# Associations of Human Crystalline Lens Retrodots and Waterclefts with Visual Impairment: An Observational Study

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**Purpose.** To investigate the relationships between visual acuity, contrast sensitivity, and 11 clinicopathologic classes of opacity in the human crystalline lens.

**Methods.** The Somerset and Avon Eye Study is an observational population study of age-related sight-threatening eye disease, based in Bristol, UK. After excluding eyes with other visually relevant disease, data from 902 individuals aged 55 years or older were analyzed. The associations of lens features (posterior subcapsular cataract, nuclear color, nuclear white scatter, cortical spokes, anterior subcapsular cataract, vacuoles, waterclefts, coronary flakes, focal dots, retrodots, fiber folds), with refracted log minimum angle of resolution (MAR) distance acuity and Pelli-Robson contrast sensitivity, were investigated. Multivariable linear regression models using data from both eyes and taking account of the intraclass correlation between eyes were used for analysis, with the lens features and age included as potential explanatory variables.

**Results.** As anticipated from earlier studies, posterior subcapsular, nuclear, and cortical cataracts were associated with visual impairment. In addition, retrodots were strongly and independently associated in the multivariable models with both impaired visual acuity ($P < 0.001$) and contrast sensitivity ($P < 0.001$). Waterclefts were strongly associated with impaired visual acuity ($P < 0.001$).

**Conclusions.** Retrodots and waterclefts are associated with visual impairment. A causal relationship between these lens features and retinal image degradation is plausible. (*Invest Ophthalmol Vis Sci.* 2002;43:2105–2109)

A variety of opacities can be observed in the aging human crystalline lens,[1,2] but not all lens opacities cause visual impairment. However, a complete description of the optical degradation effects caused by the different types of media opacity in the eye is still unavailable, despite awareness of the problem for at least 15 years.[3] There is still clinical difficulty in differentiating cataract from normal changes due to age,[4] and there is variable practice in regard to which lens features ophthalmologists assess when deciding whether to offer cataract surgery.[5]

It is commonly assumed that there are three major types of cataract: nuclear, cortical, and posterior subcapsular (PSC).[6] The possibility that other common age-related lens opacities may cause visual impairment has not been investigated in detail. A simplified scheme of nuclear, cortical, and posterior subcapsular opacification may be satisfactory for studies of severe cataract, but it does not take into account the subtleties of lens examination in clinical ophthalmology practice. In a recent national survey of surgeons in the United Kingdom, 74% of respondents assessed opacities which have been traditionally disregarded in many research studies, when deciding whether to offer cataract surgery.[5]

The purpose of the present study was to investigate the possibility that a broader range of lens features may be associated with visual impairment.

## Methods

### Subjects

The subjects of the present investigation were 1078 individuals who attended the research clinic of an observational population study of age-related eye disease. These individuals were part of an age–sex stratified random sample drawn from the population originally sampled for the Somerset and Avon Survey of Health (SASH).[7,8] The eye study was approved by the Local Research Ethics Committee. Informed consent was obtained from participants in accordance with the tenets of the Declaration of Helsinki.

To examine the relationships between the specified lens opacities and vision, eyes with coexisting ocular disease were excluded. The exclusion criteria were as follows: history of strabismus, amblyopia, retinal disease, or poorly described eye conditions. Examination finding of relative afferent pupil defect, abnormality of the central cornea, anterior chamber abnormality (e.g., uveitis) diabetic maculopathy, exudative age-related maculopathy (ARM), geographic atrophy, or any other retinal disease involving the fovea (with the exception of drusen or minor pigmentary abnormalities) or a vertical cup-to-disc ratio greater than 0.7.

### Ocular Examination

Cataract was measured according to the decimalized version of the Oxford Clinical Cataract Classification and Grading System (OCCCGS).[9,10] The lens was examined at the slit lamp and the appearance compared to standard diagrams. Each lens feature was graded from 0.0 (minimal or absent) to 5.0 (severe) in 0.1 steps. Eyes with opacities not graded by the OCCCGS (e.g., blue dot opacities) were also excluded. Early age-related macular degeneration (drusen, hyperpigmentation or hypopigmentation) was classified as present or absent at the fovea.

