Digital Image Capture and Automated Analysis of Posterior Capsular Opacification

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PURPOSE. To develop and validate a digital imaging and analysis technique for assessing the extent of posterior capsular opacification after cataract surgery.

METHODS. Retroillumination images of the posterior capsule were obtained by using a digital camera mounted on a slit lamp. The images were analyzed using an available image analysis software program. The image acquisition and analysis techniques were tested for face validity, reproducibility, and the ability to detect progression of capsular opacity over time.

RESULTS. Digital retroillumination images were obtained without patient discomfort. Automated analysis of images correlated well with clinical grading both at slit lamp examination and when looking at the images themselves (Spearman’s correlation coefficient >0.7). Analysis of images taken at different times showed high reproducibility (intraclass correlation >0.9), and the system was able to identify progression of capsular opacity over a 2-year period with a mean increase of 15.8% in progressors versus an increase of 0.6% in nonprogressors (P < 0.05).

CONCLUSIONS. Digital retroillumination images of the posterior capsule can be obtained reliably, and automated analyses correlate well with clinical assessment. The system presented here uses commercially available instruments and software, and it is practical for use in longitudinal studies of posterior capsule opacification. It is reliable, easy to use, and can detect small changes in the percentage area covered by posterior capsule opacification over time. (Invest Ophthalmol Vis Sci. 1999;40:1715–1726)

More than 1 million cataract surgeries are performed annually in the United States, and virtually all are performed using extracapsular extraction techniques in which the posterior capsule of the lens is left intact. Lens epithelial cells that remain adherent to the lens capsule have the potential to proliferate and transform into fibroepithelial sheets, which may lead to significant posterior capsular opacification (PCO) and necessitate laser capsulotomy to restore vision.1 This procedure, Nd:YAG capsulotomy, is associated with ocular morbidity and considerable costs. It has been estimated that approximately 25% of cataract surgical patients in the United States undergo this treatment within 2 years of cataract surgery.2–5 Nd:YAG capsulotomy is now the second most commonly billed procedure among Medicare beneficiaries. In 1995, approximately 650,000 Nd:YAG capsulotomies were performed on Medicare beneficiaries at charges for that year of approximately $300 million (Earl Steinberg, Medicare Cataract Surgery records, 1995; personal communication, April 18, 1998).

Although the Nd:YAG capsulotomy rate is important for estimating health care costs, the reported rate is a poor surrogate for studying the biology of PCO. The rate of capsulotomy varies by surgeon,1 geographic region,5 and patient needs. A reliable and valid method of measuring the degree of PCO is needed to assess risk factors and potential mechanisms for posterior capsule opacification. Desirable features of a grading scheme for PCO would include high reproducibility and validity, sensitivity to PCO progression, ease of use, straightforward archiving and recall of images, suitability for standard image analysis strategies, instant feedback on image quality to allow for correlation between the image and the clinical picture, and generalizability to other investigators for facilitation of future research.

To date, there has been little published on the grading of PCO.6–8 Lasa et al.6 used a Scheimpflug slit lamp camera (Anterior Eye Segment Analysis System, EAS-1000; Nidet, Gamagori, Japan) to capture a still image of the posterior capsule and image analysis software to calculate density and thickness. Although this technique could, on average, separate patients clinically thought to have hazy capsules, it is limited by the small area of the slit beam that is assessed, the high cost of the instruments used, and the inability of the system to assess total area of the capsule covered by opacity without using multiple images. In addition, its reliability and ability to detect progression over time have not been reported. Hayashi et al.7 used the Scheimpflug to assess the central 3 mm of the posterior capsule to determine “density,” measured in computer-compatible tapes. They found their measurements to be correlated with visual acuity but have not yet documented the reproducibility of their approach or the ability to detect pro-
gession over time. In addition, their technique only images four slices through the capsule, raising the possibility that capsule opacities can be missed. These investigators recently used their system to demonstrate that polymethylmethacrylate (PMMA) lenses are associated with greater posterior capsule opacification than silicone or acrylic lenses in a randomized controlled clinical trial. Tetz et al. described a PCO grading system based on standard retroillumination photography, in which the observer subjectively assigns an integer density score from 0 to 4 that is then multiplied by the fractional area of coverage behind the intraocular lens (IOL) optic to generate a single metric for PCO. The study was small with only five eyes evaluated by multiple observers, and one observer re-evaluated three eyes to assess intraobserver variability. The system was not assessed for its ability to identify progression.

