Assessment of Age Effect in Structural and Functional Glaucoma Progression Analysis

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Purpose: To assess the age effect in glaucoma progression using a novel 2-D state-based continuous-time hidden Markov model (2D CT-HMM)

- Glaucoma progression: structural (retinal nerve fiber loss) and functional (visual field loss) degeneration processes often occur asynchronously over the disease course.
- The proposed 2-D state-based CT-HMM model:
  * Define disease states based on joint structural and functional measures, and model their transition intensities to capture their intricate dynamic relationship.
  * The learned state transition intensities, and state dwelling time distribution, can be intuitively visualized for progression understanding.
  * Covariate (such as age, treatments, etc.) effects can also be learned and incorporated into the model for individual-specific disease state decoding and future state path prediction.

Methods: Cox proportional hazard model is used to assess the age effect in state transition intensity

- 2-D disease state definition: visual field index (VFI) and global mean circumpapillary retinal nerve fiber layer (RNFL) thickness from OCT.
- Age effect: age-varying state transition intensity ($q_{ij}^{<k,t>$} using Cox proportional hazard model:
  $$q_{ij}^{<k,t>} = q_{ij}^{<0,t>}e^{w_{m}-w_{0}^{<0,t>}t_{k}}$$
  where 1 year of aging is associated with a factor $e^{w_{m}}$ of baseline transition intensity $q_{ij}^{<0,t>}$.
- The likelihood function for one individual:
  $$p(O,S^* | \lambda) = \max_{s_{1},s_{2},...s_{n}} \{ p(o_{1} | s_{1})p(o_{2} | s_{2})...p(o_{n} | s_{n}) \prod_{k=2}^{n} p(s_{k} | s_{k-1})[P_{s_{k}}(t_{k} - t_{k-1})]_{t_{k},t_{k-1}} \}$$

Results: Significant age effect in functional degeneration

- Dataset: 197 glaucomatous eyes followed for 10.6+/-.5 years.
- Results of age effect assessment:
  
<table>
<thead>
<tr>
<th>Loss Type / Risk</th>
<th>1-Year Aging Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Functional (F) loss</td>
<td>2.24% (96% CI: 0.87%-3.61%)*</td>
</tr>
<tr>
<td>Structural (S) loss</td>
<td>0.84% (96% CI: -0.16%-1.62%)*</td>
</tr>
<tr>
<td>Concurrent F and S loss</td>
<td>0.30% (96% CI: -1.59%-2.19%)*</td>
</tr>
</tbody>
</table>

Conclusion and Future Work

- Age-varying modeling: may aid in more informed progression analysis and prediction.
- Intuitive state-based visualization: our model can quantify and intuitively visualize the intricate relationship between structural and functional progression.
- Future work: model more covariates (age, treatment options, etc.) together, design and test different hazard models, test on prediction tasks.

Reference


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