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OFTALMOLOG

Welcome to

the Nordic Congress of Ophthalmology 2022

Reykjavík, Iceland

Dear Colleagues,

Tor P. Utheim

We begin this issue with the 2021 Best Paper Awards and congratulate Vinita Rangroo Thrane, Alexander Thrane, Leif Hynnekleiv, Hans Olav Ueland, and Atle Einar Østern. We would like to thank our evaluation committee, comprised of representatives from each of the Nordic countries as well as Harvard Medical School.

The Editorial Board would also like to congratulate Yousif Subhi, a young Danish eye doctor honored with three prestigious awards in 2021.

This year, the Editorial Board is pleased to launch Oftalmolog's Portrait of Excellence. In this series, we will highlight some of the exceptional achievements of our colleagues in eye care, research, innovation, and leadership within the Nordic region and beyond. We are honored to kick off this series with Sten Kjellström, the new CEO of St. Erik's Eye Hospital.

In this issue, you can read the highlights from five recent Nordic dissertations. As last year, there will be three Outstanding PhD awards (gold, silver, and bronze), totaling NOK 125,000. The recipients will be presented in the upcoming December issue. All dissertations defended in the Nordic region between January 1 and December 31, 2021, are eligible for nomination for the 2021 Outstanding PhD awards. Oftalmolog is hoping to receive many nominations from our readers by October 1, 2022.

We are excited to bring you the latest news from the Nordic Congress of Ophthalmology 2022, including some thrilling opportunities Iceland has to offer. A most exciting scientific program with several outstanding speakers is outlined. Finally, we present thought-provoking discussion on decision making as well as principles and opportunities of network meta-analysis in clinical ophthalmology.

Special thanks to Professor Jakob Grauslund for his great work as the Guest Editor for our Special Issue on diabetic retinopathy. Here, you can read more about the highlights from The European Association for the Study of Diabetes Eye Complications (EASDec) 2021 conference, dive deeper into some featured work, and read more about two authors recognized at the conference: Hanagh Winter and Lasse Jørgensen Cehofski.

The Editorial Board wishes you all a happy summer and hopes to see many of you at the Nordic Congress of Ophthalmology 2022 in Reykjavík.

Tor Paaske Utheim
Editor-in-Chief

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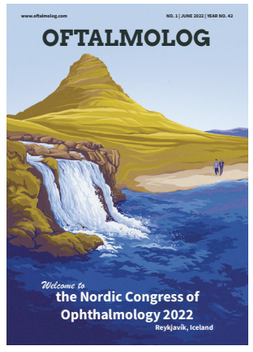
MANUSCRIPTS:

Manuscripts can be sent to info@oftalmolog.com. For guidelines about manuscripts, deadlines, and distribution, visit www.oftalmolog.com

NEXT ISSUE:

December 2022

COVER:



For this cover, we were inspired by the natural beauty of Iceland. We wanted to create an image in the style of a vintage travel poster to excite readers about the upcoming conference in preparation for their trip. The proximity of the breathtaking vistas to the urban capital is exemplified by the two people casually strolling along the beach. We hope that the cover helps you picture yourself here and that the conference will be the beginning of a wonderful summer.

We want to thank the illustrator, Agnes Guttormsgaard, for her work on both covers. If you want to see more great landscape art and to learn more about the illustrator, follow @agnesguttormsgaard on Instagram.

Best Nordic Paper Awards

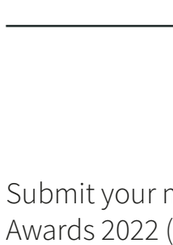
Submit your manuscript by October 1, 2022, to be considered for the Best Nordic Paper Awards 2022 (NOK 125,000). More information on these and other awards can be found on our webpage, oftalmolog.com.

Evaluation criteria

1) How interesting the subject is to our readers
2) Quality of language, pictures, illustrations, and figures

Points (1) and (2) have equal weight. Articles will be evaluated by an independent panel of judges, chosen by the Editor-in-Chief.

Evaluation committee **2021**



Madeleine Zetterberg, *MD, PhD, Professor of Ophthalmology, Senior Consultant, Department of Ophthalmology Sahlgrenska University Hospital Institute of Neuroscience and Physiology University of Gothenburg, Sweden*

Jukka Moilanen, *MD, PhD, FEBO Head Ophthalmology, University of Helsinki and Helsinki University Hospital*

Dong Feng Chen, *Associate Professor Schepens Eye Research Institute/ Massachusettes Eye and Ear, Department of Ophthalmology, Harvard Medical School, Boston, US*

Sigrid de Rodez Benavent, *MD, PhD, Senior Consultant, Department of Ophthalmology Oslo University Hospital, Oslo, Norway*

Anders Ivarsen, *MD, PhD, Department of Clinical Medicine - Department of Ophthalmology, Aarhus University Hospital, Århus, Denmark*

Yrsa Yngvadóttir, *Ophthalmology resident at Landspítali, The National University Hospital of Iceland*

We are grateful to our committee for their diligence in evaluating the great work of their peers.

The following articles were excluded from evaluation at the request of the authors:

- MicroRNAs: the new frontier in personalized medicine for AMD?
  by Juha M. T. Hyttinen, Szabolcs Felszeghy, Mikko Liukkonen, & Kai Kaarniranta

First Prize

Award of NOK 80,000

GOLD
2021
AWARD WINNER
BEST NORDIC PAPER
2021

KEY POINTS

- We discovered a novel ocular glymphatic system, which selectively transports solutes and fluids from the retina, along axons, across the lamina cribrosa, to the lymphatic system.
- The pressure gradient between the eyes and the brain is key to this transport, and clearance is stimulated by pupil movement.
- Damage caused by glaucoma can impact this system, potentially preventing proper clearance of neurotoxic solutes.

Leif Hynnekleiv, MD
Department of Ophthalmology, Haukeland University Hospital, Bergen, Norway
Department of Plastic and Reconstructive Surgery, Oslo University Hospital, Norway

Alexander S. Thrane, MD PhD
Volvat-ORBITA Eye Center, Norway
Center for Basic and Translational Neuroscience, University of Copenhagen, Denmark

Vinita Rangroo Thrane, MD PhD
Department of Ophthalmology, Haukeland University Hospital, Bergen, Norway
Center for Basic and Translational Neuroscience, University of Copenhagen, Denmark

In their own words

"We are grateful and excited to share this fundamental discovery regarding eye and brain physiology. Our basic understanding of sight-threatening diseases like glaucoma is still very limited. Breakthroughs like these can inspire us to stay vigilant and keep searching for answers."

The full article can be found on our website at www.oftalmolog.com/articles/ For direct access, scan the QR code.

SILVER
2021
AWARD WINNER
BEST NORDIC PAPER
2021

Second Prize

Award of NOK 30,000

KEY POINTS

- Surgical reconstruction to correct post-inflammatory changes is required in a subgroup of patients with thyroid eye disease.
- The different rehabilitative procedures have to be performed in the following order: first, orbital decompression; then, strabismus surgery; and finally, correction of eyelid malposition.
- The introduction of new anti-inflammatory treatment might reduce the need for surgery in this group of patients.

The full article can be found on our website at www.oftalmolog.com/articles/
For direct access, scan the QR code.

Hans Olav Ueland, MD, PhD
Department of Ophthalmology, Haukeland University Hospital, Bergen, Norway

In their own words

"Thyroid eye disease has a significant negative impacts on vision and well-being. Luckily, we have several surgical procedures to reconstruct the residual disfiguring changes. This article presents some of the most commonly used surgical techniques, and I am thrilled to hear that it has received this prize."

BRONZE
2021
AWARD WINNER
BEST NORDIC PAPER
2021

Third Prize

Award of NOK 15,000

Atle Einar Østern,
Oslo University Hospital HF (Ullevål), Oslo, Norway

KEY POINTS

- Hallucinations are a quite common result of tiredness and several eye diseases.
- The perception of a perfect visual field is a delusive sensation since the brain fills in the peripheral colors and our large physiological blind spot.
- After visual input or even in total darkness, the cells in the visual system generate electrical signals perceived as afterimages or lights.
- The brain can misinterpret visual information, causing illusions and problems with comprehending the external world correctly.

In their own words

"The thought-provoking question whether what we see is real or not has remained with me since I experienced sleep-deprived hallucinations many years ago. So now I wanted some answers."

The full article can be found on our website at www.oftalmolog.com/articles/
For direct access, scan the QR code.

In the spotlight

This year, the editorial board is pleased to launch ***Oftalmolog's Portrait of Excellence***. In this series, we will highlight some of the exceptional achievements of our colleagues in eye care, research, innovation, and leadership within the Nordic region and beyond.

Oftalmolog's Portrait of Excellence

Sten Kjellström, MD, PhD. Photo: Johnny Ring

Sten Kjellström—the new CEO of St. Erik's Eye Hospital

We are honored to kick off this series with Sten Kjellström.

In the next issue, we will get to know the new CEO of the highly reputed St. Erik's Eye Hospital. What is his vision for the hospital in terms of eye care, research, and innovation? This and much more will be presented in the December issue of Oftalmolog. ***Stay tuned!***

Want to highlight the excellent work of one of your colleagues? Nominations can be sent to info@oftalmolog.com. Submit a 1-page description of the nominee, and tell us why they shine.

Our dubious decisions

How to improve decision strategies in ophthalmology

Atle Einar Østern, MD,
Oslo University Hospital HF (Ullevål)

In August 2021, external ophthalmologists referred a patient with fungal septicemia to the Eye Department in Oslo for a second opinion. Did the patient have fungal endophthalmitis, needing intraocular vitrectomy and treatment? The Optomap image was presented at the morning meeting, where our experts agreed that the visible ocular findings could indicate vitritis and chorioretinitis. However, the senior consultant in charge returned at the following session and informed us that a proper eye examination had revealed only vitreous opacities and myelinated nerve fibers, with no pathological consequences.

This case was a real eye-opener. How were we misled? The patient was severely ill, and another ophthalmological department suspected an associated eye infection; this information influenced our first perception. In short, we suffered from a bias (Figure 1). There are many different biases, which include the following:[1]

- **Anchoring** occurs when we rely too much on the first piece of information about something without adjusting our beliefs when we learn more later.
- **Availability bias (recent case bias or posterior probability error)** is the tendency to think about a particular diagnosis because of the influence of an easily remembered event or a recent experience.
- **Base rate neglect** is the inclination to ignore the true prevalence of a (rare) disease during diagnostic judgments (skewed Bayesian reasoning), resulting in false positives and adverse events.
- **Confirmation bias** is the premature closure because of the tendency to search for, interpret, favor, and recall information that supports our initial diagnosis.
- **The gambler's fallacy** means that the frequency of preceding cases influences our estimation of the probability of a random event.
- **Loss aversion (and the sunk cost fallacy)** is the tendency to avoid losses more than acquiring the same gains and for a physician not to abandon a diagnosis once mental energy and time have been invested.
- **The overconfidence effect** is when the subjective certainty of internal judgments is greater than the objective accuracy.
- **Representativeness heuristic bias (restraint)** occurs when we misjudge the probability of something because we overestimate its resemblance to a mental stereotype.

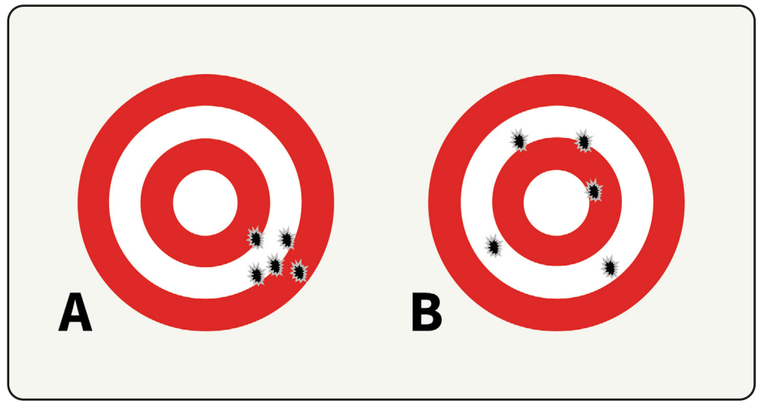


Figure 1. Visualizing the terminology. Bias (A) in psychology occurs when judgment errors diverge in one direction (invalid results). Noise (B) is the variable and random distribution of judgments that should not differ—for instance, among clinical experts (unreliable results). A fallacy is incorrect logical reasoning. Heuristics are simplified, practical problem-solving methods that include mental shortcuts. Illustration: Atle Østern

This story also illustrates another point. Group discussions frequently generate better outcomes after exchanging ideas and regression to the mean, especially when all opinions are respected and the participants have diverse areas of experience. However, there is also a risk that, due to group dynamics, the conclusion may be more extreme than the average opinion of the individual participants. This outcome is attributable to various cascade effects and group polarization, which increase noise (**Figure 1**).

