

Systems of analysis of posterior capsule opacification

T M Aslam, B Dhillon, N Werghi, A Taguri, A Wadood

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This paper demonstrates the wide variety of systems for the analysis of posterior capsular opacification (PCO). No single system has been proved to be a gold standard and it is difficult to comment on the advantages of one system over another with the limited current knowledge on the effects of PCO on vision. There are few studies that actually compare the different systems of analysis. Researchers must ensure that the systems they use for PCO analysis are objective and must give maximum consideration to ensuring potential systematic errors are reduced to a minimum. Further research is required into how the various types and locations of PCO affect vision and how well different systems of analysis perform.

Advances in microsurgical practice have transformed outcomes in cataract surgery and intraocular lens implantation. However, posterior capsular opacification (PCO) remains one of the most common postoperative morbidities,^{1,2} and Nd:YAG capsulotomy is one of the most commonly performed surgical procedures.³ While Nd:YAG laser availability has led to an effective treatment for PCO, this procedure is not without risks. Lack of access to a Nd:YAG laser deprives less affluent countries of an optimal long term visual outcome. Also, when patients cannot be safely positioned—for example young children, they are unable to enjoy the benefits of the relatively simple and safe capsulotomy procedure. Thus, the study of PCO has a high level of clinical relevance and the aim of this article is to review current methods of analysis of PCO. Technological advances have meant that a wide variety of mechanisms have become available and we describe techniques of PCO assessment and their clinical and scientific relevance. The most commonly utilised methods of analysis will be discussed in terms of their principles, availability, advantages, and disadvantages.

It is neither an exhaustive list of all systems ever used nor a description of historical development of current systems. It will outline the best examples of those systems currently in use and that have been shown to be scientifically valid.

USES OF PCO ANALYSIS SYSTEMS

Accurate PCO analysis is important for measuring the effect of treatments that aim to reduce PCO such as intraoperative pharmaceutical treatments or varying types of surgery. It is also an important tool for comparing rates of PCO between the many available lenses, and the rates of progression with these lenses over time. The systems may

potentially have other clinical uses such as assessing amount of PCO with regard to potential Nd:YAG capsulotomy surgery.⁴ Systems used vary from those using simple slit lamp analysis observation and subjective grading by the observer,^{5–10} to much more complex computerised analysis of digital images obtained with specialised photographic equipment.¹¹

Properties of an optimal analysis system

The ideal system for analysis should be objective and produce quantifiable values for PCO that correlate well with changes in visual psychophysics and other indices of visual morbidity. The system should have the minimum amount of bias caused by inconsistent, human processing, with a grading system shown to have a high degree of reproducibility and validity.¹² It should be sensitive enough to pick up small differences in PCO anywhere in the visual axis and also sensitive to PCO progression, yet be specific enough to avoid registering artefacts such as lens edge, capsulorhexis edge, flash reflections, and poorly illuminated areas of capsule.

For those systems analysing photographic images, it is important that the photographic images are of sufficient detail to permit analysis,¹³ and also that the analysis has some mechanism for taking into account artefacts such as reflections and variable brightness at different areas of the capsule.

Retroillumination images have inherently uneven backgrounds caused, for example, by different degrees of pupil dilation and fundus pigmentation. This combined with low resolution of some imaging systems may lead to difficulties in assessment of PCO¹¹ by simply calculating brightness thresholds of pixels in digital images. Texture analysis aims to resolve some of these problems by analysing the local variance of pixel intensities.¹¹ Reflections may be removed before image analysis through software design¹¹ or by the merging together of two separate images to form a composite containing no reflection.¹⁴ Systems which rely on cross sectional analysis of the posterior capsule need to use a range of measurements across the capsule to obtain accurate representation of the degree of opacity of the area about the visual axis.¹⁵ At present, knowledge of the clinical importance of the various forms and distributions of PCO is limited. Recent articles suggest that different types of PCO affect vision and contrast sensitivity to different extents.¹⁶ Specifically, pearl type PCO was found to affect vision (acuity and contrast sensitivity) to a greater extent than pure fibrosis.¹⁶

The ideal analysis system should preferably be able to provide for varying ways of analysing the PCO. The researcher may wish to explore the

See end of article for authors' affiliations

Correspondence to:
Dr Aslam, Eye Pavilion,
Edinburgh, UK;
TAslam@aol.com

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Table 1 Summary of some of the advantages and disadvantages of PCO evaluation systems