### Vision Tests

Subjective refraction was performed on all subjects. The vision tests were performed with correction for refractive error. Monocular visual acuity was measured at 4 m with the Early-Treatment Diabetic Retinopathy Study (ETDRS; log minimum angle of resolution [MAR]) chart,[11] using a forced-choice testing procedure, scoring individual

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**TABLE 1.** Subject Prevalence and Severity of OCCCGS Features

| | Subject Prevalence % | Mean of Nonzero Values | Intraclass Correlation | N1 | N2 |
|---|---|---|---|---|---|
| Posterior subcapsular opacity | 8.5 | 0.80 | 0.74 | 195 | 671 |
| Brunescence | 99.7 | 1.12 | 0.94 | 203 | 666 |
| White scatter | 100.0 | 1.92 | 0.93 | 199 | 668 |
| Cortical spokes | 33.5 | 0.52 | 0.77 | 198 | 671 |
| Anterior subcapsular opacity | 2.9 | 0.75 | 0.86 | 198 | 671 |
| Vacuoles | 46.4 | 0.38 | 0.46 | 197 | 671 |
| Waterclefts | 23.7 | 0.40 | 0.82 | 197 | 671 |
| Coronary flakes | 24.7 | 0.90 | 0.85 | 205 | 652 |
| Focal dots | 96.2 | 1.41 | 0.80 | 198 | 661 |
| Retrodots | 30.1 | 1.26 | 0.84 | 198 | 670 |
| Fiber folds | 15.9 | 0.89 | 0.74 | 197 | 671 |

The subject prevalence was based on the mean grade of the two eyes, or of one eye if data were missing from the contralateral eye. The mean of nonzero scores was also based on the mean grade per individual. N1, number of individuals who provided data from one eye; N2, number of individuals who provided data from both eyes.

letters. The chart was illuminated using the Lighthouse Chart Illumination Unit (Lighthouse Low Vision Products, New York, NY). The average luminance of the white areas of the chart was 248 cd/m$^2$, measured at the beginning of the study. If a subject was initially unable to read any of the letters at 4 m, the chart was brought progressively closer, to a minimum testing distance of 0.5 m. The acuity result was adjusted for the distance of the chart.

Monocular contrast sensitivity was measured at 1 m with the Pelli-Robson chart,[12] also using a forced-choice testing procedure and scoring individual letters. The average luminance of the white areas of the chart was 97 cd/m$^2$, measured at the beginning of the study. Eyes with non-logMAR acuity (e.g., hand movements) were excluded from the analyses.

## Statistical Analysis

For ease of presentation the prevalence and severity of the cataract features shown in Table 1. were calculated from the mean grade of the two eyes[13] or from one eye if data were missing from the contralateral eye. A feature was deemed to be present if the mean grade was equal to 0.05 or greater. Note that the mean grades of the two eyes were not used in the multivariable analyses.

Multivariable linear regression models were used with the vision test results as dependent variables and ocular examination findings as potential explanatory variables.

Initial analyses (not presented in this report) were performed separately for right and left eyes (one-eye models) to examine five explanatory variables of known importance (PSC, nuclear brunescence [color], nuclear white scatter [opalescence]), cortical spokes, and presence or absence of early age-related macular degeneration) and to check the distributions of the dependent variables and residuals. The distributions of both logMAR acuity and contrast sensitivity were highly skewed.

