Macular Pigment Optical Density before and after Cataract Extraction

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Purpose. Psychophysical methods of measuring macular pigment (MP) use comparisons of short- and midwave light in the fovea and parafovea to derive optical density estimates. This light must pass through the crystalline lens before absorption by the MPs can occur. The effect of lens absorption on these measures has not been adequately determined. The present study assesses the influence of lens absorption on MP measurements by comparing MP optical density (MPOD) measured before and after cataract extraction.

Methods. MPOD was measured using flicker photometry in free view at 458 nm with a 1° stimulus. Twenty-nine eyes from 24 patients with cataracts sufficiently severe to require cataract extraction were evaluated.

Results. In the entire group of 24 patients, the mean (±SD) age measured 68.7 ± 9.5 years, and the mean MPOD measured 0.19 ± 0.11. For all 29 eyes measured, MPOD averaged 0.206 ± 0.13 before and 0.18 ± 0.12 after cataract extraction. MPOD measurements at the two time points (mean 8.1 ± 4.7 weeks after surgery) were highly correlated ($r = +0.58$), suggesting that a cataractous lens does not influence the MP measurement technique.

Conclusions. Psychophysical techniques can be used to obtain reliable measurements of MP in elderly subjects, even in those with cataracts. Moreover, differences in retinal illuminance due to varying opaqueness of the crystalline lens do not seem to have a measurable influence on MPOD. (*Invest Ophthalmol Vis Sci.* 2001;42:1338–1341)

Before the neural retina can process light, it is reflected, absorbed, and scattered by the anterior structures of the eye. Of these structures, it is the crystalline lens that tends to influence visible light most strongly and that may therefore impact visual performance most significantly.[1] For instance, a dense lens increases the forward scatter of light, reducing contrast sensitivity by producing a veiling illumination across the retinal image.[2] The crystalline lens also decreases retinal illumination as a function of age, particularly at short wavelengths.[3]

Measurements of the retina are therefore affected by light loss due to lens absorption. For example, Maxwellian view optics focus a narrow ray of light through the center of the pupil, and this light passes through the central nucleus of the lens. Stimuli seen in natural view must pass through a wider area of the lens defined by the size of the pupil. Both psychophysical and physical methods must correct for the wide individual differences in this type of preretinal light loss to precisely specify retinal illuminance. Psychophysical methods are further limited, in that corrections are made for light absorption but not for the negative effects of a dense lens on visual performance.

There are generally two methods used to correct for absorption by the crystalline lens. One method involves measuring the optical density (OD) of the lens at specific wavelengths (see Snodderly and Hammond[4]) and then subtracting these values from the overall amount of light used in retinal measurements. Another method used to correct for lens absorption is to compare measures of retinal areas that differ only in the parameter being measured. In this way, light absorption by the lens is the same for both measures, and the only factor that differs is the variable being measured. This is the basic psychophysical method used when measuring macular pigment optical density (MPOD). In essence, retinal sensitivity to visible light is measured in an area where MP is dense (the fovea), and that measure is compared with an area where MP is optically immeasurable (usually at approximately 4°–8° in the parafovea). When these two photopic sensitivity curves are equated at long wavelengths, they differ in the short-wave end of the visible spectrum. When these differences are plotted against wavelength, a spectral density curve is generated that has the same basic shape as the extinction spectrum of xanthophylls.[5] Because absorption by the lens is equal in both cases, it is assumed that lens absorption does not influence the difference in these two spectral curves. Simulation data from Wooten et al.[6] suggest that this is the case.

In the present study, we assessed the influence of lens absorption on MP measurements by comparing MP measured before and after cataract extraction. Although the subjects' overall sensitivity to light increased after the extraction, their measured MPOD did not change significantly.

Methods

Subjects

Twenty-four patients (age range, 48–82 years) from a university-based general ophthalmology practice in Indianapolis were recruited for this study. All subjects were recruited from a cohort of patients who had initially had cataract sufficiently symptomatic to warrant extraction. All patients underwent dilated fundus examination before and after cataract extraction. Only patients with normal results from retinal evaluations were asked to participate in this study. In particular, no patient showed optic nerve cupping, diabetic retinopathy, or signs of macular degeneration. The mean age of the subjects was 68.7 years; 21%, 29%, 42%, and 8% of the subjects were aged 45 to 60, 60 to 70, 70 to 80, and 80 to 90 years, respectively. Moreover, 67%, 21%, 8%, and 4% had brown, blue, green, and gray irides, respectively. Fifty percent of the subjects were past smokers, 42% had never smoked, and 8% were current smokers. In short, the subjects were representative of the population of patients under the care of an attending comprehensive ophthalmologist at a teaching hospital in a major midwestern city.

