Spotting cataracts at the earliest stages

Manuel B Datiles III, MD

“Early detection of cataracts before symptoms appear is a long sought goal of ophthalmology. A new instrument originally developed for research in zero gravity may be what the eye care community has been waiting for.

The new instrument uses a laser-based dynamic light scattering (DLS) to measure cataract-associated proteins in the lens. It was originally developed by Rafat Ansari PhD, senior scientist at NASA’s John H Glenn Research Centre to analyse the growth of protein crystals in a zero gravity space environment.

Dr Ansari came up with the idea of using his instrument for clinical medicine after his father developed cataracts. He researched the topic of cataract formation, and upon learning that several proteins are involved in cataract development, began to look at ways to measure proteins associated with early stage cataracts, particularly alpha-crystallin.

After doing some basic research to evaluate his theory, Dr Ansari shared his ideas with medical researchers at the National Eye Institute, a division of the US National Institutes of Health. More than a decade of research culminated in a recent publication in the Archives of Ophthalmology (Arch Ophthalmol, Dec 2008; 126: 1687 – 1693) indicating significant clinical potential for the new approach.

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“We have shown that this non-invasive technology that was developed for the space programme can now be used to look at the early signs of protein damage due to oxidative stress, a key process involved in many medical conditions, including age-related cataract and diabetes, as well as neurodegenerative diseases such as Alzheimer’s and Parkinson’s. By understanding the role of protein changes in cataract formation, we can use the lens not just to look at eye disease, but also as a window into the whole body,” said Dr Ansari.

In the recently published study, the researchers used dynamic light scattering to clinically assess early pre-cataractous lens protein changes in 380 eyes of 235 people ranging in age from seven to 86 years. Participants had clinical nuclear lens opacities ranging from zero to 3.8 on the AREDS scale, i.e. from clear to extremely cloudy lenses.

Dynamic light scattering analysis revealed a statistically significant decrease in the alpha-crystallin index associated with increasing nuclear opacity and ageing. The testing revealed significant losses of alpha-crystallin, even in clinically clear lenses of elderly patients.

“By the time the eye’s lens appears cloudy from a cataract, it is too late to reverse or medically treat this process. This technology can detect the earliest damage to lens proteins, triggering an early warning for cataract formation and blindness,” said Manuel B Datiles III, MD, NEI medical officer and lead author of the clinical study.

Clinical detection of pre-cataractous lens damage is not possible with current imaging modalities. This new ability has many potential applications, according to Dr Datiles. For example, early identification of increased risk for cataract development could be used to encourage patients to modify risky lifestyle practices such as sun exposure, smoking, and alcohol intake. It also adds yet another reason to encourage patients to strive for tight control of diabetes.

Measuring the alpha-crystallin index could also be an important new outcome variable in clinical trials. It could help select patients for medical studies involving anti- cataract drugs, eliminating those whose cataracts may have progressed too far. It could also prove useful in evaluating such drugs in appropriate patients. Conversely, dynamic light scattering lens evaluation could also be useful in evaluating the potential cataractogenic side effects of all manner of drugs in clinical studies.

“Because the development of overt nuclear cataracts can proceed slowly, a highly sensitive and quantitative means of assessing pre- cataractous changes also would be useful as an outcome variable in clinical trials for assessing treatment effects (protective or toxic) on the lens,” the researchers emphasise.

The DLS device developed by Dr Ansari includes a fibre-optic probe mounted on a movable carriage inside a keratoscope (Keratron, Optikon) with a three-dimensional aiming system. Over the past dozen of years Dr Ansari and colleagues evaluated the potential of this approach in different animal models of cataract, including cold cataract, radiation, diabetic, selenite, and hyperbaric oxygen-induced cataracts. Clinical trials were instituted after these studies showed a high degree of safety and repeatability.

The device directs a beam of light to a specific area in the lens, collecting light scattered by randomly moving particles during a five second interval. The device then uses the time-autocorrelation function of the measurements to calculate a profile of intensities. This provides an estimate of the frequency distribution of particle sizes. From this the instrument can measure the presence of alpha-crystallin and other lens proteins.

“A delay in cataract formation of about 10 years would reduce the prevalence of visually disabling cataracts by about 45 per cent,” notes Carl Kupfer MD, former director of the National Eye Institute.

The new device should also be a boon to NASA, which is setting its long-term sights on a manned mission to Mars, added Dr Ansari.

“During a three-year mission to Mars, astronauts will experience increased exposure to space radiation that can cause cataracts and other problems. In the absence of proper countermeasures, this may pose a risk for NASA. This technology could help us understand the mechanism for cataract formation so we can work to develop effective countermeasures to mitigate the risk and prevent it in astronauts.”