Pande et al. described a slit lamp–mounted digital camera for imaging the posterior capsule. The system required special adaptation of the slit lamp and camera to obtain a coaxial illumination and imaging path. Ursell et al. used this system to assess the relationship between intraocular lens material and the development of PCO. They relied on automated analysis to determine the presence of texture on the posterior capsule. PCO was present for any texture above some unstated threshold. The average percent area of the posterior capsule covered by texture was compared between groups. The reliability and validity of this system have not been published.

We report the use of a digital camera to obtain retroillumination photographs of the posterior capsule after cataract extraction and the analysis of the images with automated algorithms. We evaluated the validity of this approach, the reproducibility of the image acquisition and analysis techniques, and the ability of the analysis system to detect progression in retroillumination photographs, subsequently digitized, which were taken 2 years apart.

METHODS

Image Acquisition

We used a digital retroillumination camera mounted on a slit lamp to photograph the posterior capsule through a dilated pupil (Marcher Case 2000 Computerized Anterior Segment Evaluation System, Marcher Enterprises, Hereford, UK). While seated, the subject is asked to place his or her chin on a standard slit lamp biomicroscope chin rest and his or her forehead against a positioning strap. The subject is then asked to look at a flashing fixation light, and the technician centers the retroillumination image in the pupil using the computer-generated centering circles. The camera gain is then adjusted manually before focusing on the plane of the posterior capsule. The image is obtained with minimal flash and appears on the screen within 1 to 2 seconds. The operator has the option to accept or reject the image and can adjust the gain as needed for the next photograph. The gain adjustments enable the operator to obtain a wide spread along the gray scale, enhancing the quality of the image. We required two acceptable images from each subject, which were archived on the local hard drive. The total time required was approximately 2 minutes per eye.

We have obtained PCO photographs with this system in approximately 200 patients, none of whom has complained of discomfort from the illumination system. The reliability and validity data are reported based on images from this data set. All subjects consented to the photographs under a research protocol approved by the Johns Hopkins University School of Medicine Committee on Clinical Investigations.

Image Processing

The images are downloaded to a personal computer and analyzed using image processing software (IPLaboratory; Signal Analytics, Vienna, VA). For each photograph a 4-mm-diameter region of interest (ROI) was outlined by the computer in the center of the visual axis after three points were manually chosen on the pupil border. Three points are sufficient to specify the center of the ROI. A 4-mm central region was chosen because it matches the most optically important portion of the visual axis, because using larger diameters frequently incorporates the anterior capsulotomy edge which almost invariably opacifies, because locating the central 4 mm is straightforward to reproduce for longitudinal analyses because the anchor is the pupil margin, and because the IOL itself may shift in position and is therefore not as good a reference for locating the ROI.

Image analysis techniques are used to suppress various artifacts that may be encountered. To suppress the reflex from the cornea, the camera system uses cross-polarized illumination and viewing. This strategy suppresses most of, but not the entire reflex. A side effect of this strategy is that the birefringence of the cornea produces a distinct Maltese cross illumination artifact in the imagery. Careful, standardized reduction of room illumination also minimizes reflex artifacts. One final artifact that is often seen is related to the expertise of the photographer. To avoid excessively illuminating the iris, the diameter of the illumination beam is adjusted to approximate that of the dilated iris. Occasionally, however, the illumination beam is positioned off center, resulting in a crescent moon artifact. The effect of all these artifacts can be mitigated in a straightforward manner using morphologic gray-scale manipulations. Specifically, a dilation operation repeated several times, followed by an equal number of erosion operations and a low-pass filtering produces an estimate of the illumination. Choice of the number of morphologic operations and their local neighborhood size is driven by the scale size of the illumination variations. All the imagery used in this study used the same compensation algorithm. For example, dividing the original image shown in Figure 1 by that of Figure 2 (the illumination estimate) produced the resultant illumination-compensated image shown in Figure 3.

Image Analysis

We created a system that would allow comparisons between clinical assessment of PCO at the slit lamp examination, clinical evaluation of retroillumination images of the posterior capsule, and automated analysis of these images using computer software. The grading scheme for PCO assessed two metrics of the opacity: density and percent coverage. For clinical assessment, the graders evaluated the central 4 mm for percent coverage by PCO, and the average density of the area that was covered was assigned a score from 0 to 4. Anchors were used to guide the graders in determining density (Fig. 4).

