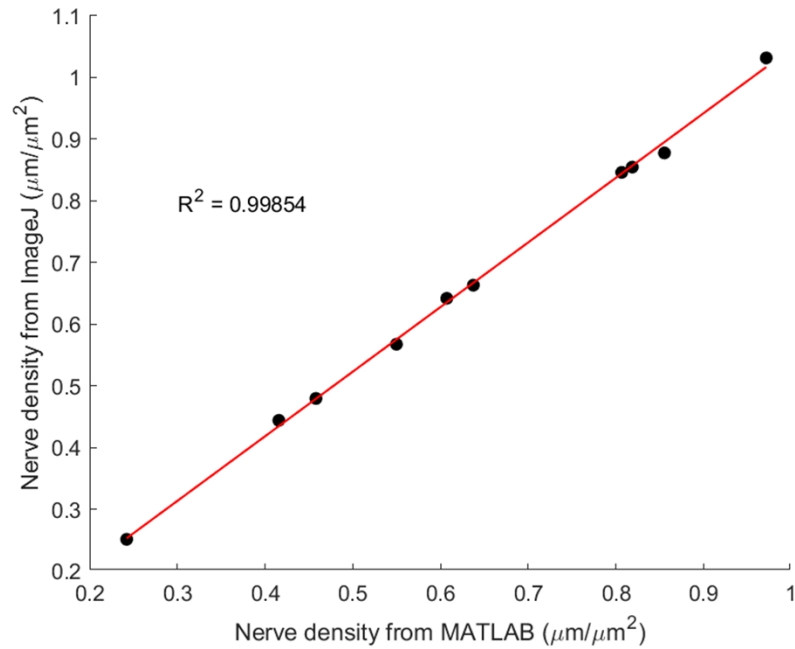
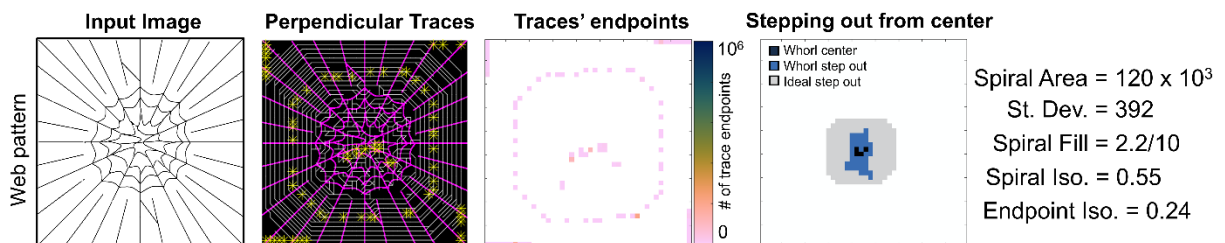


