eye on Ophthalmology

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Recent Advances in Cataract Research

Cataract is the leading cause of blindness worldwide, accounting for more than 20 million of the world population, a figure estimated to reach 40 million by 2020.1 The removal of cataract is the most common surgical procedure performed in those over the age of 65 in New Zealand.2

The Department of Ophthalmology at the University of Auckland has established major research projects involving the clinical and scientific aspects of cataract formation.

Clinical research

Currently in ophthalmic clinical practice, the classification of cataract primarily involves a subjective clinical grading. Classification schemes for grading lens opacities include the Lens Opacities Classification Scheme (LOCS III) and the Oxford Clinical Cataract Classification and Grading System (OCCGS); however, these are mainly reserved for research purposes. We are presently investigating the use of novel techniques for additional pre-operative assessment of cataracts and post-operative outcomes of cataract surgery and its application to the clinical setting.

Scheimpflug photography

The Anterior Eye Segment Analysis System (NIDEK EAS-1000, Japan) is an imaging technique based on the Scheimpflug principle that is relatively new to New Zealand and is used for assessing lens abnormalities such as cataract. This is an accurate, reproducible and observer-independent system that can be used to classify cataract. Scheimpflug photography has been in use over the past decade as a non-invasive tool for in vivo examination of the lens, however this has been a technique mainly limited to research centres.3 It captures several types of images, including single photographic slit sections of the anterior segment (Fig 1a) and retroillumination images of the lens, (Fig 1b) and can be used as a postoperative imaging tool to calculate the position of an intraocular lens implant. A unique feature of this imaging technique is the ability to create a three-dimensional reconstruction of a lens by capturing several static slit images (eg. Sixty images at three-degree intervals around a central axis), providing sufficient information to determine the volume of opacity of the lens and the exact location of the opacity.4

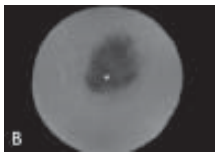

Figure 1. Scheimpflug slit photograph (A) and retroillumination image (B) illustrating a dense posterior subcapsular opacity

Analytical functions of The Anterior Eye Segment Analysis System of these slit images include linear densitometry of lens opacity, integral density of the lens and biometry (see fig 2).

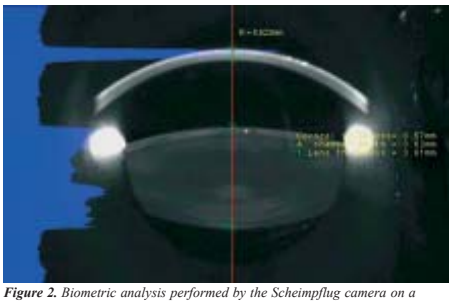

Figure 2. Biometric analysis performed by the Scheimpflug camera on a normal eye.

Wavefront aberrometry

A recent introduction to the ophthalmic clinical world is wavefront aberrometry.5 This is a novel technique for quantifying the aberrations produced by the eye as a whole optical system. It assesses the higher order aberrations (ie. aberrations beyond defocus and astigmatism) emanating from a human eye, practice that is not routine in clinical ophthalmology (fig 3). Wavefront aberrometry has been utilised to refine corneal refractive surgery and has recently been adapted to quantify and analyse the aberrations induced by cataract.6 The use of this technology in assessing patients with cataract could provide a possible explanation for patients with visual symptoms such as glare and night driving difficulties and a relatively good high-contrast Snellen visual acuity.

Order of aberration	Name of aberration
0	Piston
1	Tilt along x and y axis
2	Spherical refractive error, Astigmatism
3	Coma, Trefoil
4	Spherical aberration, Secondary astigmatism, Tetrafoil
5	Secondary coma, Secondary trefoil, Pentafoil

Figure 3. Table indicating each order of aberration.

The combination of Scheimpflug photography and wavefront aberrometry in the assessment of cataract will allow the correlation of the type of cataract with the higher order aberrations induced by each type of cataract. This will be particularly useful in patients with posterior subcapsular lens opacities where symptoms are dependent on level of illumination and pupil size.

A recently conducted study of twenty patients presenting with cataract to Auckland Public Hospital reveals different wavefront aberrometry patterns with different types of lens opacities. Nuclear opacification induces a higher amount of negative spherical-like aberration (fourth order aberration), whereas cortical lens opacities induce a high amount of coma (Figure 4).

