

Glaucoma Research Society



President's Summary of discussions Glaucoma Research Society Meeting, Kyoto, 2010 Prepared by Harry Quigley

Overall comments during business meeting regarding the format:

1. Extended discussion at a high level of important topics selected in advance is an improvement
2. Materials circulated prior to the meeting to allow attendees to start with a fund of knowledge on the subject matter was useful, but came too late to the website and email, and were only read by a minority of attendees.
3. Asking the presenters to use only 2-3 slides for introduction of the subject matter is insufficient in most cases and 10 slides might be a more practical alternative. Panelists who go well beyond this limit should be stopped by the Chair.
4. We should invite outside experts to lead or contribute to discussions in some areas
5. 10 topics seemed too many for the 2 ½ day meeting and 5-7 might be more useful to allow longer discussion of some areas. Flexibility when discussion lags might dictate shortening some topics.
6. A summary session on the last day should evaluate potential research areas and projects identified by the discussions.
7. WiFi in the room would more easily allow access to pre-meeting materials and published data needed during discussion (though it would also facilitate distractions for attendees).

Specific discussion areas and their proposed outlines (*italics*) followed by summary of discussions

1. Angle closure glaucoma: the important issues

(Friedman, Sihota, Thomas, Tomita, Aung)

- *Mechanisms of angle closure*
- *Definitions of angle closure*
- *Who should have an iridotomy*
- *Cataract and other LPI complications*
- *Primary lens extraction for angle closure*

Summary points of discussion:

- While the Foster et al classification is now often used in publications and prevalence surveys to denote definitions in ACG, re-evaluation of the categories, definitions, and examination methods to identify and classify ACG are needed
- More clinical trials are needed to identify the value of various surgical approaches to ACG
- At this time a principal question needing research is which narrow angle suspects benefit from laser iridotomy.

2. Worldwide glaucoma management

(Budenz, Sekhar Tuulonen, Robin, Yamamoto)

- *Could we agree on a consensus worldwide therapeutic approach to primary open angle glaucoma and primary angle closure disease?*
- *How does the GRS membership view the W.H.O. April, 2009 Geneva report*
- *Can we apply cost-effectiveness criteria to glaucoma therapy without losing safety?*
- *Challenges and opportunities for glaucoma care in developing countries?*

Summary points of discussion:

- Glaucoma is over-treated in the developed world and under-treated in the developing world. Additional education is necessary to eye care providers in the developed world regarding the overtreatment of ocular hypertensives so that time and resources can best be spent on those patients with manifest glaucoma. One reason for over treatment might also be improper interpretation of the optic nerve head imaging and field testing
- Identification of undiagnosed glaucoma in the developing world is best accomplished through case detection as part of eye health exams rather than population screening.
- Skills transfer in the diagnosis and management of glaucoma from specialists in the developed world to ophthalmologists in the developing world would be beneficial.
- There is a potential for research into patient care models to optimize the follow-up in stable versus rapidly progressive cases. There was discussion of how to involve other eye care professionals in efficient systems of eye care (a model being planned in Canada).

3. Long-acting glaucoma drug therapy

(Araie, Wax, Epstein, Kaufman, Lu, Tamm)

- *What research is needed to produce long-lasting IOP lowering?*
- *What would be the best drug delivery method?*
- *What effect would such therapy have on our approach to glaucoma?*
- *Could we develop treatments to lower IOP for 6 months to one year at a time?*
- *What new delivery methods have promise? Pharmacogenomics, receptor mechanism and new potential therapeutics*

Summary points of discussion

- There remain unmet needs for long-acting glaucoma drug therapy to reduce the treatment burden and improve patients' adherence.
- Periocular or intravitreal sustained-release systems encapsulating drugs or transfected cells targeting conventional, uveoscleral outflow system, ciliary epithelium, retina or optic nerve head have potential in long-acting glaucoma drug therapy.
- Application of nanotechnology is promising in delivering various agents including si-RNA or genes, but gene delivery techniques need further improvement.
- Attention must be focused on development of noninvasive, safe and biocompatible sustained drug delivery system targeting both anterior and posterior segments of the eye.

4. Basic mechanisms of glaucoma damage

(Martin, Crowston, Gupta, O'Brien, Yu)

- *Role of glia*
- *Role of vasculature*
- *Role of biomechanical factors*
- *Role of mitochondria/oxidative stress/autophagy*

Summary points of discussion

- An explant culture system for the optic nerve head would be useful to help tease out the ways in which optic nerve glia impact RGC survival
- The effect of ageing on RGC response to injury remains poorly understood. Studying ageing effects on RGC survival in different species may give new insights
- Glial and mitochondrial contributions to RGC degeneration are an important focus for future work.
- Translation of new treatment candidates is currently limited by noisy endpoints which make clinical trials long and expensive. Better surrogate endpoints are needed for clinical trials.

