Supplementary Figure S1. Calculating center-to-center cone spacing (c).

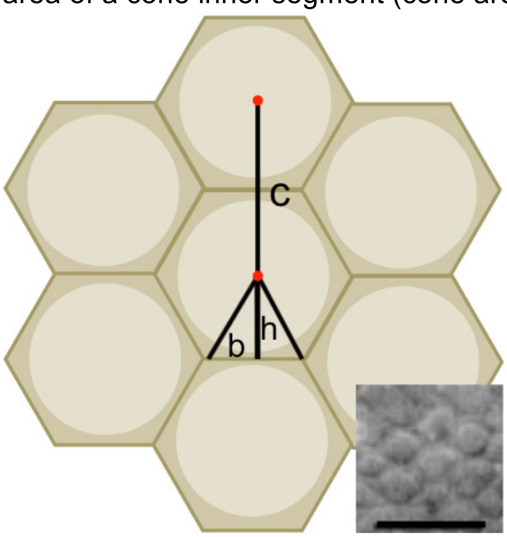
The packing of cone photoreceptor inner segments and Müller cells at the external limiting membrane is a triangular array with hexagonal elements (example from a human retina flatmount, inset. Scale bar, 10µm. [Adapted with permission[13]]). Light tan circles are inner segments in cross-section, and red dots are centers. The darker tan is the Müller cells that surround each cone, and edges of hexagons (which do not represent anatomical structures) are shown as lines. At light microscopy resolution in Figure 6, we assume that the width of the bounding hexagon is the same as the diameter of the cone inner segment, which can be measured in a flatmount retina. The area of each hexagon can be determined from 12 right triangles that make it up. Two of these triangles are shown. Each triangle has a height (h) and base (b).

h = ${}^{1}\!/_{2}\ c$ and b = $\frac{{}^{1}\!/_{2} \times c}{\sqrt{3}} = \frac{1}{c \times 2\sqrt{3}}$

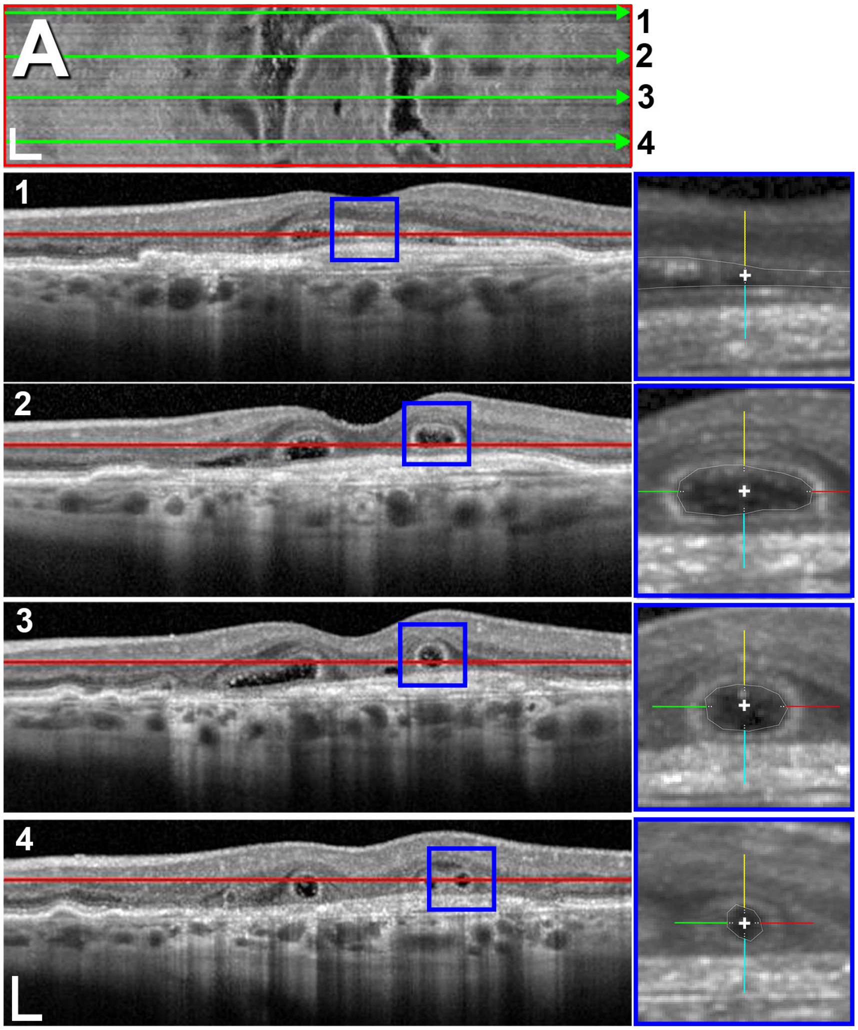
Area of one triangle = ${}^{1}\!/_{2} \times (b \times h) = {}^{1}\!/_{2} \times \frac{1}{c \times 2\sqrt{3}} \times {}^{1}\!/_{2}\ c$

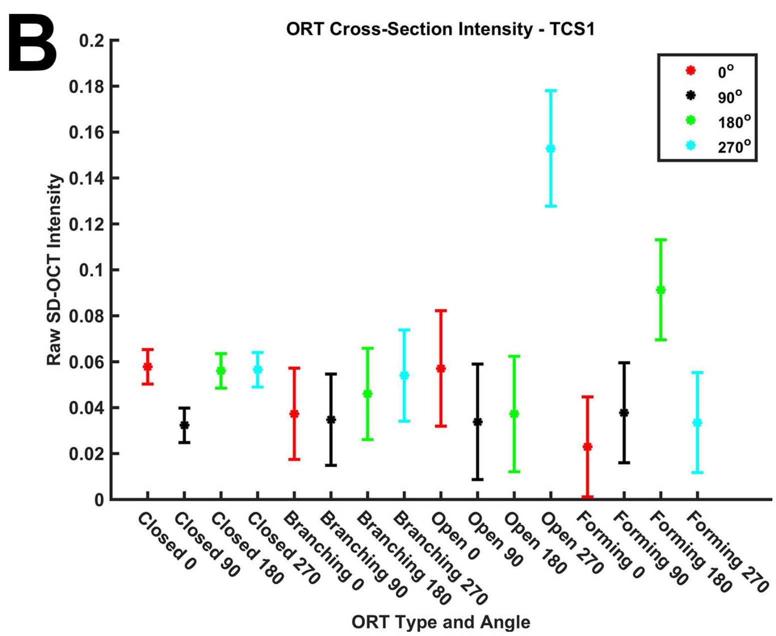
Area of 12 triangles = 1 hexagon = $\frac{\sqrt{3}}{2} \times c^2$