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Supported by an unrestricted grant from Research to Prevent Blindness. TAC is a recipient of a Career Development Award from Research to Prevent Blindness.

Submitted for publication September 19, 2000; revised December 15, 2000; accepted December 20, 2000.

Commercial relationships policy: N.

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Investigative Ophthalmology & Visual Science, May 2001, Vol. 42, No. 6

All patients underwent planned phacoemulsification and placement of a foldable acrylic posterior chamber intraocular lens for cataract of sufficient severity to interfere with their activities of daily living. The median preoperative best corrected Snellen distance visual acuity measured 20/50. Patients were deemed eligible for this study if their near acuity could be refracted to 20/25 or better. In five patients, both eyes were considered cataractous, and MPOD was assessed in both. MP was originally measured before cataract extraction and then a mean (±SD) of 8.1 ± 4.7 weeks (range, 3–17; median 6 weeks) after completion of the surgery. During MPOD measurement, visual acuity was corrected to 20/25 near acuity. All subjects were naïve about the purpose of the study and were not experienced in psychophysical tasks. Informed consent was obtained, and the tenets of the Declaration of Helsinki were followed.

Measurement of MPOD

Schematics and an expanded discussion of the device and stimuli used in the present study can be found in Wooten et al.[6] For details regarding the procedure used, see Snodderly and Hammond.[4]

Stimuli. A circular test stimulus was presented near the center of a 6°, 10.5-candelas (cd)/mm^2, 470-nm circular background. The size of the test stimulus was 1°. The wavelength composition of the test stimulus alternated between a 458-nm measuring field (peak MP absorbance) and a 570-nm, 16.7-cd/mm^2 reference field (minimal MP absorbance). The measuring and reference fields were superposed and presented out of phase in a square wave alternation rate of 11 to 12 Hz in the foveal condition and 6 to 7 Hz in the parafoveal condition.

Apparatus. The apparatus used for the MP measurement delivered the stimulus in natural view but used a stimulus that was similar to configurations used in past studies in which the stimulus was presented in Maxwellian view.[7–11] Recent data[6] on 32 subjects (age range, 18–72 years) have shown that MPOD measured in natural view, with a slightly different stimulus configuration (e.g., this study used a 4° rather than a 6° parafoveal reference), provides the same values as MPOD measured in Maxwellian view.

Light for the 6° background was produced by three LEDs (packed tightly in a triangular array) with peak energy at 470 nm and half-widths of approximately 20 nm. Light for the 570-nm reference field was produced by an LED with peak energy at 570 nm (half-width, 20 nm). Light for the 458-nm measuring field was produced by two LEDs with peak energy at 458 nm (half-width, 20 nm). Light from the LED sources was collimated with planoconvex lenses and was then passed through polycarbonate diffusers (high-efficiency, holographic type; Physical Optics, Torrence CA), which served essentially as back-projection screens.

The sizes of the background and test stimulus were defined by circular apertures (constructed by computer-generated images exposed on high-density, photographic mylar film) placed after the collimating lenses. The background and test stimuli were then combined and reflected to the subject by a 2-in. beam splitter with the front surface located 16 in. from the subject's eye. The entire optical system was contained in a rectangular, black plexiglas box. One side of the box contained a 1-in. hole centered on the subject's optical axis through which the stimulus could be viewed. Subjects requiring refractive correction were allowed to wear the appropriate corrective lenses for the viewing distances used, provided these lenses were not tinted. Head alignment was accomplished by the use of an adjustable head and chin rest assembly and, when properly aligned, the subject viewed the hole in the box as slightly larger than and concentric with the background field.

Stimuli were calibrated using a photocell (PIN-10; UDT Sensors, Hawthorne, CA). The LEDS were driven by a constant-current power supply. Radiance variation was achieved by varying the frequency of a 1.5-μsec pulse over a range of 300 to 300,000 Hz. Calibration of the high-frequency pulse rate showed that the frequency delivery was proportional to the radiance output. Thus, MPODs could be derived by simply calculating the log ratio of the frequencies of the 458-nm measuring field at the foveal and parafoveal eccentricities, respectively.

