EYE HYDRODYNAMICS AND ANATOMICAL TOPOGRAPHIC FEATURES OF ANTERIOR EYE SEGMENT BEFORE AND FOLLOWING CATARACT PHACOEMULSIFICATION

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SUMMARY

Different aspects of eye hydrodynamics before and following complicated cataract surgery as well as its impact on IOP levels are observed. Trabecular and uveoscleral outflow features, anterior eye segment anatomy and topography, associations between accommodation and aqueous humor outflow regulation in elderly patients are analyzed. Besides, optimal clinical refraction and IOL model selection are of special importance in cataract and glaucoma patients.

Keywords: cataract, IOP, uveoscleral outflow, accommodative IOLs

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Ocular connective tissue changes while being an essential part of aging process significantly affect eye hydrodynamics. Normally, anterior chamber (AC) volume in human is 0.15-0.25 cm^3 and AC depth (ACD) is 2.6-4.4 mm. However, in people over 40, AC volume progressively decreases approximately by 0.01 mm per year. In hyperopic eye this decrease is higher than in myopic one (ACD increases by 0.06 mm for each diopter of myopia). This phenomenon is accounted for continuous lens growth during the life and anterior displacements of the iris-lens diaphragm observing in elderly persons due to vitreous dilution or posterior vitreous detachment and fluid accumulation [1-5].

Age-related ciliary body changes occur after age 50. They are found in ciliary muscle and ciliary processes, i.e., ciliary body mass increases while ciliary processes become elongated and thicker. This results in forward displacement of the iris-lens diaphragm, stepwise AC angle closure and aqueous humor outflow reduction [2]. Muscle tissue degenerates and is displaced by the structures histologically resembling connective tissue. The density of the connective tissue filling the spaces between muscle fibers increases. Additionally, ciliary muscle total length decrease and its contractility reduction are observed. The changes of multidirectional muscle fibers are different, i.e., the number of longitudinal and radial fibers decreases while the number of circular fibers significantly increases. This causes the whole ciliary muscle displacement towards the

anterior chamber. Among other morphological changes, the increase in the number of pigmented cells localized between the bunches of muscle fibers (with subsequent outflow decrease through the ciliary body) is also observed.

In a human eye, two regulating systems coexist, first-order one is accommodation and second-order one is aqueous humor outflow regulation. Both systems have common acting mechanism that consists of ciliary muscle, zonular fibers and posterior chamber.

Uveoscleral outflow pathway is preserved in human from animals (see Fig. 1). Ciliary body anterior surface, trabecular apparatus uveoscleral part and iris anterior surface are potential routes for aqueous humor outflow into suprachoroidal space. This was demonstrated by many authors [7-9]. Aqueous humor drains through the stroma of above-mentioned structures into suprachoroidal space and then through the sclera into vascular system including vorticose veins. Uveoscleral outflow can account for 5% to 25% of total outflow [7, 10].

In 2006, Zolotarev AV et al. hypothesized that aqueous humor drains through the single route with two functional paths. At the initial stage aqueous humor drains through the trabecular meshwork. The differences lie in the directions of fluid movements as two types of spaces coexist in trabecular meshwork, i.e., holes in trabecular lamellae and fissures between them. Aqueous humor flows across trabecules (trans-trabecular direction) through the intra-trabecular spaces towards juxtacanalicular layer and crosses Schlemm's canal (trabecular pathway). Aqueous humor also flows along the uveal trabecules (para-trabecular direction) into inter-fiber spaces (uveoscleral pathway) [11]. When ciliary muscle tone is depressed, aqueous humor outflow through the trabecular and uveoscleral drainage routes reduces, especially in dense swollen lens.

In the higher primates and humans, a novel trabecular pathway of aqueous humor outflow has evolutionally evolved (see Fig. 2). This route is more significant for eye hydrodynamics as it mostly regulates ocular tension. The life activity of sub-human primates and humans requires frequent and extensive accommodation. This results in accommodative apparatus development, ciliary muscle volume increase and AC volume decrease in humans as compared with the lower mammals. When viewing a near object (ciliary muscle contracts), uveoscleral outflow is usually blocked. When viewing a far object (ciliary muscle relaxes), trabecular outflow is blocked while uveoscleral outflow is opened. However, uveoscleral pathway cannot provide the exit of the whole of the used aqueous humor, otherwise, trabecular route would not evolutionally develop. Active functioning of the ciliary muscle contributes to the variations of anterior and posterior chambers volume and eye hydrodynamics changes. Evolutionally this results in the development of a specialized trabecular apparatus that is evident in humans but not in animals [6].