5. Non-IOP lowering neuroprotective treatment

(Danesh-Meyer, Quigley, Mills, Pillunat, Varma)

- *How can studies be designed to show effectiveness more efficiently?*
- *What are the most likely candidate agents for neuroprotection now?*
- *Why do animal studies not translate into human drug treatments?*

Summary points of discussion

- The present view is that it is too hard to prove neuroprotection in ophthalmological clinical trials in glaucoma due to large patient numbers needed and the difficulty of visual field change being the outcome.
- This is compounded by the apparent failure of the Memantine trials and multiple trials in neurological diseases.
- If we utilize new designs rather than “standard” clinical trials methods, neuroprotection trials may be accomplished—including so-called futility approaches.
- Large collaborative groups of ophthalmologists are already being formed to do research efficiently and this may allow neuroprotection studies at lower cost and faster time frames.
- Features of glaucoma injury that are at a reversible stage and that can be detected/imaged in real time are an important area of research to make neuroprotection trials more practical.

6. New tonometers and telemetric IOP measurement

(Burgoyne, Kuwayama, Brandt, Zeyen)

- *Do any of the new tonometers represent an improvement in management?*
- *Which emerging methods for continuous/telemetric tonometry are most promising?*
- *What research do we need to link telemetric measurement and control of IOP to progression?*
- *Would continuous IOP measurement add valuable information for therapeutic decisions?*

Summary points of discussion

- A summary of the ICare, Pascal (DCT), applanation and other instruments shows advantages and disadvantages of each
- The role of variability in IOP from moment to moment, diurnally, and change over days/weeks is not fully understood in terms of its real impact on glaucoma damage
- Extraocular (contact lens) and intraocular methods for telemetric IOP measurement are in development but none is ready for human use—their implementation should have a high priority for understanding of IOP risk and adherence with therapy.

7. How can we improve glaucoma surgery?

(Heuer, Shirato, Jampel, Traverso, Grehn)

- *IOP effectiveness of various methods at long term*
- *complications in the long term*
- *basic research aspects (including animal models)*
- *new methods—any ready for prime time?*
- *How can “success” be defined?*

Summary points of discussion

- Complications of trabeculectomy (particularly cataract worsening, late infection, and hypotony) need to be addressed or new surgical approaches found

- The assessment of new (and old) forms of surgery should follow strict and objective guidelines outlined in available publications

8. Health economics, glaucoma outcomes and progression (Heijl, Tuulonen, Douglas, Wormald)

- *Can we justify the way we look for and treat glaucoma?*
- *What is the outcome of present glaucoma management?*
- *Are we performing too many tests, not enough, or the wrong ones?*
- *What is the best way to measure progression?*

Summary points of discussion

- Outcomes of even the best glaucoma centers under ideal conditions show unacceptably high rates of patient progressive worsening—potentially related to failure to recognize findings in field testing
- Despite this, most glaucoma patients, once in care, do not become significantly impaired, though measurement of impairment (as compared to clinical tests) is an important area for research
- Ophthalmologists in the developed world fail to perform testing appropriately, especially gonioscopy

9. Clinical Implications of SD-OCT imaging of the ONH, NFL and retina in glaucoma (Park, Medeiros, Burgoyne, Araie, Garway-Heath, Schuman)

- *What is new in what we are seeing?*
- *What are the anatomic targets and why?*
- *What are the clinical implications for risk characterization*
- *What are the clinical implications for longitudinal change detection*
- *How should we design studies of diagnostic accuracy (cross-sectional and longitudinal) for imaging devices?*

Summary points of discussion

- There is a rapid development of SD OCT technology and it is not clear which system will ultimately show greatest usefulness
- Imaging of the lamina cribrosa and nerve head area with SD OCT should be a high priority
- Studies of “accuracy” in prediction are frustrated by the lack of gold standards against which progression can be judged.

10. Biomarkers

(Gandolfi, Kee, Tanihara, Coleman, Jonas, Sugiyama, Alward)

- *Factors that influence outcome*
- *Secondary glaucomas, exfoliation*
- *Gene polymorphisms*
- *Measurable serum molecules*

Summary points of discussion

- In spite of a considerable body of data collected in several laboratories, there is no strong enough clinical evidence speaking for (a) any measurable serum molecule or (b) detectable gene polymorphisms that might be currently offered as "biomarkers" in glaucoma.
- We need to implement translational research by supporting/performing long-term clinical trials to possibly validate those molecules/gene mutations that show promising results in both animal models and human cross-sectional research