisons Across all Layers

<table>
<thead>
<tr>
<th>Device Comparison</th>
<th>Full Retina</th>
<th>Superficial Layer</th>
<th>Deep Layer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avanti-Cirrus</td>
<td>ns (p=0.107)</td>
<td>p&lt;0.0001</td>
<td>p=0.001</td>
</tr>
<tr>
<td>Avanti-Plex</td>
<td>ns (p=0.244)</td>
<td>p&lt;0.0001</td>
<td>p=0.042</td>
</tr>
<tr>
<td>Cirrus-Plex</td>
<td>ns (p=1)</td>
<td>ns (p=1)</td>
<td>ns (p=0.444)</td>
</tr>
</tbody>
</table>
## Specifications of OCTA Devices

<table>
<thead>
<tr>
<th></th>
<th>Cirrus HD-OCT</th>
<th>RTVue XR Avanti</th>
<th>Zeiss PLEX Elite 9000</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>OCT</strong></td>
<td>Spectral-domain</td>
<td>Spectral-domain</td>
<td>Swept-source</td>
</tr>
<tr>
<td><strong>Wavelength</strong></td>
<td>~840 nm</td>
<td>~840 nm</td>
<td>~1060 nm</td>
</tr>
<tr>
<td><strong>Acquisition speed</strong></td>
<td>68,000 (A-Scans/second)</td>
<td>70,000 (A-Scans/second)</td>
<td>100,000 (A-Scans/second)</td>
</tr>
<tr>
<td><strong>A-scan depth</strong></td>
<td>2 mm</td>
<td>~ 3mm</td>
<td>3 mm</td>
</tr>
<tr>
<td><strong>Available default OCTA scan protocols</strong></td>
<td>3x3, 6x6 mm centered on macula</td>
<td>3x3, 6x6, 8x8 mm centered on macula; 3x3, 4.5x4.5 mm centered on ONH</td>
<td>3x3, 6x6, 9x9, 12x12 mm centered on macula (montage available with manual positioning of focus point)</td>
</tr>
</tbody>
</table>
# Specifications of OCTA Devices

## Continued

<table>
<thead>
<tr>
<th></th>
<th>Cirrus HD-OCT</th>
<th>RTVue XR Avanti</th>
<th>Zeiss PLEX Elite 9000</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Axial resolution</strong></td>
<td>5 microns</td>
<td>5 microns</td>
<td>6.3 microns</td>
</tr>
<tr>
<td><strong>Transverse resolution</strong></td>
<td>15 microns</td>
<td>15 microns</td>
<td>20 microns</td>
</tr>
<tr>
<td><strong>Acquisition Scan</strong></td>
<td>1 acquisition scan with eye-tracking</td>
<td>2 co-registered acquisition scans with eye tracking</td>
<td>1 acquisition scan with eye-tracking</td>
</tr>
<tr>
<td><strong>B-scans/cube</strong></td>
<td>245 (repeated 4x at each position for 3x3mm) 350 (repeated 2x at each position for 6x6mm)</td>
<td>304 (repeated 2x at each position in X and Y direction)</td>
<td>300 (repeated 3x at each position for 3x3mm) 500 (repeated 2x for 6x6, 9x9, and 12x12mm)</td>
</tr>
<tr>
<td><strong>Acquisition Time</strong></td>
<td>~3.5 seconds</td>
<td>~3 seconds</td>
<td>~2.6 seconds for 3x3 ~5 seconds for 6x6</td>
</tr>
<tr>
<td><strong>Algorithm</strong></td>
<td>OMAG</td>
<td>SSADA</td>
<td>OMAG</td>
</tr>
</tbody>
</table>
VSD decreases with increasing number of averaging frames

SRL: greatest reduction in VLD occurs with averages of 2-5 frames

DRL: greatest reduction in VSD occurs with averages of at least 3-6 frames