The automated analysis algorithm determines the percent area covered by opacity and assigns a gray level for each unit of areas. The gray levels are weighted by the area covered at each
level, and an average is calculated. Identification of the regions of opacification is achieved by a simple thresholding operation. Specifically, the threshold is chosen as 95% of the modal (normalized) gray level. This modal gray level corresponds to the nonopacified regions of the capsule. Even though the clear region of the capsule may be small in proportion to the opacified region, its gray level is very consistent, thus producing a strong peak in the gray-level histogram. Such a simple thresholding operation is not possible on the uncompensated image, because the density of the illumination artifacts is often comparable to that of the opacification. Its successful operation depends on the illumination compensation process described earlier. An additional benefit of this compensation technique is that it provides self-referencing for each photograph. As a result, variations in illumination levels caused by flash variation, film processing, and fixation are obviated. This elegant approach performs as well as and far faster than more sophisticated algorithms and is more accurate and reproducible than manual methods.

Figures 3 and 4 illustrate examples of the images obtained with this system, and Figure 5 shows the resultant regions of opacification that were identified in Figure 3 using our algorithm. The fractional area of coverage was determined by integrating the various thresholded areas and dividing by the area of the (4-mm diameter) ROI. The density is not a photometric density per se, but rather an area-weighted normalized gray level. Each thresholded region in the segmented image (see Fig. 5) was multiplied by its average normalized gray level. The sum of all these weighted areas was then divided by the total area of opacification. Coverage was reported as a percentage of the ROI, and density was converted to a scale ranging from 0 to 4 for comparability with the clinical grading.

Assessing the Validity and Reliability of the System

Three data sets were used to evaluate the validity and reliability of the image acquisition and analysis system. Face validity was determined by comparing the clinical grade with that generated by the automated algorithm using the computer. This was tested on 14 eyes of 12 subjects graded at slit lamp examination. In addition, a separate set of 27 digital photographs representing a range of capsular opacification were graded by consensus by two cli
cians (ODS, DSF) and these grades were compared with the automated analysis. These analyses were intended to determine whether that which the computer identifies as PCO is the same thing that a clinician would call PCO, not to evaluate the reliability of clinicians’ grading of PCO.

Two further analyses were performed to test the reliability of the system. First, we ran the analytic algorithm on the same set of 20 digital images two times. The results were identical with 100% correlation, as would be expected using a computer to perform the analysis. Second, we evaluated test–retest reliability by having the technician take two sets of digital images of the posterior capsule on 13 subjects 10 minutes apart. Between each set, the subject was separated from the slit lamp, and the technician left the room, so that the technician had to reposition the subject before taking the second set.

Determining the Ability of the System to Detect Progression

To evaluate the system’s ability to detect progression, we reviewed existing standard photographic data from a previous study. We used retroillumination photographs from the Salisbury Eye Evaluation, a population-based longitudinal study of eye disease in rural Maryland. Photographs of pseudophakic eyes were taken in patients 2 years apart with a retroillumination camera (Neitz) using 200 ASA film (Ektachrome; Eastman Kodak, Rochester NY). These photographs were taken to document the lens status of the participants. No specific effort was made at the time of photography to obtain high-resolution images of the posterior capsule itself. Twenty photographic pairs were selected from approximately 100 subjects with photographs taken 2 years apart. Approximately 50 of the original 100 photographs were excluded because of the presence of a Nd:YAG capsulotomy in one or both photographs. An additional 30 images were excluded because of poor focus on the posterior capsule. We selected photographs to determine whether the computer could detect change in capsular opacification, not to estimate expected rates of progression in the general population. In fact, we excluded most with progressive opacity (progressors) from the data set through our selection pro-

![Figure 2](http://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933583/)
cess. The 35-mm color slides were digitized to black and white with a scanner (Coolscan; Nikon, Melville, NY). These images were processed as has been described and graded in two ways. First, the images were shuffled and randomly presented on the computer monitor to the two clinicians who graded each of the 40 photographs independently. Then the pairs were presented to the clinicians together to determine whether there was clear progression or not.

**Statistical Analysis**

All data were analyzed using commercial software (Stata) Spearman’s correlation coefficients were calculated because the data were not normally distributed. The intraclass correlation coefficient was used to test the reliability of repeated measures. The rank sum test was used to test for differences between groups because an assumption of normality could not be made.