Our flaws

Most of us aspire to become better at diagnosing and treating patients through lifelong learning founded on updated evidence-based medicine. Knowledge is vital and matters a great deal, as might be expected. The more experienced a doctor is, the more likely their decisions are to be correct. For instance, variation in skills can explain 44% of discrepancies in diagnostic decisions about pneumonia. The best evaluations come from professionals with procedure-specific expertise, good comprehension, and an open-minded cognitive attitude. However, doctors are only human—we are not immune to bias and noise, as the above case demonstrates.

Many factors influence decision-making. Before a decision, there will be a judgment. Judgment in this context refers to a measurement where the human mind provides a qualitative or quantitative assessment of something. Most medical judgments are predictive and later verifiable during follow-ups. However, as a clinician, you usually make judgments independently without the simultaneous, systematic evaluation of other experts.

Judgments can vary over time, and they can be shaped by factors as diverse as the doctor's mood (including fatigue and stress) or even the time of the day (for instance, when one is behind schedule). Hypotheses are often generated prematurely, only a few are actively considered, new information is discarded, distractions lead us astray, prior experiences are not fully taken advantage of, and our competence varies for different topics. In addition, reliance on memory alone is risky because it is selective, inaccurate, and changeable.

A clinical examination involves numerous decisions, both conscious and unconscious. Whether small or large, each decision opens up potentially divergent pathways for different outcomes. Even though the purpose of continuing education programs and revised guidelines is to minimize mistakes, research shows an astonishing level of disagreement among medical experts due to noise.[2] The resulting amount of damage can be devastating. For example, if two doctors give different diagnoses, at least one of them is wrong. Depending on which physician a patient meets, this could mean the difference between life and death.

Review your last day at work. Were all your judgments and clinical decisions of the "highest standard," utterly free of mistakes—or unacceptable risk thereof? Remember that the outcome—for example, an improved disease status in a patient—is not always proof positive that the prior treatment decision was sound. Perhaps the change coincided with a random variation. How systematic were you during the decision-making process in each case? Have you reflected on the decision strategies you apply at all times? Most of us will honestly realize that there is significant potential for improvement. Let us now dwell on the answers to these questions.

Figure 2. Consequence analysis. Chess is the ultimate decision-making board game. Our limited short-term memory makes foreseeing all possible outcomes challenging, especially in situations with many uncertainties and possibilities. Photo: Atle Østern

The two systems

The brain is not like a computer that can calculate the consequences of all potential moves (**Figure 2**). Instead, our mind is the overall manifestation of the network of integrated neurons interacting on all levels. Dreams and conversations show how we seamlessly drift from one topic to another associated theme. Furthermore, we are selective and tend to apply categories to make sense of all the sensory information we receive. Consequently, we are often right but also prone to errors.

The 2002 Nobel Prize winner in Economics, psychologist Daniel Kahneman, describes the workings of the human brain in his bestselling book: *Thinking, Fast and Slow*.[3] As Kahneman tells it, the mental process is divided into two parts, which he labels "System 1" and "System 2." System 1 is the simple, automatic and effortless, intuitive approach based on gut feeling. Intuition is deeply rooted in experiences and feelings from a lifetime; it is lightning-quick—and, most of the time, it is correct. In our distant past, this decision style helped us survive. For example, if a lion threatened you, you had to decide immediately: fight, flight, or freeze. Intuition differs from instinct, which is the genetically preprogrammed behavior found in all members of a particular species (**Figure 3**). Yet, the remarkable fact is that our brain decides what to do as early as several seconds before we become consciously aware of it. Thus, we may ask questions about our assumptions of free will.

The alternative is System 2, the analytical decision strategy, wherein a systematic, logical, rational, and calculated assessment is made that is time-intensive and deliberate. Even so, emotions remain crucial for analytical decision-making as well. It is generally good to keep a cool head, but even minor decisions are difficult to reach without an emotional push. The link is in the brain's ventromedial prefrontal cortex, which is involved in both decision processes and the regulation of feelings.

In reality, the two systems are not exclusive. Rather, they are distinct yet related styles used by all people, depending on the situation and personality traits.

Figure 3. Animal instincts and decisions. Decisive responses exhibited by animals are primarily instinctive. Birds, modern descendants of the relatively small-brained dinosaurs, have evolved remarkably complex brains. As a result, some crows can flexibly make profitable decisions in tool-using tasks, similar to humans.[4] Diorama and photo: Atle Østern

How to proceed

Aviation safety was famously revolutionized by the introduction of checklists, a powerful tool in many situations. They are now implemented in healthcare—for instance, to ensure "safe surgery."[5] A procedure, similar to a checklist in some ways, is more extensive. In my opinion, such schemes, whether written or informal, are fundamental to all good decisions and task performances in one way or another.

There are many decision strategies we can draw upon.[6] Consider the following examples:

- **Exclusion method**: The least likely hypotheses are eliminated through pairwise comparisons.
- **Pattern recognition (or associative model)**: The automatic identification of perceived inputs that match internalized pre-existing patterns.
- **Multiple criteria decision analysis (MCDA)**: An additive sum of weighted scores for different criteria.
- **Flow charts (algorithmic model)**: A diagrammatic representation of a step-by-step approach to solve a task.
- **Even swaps**: A method for making trade offs through sequential elimination of alternative solutions by equalizing the values of one selected measure in exchange for adjusting another.
- **Pro et contra**: The well-known list of arguments for and against an option.

Each of these decision strategies has advantages and limitations. Although we might not know the procedure by name, pattern recognition is likely the most commonly used method among ophthalmologists. It is fast, and its accuracy increases with experience—but the risk of bias or noise is relatively high. Measurable tests, calculations, and quantitative scores reduce or erase noise. However, a problem with MCDA is that pattern noise may emerge if the criteria are not interpreted equally by all users. Flow charts visualize the decision-making process, and a great many exist for various eye conditions. Flow charts can be a great aid in decision-making, but they are difficult to recall and you may not always have access to them.[7]

I will now describe my strategy, as of 2022, for adopting System 2. It is certainly not the only or necessarily the best solution, and you may disagree with it. My aim is to inspire (or provoke) you to think through your strategy.

A suggested strategy for ophthalmology

1. **Medical interview (a thorough history-taking):** What is the (real) problem (root cause analysis)? Why has the patient asked for help (chief complaint)? A systematic template for potential questions is of great assistance regarding possible vision loss/disturbance or pain/discomfort. Ask when the symptoms started (chronology), whether the onset was sudden or gradual, whether the symptoms have varied over time, and what their relationships are to other factors. Screen, then elaborate. What does the patient understand, feel, and expect?
2. **Systematic physical examination:** Gather diagnostic clues—for instance, by asking myself, "is the cornea transparent (yes or no)?" I use the abbreviation "ABC" to remember to determine the Anatomical location, Be descriptive of and Classify the pathological conditions (e.g., infiltrates, exudates).
3. **Diagnostic hypothesis generation:** What are the alternative explanations? A starting point can be a crude division of conditions and anatomical sites that fit in with voiced pain/discomfort (inflammation, infection, ischemia, injury, increased intraocular pressure), photophobia (keratopathy, uveitis), and vision loss (refractive error, opaque media, retinal disease, optic neuropathy, brain disorders), but also different pathophysiological categories. I also ask, "what is the most likely (expressed as a quantified probability when possible; see **Figure 4**), severe and treatable diagnosis I should consider?" Resist premature intuitions before balanced information has been obtained and the evidence considered.
4. **Diagnostic tests:** Decide on supplementary workups to gather appropriate data if the results can change the management, based on an estimate of the prior probability of a particular disease. Assess their accuracy (predictive values, sensitivity, and specificity). Stop when you have enough relevant information.
5. **Rank the different alternatives in order of plausibility:** I often apply a combination of the exclusion method, pattern recognition, multiple criteria analysis, flow charts (occasionally), and finally, pro et contra until one or a few diagnoses remain. Pathognomonic signs (such as jaw claudication in giant cell arteritis) are rare. Then, combine diagnoses with the same consequences and judge whether one diagnosis may explain everything (rule of parsimony). Regarding treatments, I try to calculate the predictive outcomes. For example, what are the benefits of treatment compared to the harms involved? Secondly, what is the risk (calculated as the multiplication of the probability of an event by its severity) of doing nothing compared to the risk of doing something? Establish the purpose or goals (these should be SMART—i.e., specific, measurable, assignable/achievable, relevant and time-bound). Prioritize and determine the sequence of actions (**Figure 5**). Finally, design a structured and feasible plan A (and B).
6. **Evaluation of the main hypothesis:** Are the symptoms, findings, and tests compatible with the diagnosis and treatment? Consider fallacies. Have I checked all clues and interpreted them correctly (constructive "Socratic questioning")? Repeat, if necessary, some of steps 1–5. Review reliable textbooks, guidelines, or meta-analyses. Discuss cases with trustworthy colleagues (second opinions). At last, revise your decisions and plan.
7. **Shared decision-making:** Explain to the patient the medical problem and treatment options at their level of understanding. Assess the patient's attitude regarding the risks and benefits (utility) and the treatment threshold probability (the level of certainty of a disease for starting treatment). Make individual adjustments. Get informed consent. Treat, test more, or observe. Agree on a follow-up.

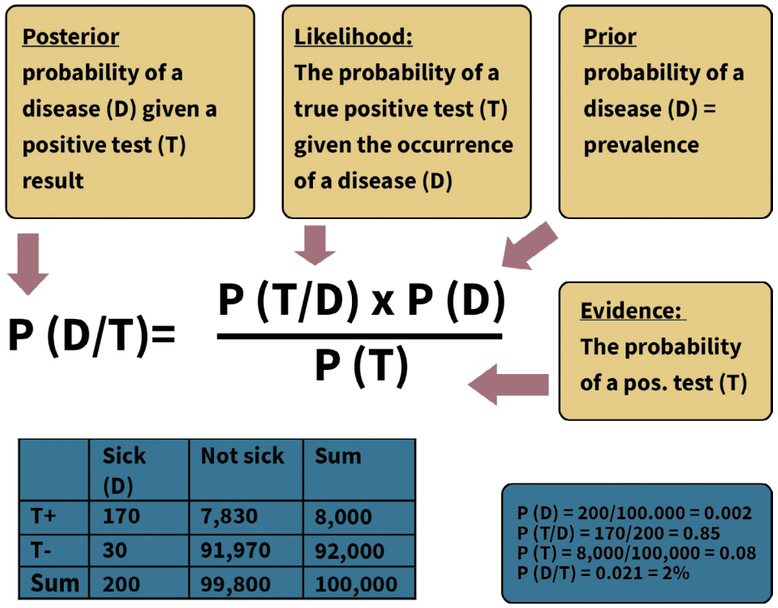


Figure 4. Bayes' theorem (or its derived odds ratio form) is a widely used method to calculate the conditional probability of events on a scale of 0 to 1. The interpretation of a test result, as new information becomes available, depends on the probability of a disease before the test.[8] Brown boxes explain the formula; blue boxes show an example.
Figure: Atle Østern

Medical decision-making is supremely complex and challenging because of the inherent uncertainty and difficulty in making accurate predictions in real time. The key is to estimate the probability before and after acquiring new information (**Figure 4**). In addition, the patient may have two or more diseases with conflicting and confusing findings—or one condition may be connected to another. For example, chickenpox during childhood can later manifest as herpes zoster ophthalmicus, possibly due to another triggering illness, with simultaneous or time-delayed neurotrophic keratopathy, secondary bacterial keratitis, uveitis, and acute retinal necrosis. To make matters worse, some clinical cases diverge from the typical presentations or prior experiences. The clinician must sort out all these possibilities, acting like a "medical detective."[10]

As shown, the decision-making process involves many choices, and it is helpful to take the outside view of the problems and break them down into several smaller, manageable tasks. Use your creativity as well to organize and plan ahead. The PDSA cycle refers to the first letters in Plan (choose a method), Do (intervene), Study (reassess), and Act (modify based on reassessment). It

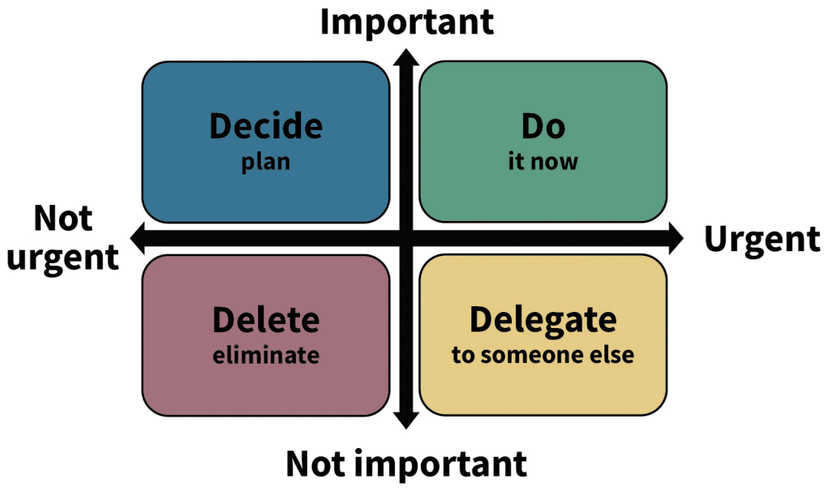


Figure 5. Prioritization: General (and later President) Eisenhower introduced the above matrix, now named after him.[9] Another solution is to assign letters to tasks: A (absolutely urgent), B (becomes necessary), C (can do), D (delegate), E (eliminate), and F (file). Scoring systems are increasingly applied to sort patients according to their treatment needs (like triage).
Figure: Atle Østern

is a problem-solving model for testing and executing change that is also employable during follow-ups. In the end, you should adhere to your values and principles and make sure that your conclusions fall within relevant frameworks (e.g., laws and financial restraints).