Procedure. Flicker photometry was used. Subjects adjusted the radiance of the 458-nm measuring field to achieve minimal flicker with the 570-nm reference. This measurement was performed in the fovea (where MP is the most dense) and at 4° in the parafovea (where light absorption by MP is negligible). A tiny (5-minute) opaque fixation point was located on the left edge of the background, and subjects fixated on this point when making the parafoveal measurement. The peak optical density of MP was derived by subtracting the log foveal sensitivity from the log parafoveal sensitivity at 458 nm. Five foveal and five parafoveal measurements were made after brief instructions and a few practice settings. The means ± SD of these numbers are provided in Table 1.

The MP measurement technique has been validated on normal subjects by measuring the entire spectral absorption curve of MP and comparing it with the extinction spectrum of the macular pigments measured in excised tissue.[5] The reliability of the method has also been evaluated[4,5,9] in younger subjects. In addition, a recent study at the same institution with the identical apparatus has demonstrated that naïve subjects recruited from the general population can reliably undergo testing.[12,13] In this study, 280 healthy adult volunteers (138 men, 142 women; age range, 18–50 years) were found to have a mean MPOD measuring 0.211 ± 0.13.[12,13]

Results

MPODs measured before and after cataract removal are presented in Table 1. As shown in the table, the average MPODs were slightly lower after cataract removal (0.18 compared with 0.206), but this effect was small and not statistically significant. As shown in Figure 1, the measured MPODs were similar before and after cataract extraction ($r = +0.58$, $P < 0.001$). This relationship improved when two statistical outliers (indicated by open squares) were removed ($r = +0.74$).

In contrast, the foveal and parafoveal values used in the derivation of MPOD were significantly different before and after cataract removal (see Table 1). For example, the values (i.e., the energy output of the LED in relative energy units) obtained in the foveal and parafoveal conditions are significantly ($P < 0.001$) lower after cataract removal. For example, average foveal settings were 651 and 305 nm before and after cataract removal, respectively. These numbers translate to a corneal irradiance of 1.55 and 3.16 nW, respectively. Because higher foveal values reflect higher energy output, this implies that cataract removal significantly increased the subject's sensitivity to light. This change, however, did not significantly alter the derived MPOD.

As shown in Figure 1, the results of this study also suggest that the method used for measuring MPOD is reliable in older experimentally naïve subjects. The two values measured before and after cataract and at disparate time points yielded similar MPODs ($r = +0.58$). The absolute value of the average change between the first and second session was 0.085 ± 0.08. Nonetheless, as also shown in Figure 1 (open squares), there were two subjects whose data did not replicate well. When these two subjects (MH and NC) were removed, the correlation was improved ($r = +0.74$).

Table 1 lists the SDs of the five foveal and parafoveal measures used to derive MPOD. Although the changes in the variance of the parafoveal measures before and after cataract were minimal, the variance in the postoperative foveal values decreased by approximately 45%. These findings suggest that a dense lens can influence a subject's performance, particularly when making the foveal settings. It is unclear, however, whether increased variability in performance actually leads to less replicable data. There were instances (e.g., subject NC) when high within-session variability predicted poor replicabil-

