Digital Image Capture and Quantitative Analysis of Posterior Capsular Opacification

Essay

Submitted in the Partial Fulfillment of M.Sc. degree in Ophthalmology

By Ahmed Abdel Sattar Dahab M.B., B.CH

Supervised by **Professor Dr. Emad Abdel Aal Sawaby**

Professor of Ophthalmology Faculty of Medicine Cairo University

Dr. Hoda Mohamed Hosam Eldin Mostafa

Lecturer of Ophthalmology Faculty of Medicine Cairo University

Faculty of Medicine - Cairo University

Acknowledgement

First and foremost thanks to **Allah** who granted me the power to accomplish this work.

I would like to express my deep appreciation to **Prof. Dr. Emad Abdel Aal Sawaby** Professor of Ophthalmology, Faculty of Medicine, Cairo University, for kind supervision, wise guidance, patience, continuous encouragement and great help throughout this work.

I am also deeply grateful to **Dr. Hoda Hosam Eldin Mostafa** Lecturer of Ophthalmology, Faculty of Medicine,

Cairo University, for her sincere supervision, great

contribution, her advice and encouragement were of tremendous

impact.

Last but not least, I thank my Family for their patience and emotional support throughout this work.

Table Of Contents

	Page
• Acknowledgement	i
• Table of Contents	ii
• List of Abbreviations	iv
• List of Tables	V
• List of Figures	vi
• Chapter I : Anatomy, Pathogenesis & Pathology	
 Anatomy of the lens capsule and lens epithelium 	1
- Pathogenesis of posterior capsular opacification	4
- Pathology	7
- Risk factors	11
Chapter II: Clinical evaluation of PCO	14
• Chapter III: Imaging systems of PCO	
- Importance of PCO analysis systems	17
- Properties of an ideal analysis system	18
- Scheimpflug system	20
Digital photographic image acquisition	25
 Retroillumination versus Reflected-Light images in 	
the photographic assessment of PCO	35
 Objective Quantification of PCO with Optical Coherence 	ce
Tomography	42

• Chapter IV: Analysis of digital image of PCO

- Brightness based analysis	47
 Computerized analysis of density boundaries 	50
- Density map system	52
- Texture analysis system	59
- Color coded grid system	70
- Comparison between methods quantifying PCO	74
• Summary	83
• References	85

LIST OF ABBREVIATIONS

AQUA : Automated Quantification of After-cataract.

AMD : Age-related Macular Degeneration.

BCVA : Best Corrected Visual Acuity.

BU : Brightness Unit.

DRCP : Digital Coaxial Retroillumination Photography.

EAS : Anterior Eye Segment Analysis System.

EPCO : Evaluation Of Posterior Capsule Opacification.

FGF : Fibroblast Growth Factor.

HGF : Hepatocyte Growth Factor.

IOL : Intraocular Lens.

LECs : Lens Epithelial Cells.

OCT : Optical Coherence Tomography.

OU : Opacity Unit.

PAS : Periodic Acid Schiff.

PCO : Posterior Capsular Opacification.

PCT : Posterior Capsular Thickness.

PMMA : Polymethylmethacrylate.

POCO : Posterior Capsule Opacification software.

POCOman: manual POCO.

PXF :Pseudoexfoliation Syndrome.

RK : Refractive Keratotomy

ROI : Region of Interest.

RP : Retinitis Pigmentosa.

SD : Standard Deviation.

TGF : Transforming Growth Factor.

VA : Visual Acuity.

LIST OF TABLES

I	page
Table 1: Classification of PCO according to visibility of	
the fundus	16
Table 2: Summary of the present techniques PCO evaluation	
systems	74
Table 3: Summary of some of the advantages and disadvantages	
of PCO evaluation systems	76

LIST OF FIGURES

ho c	ige
Figure 1: The Scheimpflug image on Pentacam	21
Figure 2: Scheimpflug slit image before capsulotomy	21
Figure 3: The opacification density value vs visual acuity	22
Figure 4: Purkinje spots	27
Figure 5: Image-fusion process	28
Figure 6: Examples from the image set, showing original and fusion images	29
Figure 7: Correlation between A and B results	31
Figure 8: Image pairs with small, larger and maximum difference in results	32
Figure 9: a. Original greyscale image, b. background removed	33
Figure 10: a. Original greyscale image, b. background removed	33
Figure 11: Retroillumination and reflected-light standard photographs used for PCO subjective density grading	37
Figure 12: Combined index of severity (PCO index) for reflected-light image plotted against PCO index for retroillumination images	38
Figure 13: Comparison of retroillumination (left) and reflected-light (right) photographs of cases of PCO	39
Figure 14: Scatterplots of the combined index of severity (PCO index) versus best corrected visual acuity (BCVA) for retroillumination (A) and reflected-light (B) images	40
Figure 15: The location of the OCT scan	42
Figure 16: PCO types	43
Figure 17(A): The anterior and posterior IOL peaks in an eye without PCO	44
Figure 17(B): Scan profile in an eye with fibrosis-type PCO	45
Figure 17(C): This scan profile showing four major peaks	45
Figure 18(A): Digital retroilluminated images clearly focused on posterior capsule	2. 48