Age-related structural changes of drainage system increase outflow resistance and favor glaucoma development. Histological findings indicate that several processes occur with ageing, i.e., extracellular material accumulation in the trabecular meshwork and ciliary muscle and trabecular meshwork cells death. This reduces aqueous humor outflow and promotes IOP elevation. A decrease in hyaluronic acid level and an increase in fibronectin and thrombospondin levels are closely related to extracellular environment changes as well. Abnormal response to oxidative stress, protein cross-linking and elasticity loss can trigger over-expression of interleukin-1, transforming growth factor beta and CD44S with subsequent elevation of fibronectin level, myoepithelial transformation of trabecular meshwork cells and extracellular matrix degradation impairment. As a consequence, trabecular and uveoscleral outflow facility reduces and IOP increases [12]. Trabecules become two or three times as thick due to spiral collagen accumulation. Basal material level increases but proteoglycan (chondroitin sulfate) level is decreased. Finally, microfibrillar component of elastic fibers disappears [13].

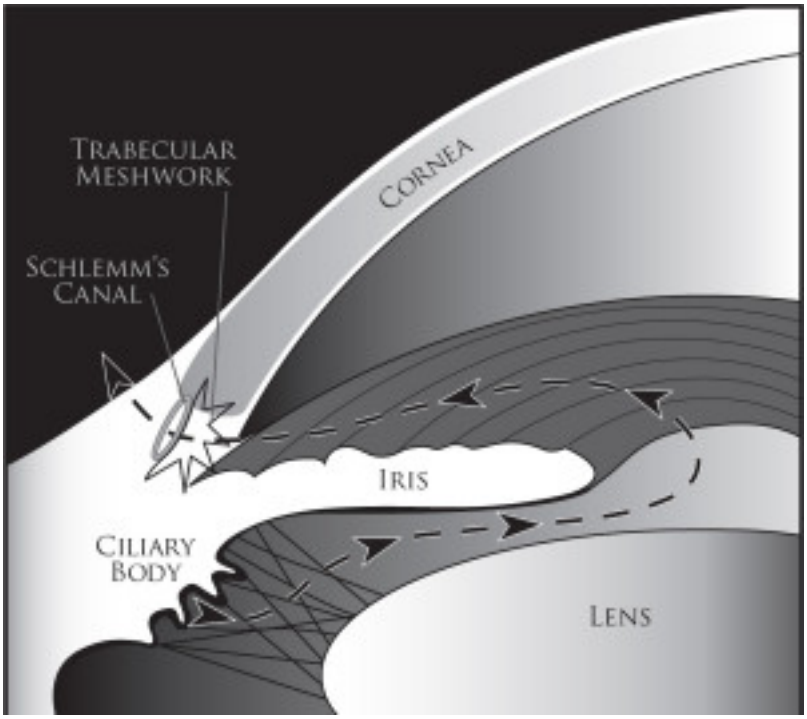

Fig. 1. Schematic diagram illustrating the uveoscleral outflow pathway.

