Significance of Progression

- Management of glaucoma depends on predicting if an eye will progress.
- Recognizing if glaucoma is stable or progressing.
- Measuring rate of progression.
- Current methods for detecting progression with visual fields.
- Non-negative Matrix Factorization (NMF) and Independent Component Analysis (ICA).

Background Premis

- Visual fields are noisy, yet we want to use them.
- Attention variability.
- Sick angling cells.
- Visual fields are noisy, yet we want to use them.
- Human limitations and bias in interpretation.
- Mathematical methods for detecting progression.
- Reduces human limitations and biases.
- Improve signal-to-noise ratio (SNR).

Methods

General Steps

- Establish environment of axes of progressing severity.
- Progression of Patterns (POP).
- Propose time sequence of VFs on axes.
- Linear regression to measure slopes of severity change.
- Define the threshold between stability and progression.
- Determine if analyzed eye exceeds threshold slope.

Database Characteristics

- 3 datasets.
  - Set 1: Cross-sectional SAP-SITA TD plots.
    - To develop environment of axes of progressing severity.
    - 1146 normal eyes.
    - 939 eyes with glaucoma determined by GHT and PSD.
    - 205 total.
  - Set 2: Longitudinal VFs in stable eyes with glaucoma.
    - 55 glaucoma eyes simulating stable eyes.
    - 5 VFs per week apart (0, 1, 2, 3, 4).
    - Linear regression to determine estimated mean slope.
    - VFs permuted (51=120) = 6600 slopes.
  - Set 1: Longitudinal VFs in eyes to be analyzed.
  - Number of VFs in sequence ≥ 5 at 1-year intervals.
  - 4260 VFs from 628 eyes in 418 patients.

Pop step 1
Projection of VF Sequence on an Axis

- Unsupervised learning creating axes.
- 3D representation of 52D.
- Axes indicate progression.
- Measuring rate of progression.
- Set 1 Axis direction.
- Variational Bayesian Independent Component Analysis Mixture Model (VIM).
- Along direction of progression.
- All glaucoma eyes in Set 1.

Pop step 2
Confidence Limit of Stability

- Unsupervised learning creating axes.
- Non-negative direction.
- V* VFI.
- 2D representation of 52D.
- Axes constrained non-negative.
- Axes indicate progression.

Pop step 3
Slope > Limit for Stability

- Unsupervised learning creating axes.
- Non-negative direction.
- V* VFI.
- 2D representation of 52D.
- Axes constrained non-negative.
- Axes indicate progression.

Non-Negative Matrix Factorization

- Unsupervised learning creating axes.
- Non-negative direction.
- V* VFI.
- 2D representation of 52D.
- Axes constrained non-negative.
- Axes indicate progression.

Results

Comparing NMF & ICG with other progression-detecting methods with PGON

- Sensitivity (%): POA-ICG 21.1, 29.7, 22.4, 28.9, 32.9, 14.5.
- Sensitivity (%): POA-VFI 21.1, 0.28, 0.41, 0.29, 0.76, 0.29, 0.01.
- Sensitivity (%): POA-VPM 16.0, 0.59, 0.78, 0.16, 0.02, 0.20.
- Sensitivity (%): POA-ICG 23.5, 0.74, 0.26, 0.09, 0.13.
- Sensitivity (%): POA-VFI 22.4, 0.17, 0.00, 0.11.
- Sensitivity (%): POA-NMF 28.9, 0.26, 0.02.
- Sensitivity (%): POA-NMF 32.9, 0.00.

McNemar comparison of sensitivities at specificity = 95%.
- NMF better than other methods except MD.
- MD, not corrected for cataract progression, may detect progressing cataract in some eyes.

Conclusions

1. Information in inherently noisy visual fields permit detection of progression.
2. Machine-learning methods can learn to detect progression well without human intervention.
3. A purely mathematical approach to improve SNR for progression detection is effective for visual fields.
4. Progression of Patterns (POP) can display the pattern that progresses the most.
5. Progression of Patterns, using NMF or ICG, is more sensitive for detecting progression at same specificity than current methods.

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