**RESULTS**

**Face Validity**

We confirmed that the automated analysis system operated on principles that reflect the subjective assessment of PCO by clinician observers. The Spearman correlation on the 27 images graded by both the clinician and the computer was more than 0.7 for both density and percent coverage (Figs. 6 and 7). The Spearman correlation between the clinical grades applied to 14 eyes at the slit lamp examination and the computer analysis of the retroillumination images obtained after the examination was 0.88 for density and 0.74 for percent coverage ($P < 0.01$, Figs. 8 and 9). In addition, even after removing the five images with the least amount of PCO, the Spearman correlation was 0.67 ($P = 0.05$) for density and 0.78 ($P = 0.008$) for percent area covered.

**Reliability**

When the first and second sets of images were compared on 13 subjects, the intraclass correlation coefficient for percent cov-
The mean absolute difference between the two readings of percent coverage was 0.73% ± 0.53. The maximum absolute difference between readings was 1.75%. The mean absolute difference between the two readings for density was 0.06 ± 0.06. The range of values for density was 0.57 to 1.17. One outlier was identified with a difference in density between the two images of 0.21. Removing this subject from the analysis decreased the absolute mean difference between the images to 0.04 ± 0.04. The data are presented graphically in Figures 10 and 11.

Detecting Progression

Both the ophthalmologists and the automated analysis detected a mean positive change in area covered by PCO between photographs taken 2 years apart. The automated analysis found a mean increase of 5.2% (−0.3, 10.6), whereas the clinical graders identified a mean change of 2% (−1.6, 5.5). When two clinicians viewed the 20 pairs side-by-side, 6 pairs were thought to have either progressed by more than 10% (3 pairs) or to almost have achieved this threshold (3 pairs). For these six progressors, the computer measured a mean 15.8% increase compared with a mean net increase of 0.6% for nonprogressors (P < 0.05, Wilcoxon rank sum test). The comparable figures for the clinician were 7.8% for progressors versus −0.5% for nonprogressors (P < 0.05, Wilcoxon rank sum test). In addition, the computer identified all three subjects categorized as definite progressors as having more than a 10% increase in percent coverage. The only other subject so identified by the computer was one of the three thought to have achieved an almost 10% progression (Fig. 12). One subject thought to have almost achieved this threshold in side-by-side grading was identified by the ophthalmologists as having improved over time in the shuffled analysis (Fig. 12).

DISCUSSION

We have designed a computer-based image acquisition and grading scheme that satisfies the needs for a valid and reliable...
We have performed a series of tests to confirm that automated analysis provides data that are clinically relevant, are reproducible with little variation, and can be used to detect change over time. The analysis grades the severity of PCO in a clinically relevant fashion. The validation studies show that the image analysis system identifies the percent coverage and density of PCO similarly to subjective assessment by an ophthalmologist. In addition, clinical grades of PCO made at the slit lamp examination correlate well with later automated analysis of retroillumination photographs. The system is ideally suited for research on the development and prevention of PCO. It was not designed for use in the clinical setting where the impact of PCO on a patient’s function may be a more relevant measure.

Others have used the Case 2000 Marcher system to obtain reproducible images of posterior subcapsular cataracts.\textsuperscript{17,18} We have applied similar strategies to develop a digital image acquisition system and an automated analysis system for assessing PCO that yields highly reproducible results. A second computer analysis of the same images showed no variation. No human system can perform at this level. Images taken at different times on the same subject showed minimal variation, especially in determining percent area covered by PCO. The sources of this variation include operator variation in image acquisition and image analysis. During the acquisition stage, several factors can affect reproducibility including patient fixation, operator focusing techniques, and gain adjustment.

\textbf{FIGURE 5.} Retroillumination image showing the area detected as opaque by the algorithm. Opacity above threshold is outlined in \textit{black}. 

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Although the system worked extremely well, we plan to improve reliability still further by automating the gain-selection process. During the analysis stage the main source of variability is the placement of the 4-mm circle that delineates the ROI. The current approach introduces very little measurement error. However, further refinement of the system is possible. For

**Figure 6.** Scatterplot of the clinician grade looking at images for average density of the capsule in the central 4 mm versus the grade generated using the algorithm in the computer.

**Figure 7.** Scatterplot of the clinician grade looking at images for percent covered by PCO in the central 4 mm versus the grade generated using the algorithm in the computer.
example, it is feasible to establish algorithms that use anatomic landmarks to automate the placement of the circle in the same place on different photographs obtained in the same subject.