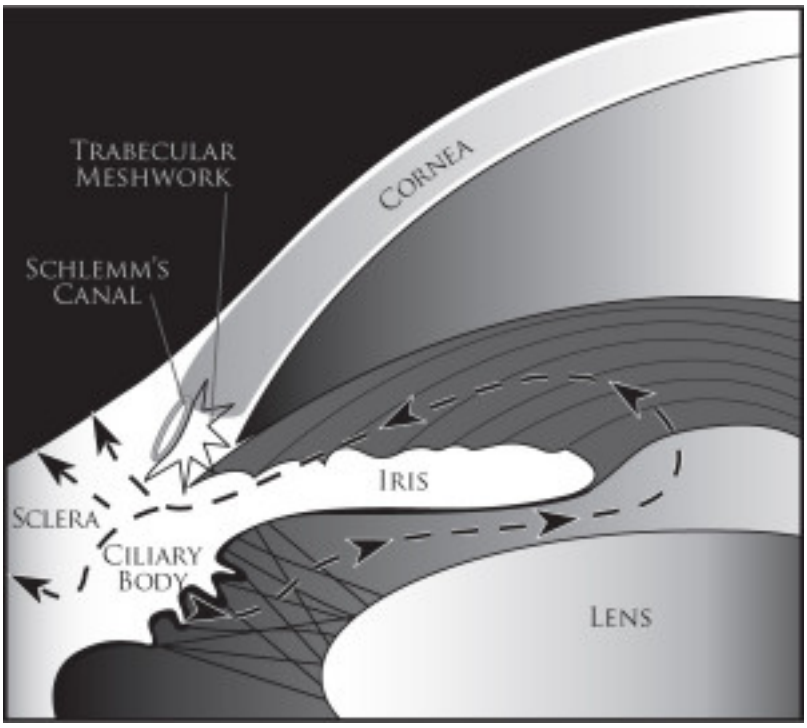

Fig. 2. Schematic diagram illustrating the trabecular outflow pathway.

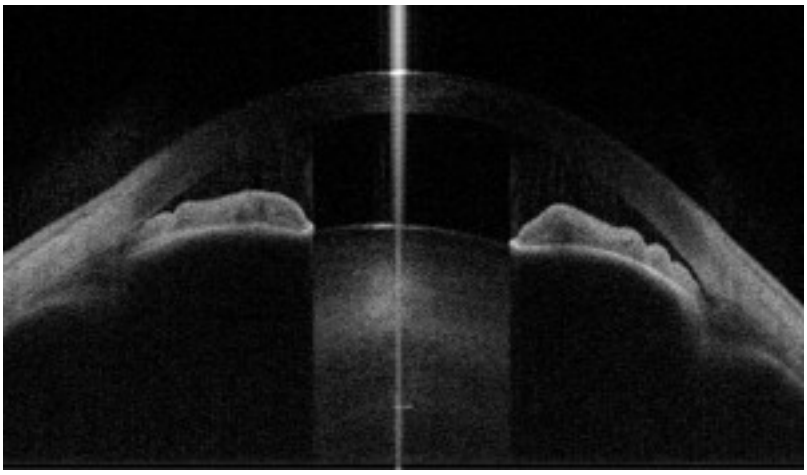

Fig. 3. AC angle topography before accommodating IOL implantation (CASIA 3D OCT).

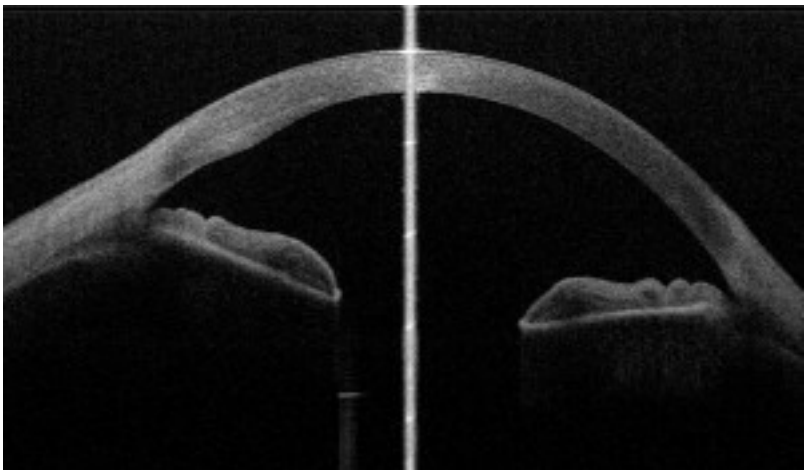

Fig. 4. AC angle topography following accommodating IOL implantation (CASIA 3D OCT).