The two-eye analyses were undertaken by computer (Stata software[14]). Intraclass correlation coefficients (ICCs) for intereye correlations were estimated using one-way analysis of variance. Multivariable linear regression models using data from both eyes and taking account of the intraclass correlation between eyes were estimated using random-effects models and generalized estimating equations.[15,16] The analyses were performed separately for visual acuity and for contrast sensitivity. For each visual impairment variable, model-building proceeded in four stages. First stage: The five established variables listed in the foregoing paragraph were included in a two-eye multivariable model. At this and each subsequent modeling stage, the assumption of a linear relationship with visual impairment was tested for each explanatory variable by the addition of a quadratic term. Second stage: Age was added, and because for acuity and contrast sensitivity the relationship with age was not linear, terms for both age and age squared were included. Third stage: The remaining lens opacities (anterior subcapsular, vacuoles, waterclefts, coronary flakes, focal dots, retrodots, and fiber folds) were then incorporated. A final model was then derived that consisted of the five established variables, age and age squared, and any of the remaining lens opacities (and respective quadratic terms) that were statistically significant. The final model was also reestimated with age (and age squared) omitted. Coronary flakes were excluded from the final model because of a very weak association with visual acuity and an absent association with contrast sensitivity (see tables and the Discussion section). Reported analyses are restricted to the subset of observed eyes for which complete data were available for all variables. Due to the skewed distribution of the dependent variables, all multivariable analyses were repeated, using transformations of these variables (decimal acuity and the antilog of the Pelli-Robson score, respectively). For both transformed and untransformed analyses, the distribution of residuals was checked, and models were reestimated with highly influential observations omitted. Because the results of these models were substantively the same, the results of untransformed analyses are presented herein, because they are most clinically meaningful and easier to interpret.

## RESULTS

After exclusions, measurements were obtained from 902 individuals; 471 (52%) were women and 431 (48%) were men. The age range was 55 to 95 years, with median 67 and mean 68 years. For each variable, measurements were not obtained in a small number of cases. Complete data for all variables included in the analysis were obtained from 1473 eyes in 839 individuals.

Better-eye logMAR visual acuities ranged from −0.30 to 1.18 (median, −0.08). The worse eye values ranged from −0.20 to 1.66 (median 0.00). The intereye correlation (ICC) for acuity was 0.70. Better-eye Pelli-Robson scores ranged from 0.35 to 1.95 (median, 1.60). The worse eye scores ranged from 0.15 to 1.85 (median, 1.50). The ICC for Pelli-Robson score was 0.67.

Table 1 shows the subject prevalence and severity of the cataract features after the exclusions relevant to vision testing and also shows the ICCs between right and left eyes. Early age-related macular degeneration (drusen, hyper- or hypopigmentation) was present at the fovea of one or both eyes in 31.2% of subjects.

Tables 2 and 3 show the results of the two-eye multivariable models. Table 2 shows the results for visual acuity, and Table 3 shows the results for contrast sensitivity. Model A is the result of the second model-building stage and includes the established cataract features, age, and early age-related maculopathy (ARM). Model B is the result of the third model-building stage

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**TABLE 2.** Summary of Two-eye Maximum-Likelihood Random Effects Models: Associations with logMAR Visual Acuity