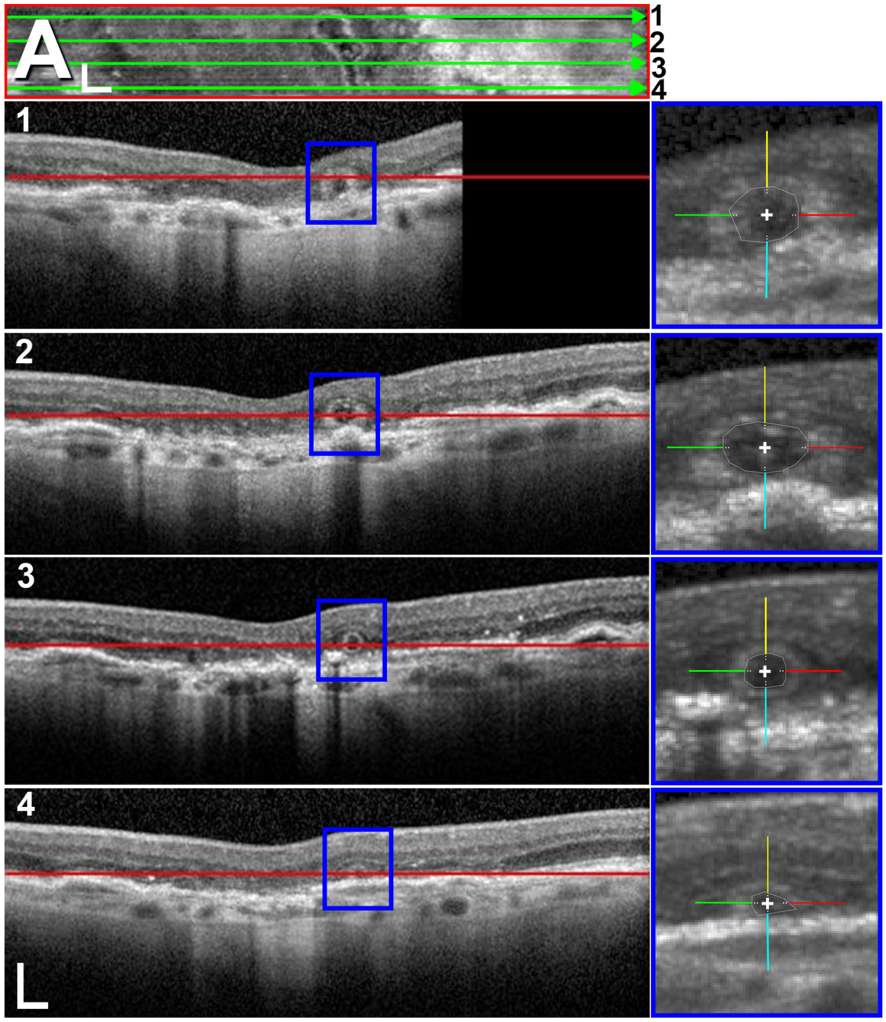
Rearranging this formula, c = $\sqrt{\frac{2 \times Hexagon\ area}{\sqrt{3}}}$, where hexagon area is the cross-sectional area of a cone inner segment (cone area).