Table 1. Comparison of Macular Pigment Measurements

Subject	Age	Eye	Suppl	Cataract Type	Pre F Mean	Pre F SD	Pre PF Mean	Pre PF SD	Pre MPOD	Post F Mean	Post F SD	Post PF Mean	Post PF SD	Post MPOD	MPOD Change
RS	67	OS	No	2 + NS 1 + PSC	570	17	244	82	0.368	164	14	86	15	0.28	−0.088
*DT	75	OS	Yes	3 + NS	734	26	465	21	0.198	436	14	338	15	0.116	−0.082
*DT	—	OD		3 + NS	952	40	497	29	0.282	379	39	233	19	0.211	−0.071
DC	60	OS	Yes	1 + cort. 1 + PSC	505	38	282	13	0.253	457	14	366	54	0.096	−0.157
JK	54	OD	Yes	1 + PSC	436	18	269	14	0.21	236	40	168	16	0.148	−0.062
NA	66	OD	Yes	2 + NS	669	15	351	32	0.28	301	32	158	19	0.279	−0.001
*CG	70	OD	Yes	3 + NS 1 + post. Polar	514	52	295	17	0.241	210	29	102	5	0.314	+0.073
*CG	—	OS		2 + NS	583	28	280	11	0.318	184	3	96	8	0.282	−0.036
MH	48	OS	Yes	3 + ant. subcapsular	852	41	356	25	0.379	358	24	315	42	0.056	−0.323
AG	77	OD	No	3 + NS	884	57	340	50	0.415	269	49	97	13	0.428	+0.013
AM	47	OS	No	3 + PSC	322	32	308	6	0.019	213	13	194	7	0.041	+0.022
NC	79	OS	Yes	3 + NS	262	24	232	21	0.053	520	83	252	33	0.315	+0.262
CW	80	OS		3 + NS	712	65	691	39	0.013	144	9	146	36	0.025	+0.012
PH	58	OS	Yes	3 + NS 1 + PSC	526	35	490	21	0.031	213	35	201	14	0.025	−0.006
BH	68	OD	Yes	2 + NS 1 + post polar	570	57	401	68	0.152	221	42	151	7	0.165	+0.013
AW	69	OS	Yes	1 + NS 2 + CS	538	27	276	20	0.29	268	16	201	5	0.125	−0.165
*FC	80	OD	No	3 + NS	453	49	367	38	0.091	652	28	645	31	0.004	−0.087
*FC	—	OS		3 + NS	552	88	357	9	0.189	331	19	215	9	0.187	−0.002
*RP	73	OS	No	3 + NS	550	40	450	31	0.088	287	31	205	28	0.146	+0.058
*RP	—	OD		3 + NS	746	26	565	31	0.121	302	17	162	55	0.27	+0.149
LH	74	OD	Yes	3 + NS	953	17	592	23	0.207	235	51	184	4	0.105	−0.102
RL	81	OD	No	3 + NS	877	85	622	36	0.149	347	13	187	33	0.268	+0.119
WM	75	OS	No	3 + NS	872	86	362	40	0.382	261	14	206	4	0.15	−0.232
*LW	67	OS	Yes	3 + NS	487	31	275	62	0.248	243	20	163	11	0.173	−0.075
*LW	—	OD		2 + NS 1 + PSC	347	21	244	22	0.153	251	12	197	20	0.105	−0.048
WH	66	OD	Yes	2 + NS 1 + PSC	625	44	552	34	0.054	296	11	293	26	0.051	−0.003
AC	72	OS	Yes	2 + NS 2 + PSC	1005	40	530	16	0.278	324	2	200	67	0.21	−0.068
SS	68	OS	No	2 + NS 2 + PSC	1130	75	353	87	0.505	442	13	140	43	0.499	−0.006
MH	75	OD	Yes	3 + NS	660	88	636	13	0.016	308	22	216	10	0.154	+0.138
Mean	68.7				651	43.5	404	31	0.206	305	24	211	22	0.180	−0.026
Stan Dev	9.5				217	23	134	21	0.13	112	17	108	17	0.12	0.116

Measurements were made before (Pre MPOD) and after (Post MPOD) cataract extraction. Eye is the eye that was tested. The ethnicity of the subjects was white (W) and African American (AA). Whether nutrient supplements (Suppl) were used is indicated by Yes or No. Cataract severity is indicated numerically, and type is specified as follows: ant. cort., anterior cortical; NS, nuclear sclerosis; CS, cortical spoking; PSC, posterior subcapsular cataract. Also included are the values used to derive MPOD using the macular densitometer. These numbers reflect the relative energy output of the LEDs. Thus, higher numbers indicate higher energy output (needing higher energy output to do the task implies reduced visual sensitivity). To derive the MPOD, the log of the measurements in the fovea (Pre F before cataract removal and Post F after cataract removal) are subtracted from the log of the measurements made in the parafovea (Pre PF before cataract removal and Post PF after cataract removal). Data are expressed as means ± SD.

* Those subjects in whom both eyes were evaluated.

ity in the derived MPODs. As shown in Table 1, however, for most subjects, variability within a session was not related to differences in the derived MPODs across sessions.