| | Model A | | Model B | | Model C | | Model D | | |
|---|---|---|---|---|---|---|---|---|---|
| | *P* | Coef. | *P* | Coef. | *P* | Coef. | *P* | Coef. | 95% CI |
| Constant | | 1.534 | | 1.227 | | −0.087 | | 1.236 | |
| Posterior subcapsular opacity | <0.001 | 0.086 | <0.001 | 0.085 | <0.001 | 0.080 | <0.001 | 0.081 | 0.061 to 0.101 |
| Brunescence | | −0.054 | | −0.062 | | −0.078 | | −0.064 | −0.117 to −0.011 |
| Brunescence$^2$ | <0.001* | 0.037 | <0.001* | 0.044 | <0.001* | 0.067 | <0.001* | 0.045 | 0.024 to 0.066 |
| White scatter | 0.020 | 0.012 | 0.148 | 0.008 | 0.046 | 0.011 | 0.277 | 0.006 | −0.004 to 0.016 |
| Cortical spokes | <0.001 | 0.048 | <0.001 | 0.043 | <0.001 | 0.050 | <0.001 | 0.042 | 0.026 to 0.057 |
| Early ARM | 0.316 | 0.007 | 0.237 | 0.009 | 0.061 | 0.014 | 0.274 | 0.008 | −0.006 to 0.022 |
| Age | | −0.053 | | −0.043 | | | | −0.043 | −0.056 to −0.031 |
| Age$^2$ | <0.001* | 0.0004 | <0.001* | 0.0004 | | | <0.001* | 0.0004 | 0.0003 to 0.0004 |
| Anterior subcapsular opacity | | | 0.430 | −0.018 | | | | | |
| Vacuoles | | | 0.913 | −0.001 | | | | | |
| Waterclefts | | | <0.001 | 0.046 | <0.001 | 0.080 | <0.001 | 0.045 | 0.023 to 0.068 |
| Coronary flakes | | | 0.014 | 0.014 | | | | | |
| Focal dots | | | 0.963 | −0.001 | | | | | |
| Retrodots | | | | −0.015 | | −0.003 | | −0.013 | −0.037 to 0.011 |
| Retrodots$^2$ | | | <0.001* | 0.016 | <0.001* | 0.022 | <0.001* | 0.016 | 0.007 to 0.025 |
| Fiber folds | | | 0.165 | −0.012 | | | | | |
| $R^2$ | 0.50 | | 0.53 | | 0.44 | | 0.52 | | |

Coef., regression coefficient; 95% CI, 95% confidence intervals for the regression coefficients in model D.

Model A is the result of the second model-building stage and includes the established cataract features, age and early ARM. Model B is the result of the third model-building stage and includes all OCCCGS features, age and early ARM. Model C is the final model, excluding age. Model D is the final model and includes the established cataract features, age, early ARM, waterclefts, and retrodots.

* Joint test, $\chi^2(2)$

and includes all OCCCGS features, age, and early ARM. Model D is the final model and includes the established cataract features, age, early ARM, waterclefts, and retrodots. Model C is the same as Model D, but with age terms omitted.

The two estimation methods produced similar results in all analyses, so only the results of random effects models are presented. The initial models confirmed that PSC, nuclear brunescence, nuclear white scatter, cortical spokes, age and age-squared were all associated with impaired acuity and impaired contrast sensitivity at the 5% level. In addition, squared terms for brunescence and retrodots were retained in the acuity models, and for brunescence, white scatter, and retrodots in the contrast sensitivity models. Early age-related maculopathy was not significantly associated with visual impairment, but this association was stronger when the terms for age and age squared were excluded.

Tables 2 and 3 show that retrodots were strongly and independently associated with both impaired visual acuity ($P < 0.001$) and contrast sensitivity ($P < 0.001$). Waterclefts were strongly associated with impaired visual acuity ($P < 0.001$) and to a lesser extent with impaired contrast sensitivity, depending on whether age was included in the final model. After transformation of the dependent variables, retrodots were still strongly associated with impaired visual acuity and with impaired contrast sensitivity. Waterclefts were still strongly associated with impaired visual acuity, after transfor-