System of analysis	Ease of availability	Objectiveness	Flexibility in use to measure varying criteria	Sensitivity	Specificity
Vision loss/visual psychophysics	+++++	++	+	++	+
Nd:YAG capsulotomy rates	+++++	++	+	++	++
Slit lamp grading	+++++	+	++++	++	++
Fundus visibility	+++++	+	+	++	++
Schiempflug system	++	+++	+	+++	+++
Density map	+++	++++	++	++++	++++
Computerised analysis of density boundaries	++++	++++	++++	++++	++++
Texture analysis	+	+++++	++	+++++	++++
Colour coded grid	+++	++++	+++	++++	++++

+ = very poor; +++++ = excellent.

effect of peripheral PCO on acuity or glare. Alternatively, the analysis may need to be modifiable to consider perhaps a small central area only. This would rely on the researcher being able to accurately determine various areas for analysis. Although the optic size might be a useful measure of intraocular distances, the borders may not be visible in some patients. The cornea is estimated to magnify capsulorrhexis size by a factor of 1.15,¹⁷ and this effect may cause a variation of about 10% between patients.¹² Algorithms are being developed to help overcome this source of error.¹² The nature of opacification varies and the system should ideally be able to distinguish, for example, among thickening, fibrosis, pearls, folds, wrinkles, and pigment deposits.

The system should be sensitive to difference among different lenses in different eyes and also to a progression of PCO within the same eye. The use of a quantification system to be able to predict outcomes following capsulotomy would be beneficial to patients and clinicians, especially in the context of comorbidities such as PCO in diabetic retinopathy, glaucoma, and age related macular degeneration (AMD). Finally, the system should be accessible to the research community and not prohibitively expensive to obtain and run.

CURRENT ANALYSIS SYSTEMS

Descriptions of current analysis systems follow, divided into those using clinical criteria, imaging systems and digital image analysis. Table 1 provides a summary of the advantages and disadvantages of PCO evaluation systems.

Clinical criteria

Vision

Light entering the eye is scattered as a result of optical imperfections such as PCO. Light scattered towards the retina (forward scatter) results in reduction of retinal contrast¹⁸ and may lead to a variety of complaints, especially glare.^{19, 20} Slit lamp image depends on back scatter,²¹ which is light scattered toward the observer. The amount of back scatter seen at slit lamp cannot, however, be used as a reliable indicator of the more relevant forward scatter at the patients retina.²²

Visual acuity, glare, and contrast sensitivity have been investigated in terms of effect from PCO.²³⁻³⁰ The effect of PCO on the various visual functions has been measured by assessment of vision before and after Nd:YAG capsulotomy.²³

Visual acuity following cataract surgery with IOL implantation can be reduced by many factors other than capsule opacification, and is therefore not suitable to be used as a sole measure of PCO grading.³¹ However, the slit lamp appearance of media opacities may not allow an all encompassing prediction of effect on patients' vision³² and full visual function assessment including contrast sensitivity and glare should be included in assessment of any patient with PCO.³³

Incidence of YAG

Oner *et al*⁶ report different rates of YAG capsulotomy for PMMA and for acrylic foldable lenses. As recently as July 2001

reduction in best corrected visual acuity leading to YAG has been used as a measure of PCO.³⁴ Apple *et al*³⁵ used YAG capsulotomy rate to document a decreased rate of PCO development in 5416 pseudophakic eyes in postmortem specimens. Although there may be no alternative in postmortem studies, the incidence of YAG capsulotomy is not ideal as a measure of PCO. Actual numbers may be too low for strong statistical significance. It may be influenced by subjective patient complaints, surgeons preferences and opinions, and even economic considerations.³¹ At the ASCRS meeting, April 2001; analysis of visual acuity, glare, contrast sensitivity and YAG rates were deemed to be unreliable methods of assessing the amount of PCO.³⁶

Slit lamp grading

Many authors have used simple observation to evaluate level of PCO; Kruger *et al*³⁷ used a grading system of 0 to 3 to evaluate capsule opacification. The criteria used were 0 = absent, 1 = very mild, 2 = moderate, 3 = dense white. The capsule behind the optic was evaluated within a central area measuring 3 mm diameter, and also evaluated in the periphery. Distinction was given to grading of Elschnig pearls and fibrosis.

