Statistical Deformation Modeling of the Optic Disk

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Background

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 $\pm$ 10.9 years
- ONH area 2.2 $\pm$ 0.5 mm^2 (Macro ONH not included)
- 149 glaucoma cases I_g (FDT test time 67.4 $\pm$ 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.

(a) (b) (c)

Figure 1: Preprocessing to eliminate disease independent variations: (a) cropped original fundus image, (b) illumination corrected reflectance image with normalized ONH location, (c) inpainted 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
     $D(R(U), T) + s \cdot S(U) \xrightarrow{u} \min$
   - 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 is calculated by an iterative procedure:
   - Reference R: Selection of initial estimate as the average of sample set I
   - Calculation of deformation fields U_i between samples I_i and current reference R
   - Average deformation field: $U_{avg} = \frac{1}{N}\Sigma_{i=0}^{N} U_i$
   - Deformation of reference $R(U_{avg})$ by average deformation field U_{avg}

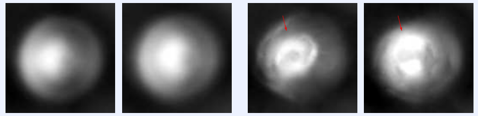
4. **Isolation of abnormal variations**
   from captured deformation field which is distorted by overlaid control deformations.
   - Deformation field U between reference ONH R and a sample
   - Model healthy ONH variability by Principal Component Analysis (PCA) on deformation fields U of controls I_c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

   $\rightarrow$ Identification of modes most discriminating between controls and glaucomatous

Results and Discussion

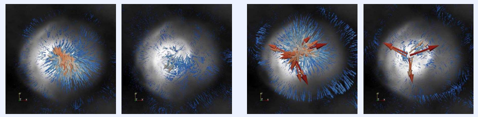
1. **Deformation based reference ONH**



(a) (b) (c) (d)

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 indentify local structures. Deformation based averaging (c,d) clearly shows a structural thining of the upper rim in case of glaucoma (d) compared to control reference (c) (red arrows).

2. **Isolation of abnormal deformations**



(a) (b) (c) (d)

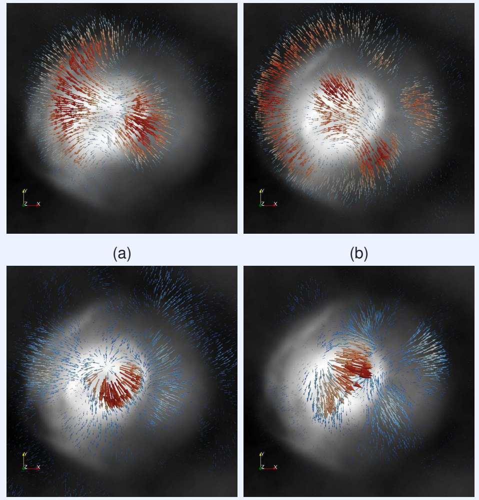
Figure 3: Isolation of abnormal deformations: (a,b) control, (c,d) glaucoma. (a,c) Captured deformations between test sample and reference. Abnormal deformations overlaid by high amount of control deformations. (b,d) Isolated abnormal deformations showing an increased cupping for the glaucomatous case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

- Visualization of ONH's deformations
- Identification of isolated abnormal deformations

$\rightarrow$ Novel representation for the physician

3. **SDM of ONH in glaucoma**
   - Discriminative modes identify patterns of variation
   - Intuitive visualization of ONH deformation (Figure 4)
   - Mathematically derived influence of rim and cup

   $\rightarrow$ Biologically interpretable descriptions of ONH deformation in case of glaucoma



(a) (b) (c) (d)

Figure 4: First four PCA modes most discriminating between control and glaucoma providing a mathematically derived and biologically interpretable description of ONH deformations: (a,b) Simultaneous deformation of the cup and rim, (c,d) local extension of the cup (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.

Deformation based morphometry of ONH shows a potential to be a **future** technique to gain novel insights into glaucomatous changes of the ONH.

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Commercial Relationship

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References

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