Critical thinking improves the quality of healthcare. For example, noise in a clinic can be measured by an audit set up by many professionals who independently judge the same cases (actual or fictitious). Thus, this evaluation can disclose deficiencies in skill and training at the workplace, necessitating altered guidelines and educational activity. Finally, a growth mindset in the doctor can enable a change of habits. One way is to recall an event, review whether the proper procedure was pursued, mentally replay a revised version, and think (procedure selection) before the task (process).

What will the future bring?

A radical solution is the replacement of judgment with rules or algorithms that eliminate noise. Artificial intelligence (AI) heralds a future where computers can assist and even out-compete humans (**Figure 6**). Even today, they are better than ophthalmologists at assessing diabetes retinopathy. Thus, the quality of ophthalmologists' decision-making strategies may become even more critical in the future. As a result, the role of doctors may change. Nevertheless, doctors can detect stupid mistakes made by AI, inspire more trust and satisfaction, resolve misunderstandings, and adjust treatment plans following feedback from patients. For the foreseeable future, most vulnerable patients will probably prefer—and need—empathetic experts to advise and help them.[11]

Let us not forget who we are. We are *Homo sapiens*, meaning "wise man" in Latin, with the means to make good decisions. Above all, the human eyes and brain are still the best tools to observe and perceive the eyes and brains of others.

Still, somehow, we failed in this respect in August 2021.

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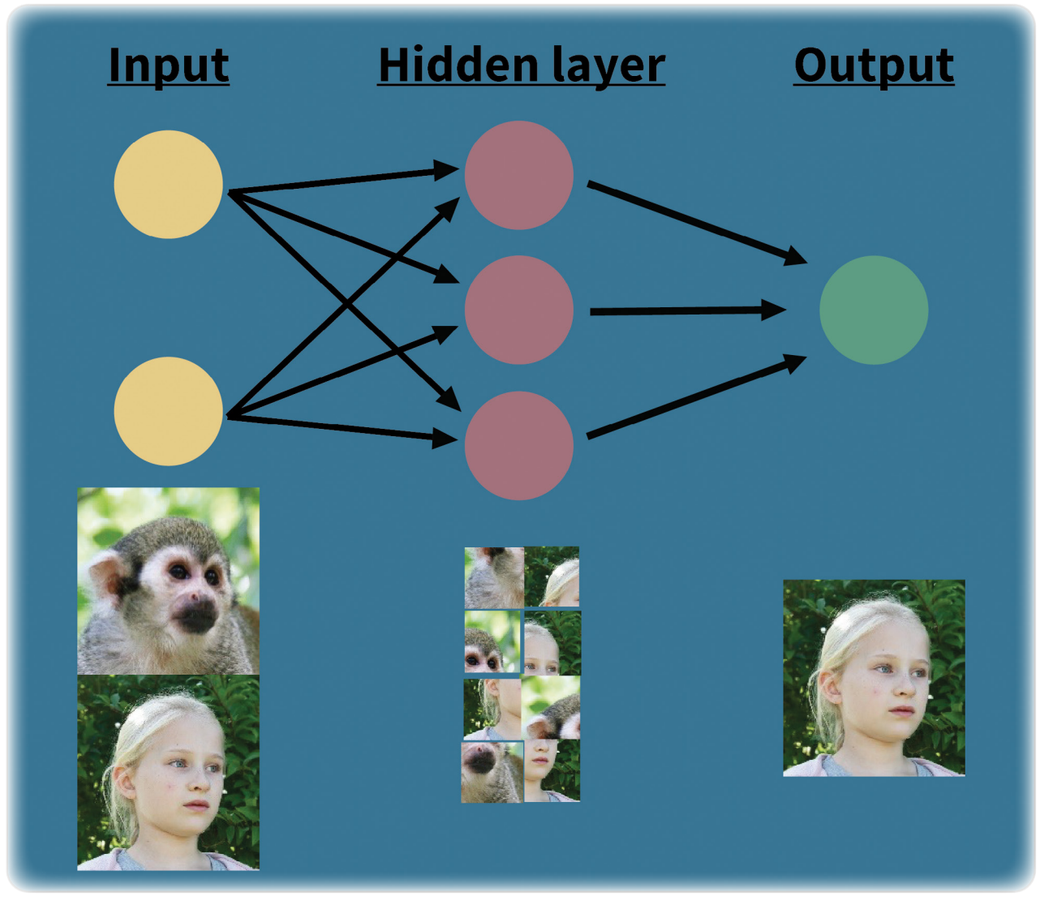


Figure 6. Artificial intelligence and machine learning. Through a hierarchical structure of neural networks with coupled nodes, the software will, over time, find patterns as a result of training and deep learning. It can, in the end, distinguish images of different categories.
Illustration and photos: Atle Østern

Evaluation criteria for Outstanding PhD Awards

We want to showcase the best and brightest PhD recipients from the Nordic region each year. To do this, we offer dissertation awards to recognize all the hard work these new doctors put into furthering the field of ophthalmology.

Prizes:

Gold: NOK 80,000

Silver: NOK 30,000

Bronze: NOK 15,000

Deadline for nominations:

October 1, 2022

More information on the award can be found on our website, www.oftalmolog.com.

We are very grateful to our generous sponsor, **Santen**, for their donation and support in making these awards possible.

Criteria

All dissertations defended in the Nordic region between January 1 and December 31, 2021, are eligible for nomination for the 2021 Outstanding PhD Awards. Nominations are accepted from anyone and must be submitted to *Oftalmolog* before October 1, 2022.

To determine the recipients of the Outstanding PhD Awards, we use the sum total of the CiteScores for each article included in the thesis. Review articles are excluded from the calculations. Although literature reviews are also valuable, not all universities accept these as thesis components. Additionally, journals solely focused on reviews generally have a higher CiteScore due to the nature of their content. Thus, by excluding reviews, we aim to make comparisons fairer.

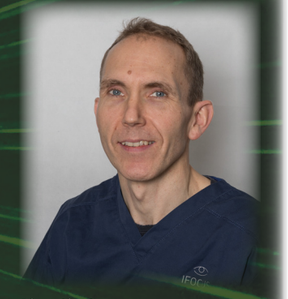
All papers accepted for publication by a journal before the submission of the thesis to the university are included in the calculation. Thus, manuscripts included in the thesis that were not accepted by a journal at the time of thesis submission are not included in the total CiteScore.

The CiteScore for each included article is determined based on the year the individual article was submitted to the given journal. For example, if a manuscript was submitted in 2018, the 2018 CiteScore was used, even if the paper was not published until 2019.

Correcting the correction:

Intraocular lens calculations after laser refractive surgery

On May 28, 2021, Bjørn Gjerdrum defended his thesis "Improvement in refractive precision for intraocular lens power calculations in patients with a history of laser vision correction for myopia" at the Department of Optometry, Radiography and Lighting Design, Faculty of Health and Social Sciences University of South-Eastern Norway (USN). The PhD project was conducted at Ifocus Øyeklinikk in Haugesund and Memira Clinics in Norway, Sweden, and Denmark. The supervisors were Bente Monica Aakre and Per Olof Lundmark, both associate professors at USN, and Kjell Gunnar Gundersen MD PhD Ifocus Øyeklinikk.



Bjørn Gjerdrum
Department of Optometry, Radiography and Lighting Design, Faculty of Health and Social Sciences University of South-Eastern Norway

In planning cataract surgery and refractive lens exchange (RLE), calculations of the intraocular lens (IOL) power depend on, at a minimum, the measurement of corneal curvature and the axial length of the eye. In general, the refractive accuracy of the procedure is high. However, for patients with previous laser vision correction (LVC), the precision is much lower because the empirical formulas do not account for the individual altered shape in these patients' corneas. Erroneous keratometric measurement due to an unstable tear film may be an additional confounding factor.

Traditionally, corneal power is predicted from reflection-based paracentral keratometry. An artificial corneal refractive index is used to account for the refractive contribution of the posterior cornea. For eyes with previous LVC, this assumption is wrong because the anterior surface of the cornea has been altered, making the prediction of the posterior corneal power erroneous. In addition, the prediction of central corneal power from paracentral measurements may be inaccurate. Special post-LVC formulas have been developed to correct for these errors, either using historic data, regression equations, or posterior corneal measurements. However, accurate IOL calculations remain challenging in these patients.

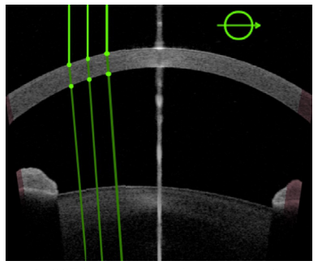


Figure 1. OCT image of anterior segment. Green lines illustrate ray-tracing calculations through different refractive surfaces at varying axes and radial distances.

An alternative approach to IOL calculations is ray tracing, where single rays at varying radial distances are calculated exactly using Snell's law (**Figure 1**). The calculation is based on individual measurements without relying on population-based assumptions or optical approximations. Instead of IOL power, the calculations use manufacturer provided lens radius, refractive index, asphericity, and thickness.

This thesis aimed to improve refractive precision for cataract or RLE in patients with previous myopic LVC. Four studies were conducted to investigate the objectives of the thesis.[1–4] Our retrospective analysis of previous RLE after LVC showed better refractive results than previously seen in the literature. However, further improvement could be achieved using a refined protocol with optimized lens constants and a target nomogram.[1] The prevalence of dry eye 5–15 years after refractive surgery suggested that LVC may induce tear film instability.[2] This was indicated by tear film osmolarity, even for subjects with few subjective symptoms of dry eye. However, a repeatability study found no evidence that the results of keratometry were influenced by tear film osmolarity.[3] A prospective treatment study showed that ray-tracing IOL calculations based on individual optical coherence tomography (OCT) measurements showed better prediction accuracy compared to reflection-based formulas in post-LVC patients (**Figure 2**).[4] Ray-tracing calculations are based on individual measurements and are independent of the patient's ocular history; therefore, they are also suitable for patients without previous refractive surgery.

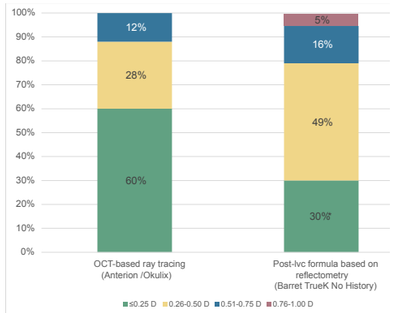


Figure 2. Percentages of refractive prediction error within certain ranges. Ray tracing showed the highest percentages of eyes with prediction errors within ±0.25, ±0.5, and ±0.75.

Key points:

- Even with few subjective symptoms, laser vision correction (LVC) may increase dry eye risk up to 15 years after surgery.
- The repeatability of keratometry with OCT-, reflection-, or Scheimpflug-based devices was not influenced by tear film osmolarity.
- Ray-tracing IOL calculations show better predictability than traditional post-LVC formulas. Calculations are based on measurements and independent of patient history.

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1. Brenner LF, et al. Presbyopic refractive lens exchange with trifocal intraocular lens implantation after corneal laser vision correction: Refractive results and biometry analysis. J Cataract Refract Surg. 2019;45(10):1404-1415.
2. Gjerdrum B, et al. Prevalence of Signs and Symptoms of Dry Eye Disease 5 to 15 After Refractive Surgery. Clin Ophthalmol. 2020;14:269-279.
3. Gjerdrum B, et al. Repeatability of OCT-Based versus Scheimpflug- and Reflection-Based Keratometry in Patients with Hyperosmolar and Normal Tear Film. Clin Ophthalmol. 2020; 14:3991-4003.
4. Gjerdrum B, et al. Refractive Precision of Ray Tracing IOL Calculations Based on OCT Data versus Traditional IOL Calculation Formulas Based on Reflectometry in Patients with a History of Laser Vision Correction for Myopia. Clin Ophthalmol. 2021; 15:845-857.