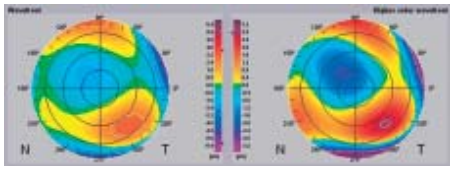

Figure 4a. Colour coded map from the Zywave Hartmann-Shack aberrometer of a patient with predominantly cortical lens opacification. The left map shows the total aberrations emanating from this eye; the right map illustrates the higher order wavefront from this eye showing a high amount of coma.

Scientific research

Protein composition of lenticular opacities

The recent sequencing of the human genome has introduced a new chapter into the analysis of the protein structure of the lens. To date, the study of protein expression (proteomics) of the lens has concentrated on crystallins and has been done predominantly in animal models with induced lens opacities.7,8 The major limiting factor in the study of proteomics in human cataract formation ins the availability of tissue for research.

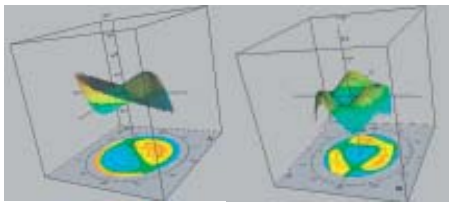

Figure 4b. Three-dimensional representation of a wavefront with predominantly and coma (left) and one with predominantly negative spherical-like aberration (right).

We hypothesised that since cataract surgery is the most common procedure performed in people over the age of 65 in New Zealand, the discarded debris from this surgery could potentially be a prolific source of research material available to study the protein structure of human lens opacities. Currently, the most common surgical technique to remove cataract is phacoemulsification. This uses ultrasound to emulsify the cataractous lens in-situ followed by aspiration of the lens fragments and cellular debris, leaving an intact capsular bag into which a synthetic intra ocular lens (IOL) implant is placed. In order to assure that this source of material is of sufficient integrity to identify the molecular changes in protein expression that are associated with the development of age-related cataract in humans, it was first necessary to determine whether phacoemulsification induces any protein degradation.

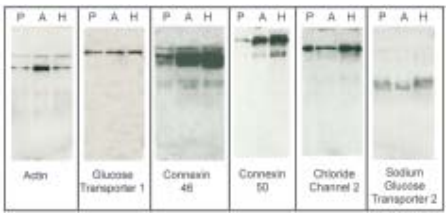

Figure 5. *Bovine lens proteins prepared by three separate methods, Phacoemulsification (P), Aspiration (A) and Homogenisation (H) were separated by molecular weight prior to individual protein identification by specific antibodies. Analysis of five membrane proteins and the intra-cellular protein actin revealed no significant differences in protein integrity between the three separate isolation methods.*

In order to test this hypothesis, normal bovine lenses were obtained. These lenses were extracted using three different methods. One group were emulsified by phacoemulsification, one group were aspirated (without phacoemulsification) and one group of lenses were dissected intact from the eye and then homogenised according to standard laboratory techniques for protein preservation. All groups were processed using 1-Dimensional gel electrophoresis, a technique commonly used in laboratory science for separating proteins by their molecular weight. Six proteins were targeted in each group using specific antibodies; five to known membrane proteins (Glucose Transporter 1, Connexin 46, Connexin 50, Chloride Channel 2, Sodium Glucose Transporter 2) and one to an intracellular protein (actin). As shown in figure 5 all three methods of extraction resulted in almost identical gel maps identifying the same protein with no evidence of any degradation of proteins. Thus, we conclude that phacoemulsification does not induce any degradation of lens proteins and therefore provides us with a abundant source of human lens material, enabling the study of the proteomics of human cataractous lenses which is now in progression in collaboration with Dr Paul Donaldson and Dr Rachelle Merriman-Smith in the Department of Physiology at the University of Auckland.

Conclusion

The development of these research tools provides a new avenue for cataract research. The combination of the classification of a subject's cataract by Scheimpflug photography with the wavefront aberrations induced by each cataract will ascertain whether certain types of cataract are associated with specific wavefront abnormalities. The assessment of the molecular changes of different types of cataract will allow the correlation of specific changes in gene and protein expression with each type of cataract.

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