Sellman and Lindstrom⁵ graded fibrosis and Elschnig pearl formation on a similar four point scale. The original paper contains diagrams to illustrate the various grades for both fibrosis bands and pearls. Those following grades were given; 1 = no or slight PCO without reduced red reflex, also no pearls at all or pearls not to the IOL edge; 2 = mild PCO reducing the red reflex, Elschnig pearls to the IOL edge; 3 = moderate fibrosis or Elschnig pearls inside IOL edge but with a clear visual axis; 4 = severe fibrosis or Elschnig pearls covering the visual axis and severely reducing the red reflex. The same protocol^{6, 7} or variations on it^{8-10, 38-41} has been referred to by many other authors. It has been suggested that for observer grading of slit lamp images, assessment using reflected light is more valid than retroillumination images.⁴²

Fundus visibility

Legler *et al*³⁸ assessed level of PCO in rabbit eyes using ease of visibility of posterior segment structures with indirect ophthalmoscope. Other studies have integrated visibility of fundus into their slit lamp grading mechanism. In the Madurai intraocular lens study IV⁴³ a grading system was used whereby at grade II PCO was present in the central visual axis, detectable with an undilated pupil. Also, in grade II optic nerve head was clearly seen with a direct ophthalmoscope, but retinal nerve fibre layer and blood vessels are not clearly seen. At grade III even margins of optic nerve head are not visible. No convincing data were offered to support the objectiveness of this assessment technique

Lens opacity meter

This has been used by Olson and Crandall⁴⁴ in a clinical study, as well as subjective slit lamp scores

Imaging systems

Scheimpflug system

Lasa *et al* showed in 1995 that Scheimpflug photography might be a useful tool⁴⁵ for future assessment of PCO. The Scheimpflug photography system was further developed by Hayashi in 1998.¹⁵ It is based on the use of the EAS-1000 anterior eye segment analysis system (Nidet, Gamagori, Japan) equipped with area densitometry to measure the scattering light intensity. This principle is applied to obtain a cross sectional image of the anterior segment. An alignment system is coupled with a television monitor and the slit image of the best quality is transferred to the online image analysis computer. The computer uses area densitometry to measure the scattering light intensity, which is deemed equal to the opacification density. To measure the central 3 mm portion, three cross sections are taken at meridians of 0, 60, and 120 degrees and averaged out to give an approximate value of PCO. The value obtained was shown to have a good correlation with the visual acuity.¹⁵ The system is objective and has been shown to correlate in one study¹⁵ with the visual acuities of the patients with PCO. The measurement method is easy to perform and can be done within a few minutes for each eye. Later papers reported that in terms of intraobserver and interobserver reproducibility the system was an efficient and reliable tool for PCO evaluation.⁴⁶⁻⁴⁷ It has also been verified by comparison with histological findings.⁴⁸ Hayashi *et al* describe the use of this system to successfully compare three lens types in a clinical trial.⁴⁶ However, the Scheimpflug system itself is not readily accessible to most ophthalmic departments. As it measures slit sections there is scope for missing areas of PCO if they do not lie on the meridians of analysis.¹² The limited number of axes of analysis used are the result of the problems of data entry, and limit the potential for comprehensive PCO analysis. Furthermore, the principal mechanism depends on back scattered and not forward scattered light. These factors contradict claims of a strong correlation between Scheimpflug PCO scores and visual function. The system may be limited for research purposes in terms of flexibility. There is a central weighting of data and it might be very difficult, for example, to modify the system to measure amounts of fibrosis against pearl formation. It has also been criticised in that it has not been formally assessed in its ability to detect progression.¹²

Digital photographic image acquisition systems

Digital image acquisition is particularly suited to the study of the biology of PCO.¹² Opacification occurs essentially in a single focal plane. The technician sees the final image while the subject is still at the slit lamp, allowing him to determine directly that the image obtained is consistent with the clinical findings. Rapid access to the images is feasible and the images are subsequently in a format accessible to a computerised analysis. The main advantage of using computer software to analyse images is that observer bias can be reduced and accuracy increased.¹¹ Differences between study groups may take less time to show up, and in general the process of assessing PCO is made easier and faster. The timing of follow up examinations was discussed at some length at the ASCRS conference May 2001 posterior capsular opacification meeting. It was agreed that although the effects of PCO did not take effect for some years after lens insertion, differences in PCO rates were measurable within 6 months and even 3 months that were significant and that were reliable indicators of future PCO rate differences between lenses.⁴⁹

Brightness based analysis

This technique relies on the image's pixel grey values (light intensity of the pixel) to classify a pixel as belonging to the