A rising star:

A young Danish eye doctor honored with three prestigious awards in 2021

In 2021, our young Danish colleague, Yousif Subhi (32), received three awards for his research: the Bagger-Sørensen Fonden Young Researcher Award, the VELUX Foundation 40-year Anniversary Award, and the Danish SOE Lecture 2021. Yousif is a resident ophthalmologist at Rigshospitalet in Copenhagen and an external Associate Professor at the University of Southern Denmark. His research is focused on clinical studies and evidence synthesis in ophthalmology, with an emphasis on chorioretinal diseases.

> "I did my PhD on age-related macular degeneration and immunological aging. Under the supervision of Prof. Torben Lykke Sørensen in Roskilde, we did some amazing studies. Shortly after my PhD, my mother unfortunately received a hematological cancer diagnosis, and I experienced the frustrations of patients and relatives first hand. That experience changed me in several aspects, including as a clinician and as a researcher. I shifted my focus from translational to clinical research. I want to help the patients in our clinic today. I am not interested in mechanisms that holds potential for therapy in 10–20 years. I want to know: What is the best treatment now? How do we best advise our patients today? Evidence synthesis and clinical research methods are my methods to answer these questions," explains Subhi.

The Bagger-Sørensen Fonden Young Researcher Award is an annual award in clinical and basic medicine given to a Danish researcher under the age of 40. The nominee is selected by an independent committee based on research content and bibliometric analysis. The award includes a personal gift of 100,000 DKK.

The Bagger-Sørensen Fonden Young Researcher Award was presented by the Board President Claus Bagger-Sørensen (left) and included a bag with gum as a reference to the Bagger-Sørensen company history of gum production.

The VELUX Foundation 40-year Anniversary Award was given to one senior scientist (Prof. Jens Folke Kiilgaard) and one junior scientist (Yousif Subhi) by an independent committee. The awards are given for a significant research contribution and engagement in the development of the specialty. The junior scientist award includes a personal gift of 50,000 DKK and a research grant of 125,000 DKK.

The VELUX Foundation 40-year anniversary was live-streamed, where Yousif explained his work and motivation. The award also included a vase from the Swedish artist Bente Brosbol Hansen.

The SOE Lecture is given in every European country by a talented young researcher selected by the national ophthalmological society. The award includes a presentation at the next SOE conference.

Let's detect progressive keratoconus correctly

Ingemar Gustafsson
Department of Clinical Sciences, Lund University, Sweden

On November 5, 2021, Ingemar Gustafsson defended his thesis "The Assessment of Disease Progression in Keratoconus and Corneal Crosslinking in Thin Corneae" at the Department of Clinical Sciences, Lund University, Sweden. His main supervisor was Anders Bergström, Department of Clinical Sciences, Lund University, Lund Sweden. His three co-supervisors were Jesper Hjortdal, Anders Ivarsen, and Anna Cardiakides.

Key points:

- Take disease severity into account when diagnosing progression.
- Consider whether to use one or the mean of several measurements.
- The ABC(D) Progression Display appears to over-diagnose subjects as progressive.
- The use of sterile water during CXL appears to be efficacious in halting disease progression.

Keratoconus generally manifests in adolescents and can progress to severely impaired vision. The risk of progression is inversely correlated to age; thus, younger patients are at higher risk than older ones. Progressive keratoconus can be halted by corneal crosslinking (CXL). The general indication for CXL is progressive keratoconus, although children are commonly treated with CXL upon initial diagnosis. Tomography is used to assess progression. Measurements made during different visits are compared to determine whether the patient's keratoconus has progressed and if they should be referred for CXL. However, there is no consensus on which parameters should be used or the magnitude of the change in these parameters that indicates progression. An increase in the curvature power of the steepest point on the anterior surface (Kmax) of 1.0 diopters is commonly used for all patients. However, there is little evidence that this is appropriate. Furthermore, inconsistent results have been presented regarding the magnitude at which progression can be detected. Such studies are often based on determinations of the repeatability of measurements made on one occasion. However, the progression of keratoconus is evaluated from measurements made on different occasions, and it is reasonable to assume that measurements obtained on different days will be subject to greater variation due to the biomechanical instability of the cornea caused by keratoconus. Additionally, it has been suggested in studies that the repeatability of measurements is lower in subjects with more severe keratoconus. Because keratoconus is a thinning disorder, a minimum corneal thickness of 400 µm has been suggested for the safe performance of CXL. Thus, a significant proportion of keratoconus patients are excluded from the standard CXL treatment protocol.

In the first study of this thesis, we elucidated the association between measurement error and disease severity. In the second investigation, we tested the inter-day repeatability of measurements, and in the third, we examined the Belin ABCD Progression Display. Finally, we assessed a protocol in which sterile water was added during the crosslinking procedure to increase the corneal thickness. We found that the measurement error was associated with the disease severity and that progression should be defined by limits of inter-day measurements. The results also suggest that the diagnosis of progressive keratoconus by the Belin ABCD Progression Display led to over-diagnosis of progression. Further, the addition of sterile water was effective in increasing the corneal thickness above the suggested safety limits.

These results have important clinical implications. The limits at which progression is defined should be stratified according to the severity of the disease. Patients with less advanced keratoconus are underdiagnosed as progressive if commonly used parameters are not stratified according to disease severity. This could lead to delayed referral for CXL, resulting in an avoidable risk of deterioration in vision. Patients with more advanced keratoconus, on the other hand, would be over-diagnosed as progressive, which could lead to unnecessary CXL, subjecting the patient to discomfort and possible treatment-associated complications. This risk of over-diagnosis is also relevant when using the Belin ABCD Progression Display. Finally, the data suggest that a simple measure, such as adding sterile water during corneal crosslinking, could enhance the corneal thickness to improve the safety of the treatment.

Future directions:

- Using artificial intelligence to diagnose progressive keratoconus
- Further randomized clinical trials on the treatment efficacy of using sterile water in different CXL-protocols

References

1. Gustafsson I, et al. Association between Keratoconus Disease Severity and Repeatability in Measurements of Parameters for the Assessment of Progressive Disease. *PLoS One* 2020; 15 (2): e 0228992O
2. Gustafsson I, et al. The Interday Repeatability of Parameters for the Assessment of Progressive Disease in Subjects with Less Advanced Keratoconus. *Am J Ophthalmol* 2021. 7; 225: 38- 46
3. Gustafsson I, et al. An Inter-day Assessment of the ABC Parameters in the Evaluation of Progressive Keratoconus. *Sci Rep* 2021.11(1):16037
4. Gustafsson I, et al. Retrospective Analysis of the Effects of Using Sterile Water in Addition to Hypoosmolar Riboflavin during Corneal Collagen Crosslinking for Keratoconus. *J Cataract Refract Surg* 2017. 43 (3): 426-427

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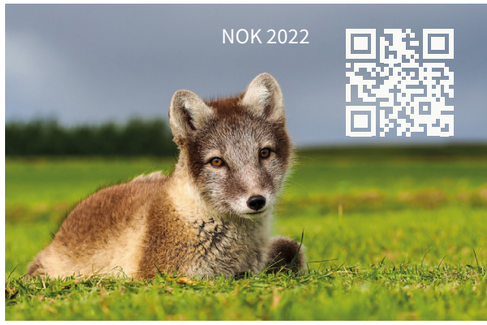
9 - 11 JUNE // REYKJAVIK, ICELAND

NOK 20//22

NORDIC CONGRESS OF OPHTHALMOLOGY



Dear colleagues,

With great pleasure and anticipation, we welcome you to the Nordic Ophthalmology Congress (NOK2022) in Reykjavík from 9 to 11 June 2022!

Together with the organizers of 32 symposia, we proudly present the final program at www.nok2022.com. There will be four parallel symposia for three whole days, and they will include all sub-specialties in ophthalmology with lecturers from Scandinavia, the UK, and the USA. Young Ophthalmologists (YO) have organized an ambitious program open to young and not-so-young ophthalmologists alike. Around 100 posters will be exhibited, and there will be many free oral presentations. The exhibition area will have many ophthalmology companies showcasing cutting-edge technologies and innovations as well as novelties in the pharmacology industry. The participants of NOK2022 will also have full access to the 21st Retina International World Congress (www.riwc2022.is).

The congress will start in the early morning of Thursday, June 9, and run until the late afternoon on June 11. Registration opens on Wednesday, June 8. Travel to Iceland is straightforward. We hope that participants will have the opportunity to enjoy Reykjavík and its surroundings before or after the congress. Since most flights from Europe arrive at Keflavik airport in the afternoon and leave for Europe in the early morning, we suggest traveling here on Wednesday, June 8, and returning home on Monday, June 13. Then, one can enjoy the incredible Icelandic nature all of Sunday, June 12.

Mother nature has been an integral part of the previous NOK meetings in Iceland, with earthquakes or volcanic eruptions interrupting the program. A small, but beautiful, volcanic eruption started one year ago, only an hour's drive from Reykjavík. The eruption had many characteristics of a shield volcano, bringing high hopes of a long-lasting volcanic eruption. Since the eruption stopped late last year, this was not to be, despite the organizing committee's encouragement. However, visiting the new lava fields is an exciting experience and well worth the effort.

The joint NOK and RIWC opening ceremony will be held in Harpas' grand hall, Eldborg. The President of Iceland will address the congress, and Professor Bart Leroy from the University of Ghent, Belgium, will give a lecture titled "Phenotyping and Genotyping in Inherited Retinal Diseases."

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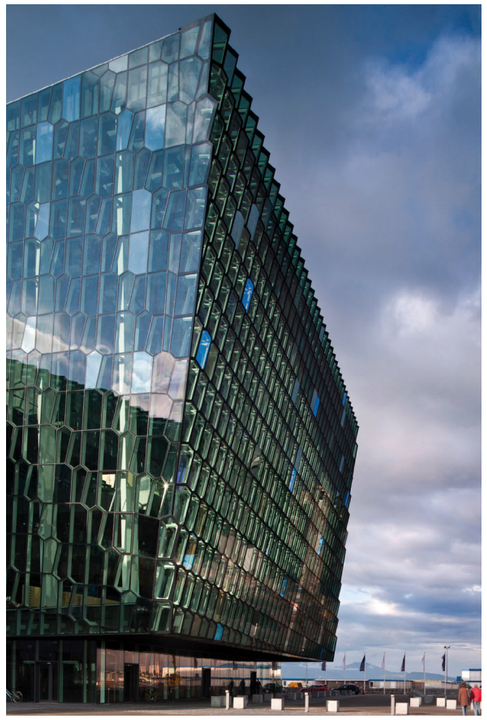
NOK2022 is honored by four outstanding keynote speakers and a special guest lecturer from the Moorfields Eye Hospital. Professor Anders Kvanta from St. Eriks Ögonsjukhus in Stockholm and Professor Leon Herndon from Duke University, North Carolina, USA, will give keynote lectures on June 9. Dr. Kvanta will take us on a journey from biological treatment to gene and cell therapy in retinal disease. In his lecture titled “Far advanced glaucoma,” Dr. Herndon will examine novel treatment approaches in managing patients with far advanced glaucoma.

From the University of California, San Francisco, USA, Professor Eugene de Juan will discuss innovation in ophthalmology in his keynote lecture titled “Physician innovators: A field guide” on Friday, June 10. He will also participate in a symposium on innovation in ophthalmology, presented at RIWC2022. The 2021 President of the American Academy of Ophthalmology, Professor Tamara R. Fountain, from Rush University Medical Center in Chicago, USA, will discuss decision-making in her keynote lecture on Saturday, June 11. The talk is titled “Pilots and physicians, passengers and patients: making decisions when the stakes are high.” Finally, Dr. Richard Collin, from Moorfields Eye Hospital, London, UK, will give a special guest lecture, titled “Tales of the unexpected,” on Saturday, June 11.

Education in ophthalmology is the theme for this year’s NOK plenary session on Friday, June 10. The ACTA honorary lecture and ACTA silver medal will be presented on Saturday, June 11. Professor Tero Kivelä will give the ACTA honorary lecture, titled “Fighting firework-related eye injuries.” YO has an exciting program covering ocular emergencies, astigmatism and cataract surgery, OCT angiographies, and neuro-ophthalmology, featuring Dr. Andrew Lee from Houston, Texas, USA.



During the congress, you will enjoy Harpa, Reykjavík’s spectacular conference and concert hall, and the surrounding harbor area in downtown Reykjavík. The word Harpa has more than one meaning. It is an old Icelandic word that refers to a time of year in early spring and is, in fact, a month in the old Nordic calendar.