Discussion

These data show that MPOD can be reliably measured in elderly subjects despite the presence of dense cataracts. These data also address the reliability of the method. As shown in Table 1, although MPOD was measured at time points differing by a mean of 8.1 weeks, most elderly experimentally naïve subjects showed low test–retest variability. There were, however, three subjects whose test–retest variability was relatively high (>0.23 OD units). In one case (subject NC), poor reliability was linked to poor task performance in the second session. The change in MPOD for the other two subjects was less clear but must have been due to measurement error not linked to task consistency (e.g., criterion changes) and/or true biologic variation (e.g., changes in diet). These two possibilities can actually be disentangled. For example, because the spectral absorption characteristics of MP are well known, measurements at differing wavelengths can be used to cross-check the accuracy of the data.[4] Moreover, physical methods for measuring MP have recently been developed that do not rely on the performance of subjects (e.g., Raman spectroscopy[14] and fundus reflectance[15]). Considered as a whole, these data confirm the tendency for flicker photometric measures of MP to be reliable in naïve older subjects. The validity of the method in older subjects with lenticular and/or retinal disease, however, remains to be determined.

The similarity in the MP measurements before and after cataract has implications for both basic and applied research. From a basic-methods perspective, techniques analogous to the flicker photometry method used in the present study can assume minimal confounding due to absorption by the lens. Thus, comparative measures of two retinal loci are valid as long as the receptor populations between the two loci are equivalent or the differences are experimentally controlled. From an applied perspective, these results further motivate the need to measure lutein and zeaxanthin within the retina in elderly subjects who are most susceptible to age-related retinal and lenticular disease. Numerous epidemiologic studies have

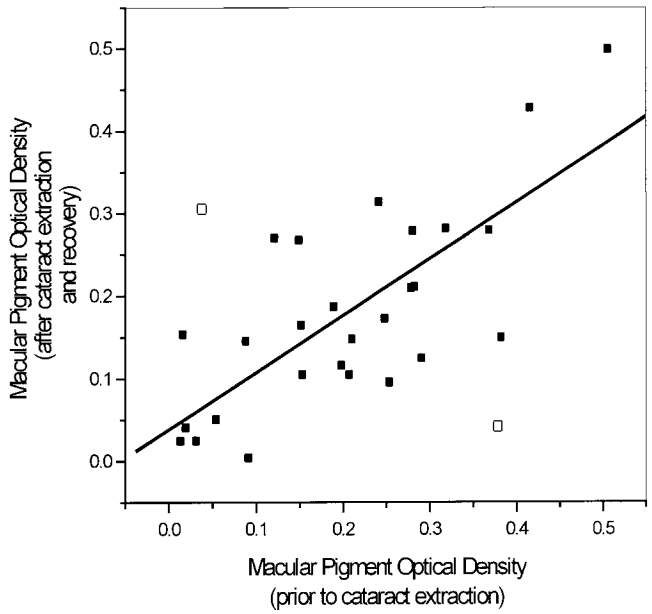

FIGURE 1. The relationship between MPOD measured before and after cataract extraction. The regression line shown ($y = 0.03 + 0.69x$, $r = +0.75$, $P < 0.0001$) was calculated without including the outliers (□). The regression line is slightly different ($y = 0.07 + 0.53x$, $r = +0.58$, $P < 0.0005$) when these outliers are included.

linked low dietary intake and blood levels of lutein and zeaxanthin to age-related cataract[16,17] and macular degeneration.[18–20] These studies, however, tend to be inconsistent.[21–23] One explanation for the inconsistencies is that dietary intake and blood carotenoid levels may actually be poor predictors of the amount of lutein and zeaxanthin available to the eye, particularly in females.[8] The ability to measure lutein and zeaxanthin directly provides a better assessment of the availability of these carotenoids to ocular tissue.

Recent years have seen a proliferation of lutein supplements being touted for their ability to protect the retina and lens from oxidative damage. It is probable that not all subjects will respond to these types of supplements equally. The ability to measure MPOD in vivo and repeatedly in the elderly would be one method of evaluating the efficacy of using these supplements and/or dietary modifications designed to increase MPOD.