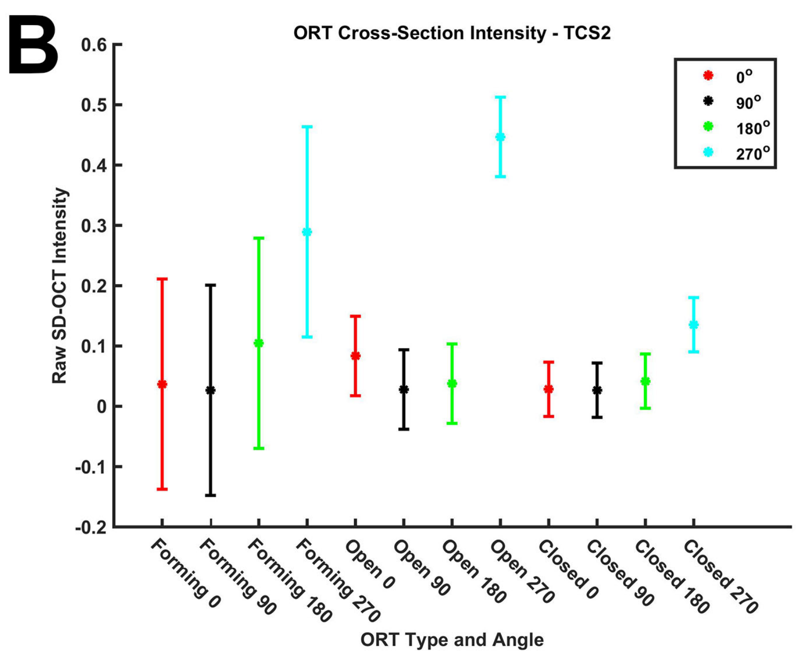


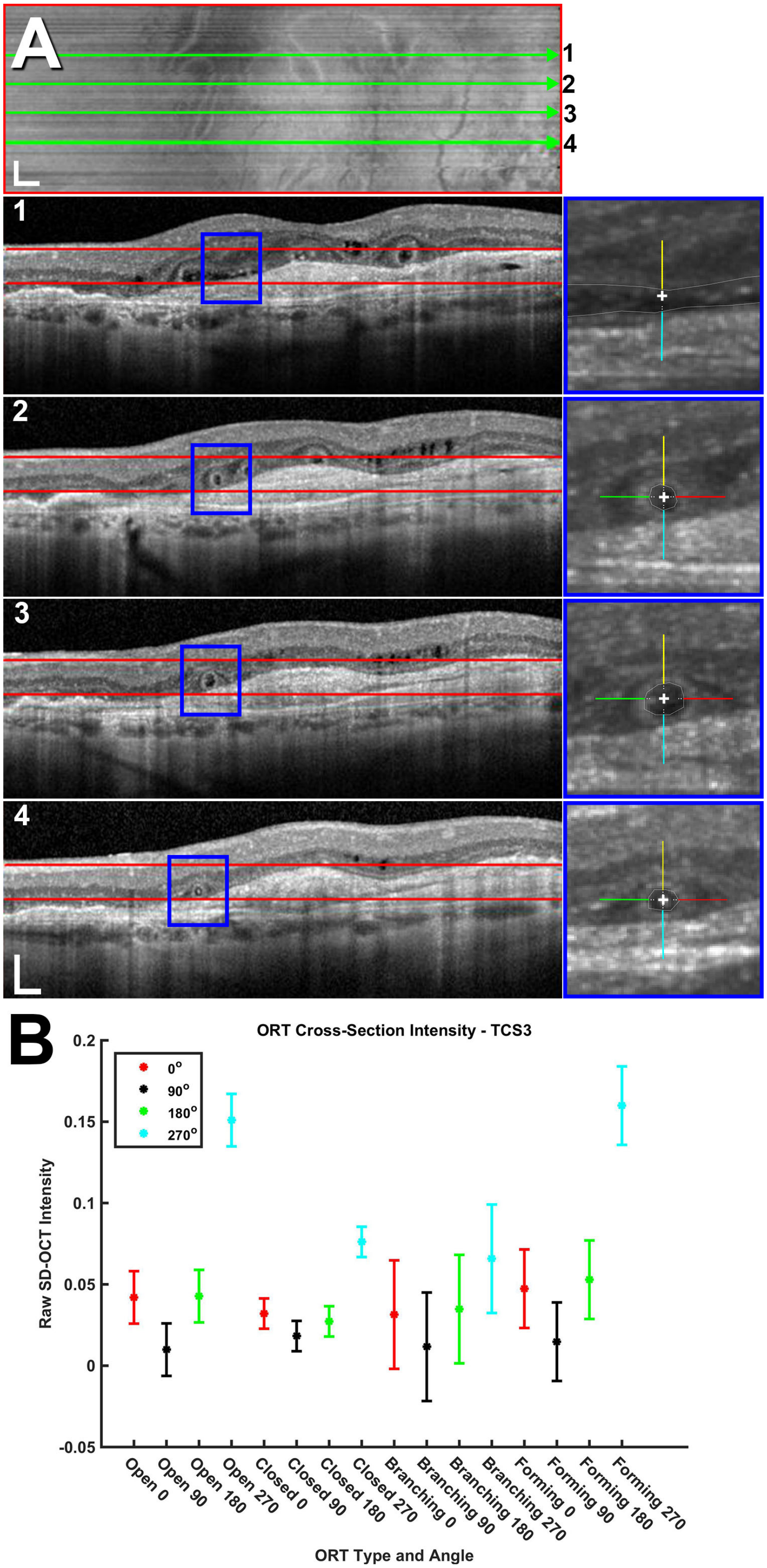
Supplementary Figure S2. Outer retinal tubulation network in spectral domain optical coherence tomography for TCS1-10. (A) En face SD-OCT scan showing complex connected ORT network. Green lines are levels of SD-OCT scans 1-4 spaced 275 μm apart, for 25 scans (TCS1), 154 μm apart, for 14 scans (TCS2), 220 μm apart, for 20 scans (TCS3), 66 μm apart, for 6 scans (TCS4), 275 μm apart, for 25 scans (TCS5), 418 μm apart, for 38 scans (TCS6), 418 μm apart, for 38 scans (TCS7), 60 μm apart for 6 scans (TCS8), 121 μm apart, for 11 scans (TCS9), and 253 μm apart, for 23 scans (TCS10) apart. Red lines in SD-OCT scans are at the levels of en face reconstruction (Heidelberg Spectralis). Blue boxes are higher magnification ORT cross-sections demonstrating ORT hyperreflective band intensity measurements at 0° (red), 90° (yellow), 180° (green), 270° (cyan) around ORT cross-section. Each line of the cross in the centroid of ORT cross-sections is 20 μm long (blue boxes). (B) Average raw (linear) SD-OCT Intensity (ranging from 0-1) by ORT type and angle sampled at 5 μm steps from the inner aspect of ORT band, representing 0 distance. Error bars, 95% confidence interval.