Harpa is also the Icelandic name for the beautiful stringed instrument, the harp, a reference to the musical activities within our stunning concert house. Harpa is home to the Icelandic Symphony Orchestra and the Icelandic Opera. The concert hall was designed by the Danish architect firm Henning Larsen. The design of the facades is based on a geometrical principle developed in Olafur Eliasson’s studio, inspired by Iceland’s characteristic basalt rocks.

You will have the chance to catch up with friends and colleagues during the get-together in Harpa after the opening ceremony on June 9 and enjoy the congress dinner on June 10 in Reykjavík’s Art Museum, Hafnarhúsið.

We recommend joining the locals in an early morning swim before going to the congress. So, make sure you pack your bathing suit! A visit to a geothermal pool is an activity you won’t want to miss. There are 17 pools to choose from in Reykjavík alone!

The day after the congress is perfect for a stroll to a local volcano (www.guidetoiceland.is) or a visit to Thingvellir, the birthplace of Iceland as a nation and the home of the oldest ongoing parliament in the world. Or you can visit the Reykjavík Art Festival (www.listahatid.is/en). The festival is a biennial, multidisciplinary festival with a particular focus on new commissions and the creative intersection of the arts. There will be exhibitions and performances of contemporary and classical works in major cultural venues and unconventional spaces throughout the city.

Iceland pools

Guide to Iceland

Reykjavík Art Festival

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We look forward to seeing you in Reykjavík on June 9–11, 2022. We hope many of you will use the opportunity to bring your families and enjoy the early Icelandic summertime. Early June is one of the best times to visit Iceland, with bright nights and blooming nature.

Gunnar Már Zoega
President NOK2022

Jóhann Ragnar Guðmundsson
President of the Icelandic Ophthalmological Society

Much to look forward to

Young Ophthalmologists

We proudly present an ambitious Young Ophthalmologist (YO) program for NOK 2022. In the first two sessions, we focus on ocular emergencies and cataract surgeries with astigmatism. Following that, we set our eyes on the future in our third session about artificial intelligence in ophthalmology. We conclude our program on the final day with two leading ophthalmologists in their fields: Andy Lee from Houston, who will tell us about seven easy steps in evaluating unexplained visual loss, and Michael Larsen from Copenhagen, focusing on the ever-growing field of OCT angiography. On the first night, we will have our very own YO night out in the magnificent Sky Lagoon.

The 21st Retina International World Congress

	RIWC 2022
	Eldborg
17:00-19:00	17:00 – 19:00 **Welcoming ceremony**
17:30-17:50	**Keynote: Phenotyping and Genotyping in inherited retinal diseases.** Speaker: Professor dr. Bart Leroy, University of Ghent, Gent, Belgium"

NOK 2022

Hall	Silfurberg AB	Norðurljós	Ríma AB	Kaldalón
08:00-08:30	*Registration*			
08:30-10:00	**Diabetic retinopathy** **Moderators:** Elín Gunnlaugsdóttir and Carin Gustavsson, Sweden	**Glaucoma surgery** **Moderator:** Maria Soffia Gottfreðsdóttir, Iceland	**Cataract surgery** **Moderator:** Jesper Hjortdal, Denmark	**YO - 2:00 am in the morning - an ocular emergency survival guide** **Moderators:** Marie Louise Rasmussen and Marie Krogh Nielsen, Denmark
10:00-10:30	***Break / Exhibition / Poster Viewing***			
10:30-11:15	KEY NOTE: From biological treatment to gene and cell therapy in retinal disease *Prof. Anders Kvanta, Karolinska Institutet, St:Eriks Eye Hospital, Stockholm, Sweden*			
11:15-12:00	KEY NOTE: Far advanced glaucoma - are we making a difference? *Prof. Leon Herndon, MD, Duke University, North Carolina, USA*			
12:00-13:30	***12:30-13:15: Lunch Symposium - Théa***	***12:30-13:15: Lunch Symposium - Bayer***	***Lunch & exhibition***	
13:30-15:00	**Retinal oximetry** **Moderator:** Sveinn Hákon Harðarson, Iceland	**Symposium - free paper**	**Corneal surgery - from innovation to clinical praxis** **Moderators:** Eydís Ólafsdóttir, Sweden and Kari Krootila, Finland	**YO - handling the astigmatic patient in cataract surgery** **Moderators:** Elisabeth Romundstad, Norway and Danson V. Muttuvelu, Denmark
15:00-15:30	***Break / Exhibition / Poster Viewing***			
15:30-17:00	**Surgical retina** **Moderators:** Jóhann R Guðmundsson, Iceland and Manoj Kakar, Sweden	**Pseudoexfoliations, snow flakes from the North** **Moderators:** Steffen Heegaard, Denmark and Tero Kivela, Finland	**Dry eye in relation to non-ocular perspective** **Moderators:** Gunnar Már Zoega and Björn Guðbjörnsson, Iceland	**Challenges in ophthalmology** **Moderators:** Nina Holst and Jan Askvik, Norway and Daksha Patel, UK
17:00-17:30	***Break / Exhibition / Poster Viewing***			
17:30-19:00	**NOK and RIWC OPENING CEREMONY @ ELDBORG HARPA.** The President of Iceland, Mr. Guðni Th. Jóhannesson, will open the congress Keynote: Phenotyping and Genotyping in inherited retinal diseases. *Prof. Bart Leroy from the University of Ghent, Gent, Belgium*			
19:00-20:00	**GET TOGETHER @ HARPA**			

Thursday, June 9

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RIWC2022
21st Retina International World Congress

Friday, June 10

NOK 2022

Hall	Silfurberg A	Silfurberg B	Ríma AB	Kaldalón
07:40-08:20		***Breakfast symposium - Miracles in Sight***		
08:30-10:00	**Vernal keratoconjunctivitis** **Moderators:** Anne K. Wiencke and Marie Louise Roed Rasmussen, Denmark	**OCT in glaucoma management** **Moderator:** Gauti Jóhannesson, Sweden	**Dry eye disease** **Moderator:** Tor Paaske Utheim, Norway	**Symposium - free paper**
10:00-10:30	*Break / Exhibition / Poster Viewing*			
10:30-11:15	KEY NOTE: Innovation in ophthalomology *Prof. Eugene de Juan, MD, University of California, San Francisco, USA*			
11:15-12:00	NOK PLENARY SESSION and ACTA OPHTHALMOLOGICA CENTENNIAL			
12:00-13:30	***12:30-13:15: Lunch Symposium - Novartis***	***12:30-13:15: Lunch Symposium - Chiesi***		
13:30-15:00	**Uveitis** **Moderators:** Noopur Kumar and Anne Kjersti Erichsen, Norway	**Future perspectives in glaucoma management** **Moderators:** Pete Williams and Gauti Jóhannesson, Sweden	**Cornea in systemic disease** **Moderator:** Berit Byström, Sweden	**YO - Artificial intelligence and screening in ophthalomology** **Moderator:** Marie Louise Roed Rasmussen, Denmark and Helgi Davíð Björnsson, Iceland
15:00-15:30	***Break / Exhibition / Poster Viewing***			
15:30-17:00	**Uveitis** **Moderators:** Noopur Kumar and Anne Kjersti Erichsen, Norway	**Pediatric anterior segment diseases** **Moderators:** Lina Kessel and Daniella Bach-Holm, Denmark	**Atypical infectious keratitis Moderator:** Emma Nivenius, Sweden	**Symposium - free paper**
17:15-18:00				
19:30	**CONGRESS DINNER @ Hafnarhús - Reykjavík Art Museum**			

RIWC 2022

Hall	Norðurljós (Professional)	The Reykjavik EDITION (Layman)
07:40-08:20		
08:30-10:00	**Age related macular Degeneration** Moderator: Dr. Jóhann Ragnar Guðmundsson	**Retinal degenerations. Clinical aspects.** Professor dr. Kapil Bharti. National Eye Institute, Bethesda, USA
10:00-10:30	**Coffee break**	
10:30-11:30	**Assessment of Endpoints in clinical studies.** Moderators Associate professor dr. Cecilie Bredrup, Bergen, Norway and Professor dr. Sten Kjellström, Lund, Sweden	**Retinal degenerations - the genetics.** Moderator: Prof. Jón Jóhannes Jónsson, national University Hospital, Reykjavík, Iceland.
12:00-13:30	**Lunch**	
13:30-14:00	**Keynote: Scientific results, a rollercoaster between hope and deception** Speaker: Christina Fasser, former president of the Retina International, Zurich, Switzerland	
14:00-15:00	**Phenotyping and Genotyping in IRD.** Moderators: Josephine Prener Holtan MD, PhD, Oslo University Hospital, Oslo, Norway, and Professor dr. Bart Leroy, Ghent, Belgium	**L.2.3 Basics of stem cell and gene-based therapies.** Moderator: Prof. Kapil Bharti. National Eye Institute, Bethesda, USA
15:00-15:30	**Coffee break**	
15:30-16:00	**Keynote: Restoration of vision** Speaker: Professor dr. Mark S. Humayun. University of Southern California, Los Angeles, USA	
16:00-17:00	**Innovations in Ophthalmology** Moderators: Christina Fasser, Retinal International, and Professor dr. Einar Stefánsson. University of Iceland, Iceland	**L.2.4 Rehabilitation and mobility training.** Moderators: Vala Jóna Garðarsdóttir and Rosa María Hjörvar Iceland.

NOK 2022

Hall	Silfurberg A	Silfurberg B	Rima AB	Kaldalón
08:00-08:30				
08:30-10:00	**YO+NOK: neuro-ophthalmology** **Moderator:** Helgi Davíð Björnsson, Iceland	**Medical retina** **Moderators:** Kai Kaarniranta, Finland	**Hot topics in ocular oncology** Moderator: Tero Kivelä, Finland	**Corneal crosslinking** Moderators: Ingemar Gustafsson, Sweden and Stine E Nielsen, Denmark
10:00-10:30	***Break / Exhibition / Poster Viewing***			
10:30-11:15	**ACTA HONORARY LECTURE:** Fighting firework-related eye injuries. Prof. Tero Kivelä, Finland. *ACTA SILVER MEDAL*			
11:15-11:50	**Keynote:** Pilots and Physicians, Passengers and Patients: Making Decisions When Stakes Are High *Dr. Tamara R. Fountain, MD, President of the American Academy of Ophthalmology*			
11:50-12:10	**Guest Lecture:** Tales of the Unexpected *Prof. Dr. Richard Collin, Moorfields Eye Hospital, London UK*			
12:10-13:30	***12.30-13:15: Lunch Symposium - AbbVie***		***12:30-13:15: YO course: OCT angiography - possibilities and limitations.***	
13:30-15:00	**Health economics** **Moderators:** Anja Tuulonen, Finland and Gauti Jóhannesson, Sweden	**Refractive surgery** **Moderator:** Jesper Hjortdal, Denmark	**Ptosis surgery, when and how!** Moderators: Haraldur Sigurðsson, Iceland. Tamara R. Fountain, USA. Richard Collin UK.	**My baby cant see, why?** **Moderators:** Dýrleif Pétursdóttir and Hanna Åkerblom
15:00-15:30	***Break / Exhibition / Poster Viewing***			
15:30-16:15	**CLOSING CEREMONY** **Prof. Einar Stefánsson, Iceland** **Prof. emeritus dr. Eberhardt Zrenner, Germany** **Introduction of NOK 2024**			

Three days, Two conferences, One great experience

RIWC 2022

Hall	Norðurljós (Professional)	The Reykjavik EDITION (Layman)
08:00-08:30		
08:30-10:00	**New Developments in IRD.** Moderator: Professor dr. Michael Larsen	**L.3.1 Clinical trials and therapies from a patient's perspective.** Moderator: Martin Smedstad, Oslo, Norway.
10:00-10:30	**Coffee break**	
10:30-12:00	**Stem cells and cell-based therapies of retinal diseases.** Moderator Professor Dr. Goran Petrovski, Oslo, Norway.	**Retina International - the global challenges** Moderator: Fiona Waters, Retina International, Ireland
12:00-13:30	**Lunch**	
13:30-14:00	**Keynote: Gene based therapies of retinal diseases** Speaker: Prof. Artur Cideciyan, University of Pennsylvania, Philadelphia, USA.	
14:00-15:00	**Gene based therapies of retinal diseases** Moderator: Eeva-Marja Sankila, MD, PhD, Helsinki University Hospital, Helsinki, Finland	**Programme in islandic for the public.** Stjórnandi: Sigþór U. Hallfreðsson, Félag blindra og sjónskertra, Íslandi
15:00	**15:00 Closing ceremony RIWC and NOK 2022 Retina innovation today and in the future** Speaker: Professor emeritus dr. Eberhardt Zrenner, University of Tübingen, Tübingen, Germany	

Saturday, June 11

RIWC2022
21st Retina International World Congress

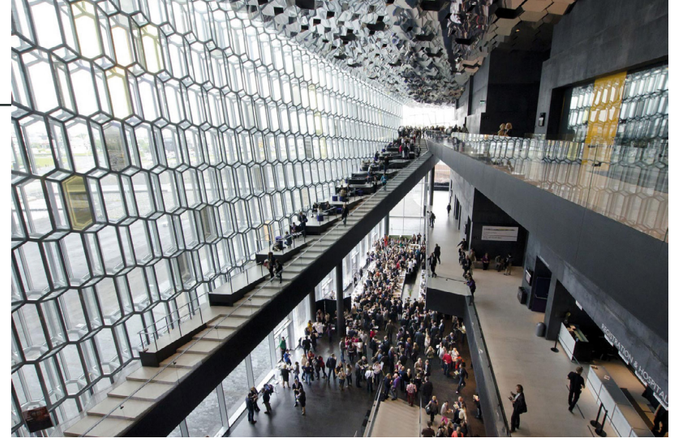
Retina International is a non-profit umbrella association of 34 national societies, each formed by people with retinitis pigmentosa (RP), Usher syndrome, macular degeneration, and allied retinal dystrophies, along with their families and friends.