References

1. Klein BEK, Klein R, Jensen SC. Visual sensitivity and age-related eye diseases: The Beaver Dam Eye Study. *Ophthalmic Epidemiol.* 1996;3:47–55.
2. van den Berg TJTP. Depth-dependent forward light scattering by donor lenses. *Invest Ophthalmol Vis Sci.* 1996;37:1157–1166.
3. Xu J, Pokorny J, Smith VC. Optical density of the human lens. *J Opt Soc Am A.* 1997;14:953–960.
4. Snodderly DM, Hammond BR. In vivo psychophysical assessment of nutritional and environmental influences on human ocular tissues, lens and macular pigment. In: Taylor AJ, ed. *Nutritional and Environmental Influences on Vision*. Boca Raton, FL: CRC Press; 1999:251–273.
5. Hammond BR, Fuld K. Interocular differences in macular pigment density. *Invest Ophthalmol Vis Sci.* 1992;33:350–355.
6. Wooten BR, Hammond BR, Land R, Snodderly DM. A practical method of measuring macular pigment optical density. *Invest Ophthalmol Vis Sci*. 1999;40:2481–2489.
7. Hammond BR Jr, Fuld K, Snodderly DM. Iris color and macular pigment optical density. *Exp Eye Res.* 1996;62:715–720.
8. Hammond BR, Curran–Celentano J, Judd S, et al. Sex differences in macular pigment optical density: relation to plasma carotenoid concentrations and dietary patterns. *Vision Res.* 1996;36:2001–2012.
9. Hammond BR, Wooten BR, Snodderly DM. Individual variations in the spatial profile of macular pigment. *J Opt Soc Am A*. 1997;14:1187–1196.
10. Hammond BR Jr, Wooten BR, Snodderly DM. Preservation of visual sensitivity of older subjects: association with macular pigment density. *Invest Ophthalmol Vis Sci.* 1998;36:1–10.
11. Werner JS, Donnelly SK, Kliegl R. Aging and human macular pigment density. *Vision Res*. 1987;27:257–268.
12. Cooper DA, Curran–Celentano J, Ciulla TA, et al. Olestra consumption is not associated with macular pigment optical density in a cross-sectional volunteer sample in Indianapolis. *J Nutr.* 2000;130:642–647.
13. Ciulla TA, Curran–Celentano J, Cooper D, et al. Determinants of macular pigment density in adult volunteers in a Midwestern population. *Ophthalmology*. In press.
14. Bernstein PS, Yoshida MD, Katz NB, McClane RW Gellermann W. Ranan detection of macular carotenoid pigments in intact human retina. *Invest Ophthalmol Vis Sci.* 1998;39:2003–2011.
15. Kilbride PE, Alexander KR, Fishman M, Fishman, GA,. Human macular pigment assessed by imaging fundus reflectometry. *Vision Res*. 1989;29:663–673.
16. Brown L, Rimm EB, Seddon J, et al. A prospective study of carotenoid intake and risk of cataract extraction in US men. *Am J Clin Nutr.* 1999;70:517–524.
17. Chasan–Taber L, Willett WC, Seddon JM, et al. A prospective study of carotenoid and vitamin A intakes and risk of cataract extraction in US women**.** *Am J Clin Nutr.* 1999;70:509–516.
18. Eye Disease Case Control Study Group. Risk factors for neovascular age-related macular degeneration. *Arch Ophthalmol.* 1992;110:1701–1708.
19. Eye Disease Case Control Study Group. Antioxidant status and neovascular age-related macular degeneration. *Arch Ophthalmol.* 1993;111:104–109.
20. Seddon JM, Umed AA, Sperduto RD, et al. Dietary carotenoids, vitamins A, C, and E, and advanced age-related macular degeneration. *JAMA*. 1994;272:1413–1420.
21. Mares–Perlman JA, Brady WE, Klein R, et al. Serum antioxidants and age-related macular degeneration in a population-based case-control study. *Arch Ophthalmol.* 1995;113:1518–1523.
22. Mares–Perlman JA, Brady WE, Klein R, VandenLangenberg GM, Klein BE, Palta M. Dietary fat and age-related maculopathy. *Arch Ophthalmol.* 1995;113:743–748.
23. Mares–Perlman JA, Brady WE, Klein BEK, et al. Serum carotenoids and tocopherols and severity of nuclear cataracts and cortical opacities. *Invest Ophthalmol Vis Sci.* 1995;36:276–88.