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Letter to the Editor

The stiffness of human cataract lenses is a function of both age and the type of cataract

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Abstract

Surgical evidence suggests that nuclear cataract lenses are generally harder than normal lenses. We examined this quantitatively using dynamic mechanical analysis of cataract lenses removed during surgery and compared the results with data from normal lenses. Stiffness of the lens centre was found to depend on the type of cataract and the age of the patient. Nuclear cataract lenses were generally stiffer than those extracted from patients with predominantly cortical cataract, with some in the latter group appearing not to differ significantly from age-matched normals. At age 40–50, the nuclear region of advanced nuclear cataract lenses was found to be approximately 46 times harder than that of normal lenses of the same age. By age 70–80 the stiffness of advanced nuclear cataract lenses had doubled, however, by this age, normal lenses had also increased significantly in stiffness so that the difference between cataract and normal lenses was much less pronounced, being a factor of approximately 2.5.

Keywords: cataract surgery; phacoemulsification; nuclear cataract; hardness; age

A change in the stiffness of normal lenses has been implicated in the process of presbyopia that becomes evident by the age of 50 and renders people unable to focus on near objects. Techniques that have been used to investigate lenticular stiffness include centrifugal methods (Fisher, 1971), impedance analysis using a probe pushed through the lens (Pau and Kranz, 1991), and more recently a method that is routinely used to measure the stiffness of polymers, dynamic mechanical analysis (DMA) (Heys et al., 2004, 2007; Weeber et al., 2005).

Nuclear cataract is characterised by oxidation of the lens proteins (Garner and Spector, 1980; Truscott and Augusteyn, 1977b), and there is clinical evidence that such cataract lenses are harder by comparison to their normal counterparts. Several physical methods have been used to investigate the stiffness of cataract lenses. These include the use of an automated guillotine (Assia et al., 1997; Heyworth et al., 1993; Tabandeh et al., 1994a,b), compression of the lenses between plates (Smith et al., 2002), and the use of penetrating indentor (Czygan and Hartung, 1997). This interest is based largely around the need to estimate the stiffness of cataract lenses, so as to gauge their suitability for extraction using phacoemulsification (Bourne et al., 2004; Gonglore and Smith, 1998). Very hard lenses present a problem during surgery. Recent studies have employed ultrasound techniques (Tabandeh et al., 2002) in an effort to obtain data *in vivo* prior to surgical extraction.

Using a DMA method that had been developed for analysis of human lenses, we examined cataract lenses of known ages and compared the stiffness data with those from non-frozen normal lenses obtained from the Sydney Lions Eye Bank that had previously been analysed (Heys et al., 2007). Twenty cataractous human lenses were sourced from an eye clinic in Rajkot, Gujarat, India, and transported in cooled containers to Australia. They were stored at 4 °C in 2 ml cryovials (Simport Plastics, Canada) to reduce possible dehydration during

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travel and were not frozen before being analysed. Lenses were analysed as quickly as possible, with most analyses occurring within 1 week of lens extraction.

Cataract lenses were placed in a holder and then sectioned equatorially using a razor blade. The instrument used for the measurement of stiffness was a Q800 DMA (TA Instruments, New Castle, DE, USA). The sample holder, DMA probe and the method of analysis were as described previously (Heys et al., 2004). In the experiments described here, stiffness measurements were carried out using the controlled force technique, and nine readings comprising a 3×3 1 mm grid pattern were taken across the centre of each lens section. An average value of these measurements was used to calculate the mean stiffness of the lens nucleus. This work was approved by the human research ethics committees of the University of Wollongong and the University of Sydney.

Fig. 1 shows that the cataract lenses were generally stiffer than those of age-matched normal lenses. In addition, the Types III and IV cataract lenses tended to exhibit higher values of stiffness than the less mature nuclear cataract group (Types I and II). This finding agrees with those of previous studies (Assia et al., 1997; Smith et al., 2002; Tabandeh et al., 1994a,b). The more advanced nuclear cataract lens group increased in stiffness with age such that on average there was a doubling in stiffness of the Types III and IV lenses over the 4 decades from age 40 to 80.

When we grouped the lenses into decades and compared cataract lenses with normal lenses as a function of age, a clear difference in the two groups emerged that was dependent on the age of the lens (Fig. 2). For the younger cataract lenses stiffness was very different from that of normals. For example, in the decade 40–49 years, stiffness values of all cataract lenses were on average approximately 32 times those of normal lenses. If only advanced nuclear cataract lenses were included, the difference was even more pronounced. Types III and IV lenses aged 40–50 were 46.5 times ($n = 3$) stiffer than comparable normal lenses. By later decades (60–70 and 70–80), however, the ratio of stiffness of normal lenses and cataract lenses had declined to approximately 2.5 (Fig. 2).

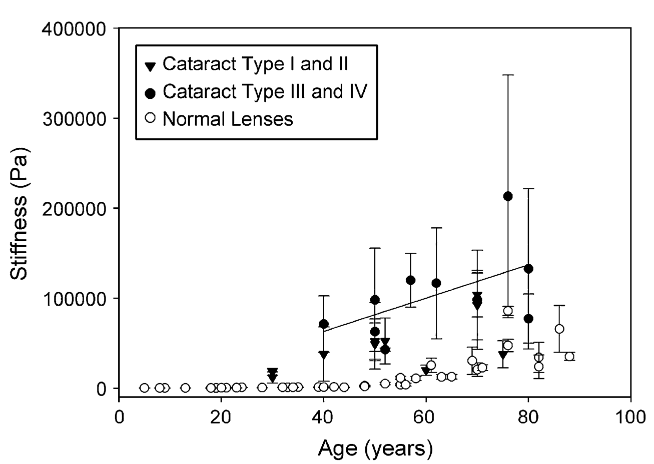

Fig. 1. The stiffness of human cataract lens nuclei as a function of age. Cataract lenses were divided into two groups: Types I and II (▼) and Types III and IV (●). Normal lens values (○) are shown for comparison (Heys et al., 2007). The trend line for the 10 Types III and IV lenses was obtained using Sigma plot ($y = 1847x - 10,700$).