Retina International is dedicated to promoting public awareness, stimulating research, and providing information on these diseases. RP is one name for a large group of inherited vision disorders that cause progressive degeneration of the retina. Usher syndrome is a rare inherited disorder primarily characterized by deafness due to an impaired ability of the auditory nerves to transmit sensory input to the brain (sensorineural hearing loss), accompanied by RP. Macular degeneration is a progressive disease affecting the macula, the center of the retina. It results in progressive loss of central vision. Occurring most often among older people, it is the most common cause of vision loss in people over age 55. It is believed that both genetic and environmental factors influence this disease.

The 21st Retina International World Congress (RICW2022) will take place on June 9–11, 2022, at the Harpa Concert Hall and Conference Centre, Reykjavík, Iceland. Being a part of a Retina International World Congress is a unique experience, bringing together some of the world's foremost retinal scientists and clinicians along with the global leaders in patient advocacy and peer support.

The RIWC2022 will be held at the same time and place as NOK2022. That will make this a very rare opportunity for practicing ophthalmologists to join both events. Together with the organizers of the Nordic Ophthalmology Congress 2022, we are preparing for a unique experience at a parallel event in the field of ophthalmology and research.

So please reserve June 9–11 for RIWC 2022 in Reykjavík, Iceland.



Anders Kvanta

"From biological treatment to gene and cell therapy in retinal disease"

Anders Kvanta is a professor in ophthalmology at Karolinska Institutet and a senior consultant in vitreoretinal surgery at St. Erik Eye Hospital. He has published more than 70 original studies on translational retinal research, ranging from angiogenesis to gene and cell therapy. Professor Kvanta is a principal investigator and lead researcher in clinical gene therapy and stem cell-based trials for retinitis pigmentosa and age-related macular degeneration.

Leon Herndon

"Far advanced glaucoma—are we making a difference?"

In this lecture, Dr. Herndon will examine novel treatment approaches in the management of far advanced glaucoma. We will also hear from a patient who has lost vision due to glaucoma as he gives us a glimpse into his life. Leon W. Herndon, Jr., MD, is a professor of ophthalmology at Duke University Medical Center in Durham, North Carolina. He has authored numerous papers, lectured nationally and internationally, and participated in several research projects related to glaucoma. He currently serves as Chief of the Glaucoma Division at the Duke University Eye Center, where he has trained 79 clinical fellows. He is the chair of the Glaucoma Clinical Committee of the American Society of Cataract and Refractive Surgeons, and secretary of the American Glaucoma Society. Dr. Herndon's research interests include novel treatment approaches in the diagnosis and management of glaucoma. He has ongoing research projects evaluating the high prevalence of primary open-angle glaucoma in Ghana, West Africa, where he travels yearly.

Eugene de Juan

"Physician innovators: A field guide"

Retinal surgeon, inventor, and entrepreneur Dr. Eugene de Juan, Jr. participates as inventor and advisor in early-stage ophthalmic opportunities. Dr. de Juan completed his medical degree and internship training at the University of South Alabama College of Medicine. He interned at the University of South Alabama Medical Center, followed by a residency at the Wilmer Ophthalmological Institute in Baltimore, Maryland, and a fellowship in vitreoretinal surgery at Duke University. He holds over 120 patents and has authored over 250 peer-reviewed academic publications. Before moving to San Francisco, Dr. de Juan was a professor of ophthalmology at the University of Southern California, the co-director of Vitreoretinal Service at Wilmer Eye Institute at Johns Hopkins, the director of the Microsurgery Advanced Design Laboratory, and the Joseph E. Green Professor of Ophthalmology. He was a member of the medical staff at the Duke University Eye Center, holding joint teaching appointments with the departments of ophthalmology and cell biology.

Tamara R. Fountain

"Pilots and physicians, passengers and patients: Making decisions when stakes are high"

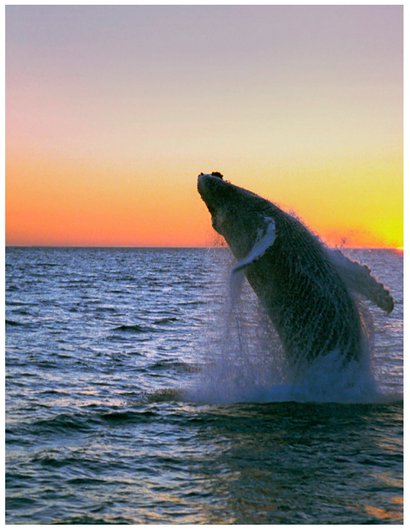
Dr. Tamara R. Fountain, MD, is a professor of ophthalmology at Rush University Medical Center and section chair emeritus of oculofacial plastic surgery. Dr. Fountain is the 2021 President of the American Academy of Ophthalmology and was previously president of the American Society of Ophthalmic Plastic and Reconstructive Surgery (ASOPRS), where she received the Robert Kennedy Presidential and Orkan Stasior Leadership Awards for service to the Society. Dr. Fountain served 15 years with the Ophthalmic Mutual Insurance Company, chairing the Audit, Strategic Planning, Risk Management, and Insurance and Marketing committees before being elected chair of the Board of Directors. She is a past president of the Illinois Society of Eye Physicians and Surgeons and has been involved in programming for the American Ophthalmological Society, Women in Ophthalmology, and the Chicago Ophthalmological Society. She previously was also an Alumni Fund Chair for Harvard Medical School.

Adventure Awaits

EXPERIENCE THE PURITY AND THE MAGIC OF ICELAND

Iceland has the lowest population density in all of Europe, with a pure, unpolluted and, magical landscape. Every day, there is an adventure waiting to happen. Here one will experience extreme contrasts and landscape that can best be described as out of this world with its abundance of mountains, volcanoes, glaciers, rivers, lakes, caves and rugged terrain.

Iceland offers a wide range of experiences regardless of when the country is visited. Every time of the year has its own unique atmosphere and there is always an opportunity to experience new things, discover beauty and marvel at the freshness and colours of nature. Every moment has its charm and will leave you with endless memories.



In winter it is a time of amazing contrasts. The placid snow accentuates the black lava fields, with a magical result. At night, the blackness of the sky is suddenly interrupted by flashes of light that flicker and dance across the sky in green, white or red: the Northern Lights often appear in cold, clear weather. Winter is a prime time for cross-country skiing and you don't have to go far from Reykjavik to find yourself surrounded by beautiful scenery and fantastic views. Summer will offer endless days thanks to the midnight sun which leaves visitors with a lot of time to travel and explore.

In Iceland there are seven regions which all have their unique characteristics be it the black sand beaches and glaciers in the South, reindeers, puffins and dramatic fjords of the East, skiing, whale watching and horses in the North, slow tourism being the characteristic of the Westfjords along with the arctic fox, culture and heritage of the West, Blue Lagoon and caves in Reykjanes Peninsula or the metropolitan capital city of Reykjavik.

Iceland has become a destination that people from around the world visit throughout the year and often visit a few times since the everchanging landscape will give a different experience every time.

Icelandic nature is fragile, as are Iceland's small communities and economy by comparison thus at the forefront of everything is sustainability and responsible tourism and we encourage travelers to integrate sustainability into their travel plans and other actions in life, as this is the key to the global and local well-being of ecosystems, cultures and the communities.

visiticeland.com

Ivan Potapenko
Department of Ophthalmology, Rigshospitalet, Copenhagen

Dr. AI will see you now...

On February 4, 2022, Ivan Potapenko defended his thesis "Artificial intelligence in age-related macular degeneration" at the Faculty of Health and Medical Sciences, Copenhagen University. The research, completed at the Department of Ophthalmology, Rigshospitalet, was supervised by Morten la Cour, Steffen Hamann, Josefine Fuchs, Javad Nouri Hajari.

Key points:

- Clinics will need to treat 50% more patients with AMD in the next 10 years.
- AI is safe and reliable for follow-up of AMD patients.
- Over half of these patients can be followed without human intervention.
- Noisy clinical training data does not impede AI performance.

Introduction

Effective treatment of patients with neovascular age-related macular degeneration (AMD) frequently requires long-term follow-up over several years. As the population ages, this growing patient group will put pressure on an already burdened public healthcare system. Staff expansion on its own is unlikely to be a viable solution; thus, innovative strategies are needed to address this issue.

In this thesis, we established the extent of the problem by modeling the number of actively treated patients and designed an artificial intelligence (AI) system to autonomously follow AMD patients.

The need for novel approaches

The direct impact of the increased AMD prevalence on the number of actively treated patients had not been previously estimated. We surveyed treatment data of 9,737 patients over 12 years. We found that the fraction of patients remaining in active treatment after initial diagnosis followed exponential decay, with a half-time of 3.6 years. This correlation appeared to be disease-specific and independent of factors such as treatment regimen and drug choice. A mathematical model based on this correlation was highly accurate in historical data (R^2=0.99; **Figure 1**). Our model predicted a linear increase of 50% in the number of actively treated patients during the coming decade. The predicted growth will mainly be driven by the demographic shift amplified by the long-term nature of treatment.

Artificial intelligence to the rescue

To address the projected patient increase, we designed an AI-based system for autonomous AMD follow-up. The system comprised two parts: an AI model to detect activity on optic coherence tomography scans and a deterministic logic to follow clinical guidelines for treatment (**Figure 2**).

The AI model was trained on noisy data taken directly from a clinical database without manual re-labeling. This previously unpublished approach allowed for the inclusion of 105,000 examinations. Up to 96% accuracy was achieved, on par with models trained on manually curated data. The deterministic logic integrated the AI model's output with patient history and clinical parameters to generate regimen-compliant treatment decisions. The algorithm was designed to handle advanced concepts such as regimen adherence, chronic edema, and concurrent ophthalmic disease. The flexibility of the two-component structure allows for later adjustment of the clinical algorithm or transition to another regimen without the need to re-train the AI model.

When validated on 200 prospectively collected cases, the system demonstrated safety on par with regular follow-ups at our clinic (92% and 88% safe decisions, respectively; p=0.33). We estimated that up to 60% of the department's AMD patient population could be followed by the system without human intervention.

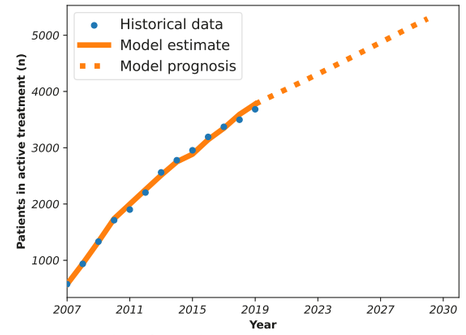


Figure 1. Number of actively treated AMD patients: model versus historical data

Looking forward

Considering the anticipated rapid growth in the treated AMD patient population, the emphasis in the coming years will be on novel follow-up strategies. As such, our proposed autonomous AI system is safe and flexible. The system can manage a large number of patients without the involvement of clinicians and can ease the pressure on public ophthalmology services in the future.

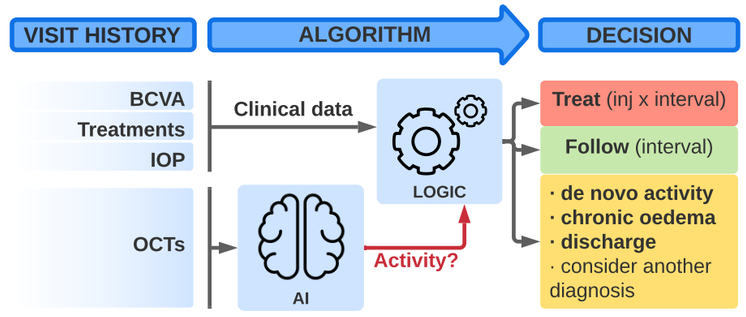


Figure 2. The design of the AI system for follow-up of AMD patients

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3. Potapenko I et al. Automated artificial intelligence-based system for clinical follow-up of patients with age-related macular degeneration. Acta Ophthalmol., epub ahead of print

Taking a sneak peek:

Preterm birth and long-term vision

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On June 12, 2021, Dýrleif Pétursdóttir defended her thesis "Ophthalmological follow-up in young adults born premature and screened for retinopathy of prematurity" at the Department of Neuroscience/Ophthalmology, Uppsala University/Akademiska Hospital, Uppsala. Her main supervisor was Assoc. Professor Eva Larsson, with co-supervisor Professor Gerd Holmström.