A
1
2
3
4

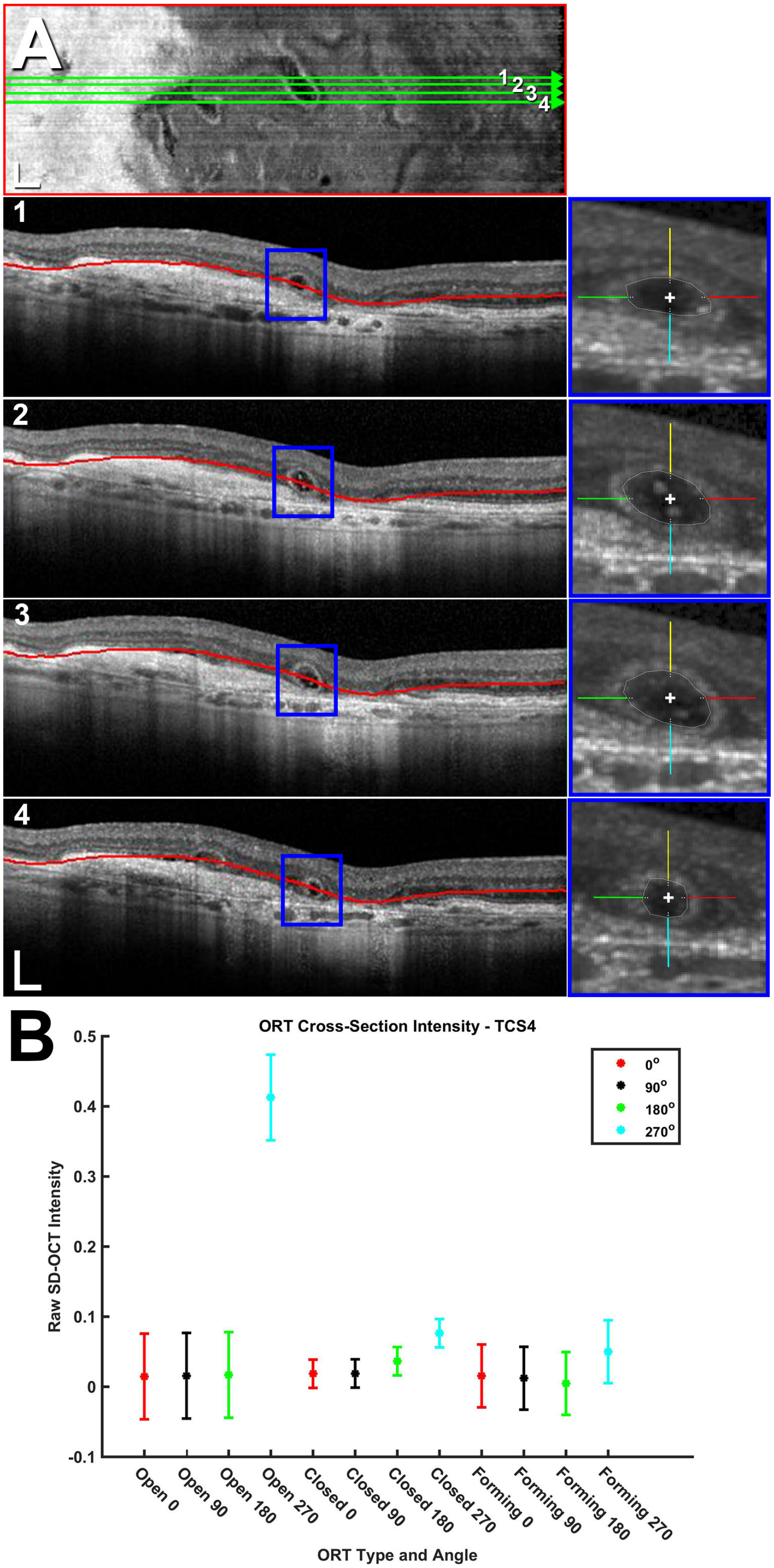

B
ORT Cross-Section Intensity - TCS1
Raw SD-OCT Intensity
ORT Type and Angle
0°
90°
180°
270°
Closed 0
Closed 90
Closed 180
Closed 270
Branching 0
Branching 90
Branching 180
Branching 270
Open 0
Open 90
Open 180
Open 270
Forming 0
Forming 90
Forming 180
Forming 270