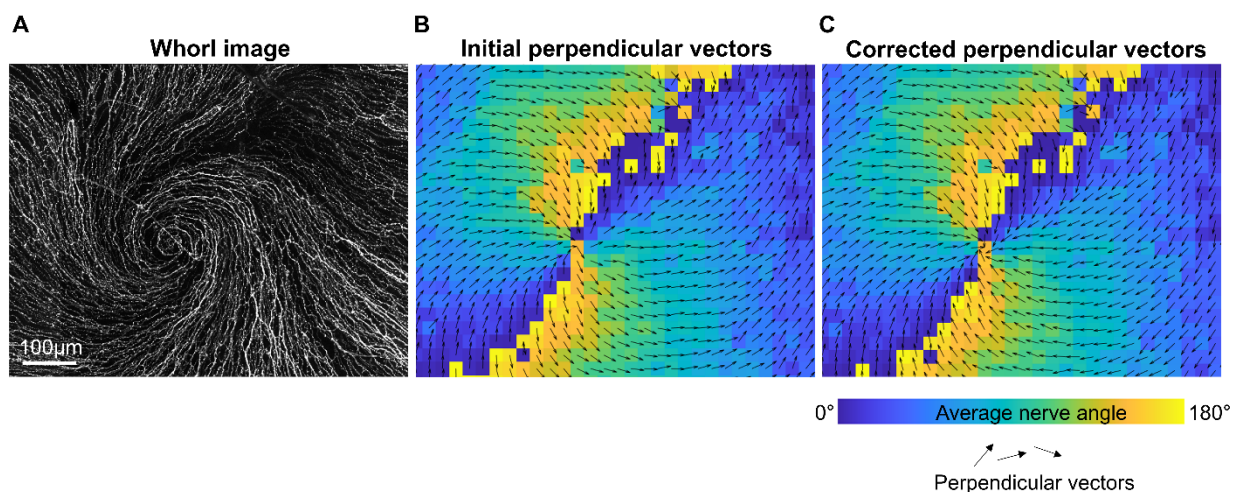
Supplementary materials



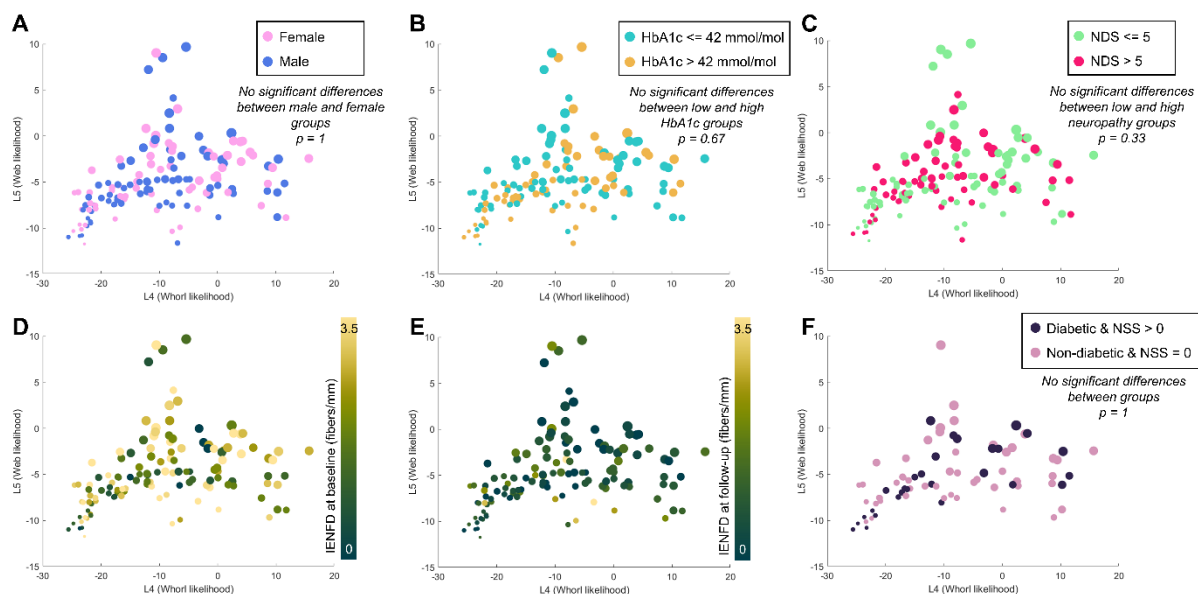
Supplemental Figure 1: Nerve density calculated using NeuronJ, an ImageJ plugin, compared to our MATLAB algorithm for 10 randomly selected human cornea images displaying a range of nerve density. $R^2=0.99854$.