**TABLE 3.** Summary of Two-eye Maximum-Likelihood Random Effects Models: Associations with Pelli-Robson Score

| | Model A | | Model B | | Model C | | Model D | | |
|---|---|---|---|---|---|---|---|---|---|
| | *P* | Coef. | *P* | Coef. | *P* | Coef. | *P* | Coef. | 95% CI |
| Constant | | 0.360 | | 0.583 | | 1.582 | | 0.595 | |
| Posterior subcapsular opacity | <0.001 | −0.099 | <0.001 | −0.094 | <0.001 | −0.094 | <0.001 | −0.095 | −0.119 to −0.070 |
| Brunescence | | 0.021 | | 0.032 | | 0.037 | | 0.033 | −0.035 to 0.101 |
| Brunescence$^2$ | <0.103* | −0.017 | 0.010* | −0.026 | <0.001* | −0.044 | 0.011* | −0.026 | −0.053 to 0.002 |
| White scatter | | 0.048 | | 0.038 | | 0.039 | | 0.041 | −0.002 to 0.084 |
| White scatter$^2$ | 0.012* | −0.013 | 0.124* | −0.010 | 0.026* | −0.012 | 0.106* | −0.011 | −0.020 to −0.001 |
| Cortical Spokes | <0.001 | −0.041 | 0.001 | −0.037 | <0.001 | −0.046 | <0.001 | −0.035 | −0.055 to −0.016 |
| Early ARM | 0.186 | −0.012 | 0.176 | −0.012 | 0.041 | −0.019 | 0.174 | −0.012 | −0.029 to 0.005 |
| Age | | 0.042 | | 0.034 | | | | 0.034 | 0.018 to 0.050 |
| Age$^2$ | <0.001* | −0.0004 | <0.001* | −0.0003 | | | <0.001* | −0.0003 | −0.0004 to −0.0002 |
| Anterior subcapsular opacity | | | 0.954 | −0.002 | | | | | |
| Vacuoles | | | 0.263 | 0.014 | | | | | |
| Waterclefts | | | 0.014 | −0.036 | <0.001 | −0.071 | 0.012 | −0.036 | −0.064 to −0.008 |
| Coronary flakes | | | 0.651 | −0.003 | | | | | |
| Focal dots | | | 0.774 | −0.001 | | | | | |
| Retrodots | | | | 0.008 | | −0.006 | | 0.008 | −0.022 to 0.037 |
| Retrodots$^2$ | | | 0.001* | −0.012 | <0.001* | −0.017 | <0.001* | −0.012 | −0.024 to −0.001 |
| Fiber folds | | | 0.698 | 0.004 | | | | | |
| $R^2$ | 0.37 | | 0.39 | | 0.33 | | 0.39 | | |

Data and models are as described in Table 2.

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mation, but were no longer associated with impaired contrast sensitivity at the 5% level. Coronary flakes were weakly associated with impaired visual acuity.

## Discussion

### Previous Studies

Several investigators have established associations between impaired visual acuity and deepening nuclear color,[17] increasing nuclear opalescence,[18,19] cortical cataract,[18] and PSC.[18] Associations have also been reported between visual contrast sensitivity and nuclear color,[20] nuclear opalescence,[18,20,21] cortical cataract,[18,20] and PSC[18,20]

### Main Findings of the Present Study

As anticipated from previous studies, posterior subcapsular, nuclear, and cortical spoke cataracts were associated with visual impairment in the present study. But in addition, retrodots were also associated with impaired visual acuity and impaired contrast sensitivity, even after adjusting for age. Waterclefts were also associated with impaired visual acuity, and there was a weaker, less-consistent association between waterclefts and impaired contrast sensitivity.

If it is assumed that the reported associations reflect a causal relationship, then the regression coefficients are estimates of the magnitudes of the vision-impairing effects of each unit grade of lens opacity. For example in Table 2, Model C, the estimated effect of waterclefts on visual acuity is 0.08 (four chart letters) per unit grade, which is comparable to the effect (grade for grade) of PSC on visual acuity. The coefficients must of course be interpreted in terms of the various different grading scales within the OCCCGS.

No association was found between visual impairment and anterior subcapsular opacity (ASC), fiber folds, vacuoles, or focal dots. ASC is associated with posterior subcapsular opacity (PSC) but the opacification in ASC tends to be less marked[22] therefore any (weak) clinical effect of ASC may have been dominated by PSC. The appearances of fiber folds may be caused by reflection[23] and may not necessarily cause degradation of the retinal image. It is possible that vacuoles or focal dots, if present in sufficient numbers, could interfere with the passage of light through the lens. The present study shows that at least at population level, these opacities are visually unimportant. When vacuoles are present in large numbers, they are usually part of another feature (e.g., PSC) and are classified as such by the Oxford system. The free-standing vacuoles graded separately tend to be isolated and infrequent.