Key points:

- Being born preterm has long-term negative effects on visual function.
- Reassuringly, no deterioration occured from age 10 to young adulthood.

Prematurely born children have a higher risk of ophthalmological and neurodevelopmental disorders than those born at term. There is a paucity of long-term, prospective follow-up studies on the visual function of prematurely born adults. The current study reported the outcome of young adults born after the introduction of treatment for retinopathy of prematurity (ROP). The study aimed to assess visual function, visual-motor integration, refraction and its development, as well as strabismus, stereoacuity, accommodation, and convergence in prematurely born young adults.

The participants were prematurely born between 1 November 1988 and 31 October 1990, having a birth weight of ≤1.5 kg, in Stockholm County, Sweden. These individuals were initially part of a prospective population-based study on the incidence of ROP in the neonatal period, followed until 3.5 years of age. The group was re-examined at age 10 and compared with a control group of term born individuals. At 25–29 years of age, 59 of the preterm patients and 44 controls underwent an extensive ophthalmological examination and a developmental test of visual-motor integration.

Those born preterm had lower visual acuity than the controls at distance and near. Mean deviation of the visual field was reduced in those born prematurely, as was contrast sensitivity. A crowding ratio of ≥1.5 was more prevalent compared to controls. In a test of visual-motor integration, the preterm group had inferior results; a neurological complication at 2.5 years of age was the strongest risk factor. Those born preterm had greater values of myopia, hyperopia, anisometropia, and astigmatism, where the highest risk was found in those who had been treated for ROP. The spherical equivalent decreased around 1 D in both groups from 10 years to 25–29 years of age. Strabismus was found in 7/59 (12%) of the preterm group and 1/44 (2%) controls. A greater proportion of those born preterm had subnormal stereoacuity and worse amplitude of accommodation than the controls, but there was no difference in convergence.

In young adulthood, prematurely born individuals had reduced visual function, worse visual-motor integration, higher prevalence of refractive errors and strabismus, and worse stereoacuity than controls. Often, these lifelong effects were correlated with previous cryotherapy for ROP or neurological complications; however, this was not always the case, suggesting that prematurity played a role.

Future directions:

- The impact of preterm birth into later adult life
- The role of neurological defects in the visual problems seen on MRI in adulthood
- The visual perception of this patient group

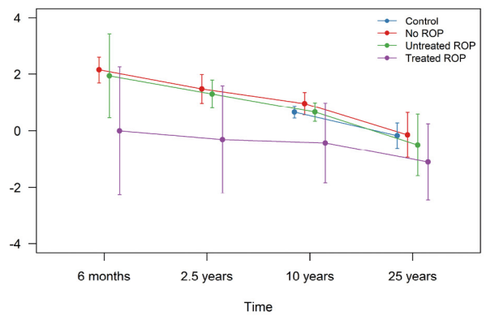

Figure 1. Development of spherical equivalent, in diopters, over time in the left eye of prematurely born individuals and term-born controls. ROP=retinopathy of prematurity. Pétursdóttir, D. 2021. Ophthalmological follow-up in young adults born premature and screened for retinopathy of prematurity. Digital Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine 1750. 71 pp. Uppsala: Acta Universitatis Upsaliensis. ISBN 978-91-513-1212-5.

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007 is best at poker. What is best for VKC?

Principles and opportunities of network meta-analysis in clinical ophthalmology

Ian Fleming's novels about the fictional agent James Bond, codename 007, have become endearing movie classics with an important cultural impact. Agent 007, of the British Secret Service, is an excellent spy, a fearsome assassin, a sharpshooter like no other, and a master of seduction. In the Casino Royale movie released in 2006, it is also revealed that 007 is the Secret Service's best poker player. A high point of the movie is when 007 wins with a straight flush against the villainous LeChiffre.

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How can one determine who is the best at playing poker in a large organization such as the British Secret Service? Although one could, theoretically, arrange multiple rounds of poker between all employees to rank individuals with certainty, this is not practically feasible. In practice, a network of comparisons can often be used for a reliable prediction of poker ranking. For example, employee A may have played against employee B, employee B may have played against employee C, and so on. Based on the results of their poker games, there is often a reasonable understanding of who is best.

Instead of 007, consider a hypothetical poker game ranking between the three authors of this paper. Marie Louise wins against Line. Line wins against Yousif. Based on this information alone, we can predict that, in terms of poker, Marie Louise must be the best (followed by Line, and then Yousif). We can put a ranking order even though we have no data on how Marie Louise performs against Yousif (**Figure 1A**). This is possible because we have data on direct comparisons, which we can extrapolate to make indirect comparisons (**Figure 1B**).

Now, consider another hypothetical poker ranking situation between the authors. Marie Louise wins against Line. Line now loses against Yousif. In this scenario, the situation is slightly more complicated, but a ranking order is still possible if we have data on the game results of the individual plays (**Figure 1C**). If we extrapolate this concept of comparisons in a network, we can use this concept in clinical ophthalmology to rank treatments according to their clinical efficacy using the principles of network meta-analysis.

Principles of network meta-analysis

Conventional comparative meta-analyses are made by summarizing the differences between pre- and post-intervention outcomes between two groups, e.g., a treatment group against a placebo group. While such meta-analyses provided a much-needed summary of evidence decades ago, the evidence base today is much larger and more diverse, and more than one or two treatment options exist. Additionally, we now have extensive computing power available at minimal cost.

Multiple treatment comparison meta-analyses allow comparison of three or more groups. Consider a simple case, where a group of studies have compared placebo against treatment A, another group of studies have compared placebo against treatment B, and no studies have compared treatment A to treatment B. A conventional meta-analysis would not be able to provide any insight into how treatment A compares against treatment B. But, if we use multiple treatment comparison meta-analysis, we can compare all groups, even treatment A vs. B in an indirect comparison, given the condition that we can draw a complete network across these groups of interest (**Figure 2**). Therefore, such meta-analyses are more popularly called network meta-analyses. In many circumstances, there is a mix of comparisons, which allows both direct and indirect comparisons as well as their summary estimate. A reference group is defined, upon which the summary estimates of all interventions can be ranked. This reference group can be placebo, but depending on the research question, it may be more appropriate to select an active treatment group as a reference, e.g., a best practice or gold standard to which other treatments can be compared.

Limitations, quality issues, and bias are important to understand when conducting and interpreting such studies. A clear research question, a well-conducted systematic literature search, and a qualitative review are mandatory aspects, just as in any other synthesis of evidence. The study design of overlapping systematic reviews is one of the main reasons why meta-analyses on the same topic can reach different conclusions.[1] For example, should different doses of the same drug be pooled into one category? Can different drugs of the same pharmaceutical category

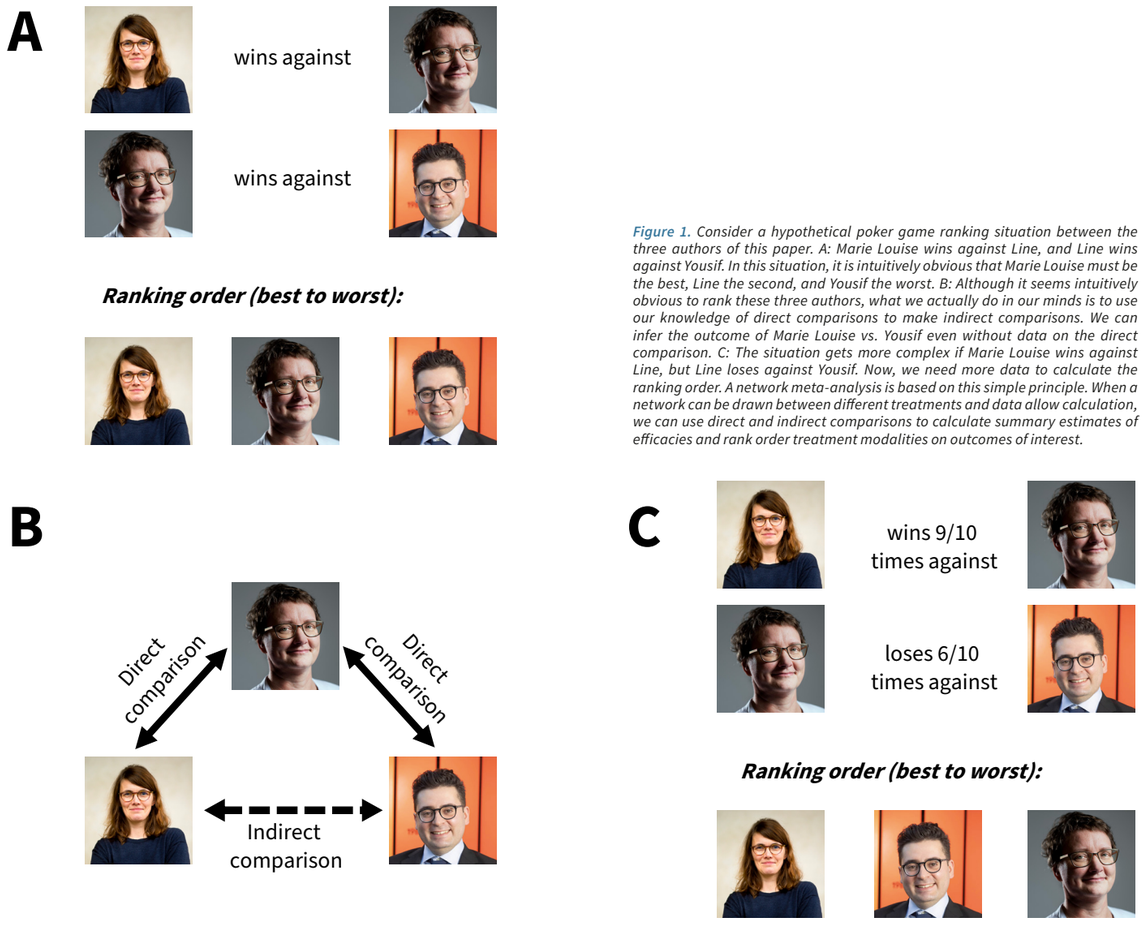

Figure 1. Consider a hypothetical poker game ranking situation between the three authors of this paper. A: Marie Louise wins against Line, and Line wins against Yousif. In this situation, it is intuitively obvious that Marie Louise must be the best, Line the second, and Yousif the worst. B: Although it seems intuitively obvious to rank these three authors, what we actually do in our minds is to use our knowledge of direct comparisons to make indirect comparisons. We can infer the outcome of Marie Louise vs. Yousif even without data on the direct comparison. C: The situation gets more complex if Marie Louise wins against Line, but Line loses against Yousif. Now, we need more data to calculate the ranking order. A network meta-analysis is based on this simple principle. When a network can be drawn between different treatments and data allow calculation, we can use direct and indirect comparisons to calculate summary estimates of efficacies and rank order treatment modalities on outcomes of interest.

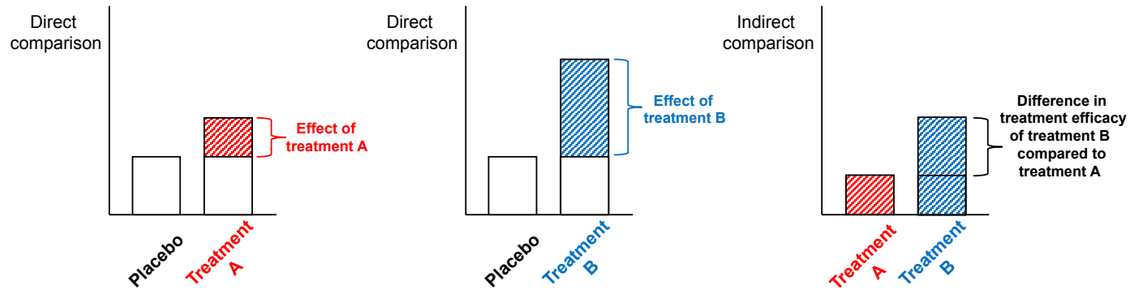

Figure 2. Consider a situation where one group of trials investigated the efficacy of placebo against treatment A (direct comparison) and another group of trials investigated the efficacy of placebo against treatment B (direct comparison), but no trials have compared treatment A and B. Using the outcomes from the direct comparisons, *it is possible to calculate efficacy estimates to perform an* indirect comparison.

be pooled into one category? How about different treatment regimens?