Figure 18 B: The percentage of transparency of the central 5.0 mm optic zone	. <i>48</i>
Figure 19:5.0 mm(A5) and 3.0 mm (A3) circle, centered on the pupil center	48
Figure 20: Unmodified image obtained using the retroillumination camera	53
Figure 21: Estimate of the illumination variation over the pupil	. 53
Figure 22: Final image used for analysis	53
Figure 23: Retroillumination image showing the level of density corresponding to clinical grades 1, 2, and 3	54
Figure 24: Retroillumination image showing the area detected as opaque by the algorithm	55
Figure 25: Scatterplot of the clinician grade at the slit lamp examination for average density of the capsule versus the grade generated using the algorithm	56
Figure 26: Scatterplot of the clinician grade at the slit lamp examination for percent covered by PCO versus the grade generated using the algorithm	57
Figure 27: Raw image with expanded views of clear and opaque areas	61
Figure 28: (A). Raw image with capsule mask applied (B). Raw image with capsule mask and light reflex mask applied (C). Contrast enhancement of the image	61
Figure 29: Examples of contrast-enhanced images containing artifacts and their corresponding segmented images	62
Figure 30: (A). Expanded view of opaque area. (B). Expanded view of transparent area	63
Figure 31: Final segmentation showing an area of 64% opacification	65
Figure 32: (A). Contrast-enhanced image. (B). Segmented image of (A) showing an area of 45% PCO	65
Figure 33: (A). Contrast-enhanced image. (B). Segmented image of (A) showing an area of 89% PCO	65
Figure 34: Comparison of findings of two clinicians (grading on slit lamp examination) versus those of the POCO image analysis software system	66
Figure 35: Comparison of images taken 1 week apart and analyzed on the POCO software system	67

Figure 36: A. The IOL optic edge is defined. B. The capsulorhexis is defined. C. A mask is applied. D. A grid overlay is placed. E. Segments with more than 50 PCO are marked. F. The PCO grades	0%
Figure 37: A. Correlation of clinically assessed area and POCOman area.	
B. Correlation of clinically assessed severity and POCOman severity	73
Figure 38: Plot of the subjective score for all cases	78
Figure 39: Box plot of PCO grade with the subjective, EPCO, POCO, and AQ methods	
Figure 40: Plot of POCO versus POCOman	80
Figure 41: The POCOman system underestimating linear opacity	81
Figure 42: Faint, low-textured opacity in some images underestimated by the computer in POCOman software	

Anatomy of the lens capsule and epithelium

The lens capsule:

The lens capsule is the ensheathing elastic basement membrane that helps to maintain epithelial cells and lens fibers as one unit. The capsule is produced anteriorly by the basal membrane of the epithelial cells while posteriorly it is produced by the basal membrane of elongating fiber cells (*Forrestre et al, 1996*).

It begins as a thin structure increasing in thickness until approximately the age of 35 years (*Olson*, 1985).

The capsule of the lens forms a transparent, homogenous, highly elastic envelope. Normally the capsule is thickest (12-21 microns) anteriorly over the lens epithelial cells. It averages 9 to 17 microns in the equatorial zone, and is thinnest (2 to 9 microns) posteriorly (*Spencer*, *1985*).

The capsule of the lens is made up of two layers; the capsule proper, which represents the main portion of the membrane, and the more superficially located, very delicate and attenuated Zonular lamella (*Duke-Elder*, 1963).

In histologic sections, the capsule is non-cellular and homogenous. It stains positively with periodic acid-schiff (PAS) indicating the presence of sulphated mucopolysaccharide component. It is dissolved in collagenase indicating a collagen component (*Rafferty*, 1985).

Under electron microscope, the capsule appears to have a relatively amorphous appearance in which the lamellar structure is suggested by coarse scattered filamentous elements. There are up to 40 lamellae, each of which is about 40nm in thickness. The lamellae are formed of fine fibrils as seen under higher resolution (*Fisher and Hayes*, 1979).

