Quantitative glaucoma indices commonly rely on geometric parameters of the optic nerve head (ONH) such as disk area or cup volume. However, the ONH is a too complex structure to be accurately analyzed by geometric morphometry because of:

- Sparse sampling of ONH
- Lack of mathematically derived and biologically interpretable ONH descriptions [2]

**Purpose**

We provide dense descriptions of the ONH variability in glaucomatous cases presented by tissue deformations.

**Data**

Erlangen Glaucoma Registry (Figure 1)

- Color fundus photographs (Kowa non-myd, FOV 22.5°, ONH centered)
- Gold standard for glaucoma diagnosis is present
  - Diagnosis by an experienced ophthalmologist
  - Complete ophthalmological examination (ophthalmoscopy, visual field test, IOP, FDT, HRT II)

**Dataset characteristics**

- Mean age 55.4 ± 10.9 years
- ONH area 2.2 ± 0.5 mm² (Macro ONH not included)
- 149 glaucoma cases \( I_g \) (FDT test time 67.4 ± 35.6 s)
- 246 controls \( I_c \)

**Methods**

1. Fundus image preprocessing [1]
   - Normalized optic nerve head images by eliminating disease independent variations (Figure 1) such as
     - Illumination inhomogeneities
     - ONH normalization
     - Vessel structures.

2. Non rigid image registration
   - Characterization of inter subject ONH variability by dense deformation fields \( U \) calculated between one reference image \( R \) and image samples \( T \in I \)
   - Variational multilevel approach
     \[ D(I, T) = \sum_i D_i + \sum_i S_i(T_i) \]
   - Distance measure \( D \): Sum of squared differences
   - Smoother \( S \): Diffusion regularizer

3. Deformation based reference ONH
   - ONH reference image \( R \) that is characterized by the minimal average residual deformation over a sample set \( I \)
   - Reference \( R \): Selection of initial estimate as the average of sample set \( I \)
   - Calculation of deformation fields \( U \), between samples \( I \), and current reference \( R \)
   - Average deformation field: \( U_{avg} = \frac{1}{N} \sum U_i \)
   - Deformation of reference \( R(U_{avg}) \) by average deformation field \( U_{avg} \)

4. Isolation of abnormal variations
   - from captured deformation field which is distorted by overlaid control deformations.
   - Deformation field \( U \) between reference ONH \( R \) and a sample
   - Model healthy ONH variability by Principal Component Analysis (PCA) on deformation fields \( U \) of controls \( I \)
   - Crop deformations by the fraction represented by PCA model of controls

5. Statistical deformation model (SDM) of ONH
   - to provide a mathematically derived and biologically interpretable description of ONH variability in glaucomatous optic atrophy.
   - PCA model on deformations \( U \) of
     - control samples \( I_c \)
     - glaucomatous cases \( I_g \)
   - Supervised attribute selection on modes
     - Identification of modes most discriminating between controls and glaucomatous

**Results and Discussion**

1. Deformation based reference ONH
   - Figure 2: Comparison of pixel wise averaging (a,b) and deformation based averaging (c,d) of ONH reflectance images. (a,c) control, (b,d) glaucoma. Pixel wise averages (a,b) are too smooth to identify local structures. Deformation based averaging (c,d) clearly shows a structural thinning of the upper rim in case of glaucoma (d) compared to control reference (c) (red arrows).

2. Isolation of abnormal deformations
   - Figure 3: Isolation of abnormal deformations: (a,b) control, (c,d) glaucoma. (a,c) Captured deformations between test sample and reference. Abnormal deformations overlaid by high amount of control deformations. (b,d) isolated abnormal deformations showing an increased cupping for the glaucomatous case (d) (red: high magnitude, blue: low magnitude of deformation vector).

**Conclusion**

Statistical deformation modelling of ONH provides

- Intuitive representation of ONH variability
- Main modes of glaucomatous deformations
- Identification of abnormal deformations.

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**References**