PCO area or not, based on a given threshold. The PCO is then evaluated by the percentage of classified pixels. Wang *et al*⁵⁰ used digital images taken with an EAS anterior segment analysis system. Brightness of different points on the digital image were graded 0 to 255 brightness units. A threshold of transparency was picked at 167 and the computer then calculated the percentage level of transparency in a particular area, with any pixel being above that value considered as being transparent. The advantage of this system is that it is objective in the sense that observers are not grading the capsules. However, there are many possible sources of bias with this approach. There are inherent variations in background intensity from factors such as pupillary dilatation and fundus pigmentation. Variations in illumination¹² arise from variations in flash, fixation, and head position. Clinical factors related to pseudophakic eyes such as IOL centration, anterior capsule relation to the anterior optic, and different refractive indices of IOL biomaterial all lead to artefacts of variable illumination in patients examined.¹³ As fixed, discrete points are taken, there may be some areas of dense fibrosis or pearl formation that are not covered by the computer analysis. Areas of fibrosis on digital images may at some points appear of quite bright intensity and it may be only when the contrast with neighbouring areas is taken into account that problems of opacity become evident. The computer generated brightness unit of a crest of a fold of fibrosis, for example, may be very bright despite the obvious problems associated with the capsular thickening. The threshold values set for analysis might not be suitable for use with other images having different luminance. An automatic selection of the threshold value using, for instance, the pixel values histogram, would make this technique more robust,⁵¹ but in general the system is little used in modern analysis because of the abundance of other potential error sources.

Density map system

Friedman *et al*¹² addressed many of the issues raised in objective analysis of digital images of PCO. The camera system they used incorporates cross polarised illumination and viewing to suppress much of the corneal reflex. This still, however, leaves a distinct Maltese cross illumination artefact in the imagery. Reduction of room illumination was also found to help minimise reflex artefacts. An uneven illumination is accounted for by an image analysis technique that involves estimating the background illumination across the capsule. The original image is then divided by the illumination estimate to provide an illumination compensated image that is relatively free of variation. As a result variations in illumination levels caused by flash variation, film processing, and fixation are obviated.¹² The grading scheme of PCO assessed both the density (based on grey level of opacification) and percentage coverage. Final coverage was reported as percentage of region of interest covered and average density was converted to scale 0-4 for comparability with the clinical grading. Friedman introduced many checks on the validity and reliability of the system. Face validity was assessed as satisfactory through comparisons to clinical grading at slit lamp by two clinicians. Test-retest reliability was assessed by having the technician take two sets of images for analysis on 13 subjects 10 minutes apart. In an attempt to determine the system's ability to detect progression photographs of patients taken 2 years apart were assessed for progression by clinicians and the computer analysis and a correlation was found. However, both sets of images were not taken by the above technique and were in fact 35 mm colour slides that were digitised with a scanner. Overall, the validation studies show that the image analysis system identifies the percentage coverage and the density of PCO similar to subjective assessment by an ophthalmologist.

The published images, however, seem to show the satisfactory identification of folds rather than areas of lens epithelial cell migration. Also, from studies on assessing the system's

ability to identify progression of PCO it was found that the area of PCO increased significantly but the average density increase did not reach statistical significance. When more area is covered by less dense PCO, for example, the average density may decrease. The authors suggest that instead of using the average density of the opacified area, use of the standard deviation of the grey scale, regionalising areas of different opacities, and assessing texture of the capsule might help in improving the assessment scheme.

Computerised analysis of density boundaries

Tetz *et al* first described a photographic analysis system in December 1997.³¹ Pictures were obtained with standard photographic slit lamp apparatus (model 40 SL/P Zeiss). Retroillumination photographs were obtained at different magnifications using coaxial illumination with standardised flash-light intensity and fully open f stop. Other photographs with diffuse illumination and with slit at different angles were used to determine other sources of opacification and to determine IOL position. On the retroillumination photographs, areas of opacification are encircled and graded 0–4 according to perceived density. The overall PCO score is then calculated by multiplying the density of the opacification by the fraction of capsule area involved behind the IOL optic. Evaluation of the photoanalysis system showed reliable and reproducible data. Interindividual variations were mild. The group showed that standardisation of the photographic technique further reduced systematic errors.

The Tetz system³¹ is now available in computerised format (EPCO), allowing calculation of areas involved in a similar means to that done previously by the observer with a photograph of the posterior capsule. The computer user traces out boundaries of different levels of PCO on digital images and the software calculates a value of PCO based on the areas and levels of PCO delineated. More recently a feature has been installed which allows merging of two images (EPCO 2000). This merge feature allows for the utilisation of two photographs of the same capsule with illumination reflections in opposite halves of the image. The halves without reflections can be merged automatically to produce a composite image without the reflective aberrations that could obscure subsequent PCO evaluation.