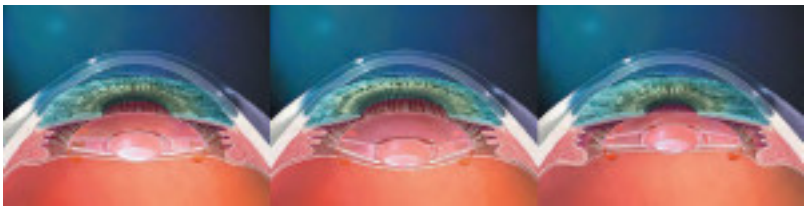

Fig. 5. Crystalens in near, intermediate and far positions.

Minor changes in drainage system (mucoid degeneration) are also observed in physiological ageing. They can provoke outflow disturbances, however, glaucoma does not develop as homeostatic mechanisms providing IOP maintenance at physiological level compensate this shift [14].

Several authors revealed degenerative changes of trabecular cells which number progressively reduces. Trabecular layer becomes thinner, trabecules “fuse”. This is considered as trabecular apparatus hyalinosis and results in outflow resistance increase and IOP elevation. The number of juxtacanalicular tissue cells decreases as well. Products of elastic fibers and spiral collagen cleavage accumulate in juxtacanalicular tissue, hyaluronic acid level also decreases with ageing. Fibronectin, collagen IV type and thrombospondin levels increase as well as laminin level decrease was biochemically established [16-17].

The aging lens growth and accommodation disorders can play a significant pathogenic role in ocular hypertension (OHT) and glaucoma development. Lens changes do not induce glaucoma but they can result in IOP elevation. In small eyes with narrow AC angle, angle closure and subsequent glaucoma development are possible. As a rule, these eyes have hyperopic refraction. In eyes with open AC angle, other changes are observed. Lens growth and sclerosis result in the contraction of cliary body excursion

amplitude with the reduction of aqueous humor volume that exits AC and drainage system hypoperfusion [17].

Hypothetically, targeted optical modification of eye static refraction may affect ciliary muscle tonus due to the stimulation of accommodation mechanisms and thus provide targeted changes of aqueous humor outflow through the trabecular and uveoscleral routes [18].

Ciliary muscle plays a significant role in uveoscleral outflow. Its constriction triggers accommodation mechanism and facilitates aqueous humor outflow through the uveoscleral route. This process appears to be the only possible way of aqueous humor movements from anterior segment to the posterior one. This movement is necessary to compensate the lack of posterior chamber volume that occurs in the course of accommodation due to lens anterior movement. In accommodation, an increase in anterior lens surface curvature as well as lens forward movements are observed [19-21]. Incompressible aqueous humor in front of the lens passes from AC through the outflow routes (most probably through the trabecular meshwork) and enters Schlemm's canal. However, behind the lens there is incompressible aqueous humor as well. Hence, the lack of the volume due to lens anterior movement should be replaced by aqueous humor inflow from the outside. Mathematical modelling of fluid movements inside the eye [22] indicates that aqueous humor produces too slowly in order to play an essential role in this process. Aqueous humor drains from AC into the posterior chamber through the uveoscleral pathway owing to ciliary muscle contractions. Therefore, ocular drainage system is morphologically related to the accommodation apparatus. This provides their active functional association.

There is an active mechanism of intraocular fluid movements in ocular chambers directly related to accommodation. With respect to accommodation at rest, this association can be represented as follows. When ciliary muscle contracts (accommodation at near), orbicular compartment decreases, pre-zonular compartment enlarges and AC volume reduces. When ciliary muscle relaxes (accommodation at far), orbicular compartment enlarges, pre-zonular compartment decreases and AC volume increases, especially as compared with focusing at near. Hence, repetitive near/far accommodative efforts known as "accommodation fluctuations" provide active fluid movements in ocular chambers from AC angle to the orbicular compartment [23].

It was demonstrated by many authors that cataract phacoemulsification with foldable IOL implantation influences IOP level. There is no definite opinion on this topic. According to some data, phaco can be considered as a risk factor for transient OHT [24-26]. However, in most cases phaco significantly lowers IOP [27-30] due to the opening of AC angle following lens removal [31, 32], the changes of anterior and posterior

chambers topography following cataract removal and thin IOL implantation, the opening of trabecular meshwork fragment that was not previously involved in aqueous humor filtration (see Fig. 3 and Fig. 4) [33, 34], and the changes of accommodation stimulus amplitude following optic system reconfiguration (the amplitude of this stimulus depends on post-op manifest refraction) [35]. These findings argue for the changes of aqueous humor outflow pathways. Still, the increase of outflow through the uveoscleral route exists only in theory since no quantitative studies were performed [36].