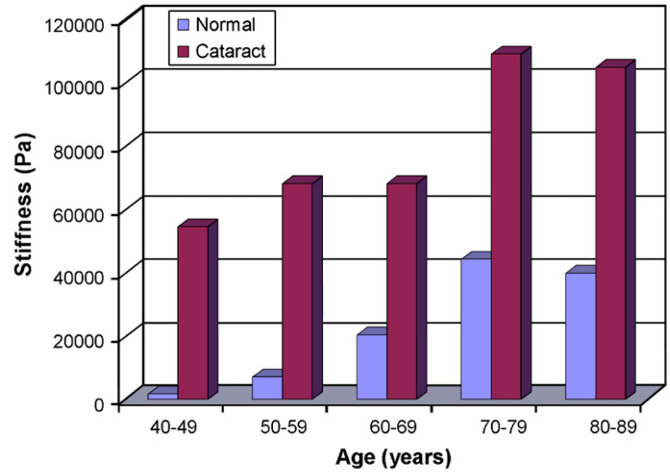

Fig. 2. A comparison of the mean values of stiffness of normal and cataract lenses as a function of age. All cataract lenses were combined, the lenses were grouped into decades and are the same lenses as shown in Fig. 1. The number of lenses in each group were as follows: 40–49 (normal: $n = 5$, 1663 ± 758 Pa; cataract: $n = 2$, 37,873 and 71,211 Pa); 50–59 (normal: $n = 5$, 7071 ± 3753 Pa; cataract: $n = 7$, $68,204 \pm 29,179$ Pa); 60–69 (normal: $n = 4$, $20,350 \pm 9051$ Pa; cataract: $n = 2$, 19,866 and 116,562 Pa); 70–79 (normal: $n = 4$, $44,226 \pm 30,385$ Pa; cataract: $n = 5$, $109,024 \pm 63,908$ Pa); 80–89 (normal: $n = 4$, $39,832 \pm 18,121$ Pa; cataract: $n = 2$, 77,288 and 132,599 Pa).

Previous investigations using a variety of approaches have shown a relationship between the degree of nuclear colouration and the stiffness of cataract lenses, with cortical cataract lenses tending to exhibit stiffness values similar to those of normal lenses (Assia et al., 1997; Smith et al., 2002; Tabandeh et al., 1994a,b). In most published studies, the relative differences in hardness measurements have been measured (Assia et al., 1997; Heyworth et al., 1993; Tabandeh et al., 1994a,b). Our data, obtained using the well-characterised DMA method, support these findings and furthermore we were able to quantify the stiffness of both normal and cataract human lenses. There was a marked difference in the ratio of normal to cataract lens stiffness that depended on the age of the individual (Fig. 2). Both normal and cataract lenses increased in stiffness with age, with the most pronounced increase in normal lenses occurring between the ages of 50 and 79. Normal lenses at age 40 are relatively soft. By age 70–79, normal lens stiffness values had approached those of 40–49 years old cataract lenses (Fig. 2).

We do not yet have a detailed picture of the reasons for the age-dependent stiffening of human lenses. In normal human and pig lenses, stiffness is correlated with the amount of free alpha crystallin that is present in the lens nucleus (Heys et al., 2007) and, after this chaperone has disappeared in man at around age 40, the stiffness of the lens nucleus increases dramatically. In humans, the increase in stiffness of normal lenses with age is not due to compaction of lens cells as has been observed in several other animals (Van Heyningen, 1972).

In the case of nuclear cataract lenses there may well be additional biochemical processes that take place which contribute to stiffness and are not observed to any significant extent in normal lenses. For example, covalent crosslinking of polypeptides (Buckingham, 1972; Truscott and Augusteyn, 1977a) is known to increase substantially as a function of the degree of nuclear cataract. In other systems, the degree of crosslinking of polymers is well known to be associated with an increase in hardness (Katime et al., 2006; Kudela, 1987). Oxidation of crystallins in nuclear cataract lenses (Garner and Spector, 1980; Truscott and Augusteyn, 1977b), which involves disulfide bond formation, may accelerate processes that contribute to hardening of the lens. Recent data (unpublished) suggest that there may be some slight dehydration in the nuclei of advanced nuclear cataract lenses. This factor too may contribute to the physical differences that we, and others, have found in the cataract lenses compared to normal human lenses.

Although the number of cataract lenses analysed in this study was relatively small, there appeared to be a limit to the age-dependent increase in lens stiffness (Fig. 2). In cataract lenses this apparent maximum was attained by approximately age 70, with the value reached being approximately double that of age-matched normal lenses.

In conclusion, age-related nuclear cataract lenses were stiffer than normal lenses for all ages examined and the stiffness values increased with age for both groups. The relative difference was, however, more pronounced for the younger lenses. These findings suggest that surgeons may well experience more problems with phacoemulsification if the nuclear cataract is present in older patients. Although we do not yet understand the reasons for the increase in lens stiffness in the case of either cataract or normal lenses, the data imply that nuclear cataract may represent an acceleration of the aging process. By contrast lenses with cortical cataract did not differ significantly from normal lenses, illustrating the different aetiologies of cortical and nuclear cataract.

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