The finding of a weak association between coronary flakes and impaired visual acuity was surprising and may be spurious. Coronary flakes are confined mainly to the peripheral (equatorial) lens and are unlikely to cause visual impairment. It is also possible that some cortical spokes could have been mistakenly classified as coronary flakes, because of the similarities between the two features.

The finding of a weak association of early age-related macular degeneration and visual impairment was consistent with the findings of Klein et al.[24] Their analyses used larger numbers of eyes and although a statistical association between such lesions and acuity impairment was found, the decrease in acuity was of small magnitude and of uncertain clinical importance.

### Mechanisms of Visual Impairment

Scattering of light by the lens occurs at all visible wavelengths. Absorption by some cataractous lenses has a poorly defined role at short wavelengths. Visible light of intermediate and long wavelengths is primarily scattered by the lens rather than absorbed.[25] Light scattered from the lens back toward the light source (back-scatter) decreases the amount of light reaching the retina,[26] but light scattered toward the retina (forward-scatter) is believed to be more detrimental to vision than back-scatter, because it is forward-scatter that may produce a "veiling luminance" over the retina and image degradation.[27]

In the cataractous lens, fluctuations in refractive index may be caused by regional changes in protein concentration or by formation of macromolecular protein aggregates.[28] An incident ray of light may meet many interfaces as determined by the degree of structural disorder within the lens.[29] At each interface the potential exists for scattering of light. From a clinical viewpoint scattering includes chaotic refraction, diffraction, and reflection.

It has been hypothesized that high-spatial-frequency contrast sensitivity (and therefore visual acuity) is predominantly affected by light scatter at narrow angles.[30,31] Consideration of the slit lamp appearances suggests that waterclefts are likely to present only a small number of refractive interfaces to incident light and may cause narrow angle forward-scatter selectively. Retrodots behave as multiple lenses within the lens and are likely to cause forward-scatter at a wide range of angles. Such a hypothesis would explain why waterclefts were more strongly associated with visual acuity, compared with contrast sensitivity, and why retrodots were associated with both visual acuity and contrast sensitivity.

It is interesting to speculate on why retrodots and waterclefts have previously escaped attention as potential causes of visual impairment. A possible explanation is the innocent clinical appearance of the lesions at the slit lamp. A conscious effort has to be made to look for both waterclefts and retrodots. Some waterclefts are barely visible in retroillumination. Retrodots are barely visible in direct illumination. The presence of both waterclefts and retrodots may be obscured easily by coexisting, more obvious opacities. Neither lesion is particularly amenable to examination using photographic techniques.

The discovery of an association between these classes of lens opacity and visual impairment highlights the difference between forward and back-scatter. Forward-scatter is difficult to measure in vivo, hence the tendency to assess back-scattered light—for example in slit lamp examination, as a proxy for forward-scatter. In clinical practice, the appearance of lens opacities is judged at the slit lamp by back-scattered light, and a subjective decision is made about whether the observed cataractous appearance is likely to be responsible for the visual impairment. Unfortunately, there is a complex and poorly defined relationship between back-scatter and forward-scatter.[29,32,33] On slit lamp examination the visible back-scattered light from the lens may contain varying amounts of reflected light that is not associated with retinal image degradation.[34] Retrodots and waterclefts may be efficient at causing forward scatter (and retinal image degradation) but cause little back-scatter, thus appearing innocuous to the clinician.

### Implications for Future Research and Clinical Practice

The findings of the present study have wide implications for cataract research. The presence or absence of waterclefts and retrodots should be considered in clinical (psychophysical) studies of vision, in epidemiologic studies of visual impairment, and when lenses are subjected to biochemical or photometric analyses. The consideration should extend, not only to cases of cataract, but also to the selection of clear lenses for use as controls in clinical, epidemiologic, and laboratory studies. Although the identification of all visually relevant lens opacities

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may be difficult when using photographic techniques, a reliable assessment at the slit lamp can be achieved after training.[10] Retrodots and waterclefts should also be considered when examining the lens in clinical practice.

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