Although relatively inexpensive and accessible, the Tetz system is not fully objective in that it relies on the human operator to assess the PCO levels in different areas of the digital computer image. The initial 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.¹²

However, from the recent ASCRS meeting, April 2001, the photographic computerised image analysis was purported to be the new standard technique.¹⁴ Throughout the talks, courses, and delivered lectures there was overall agreement that the German evaluation of PCO system (EPCO) initially forwarded by Tetz³¹ had become the new standard benchmark system for comparison of PCO rates. Credit was given to Spalton for his original objective analysis system (POCO), but this was not used by any other authors as it was deemed too expensive or commercially unavailable.⁵² The new version of EPCO, EPCO 2000 was proposed as the best currently available system for PCO evaluation.³⁶

Texture analysis

Many techniques have been developed in the computer vision community for medical applications to classify images into textured and non-textured areas.^{53–54} In November 2000 Barman *et al* described a software application which combined with specialised photographic equipment produces a fully objective assessments of the amounts of PCO in high

resolution digital images.¹¹ It has been used in some form in various studies by the original investigators at St Thomas's Hospital, London.^{55–57} The digital camera system has optics adapted to produce a high definition, evenly illuminated image of the posterior capsule.¹³ In an ordinary slit lamp, even for retroillumination, the illumination system is angled at 14 degrees to enable binocular viewing with stereopsis. In the high resolution system the illumination module was designed to be truly coaxial to the imaging objective of the slit lamp. Comparisons with standard photographs show a higher resolution and the identification of areas of PCO that may have otherwise been disregarded. Purkinje reflexes are however still ever present in images published.¹³ The anterior capsular margin or optic margin if this is smaller, is used as the template, or mask, for the area to be studied. A high resolution system has also been described by Buehl *et al*,⁵⁸ based on the same principles, in which a coaxial system of illumination and photography is connected to a digital camera. The main advantage is reported to be the higher light sensitivity of the larger chip with higher signal to noise ratio in images. The authors admit that artefacts that still exist in their images may be mistaken as PCO by automated digital image analysis systems. Their images are still limited by the persistence Purkinje reflections induced by the flashlight. The digital coaxial retroillumination system proved highly reproducible, however, in a study of 30 eyes⁵⁸ when pairs of images of each eye were compared when taken at 1 minute and also at 5 day intervals.

The image analysis involves a series of complex processing steps outlined in detail in papers describing the St Thomas's system.¹¹ Removal of Purkinje light reflexes is performed by the software automatically blanking off areas where the image is saturated. The image is then contrast enhanced. Next, a process termed "mean filtering" is used to combat the fact that as texture is used as the prime means of defining PCO, smooth areas that might still be opaque (such as fibrosis) might have a texture similar to transparent areas. These filtering steps are used to enhance the texture of these areas of opacity. After these pre-processing steps there is a computerised assessment of the level of texture of the digital image mask—each pixel is ascribed an area of 25 pixels continuous with it on either side. The variance of these neighbouring pixels is proportional to the level of texturing at the pixel in question.¹¹ The image is classified into areas of either opacity or transparency. Algorithms are used to group together classes of the image that correspond to opaque areas and classes that correspond to transparent areas of image. The final output of the program is a calculation of the percentage area of opacification based on the number of opaque pixels in the mask area compared with the total number of pixels within the mask area.

Independent masked operators tested the validity of the system against clinical observation. Repeatability of the system was also assessed of the entire photographic image acquisition and analysis system in 32 eyes 1 week apart. Inter-operator reproducibility was also verified. This may be the nearest to a fully objective system for analysis. However, although the Purkinje images are removed from the overall analysis, the area of PCO that they hide is not actually measured and, if central, this may be of significance between images. The system involves a specialised digital retroillumination system and specialised software, neither of which are readily available for general use. Furthermore, the authors fail to prove that the values given for PCO after advanced detailed and expensive imaging with subsequent extensive image processing and manipulation has led to a system that is of greater practical clinical relevance when assessing a level of PCO that affects functional vision. For example, although after the various processing steps different forms of PCO would give different values for PCO density, the system has not been specifically programmed to recognise a distinction between pearls and fibrosis.

A similar objective texture based analysis system has more recently been proposed by Findl *et al.*⁵⁹ It is also fully automated with no subjective steps in the evaluation process, but uses a different algorithm from the St Thomas's system described above.

Colour coded grid system

The POCO-MAN system⁶⁰ has been developed by those involved in the original Spalton system with the aim of developing a simple and cheap method for objective measurement of PCO. The software places a grid over the digitally captured image and the user identifies areas of PCO. The system then automatically calculates the area of PCO in the image as a percentage. It is freely available but has not been extensively tested in clinical trials. Although this system is not as complex in terms of image processing, and is not as objective as POCO, its quantification of images has been correlated with those of the original Spalton POCO system.⁶⁰

Authors' affiliations

T M Aslam, B Dhillon, A Taguri, A Wadood, Eye Pavilion, Edinburgh, UK

N Werghi, Department of Computing, Glasgow University, UK

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