Impaired Layer Specific Retinal Vascular Reactivity Among Diabetic Subjects

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Conclusions

• We developed an *in vivo* OCTA based assay of human retinal capillary reactivity in response to physiologic changes in inhaled oxygen and carbon dioxide.

• Compared to non-diabetic controls we found significant attenuation or complete loss of capillary reactivity to hypercapnia and hyperoxia in both the superficial and deep retinal capillaries of subjects with diabetes and minimal to no diabetic retinopathy.

• Our results were not changed when we included relatively large caliber arterioles or venules in our analysis. This suggests retinal vascular reactivity is mediated by changes in capillary properties.

• OCTA based retinal vascular reactivity assessment in humans is feasible and may play a useful role in detecting impaired capillary function before onset of clinically apparent diabetic retinopathy.
Vascular tissue is designed to modulate blood flow in response to physiologic stimuli such as changes in inhaled oxygen and carbon dioxide.

In 2019 we published a novel method of assessing changes in retinal vascular reactivity to physiologic manipulations of inhaled oxygen and carbon dioxide.
Retinal Vascular Reactivity Assessment via OCTA

Full Thickness OCTA of Normal Human Subject Breathing Various Gas Mixtures

O$_2$  Room Air  CO$_2$

Retinal vascular reactivity in diabetic subjects is impaired.

Impairment is more profound to hypercarbia than hyperoxia

To investigate layer specific and vessel caliber specific retinal vascular reactivity in healthy controls and subjects with mild non-proliferative diabetic retinopathy (NPDR) or no diabetic retinopathy (DR).
Methods: Gas Delivery System

OCTA acquired using SS-OCTA system (Carl Zeiss PLEX Elite 9000) during room air, 5% CO₂, or 100% O₂ delivery

Methods: Scan Segmentation

3x3mm OCTA acquired using SS-OCTA system (Carl Zeiss PLEX Elite 9000)

Automated segmentation of SRL and DRL performed

Segmentation was manually reviewed for each subject
Methods: Morphometric Measures

Vessel Skeleton Density (VSD) = \frac{\sum_{(i,j)}^{n} L(i,j)}{\sum_{(i,j)}^{n} X(i,j)}

Vessel Area Density (VAD) = \frac{(\sum_{(i,j)}^{n} B(i,j))^2}{(\sum_{(i,j)}^{n} X(i,j))^2}

where \( L_{(i,j)} \) represents pixels occupied by blood vessel length (white pixels in the skeletonized image) and \( X_{(i,j)} \) are all pixels in the skeletonized image.

where \( B_{(i,j)} \) represents pixels occupied by blood vessels (white pixels in the binarized image) and \( X_{(i,j)} \) are all pixels in the binarized image.

Methods: Large Vessel Exclusion

Original Image

Original Image with Large Vessel Removal

Skeletonized Image with Large Vessel Removal

(Singer M et al., in submission)
### Results: Subject Demographics

#### Disease Classification

<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>Diabetics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (Subjects)</td>
<td>41</td>
<td>22</td>
</tr>
<tr>
<td>Age</td>
<td>53.0 ± 18.9</td>
<td>53.7 ± 16.7</td>
</tr>
<tr>
<td>Female Gender</td>
<td>20 (48.8%)</td>
<td>9 (40.9%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>10 (24.4%)</td>
<td>6 (27.3%)</td>
</tr>
<tr>
<td>Severity of diabetic retinopathy</td>
<td>N/A</td>
<td>15 no DR, 7 mild NPDR</td>
</tr>
</tbody>
</table>

(Singer M et al., in submission)
Results: Superficial Retinal Layer

Retinal vascular reactivity to CO$_2$ is absent in superficial retinal layer of diabetic subjects

(Singer M et al., in submission)
Results: Deep Retinal Layer

Retinal vascular reactivity to CO$_2$ and O$_2$ is impaired in deep retinal layer of diabetic subjects

(Singer M et al., in submission)
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(Singer M et al., in submission)
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