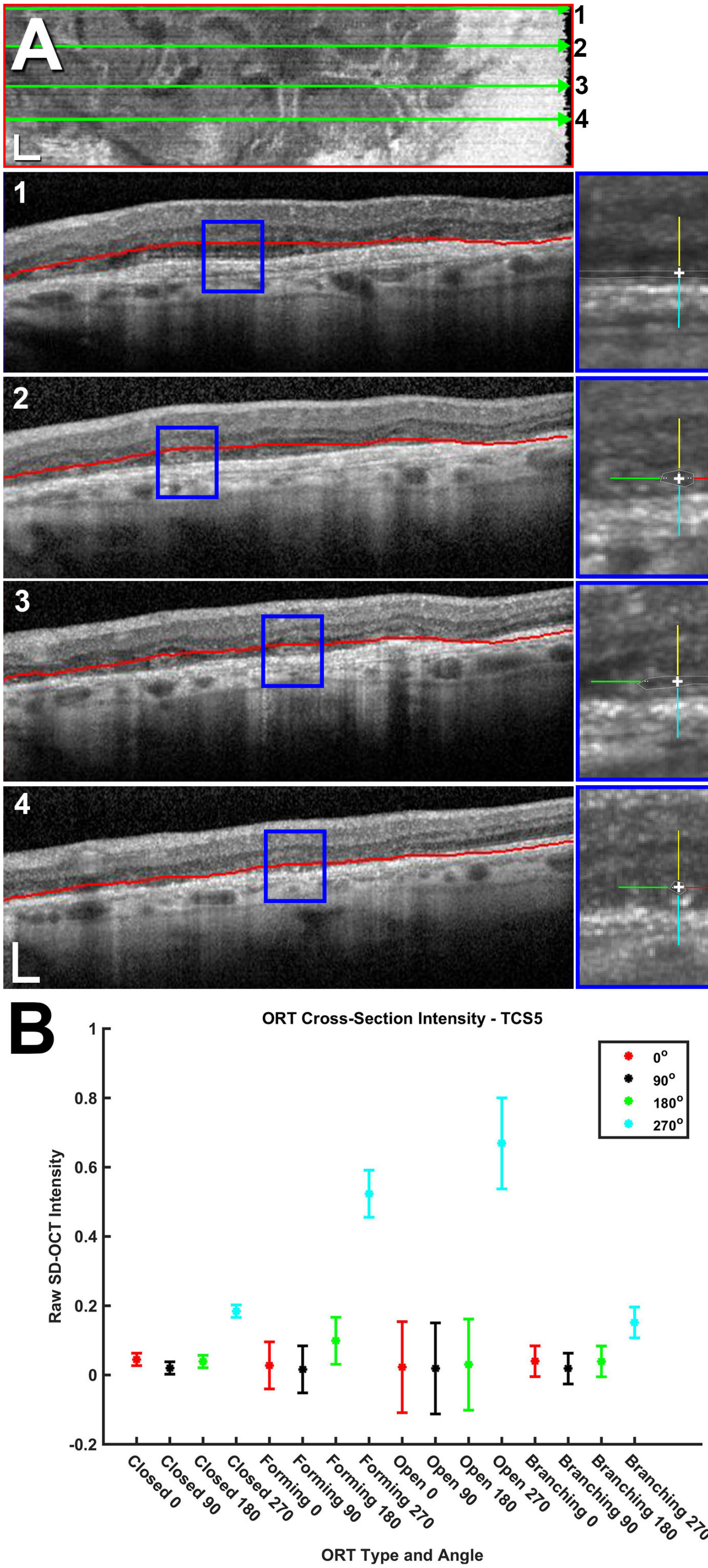

A
L
1
2
3
4
1
2
3
4
L

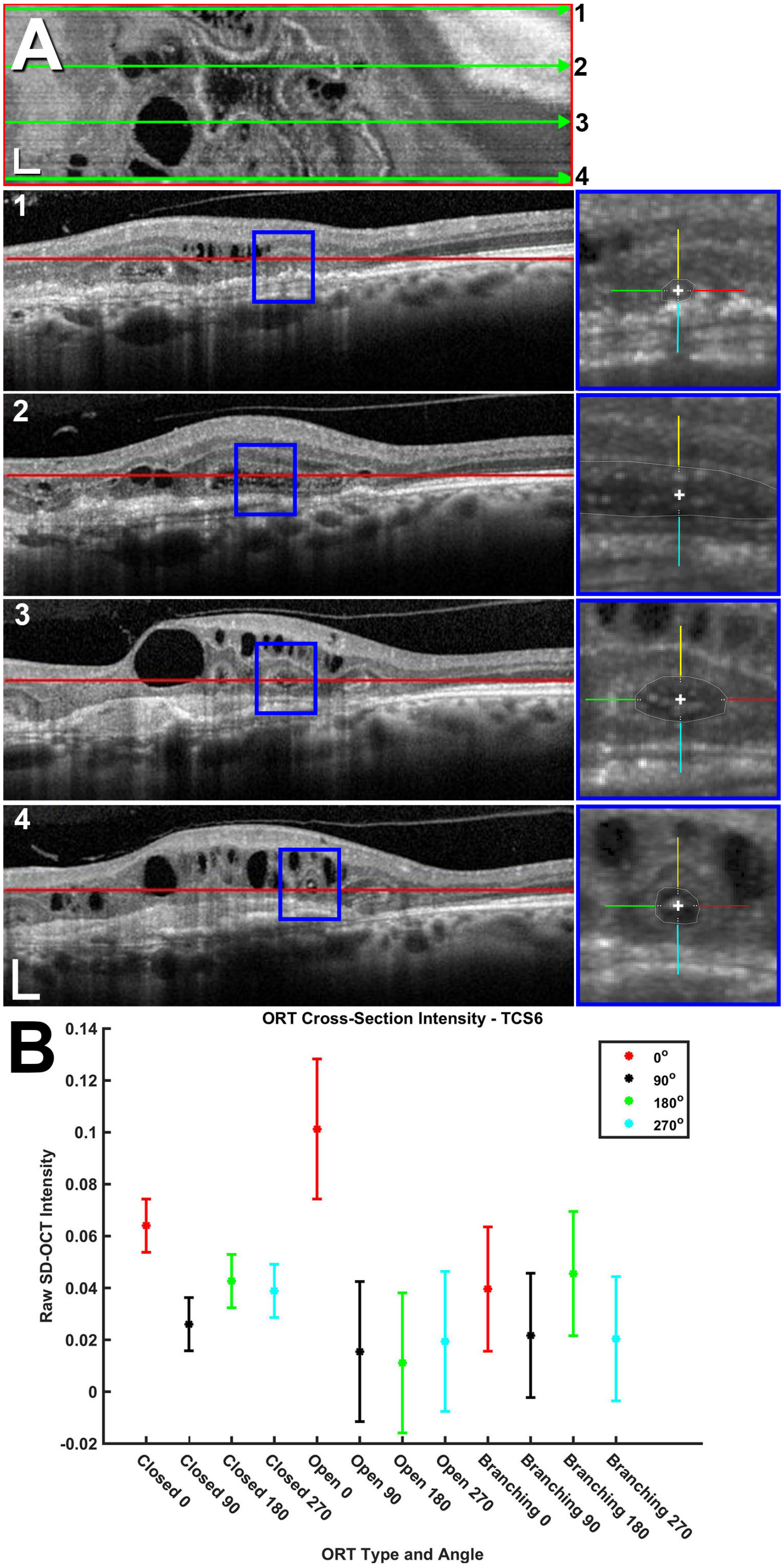

B
ORT Cross-Section Intensity - TCS2
0°
90°
180°
270°
Raw SD-OCT Intensity
0.6
0.5
0.4
0.3
0.2
0.1
0
-0.1
-0.2
Forming 0
Forming 90
Forming 180
Forming 270
Open 0
Open 90
Open 180
Open 270
Closed 0
Closed 90
Closed 180
Closed 270
ORT Type and Angle