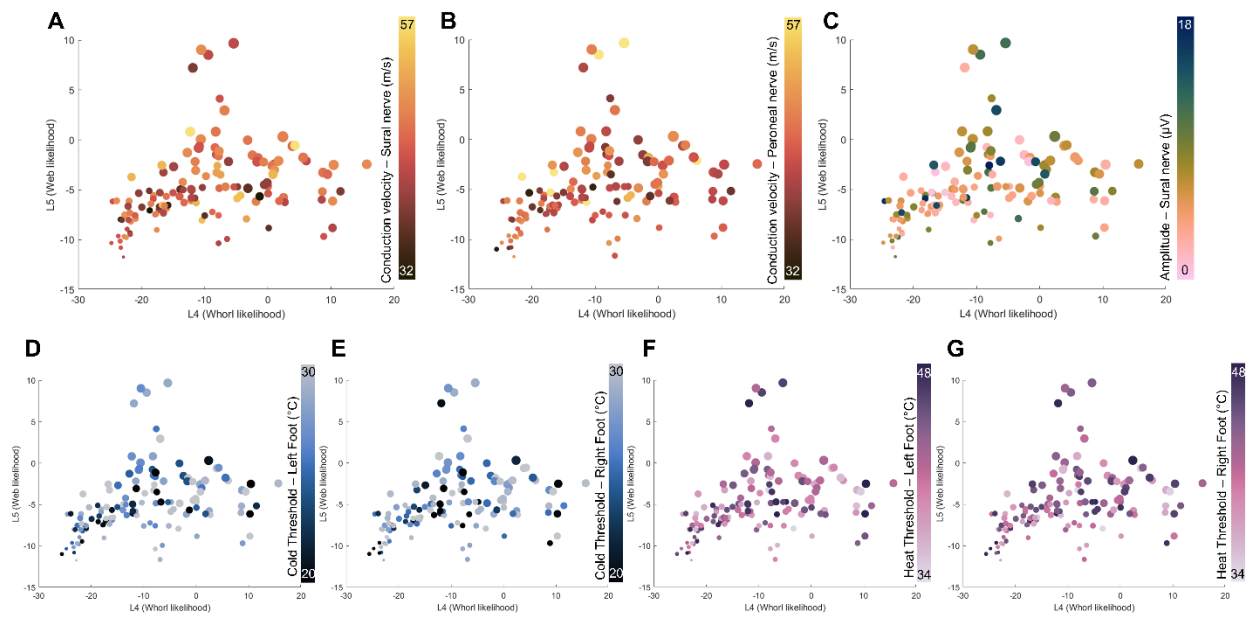
Supplemental Figure 2: Demonstration of whorl metrics on a synthetic image of a web pattern which leads to a “ring” of trace endpoints. To detect the presence of this ring, the isotropic endpoint score (Endpoint Iso.) is calculated as the coefficient of variance of the trace endpoints in the 45° slices around the center. A low isotropic endpoint score (<0.5) indicates that endpoints are equally numerous in all directions around the center, indicating the presence of a ‘ring’.



Supplemental Figure 3: Creating the vectors perpendicular to the nerves. **(A)** Example mouse whorl image with a counterclockwise orientation. **(B)** Perpendicular vectors (arrows) calculated for each image patch based on the average nerve angle in each patch. **(C)** Corrected vectors where the vector angles were kept as-is or rotated by 180° so that the vectors are pointing preferably clockwise and toward the whorl center. If the whorl had a clockwise orientation in (A), the perpendicular vectors in (C) would be corrected to preferably point counterclockwise.



Supplemental Figure 4: Comparison of whorl shapes for different patient populations. Corneas are plotted on axes representing the whorl likelihood (x-axis) and web pattern likelihood (y-axis) following linear discriminant analysis. Individual corneas are colored based on **(A)** sex, **(B)** blood HbA1c scores, **(C)** neuropathy disability scores (NDS), **(D)** intraepidermal nerve fiber density (IENFD) measured at baseline, 10 years prior to IVCM imaging, and **(E)** current IENFD results. **(F)** Only corneas from patients with diabetes and a non-zero neuropathy symptom score (NSS) vs non-diabetic subjects with a NSS of zero. For results in A, B, C, and F, the Peacock's test is used to test for significant differences between populations. Peacock's test is not appropriate for continuous distributions as in D and E.



Supplemental Figure 5: Comparison of whorl shapes as a function of different assessments for neuropathy. Conduction velocity in (A) the sural nerve and (B) peroneal nerve, (C) amplitude of the sural nerve, cold threshold in (D) the left foot, and (E) right foot, and heat threshold in (F) the left foot and (G) the right foot.