The capsule is basically formed of type IV collagen but also contain type I and III collagens in addition to other extracellular matrix components as laminine, fibronectin, heparin sulphate proteoglycan entactin and vitronectin (*Dische and Zelmenis*, 1965; *Lisa*, 1999).

Epithelial cells:

The lens epithelium arises as a single layer of cells beneath the anterior capsule and extending to the equator of the lens. There is no corresponding posterior layer since the posterior embryonic epithelium is involved in the formation of the primary lens fibers (*Anthony et al*, 1997).

The basal surface of the epithelial cells adheres to the capsule. The rest of the cell membrane is relatively complex. The lateral margin shows undulations whereas the apical membrane shows interdigitations with the underlying lens fibers. The cells are attached to each others by desmosomes and to the underlying capsule by hemidesmosomes (*Bron et al, 1997*).

The cells are polygonal (in surface view) cuboidal (in sagittal section), being approximately 10 microns high and 15 microns wide (*Anthony et al, 1997*).

By electron microscope the epithelial cells show few organelles as rough endoplasmic reticulum, Golgi apparatus, free ribosomes and small mitochondria lying in coarse granular cytoplasm (*Yeh et al, 1986; Rafferty and Scholz, 1989*).

The central cells are located near the anterior pole. They are polygonal with rounded nuclei that show no mitotic figures except when stimulated mechanically (*Bron et el, 1997*).

Pathogenesis of posterior capsule opacification

Capular opacification is a misnomer as it is not really an opacification of the lens capsule but an opaque material that lines the capsule rendering it non transparent (*Pandy et al,2004*).

Posterior capsule opacification is due to presence of remnants or regenerated lens epithelial cells following cataract surgery that migrate centrally to opacify and reduce visual acuity. Three sources produce visual opacification; (1) cuboidal anterior epithelial cells, (2) remnant epithelial cells from the equatorial lens bow and (3) dislodged cortical fibres.

Anterior epithelial cells that form the equatorial lens bow become germinal centers that have an inclination to grow along the posterior capsule after surgery (*Legler et al, 1993*).

Cuboidal cells making up the anterior epithelium lining the anterior capsule can transform into fibrocyte-like cells. These cells can proliferate but do not migrate. The germinal epithelial cells of the equatorial lens bow show mitotic activity. When disturbed during surgery, they migrate to form epithelial pearls on the posterior capsule (*Apple et al*, 1992 and *Marc Antionio et al*, 1999).

Types of PCO:

When proliferation and posterior migration of epithelial cells occur, the resulting opacity takes one of two morphological forms or a combination

of both: epithelial pearls (cellular element) and fibrous membranes secondary to metaplasia of the epithelial cells (fibrous element)(Jaffe et al,1997). The individual subcapsular epithelial cells enlarge and swell to such a degree that they have the appearance of soap bubbles and are referred to as 'Elschnig's pearls'. It has been suggested that these pearls represent the aberrant attempts of the lens epithelial cells (LECs) to differentiate into lens fibres (McDonnel et al, 1984 and Kappelhof et al, 1986). The fibrous type represents hyperplastic lens epithelium that had apparently undergone fibrous metaplasia. These aggregates hyperplastic cells always originate at the site of apposition of an anterior capsular flap to the posterior capsule and extend to a variable degree centrally towards the papillary axis. The presence of folds suggests that these cells have contractile power (McDonnel et al, 1984).

Although the proliferative activity of the epithelium is more intense in younger persons, it is by no means limited to the epilhelia of younger people (*McDonnell et al, 1984*).

Factors modulating PCO:

Certain chemical substances play a role in the pathogenesis of capsule opacification namely:

- Cytokines: cytokines are peptides secreted from cells after cell injury (*Duncan et al, 1997*).
- Transforming growth factor-beta [TGF-b]: TGF-b promotes cellular adhesions (*Hynes*, 1987).
- Fibroblast growth factor [FGF]: FGF was found to increase epithelial mitosis and collagen production (*Nishi et al*, 1996).

• Hepatocyte growth factor [HGF]: secreted by mesenchymal cells and acts upon epithelial cells influencing their migration and survival (*Grieson et al,2000*).

Less common factor in the pathogenesis of capsular opacification is the break down of blood ocular barrier with release of inflammatory mediators and cells into the aqueous humour (*Saxby*, *1999*).

Pigmentations arising from the posterior surface of the iris and ciliary body may also play a role in posterior capsular opacification. Iris melanocytes are sometimes found on the posterior capsule (*Saxby et al, 1998*).