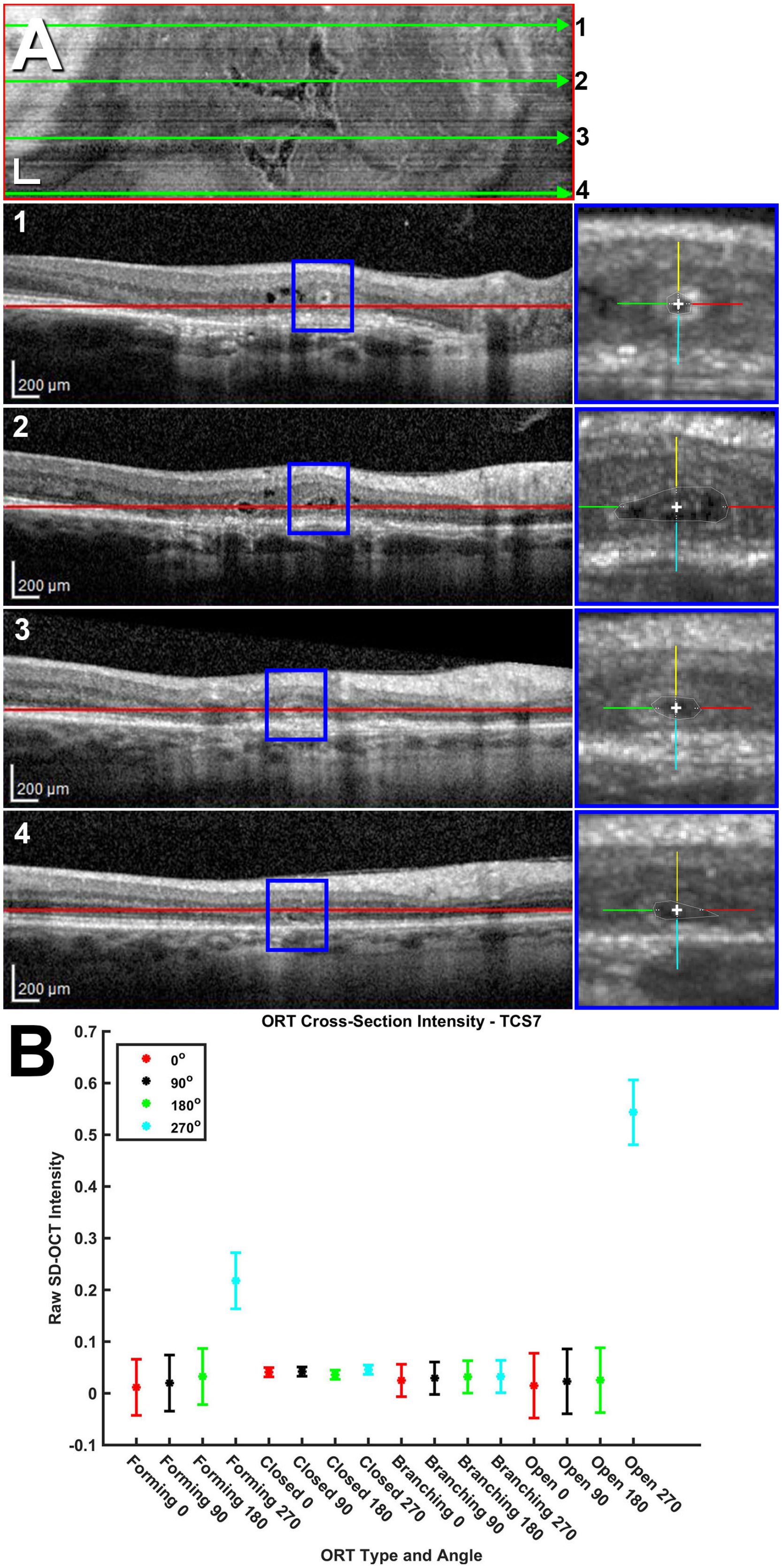

A
1
2
3
4
B
ORT Cross-Section Intensity - TCS3
0°
90°
180°
270°
Raw SD-OCT Intensity
0.2
0.15
0.1
0.05
0
-0.05
Open 0
Open 90
Open 180
Open 270
Closed 0
Closed 90
Closed 180
Closed 270
Branching 0
Branching 90
Branching 180
Branching 270
Forming 0
Forming 90
Forming 180
Forming 270
ORT Type and Angle

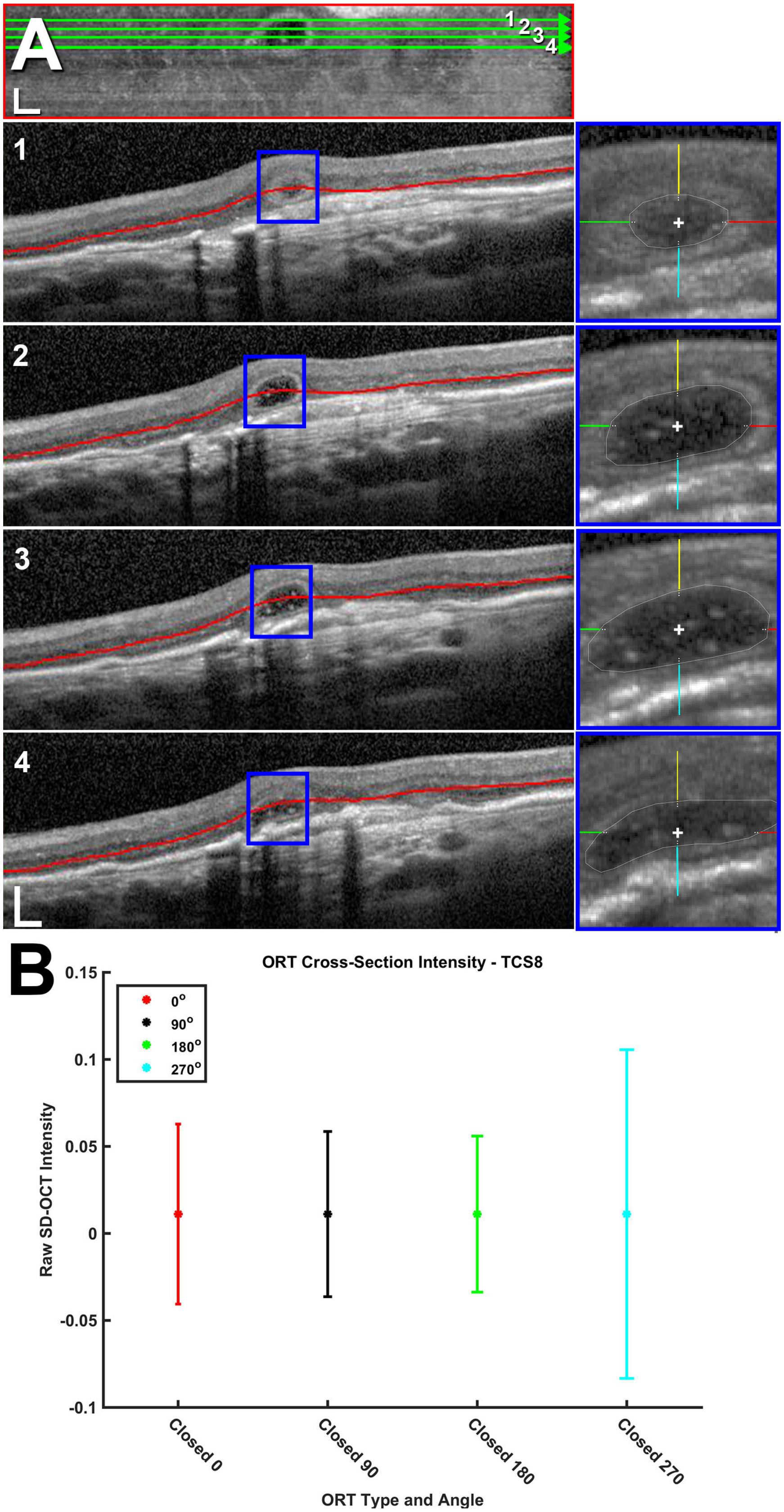
Litts, Ach, Hammack, Sloan, Zhang, Freund, Curcio: Quantitative analysis of outer retinal tubulation in age-related macular degeneration from spectral domain optical coherence tomography and histology. IOVS.