When dealing with network meta-analyses, it is important to keep in mind that the network of direct and indirect comparisons affects the overall summary estimate of a certain treatment and that different approaches to generate the network can lead to different outcomes. For example, consider a case where one systematic literature search excludes outdated treatments while another search includes such treatments. Because of direct and indirect comparisons, the summary estimates of different treatments will differ between the two network meta-analyses. This circumstance favors a more comprehensive literature search and broader eligibility criteria when conducting such network meta-analyses, but it also highlights the necessity of careful consideration of study design when planning such studies.

Another interesting aspect of network meta-analyses is that within the network, there can be groups or areas with specific biases that do not exist in other areas of the network. For example, the presence of publication bias in industry-sponsored trials is well-documented. If the network includes both industry-sponsored and investigator-initiated treatments, then a part of the network may be affected by this publication bias. In a similar fashion, other biases specific to treatments may affect one part of the network but not the other. It is unrealistic to expect to fully control such biases or a situation without any source of bias when conducting network meta-analysis. Therefore, careful consideration and discussion are the cornerstones of every such evidence synthesis, preferably facilitated by tools developed to summarize and ease the interpretation of these biases within and across studies.

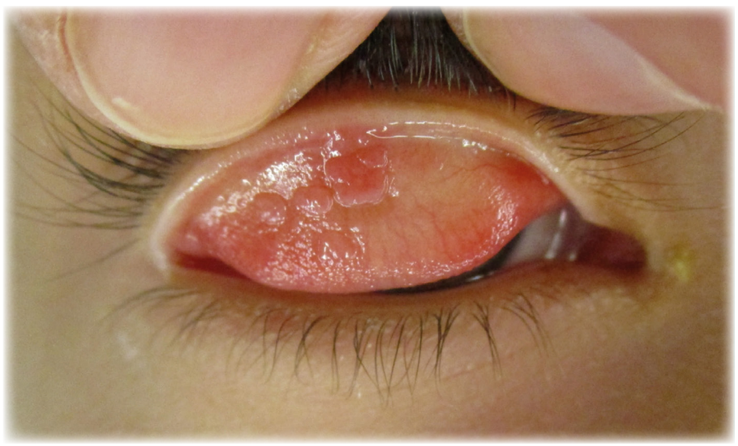

Figure 3. Clinical example of vernal keratoconjunctivitis with hallmark giant papillae located on the upper tarsal conjunctiva, clearly visualized on eversion of the upper lid.

Vernal keratoconjunctivitis: Many comparisons, ideal case

Vernal keratoconjunctivitis (VKC) is a disease of chronic conjunctival inflammation with hallmark giant papillae and Horner-Trantas dots (Figure 3). Although its pathophysiology remains incompletely elucidated, we know that it is in the category of allergic keratoconjunctivitis due to similarities in terms of allergic predisposition, eosinophilic infiltration, and inflammatory milieu. VKC is a relatively rare disease in Nordic countries, with an estimated prevalence of 3.2 per 10,000, and usually presents in pediatric populations.[2]

The overlapping allergic and inflammatory pathophysiology may allow for a range of clinical trials using different treatment modalities. No perfect treatment exists, to the frustration of the patient, parents, and physicians. Interestingly, this is an area where the broad range of treatment modalities have been compared in a fashion that allows a complete network (**Figure 4**); thus, it is a good case for a network meta-analysis to compare clinical efficacy.

Comparative efficacy of medical treatments for VKC across symptoms and signs

We began our work by conducting a state-of-the-art systematic review following PRISMA and the Cochrane Handbook. Our review was based on 39 comparative studies, of which 23 provided data that allowed meta-analyses. We evaluated efficacy as the change in four symptoms (itching, tearing, photophobia, and foreign body sensation) and four signs (hyperemia, punctate keratitis, Horner-Trantas dots, and giant papillae).[3] Effect size was measured by the standardized mean difference and calculated relative to placebo. The analysis of the Horner-Trantas dots is provided as

an example in **Figure 5**. Considering the comparisons available, it becomes clear that conducting conventional pairwise comparative meta-analyses of identified treatments could lead to difficulties in interpretation, counteracting the purpose of providing an overview.

Our study found a general trend of better efficacy using corticosteroids and highlighted that the range of therapies provided different efficacy across signs and symptoms. This is an excellent example of how network meta-analyses can help clinical practice. These rankings provide better certainty in how to interpret and rank existing therapies, which we used to create a national guideline for the treatment of VKC.[4]

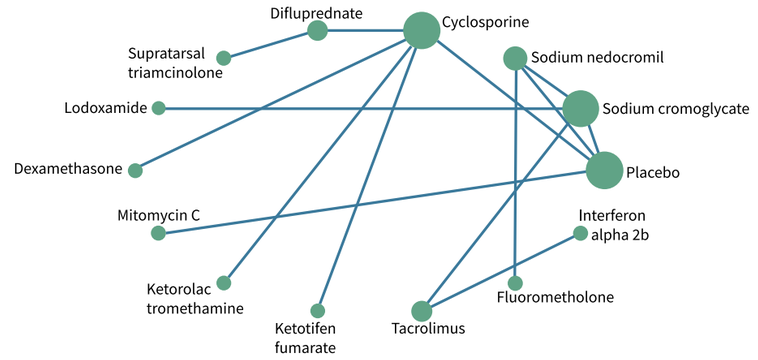

Figure 4. A network plot from a network meta-analysis on the comparative efficacy of medical treatments for vernal keratoconjunctivitis.[3] This network plot is from the analysis of the efficacy on Horner-Trantas dots. The size of the dots indicates the number of studies available with that individual treatment or placebo group. Lines between the dots indicate the existence of at least one study. In this example, a network can be drawn between all studies that evaluate Horner-Trantas dots.

Direct estimates

Active	Control	Cohen's d	LCI 95%	HCI 95%
Sodium cromoglycate	Placebo	-0.71	-1.09	-0.32
Sodium nedocromil	Placebo	-0.68	-1.11	-0.25
Cyclosporine	Placebo	-0.69	-1.60	0.22
Difluprednate	Cyclosporine	-1.14	-4.04	1.77
Difluprednate	Supratarsal triamcinolone	0.00	-3.96	3.96
Lodoxamide	Sodium cromoglycate	-0.38	-1.41	0.64
Dexamethasone	Cyclosporine	-0.18	-0.39	0.02
Mitomycin C	Placebo	-0.99	-1.79	-0.19
Ketorolac tromethamine	Cyclosporine	0.15	-0.94	1.25
Cyclosporine	Ketitofen fumarate	-0.39	-1.07	0.29
Tacrolimus	Sodium cromoglycate	-0.15	-1.30	0.99
Sodium nedocromil	Fluorometholone	0.32	-0.71	1.35
Sodium nedocromil	Sodium cromoglycate	0.07	-0.60	0.74
Tacrolimus	Interferon alpha 2b	0.00	-0.62	0.62

Summary estimates (direct + indirect estimates) with placebo as the reference in a forest plot

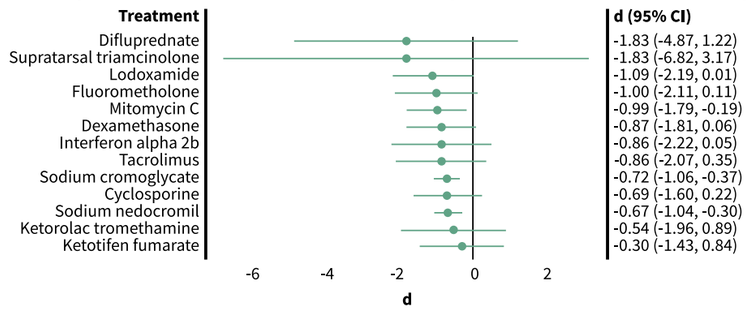

Figure 5. This is an example of the calculations from a network meta-analysis on the comparative efficacy of medical treatments for vernal keratoconjunctivitis, specifically from their analysis of the efficacy on Horner-Trantas dots.[3] Each of the rows in direct estimates are similar to the results that would be obtained from a classical pairwise meta-analysis, e.g., the meta-analysis of all studies comparing sodium cromoglycate vs. placebo lead to a lower degree of Horner-Trantas dots in the group of sodium cromoglycate at a Cohen's d of -0.71 (CI 95%: -1.09 to -0.32). After calculating indirect comparisons, the results are summarized into a final summary estimate, which is, in this case, ranked in order of efficacy and presented in a forest plot.

Concluding remarks

The network meta-analysis is a great tool for evidence synthesis and allows for comparison of three or more groups. Clinical ophthalmology can benefit from such analyses, especially considering the incredible amount of clinical evidence published today. However, careful conduct and interpretation are necessary to avoid being misled rather than being guided for better patient care. Ideally, we want to be like 007—careful in handling situations, with an eye for detail, and triumphant in the end.

Key points:

- The large evidence base of modern medicine provides data on a diverse range of treatment options.
- Network meta-analyses enable comparison of 3+ groups between one another and allow ranking of multiple treatment options.
- Methodological limitations and sources of bias necessitate a careful approach to conducting and interpreting such analyses.

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Fuchs' endothelial corneal dystrophy:

Heredity behind common corneal disease

On October 15, 2021, Andreas Viberg defended his thesis "Fuchs' endothelial corneal dystrophy—Genetic etiology and as a risk factor in cataract surgery" at the Department of Clinical Sciences, Ophthalmology, Umeå University. The PhD project was supervised by Berit Byström, MD, PhD, Department of Clinical Sciences, Ophthalmology, with co-supervisors Irina Golovleva, PhD, Department of Medical Biosciences/Medical and Clinical Genetics and Patrik Danielson, MD, PhD, Department of Integrative Medical Biology, Anatomy, Umeå University, Sweden.

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Key points:

- FECD is associated with $(CTG)_n$ expansion in *TCF4*, and repeat length is associated with disease severity.
- Patients with cataract and concomitant corneal guttata benefit from cataract surgery, but corneal guttata is associated with inferior results in both visual acuity and patient self-assessed visual function.

Nine out of ten of those with a common corneal disease have rare genetic changes. The findings of this dissertation may be important for the choice of treatment, which often includes corneal transplantation.

Fuchs' endothelial corneal dystrophy (FECD) causes visual impairment and pain. The hallmarks of FECD include corneal guttata, which is the excessive accumulation of extracellular matrix in the corneal endothelial basement membrane and the loss of endothelial cell function. In order to develop new treatment strategies that increase the patient's quality of life, it is valuable to understand the disease mechanisms. Although the disease affects only around 4% of the population, it is the most common cause of corneal transplantation in Sweden and many other countries.

The first portion of this dissertation studied the genetic cause of FECD by looking at 102 cases and an equally large healthy control group. Of the patients studied, 90% had changes in the gene *TCF4*. The change, which consisted of an increased number of repetitions of a specific DNA sequence, was only seen in 4% of the general population. There was also a connection between the repetition length of the DNA sequence and the severity of the disease.

The second part of the dissertation studied the outcome of cataract surgery in patients with both cataracts and FECD. This study was based on quality registers from the Swedish national cataract registry and the Swedish cornea transplant registry with several thousand people. The results suggest that FECD patients benefit from cataract surgery, but, at the same time, they are at risk of poorer results than patients with only cataracts, and they have an increased risk of subsequent corneal transplantation.

Because it is not uncommon for visual problems to be caused by a combination of cataracts and FECD, I hope the results of this dissertation can be helpful in choosing treatment for these patients.

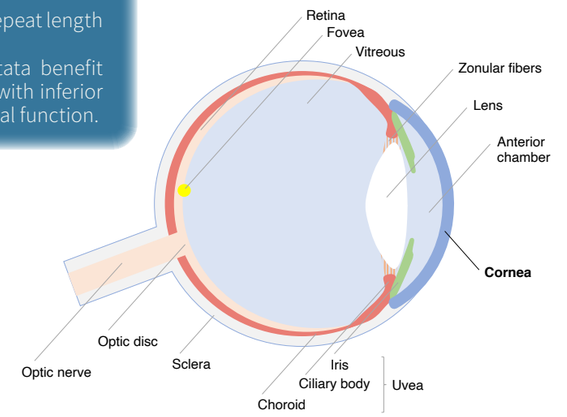

Figure 1. Basic eye anatomy and localization of the cornea (upper). The corneal layers (bottom left) and histological presentation of the hexagonal cells in the endothelial layer (bottom right), without and with corneal guttata (in orange). Illustrations by Andreas Viberg.

Remaining questions:

- Does a $(CTG)_n$ repeat expansion in *TCF4* impact cataract surgery results in patients with FECD?
- Can the development of a genetic test be useful in difficult cases?

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