The Marcher camera has a greater depth of focus than other retroillumination cameras that have been used to study PCO in the past, making it more likely that vitreous opacities will be accidentally interpreted as PCO. Subjective review of the images analyzed using our system indicated that vitreous opacities contribute, but rarely, to the computer estimate of the total percent area covered with PCO. However, analyses of 20 retroillumination images of the posterior capsule taken within 14 days of cataract extraction found the mean percent covered was 5.3 ± 3.4 (range, 0.8–11.7). In the three images where probable vitreous opacities were seen, these opacities covered less than 0.6% of the ROI. We do not believe that the occasional inclusion of small vitreous opacities significantly affects the overall image analysis.

Using an absolute increase in area covered by PCO of 10% or more as a cutoff, the computer was able to separate progressors from nonprogressors on digitized photographs taken 2 years apart. This is especially encouraging, given the significantly worse quality of the digitized photographs compared with digitally obtained images. Mean density also increased over the 2-year period, but the difference identified between the amount of increase in density between progressors and nonprogressors did not achieve statistical significance. Average density over the area of interest does not appear to be an ideal measure of progression, however. When more area is covered

**Figure 8.** Scatterplot of the clinician grade at the slit lamp examination for average density of the capsule in the central 4 mm versus the grade generated using the algorithm in the computer.

**Figure 9.** Scatterplot of the clinician grade at the slit lamp examination for percent covered by PCO in the central 4 mm versus the grade generated using the algorithm in the computer.
by new, less dense PCO, the average density does not change and can even decrease. One possible approach to this problem is to use the SD of the gray scale rather than the mean gray level to calculate density. A minimally opacified capsule would have a very narrow gray level distribution and thus a small SD, whereas an opacified capsule would have a wider range of densities and thus a larger SD. Opacity could be viewed on a regional basis and algorithms constructed taking into account local changes throughout the central 4 mm. A third approach is to assess the texture of the capsule by dividing the SD of the gray scale by the mean gray level for each distinct area of opacification. Further research on quantifying these measures will be helpful in improving the classification scheme for PCO progression.

Image magnification by the cornea can affect the size of the circle drawn to delineate the ROI. Although this source of variation would not affect intrasubject assessment of PCO over time, it may theoretically result in differences in the size of the ROI between subjects, up to approximately 10%. We are developing algorithms to minimize individual differences by incorporating keratometry and axial length readings into the calculation of the ROI.

**Figure 10.** Scatterplot of the test-retest reliability for density of PCO using the image acquisition and analysis system on two photographs taken at separate times.

**Figure 11.** Scatterplot of the test-retest reliability for percent area covered by PCO using the image acquisition and analysis system on two photographs taken at separate times.
Some areas of PCO have sharp borders and relatively clear centers. The system tends to identify the edges of such areas and ignore the clear central zones. This is a potential limitation of the current algorithms in detecting the very early stages of capsule opacification. However, it is not certain that relatively clear central regions are clinically significant. Newer algorithms that take into account texture may characterize these clear zones more precisely.

Digital image acquisition is particularly suited to the study of the biology of posterior capsular opacification. Unlike cataracts, opacification of the posterior capsule occurs essentially in a single focal plane. This removes much of the variability and difficulty associated with trying to photograph the crystalline lens (e.g., separating nuclear, cortical, and posterior subcapsular cataracts). In addition, the technician sees the final image while the subject is still at the slit lamp. This not only removes the uncertainty about image quality when taking a photograph, but also allows the technician to determine directly that the image obtained is consistent with the clinical findings. This both increases the validity of the data and avoids the loss of data that can occur when poor photographic quality precludes accurate grading. Another advantage of digital image acquisition is enhanced quality control. All images of a particular type in the data set can be called up with a single command. This rapid access to the images is impossible using conventional photography. Finally, the low level of noise in the digital system will enable clinicians in longitudinal studies to identify changes in posterior capsular opacity well in advance of the need for laser capsulotomy.

In summary, the digital acquisition and automated analysis of retroillumination images of the posterior capsule provided reliable and valid data. The system produced highly reproducible results and drew conclusions about the capsule similar to those of a human grader who is grading the capsule both clinically and from a photograph. In addition, the image analysis system detected progression of capsular opacity in digitized retroillumination photographs taken 2 years apart.

Acknowledgment

The authors thank Stacey Seabrook for her assistance with this project.

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