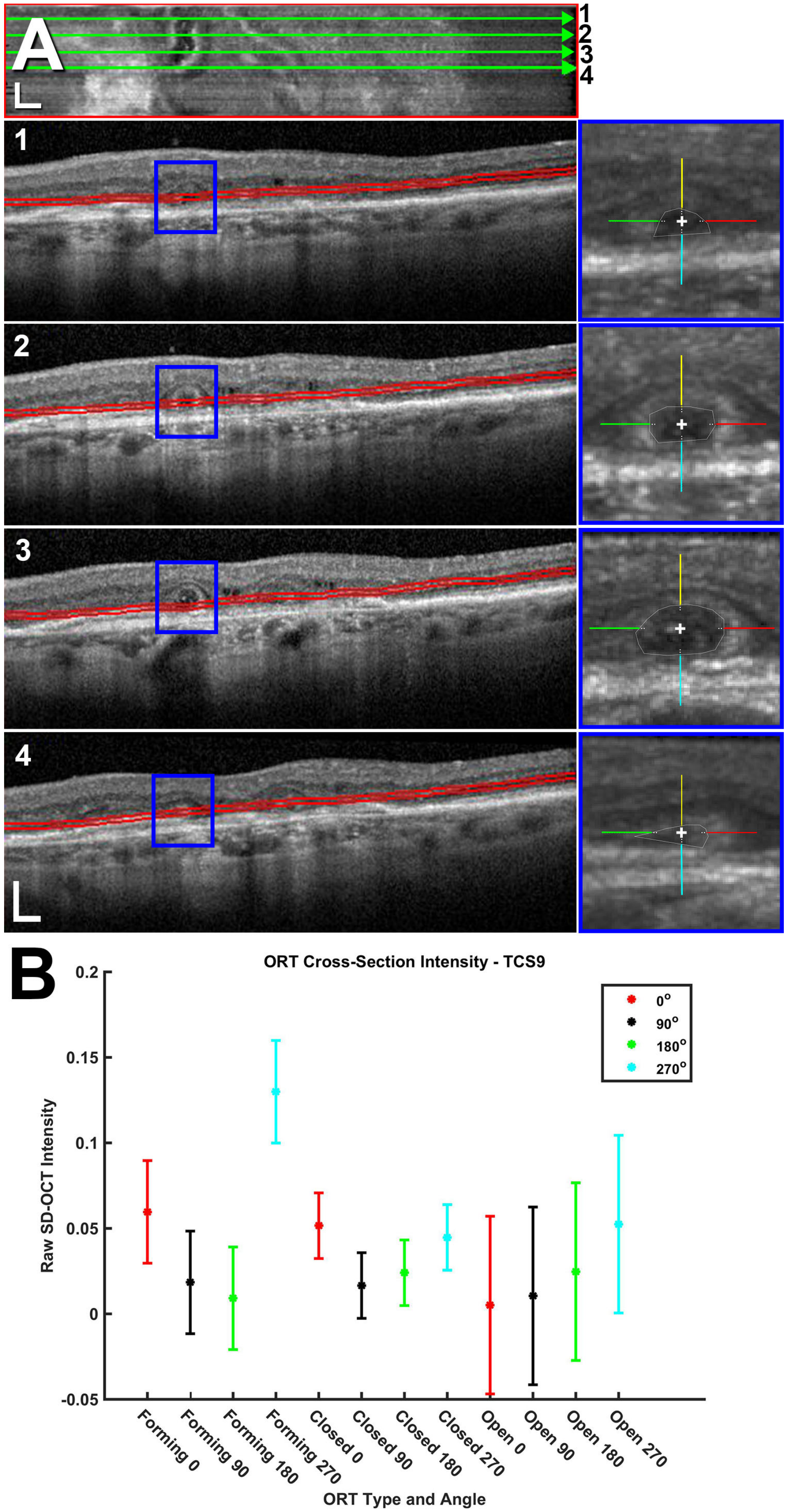


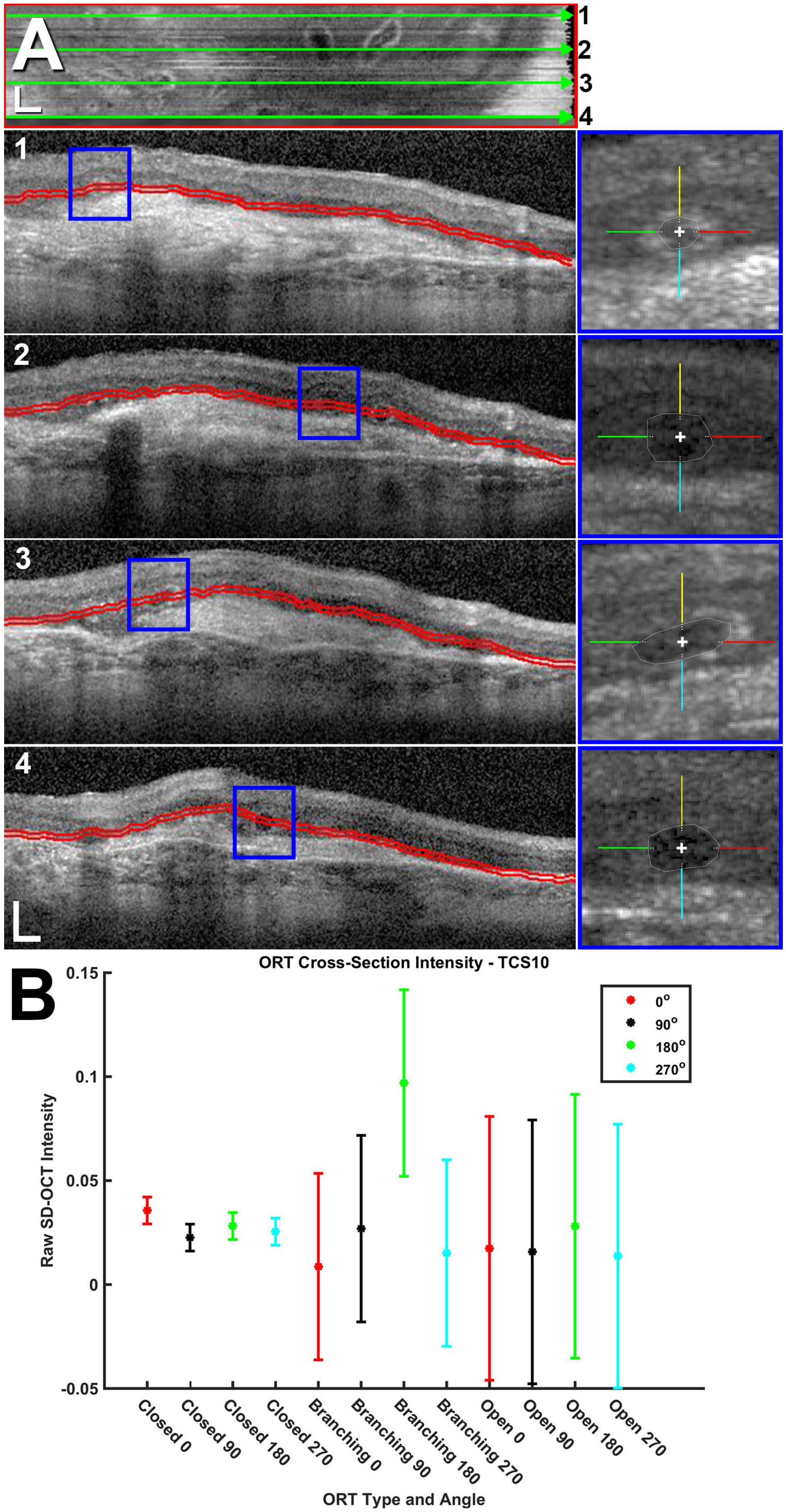

A
1
2
3
4
B
ORT Cross-Section Intensity - TCS5
0°
90°
180°
270°
Raw SD-OCT Intensity
1
0.8
0.6
0.4
0.2
0
-0.2
Closed 0
Closed 90
Closed 180
Closed 270
Forming 0
Forming 90
Forming 180
Forming 270
Open 0
Open 90
Open 180
Open 270
Branching 0
Branching 90
Branching 180
Branching 270
ORT Type and Angle


A
1
2
3
4
B
ORT Cross-Section Intensity - TCS6
0°
90°
180°
270°
Raw SD-OCT Intensity
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
-0.02
Closed 0
Closed 90
Closed 180
Closed 270
Open 0
Open 90
Open 180
Open 270
Branching 0
Branching 90
Branching 180
Branching 270
ORT Type and Angle


A
1
2
3
4
200 µm
200 µm
200 µm
200 µm
B
ORT Cross-Section Intensity - TCS7
0°
90°
180°
270°
Raw SD-OCT Intensity
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
-0.1
Forming 0
Forming 90
Forming 180
Forming 270
Closed 0
Closed 90
Closed 180
Closed 270
Branching 0
Branching 90
Branching 180
Branching 270
Open 0
Open 90
Open 180
Open 270
ORT Type and Angle


A
1
2
3
4
B
ORT Cross-Section Intensity - TCS8
0°
90°
180°
270°
Raw SD-OCT Intensity
0.15
0.1
0.05
0
-0.05
-0.1
Closed 0
Closed 90
Closed 180
Closed 270
ORT Type and Angle


A
1
2
3
4
B
ORT Cross-Section Intensity - TCS9
0°
90°
180°
270°
Raw SD-OCT Intensity
0.2
0.15
0.1
0.05
0
-0.05
Forming 0
Forming 90
Forming 180
Forming 270
Closed 0
Closed 90
Closed 180
Closed 270
Open 0
Open 90
Open 180
Open 270
ORT Type and Angle


A
1
2
3
4
B
ORT Cross-Section Intensity - TCS10
Raw SD-OCT Intensity
0.15
0.1
0.05
0
-0.05
0°
90°
180°
270°
Closed 0
Closed 90
Closed 180
Closed 270
Branching 0
Branching 90
Branching 180
Branching 270
Open 0
Open 90
Open 180
Open 270
ORT Type and Angle