Ciliary muscle activation facilitates aqueous humor outflow through the uveoscleral pathway thus providing an IOP-lowering effect [37]. The level of accommodative load depends on clinical refraction, hence, IOP value following cataract removal is determined by the clinical refraction and ciliary muscle elasticity. Maximum IOP decrease compared with initial IOP is observed in hyperopic refraction due to more active ciliary muscle functioning and iris-lens diaphragm movements [38] while minimal IOP decrease is observed in myopic refraction. Therefore, mild post-op hyperopic refraction following cataract removal is considered as a pathogenically substantiated method of OHT treatment [35].

Additionally, elastic IOL that moves along the axis of the eye activates ocular hydrodynamic as well. This results in aqueous humor outflow increase and IOP lowering. Here, the problem of IOL selection arises. Multifocal IOLs are very popular today as they provide vision at different distances and minimize the use of glasses. However, their mechanism of action is based on light dividing between two focuses, and image contrast is reduced in both focuses. In glaucoma, these lenses further decrease the reduced contrast sensitivity and functional vision. Multifocal IOLs make difficulties for glaucoma progression analysis as they can induces visual filed tests and OCT artifacts. Finally, these implants are thicker and less elastic as compared with monofocal IOLs owing to their design.

Mechanism of action of IOLs with significant constructive elasticity (Crystalens AO, Crystalens HD500, MI-60) is different. It is well-known that the whole of light passes through these implants, however, detailed mechanism remains to be solved. A theory postulates that “accommodative arching” of the lens results in enhanced depth of focus compared with another intraocular implants [39-42]. This process is very similar to that of crystalline lens – it changes the curvature and acquires the gradient of refractive power. It is likely that Crystalens has several mechanisms of action. The first is moderate axial movements by 0.1-1.4 mm in response to ciliary muscle contraction [43, 44], the second is “accommodative arching” with minimal static pseudo-accommodation, the third is asymmetric tilting of the lens (see Fig. 5) [45]. “Pseudo-accommodation” is a term for optical phenomenon which enables to produce three-dimensional image without real accommodation. This can be achieved by different means, e.g., by the

increase in higher-order aberrations (especially primary spherical aberrations) that provides enhanced focus depth [46-47].

It was demonstrated [48, 49] that following accommodating IOL implantation (i.e., Crystalens), iris-lens diaphragm moves approximately by 0.25-0.5 mm. This is indicative of ciliary body excursion and ciliary muscle activation. The above-mentioned data suggest that these events facilitate aqueous humor outflow through the trabecular and uveoscleral routes.

Accommodating IOLs are implanted through the 2.8-3.2 mm clear corneal incision using special injectors. This procedure requires maximal mydriasis which is achieved by using topical Irifrin®/Cyclomed® and Mydrimax® (Sentiss, New Delhi, India) 30-90 min before surgery. Capsulorhexis 5.5.-6.0 mm in diameter is recommended. IOL should be rotated at the moment of implantation. These manipulations provide capsular bag expansion and tension and, therefore, proper IOL centration and haptic elements unfolding.

Thereby, cataract removal impacts on ocular hydrodynamics. These changes result from the significant increase of ACD, trabecular iris angle, AC angle, scleral iris angle and scleral ciliary processes angle. Additionally, iris thickness near the root tends to decrease while maximal posterior chamber depth, trabecular ciliary process distance and ciliary body thickness slightly change. IOP-lowering effect depends on glaucoma stage, i.e., it is more significant and long-lasting in early and advanced glaucoma.

Data available on the interaction between trabecular and uveoscleral pathways and their morphology confirm the strong association between accommodation and hydrodynamics. This argues for the possible influence of accommodation on IOP regulation. Ciliary muscle activation may facilitate aqueous humor outflow and decrease IOP level. The degree of ciliary muscle accommodation load depends on clinical refraction, therefore, one can modify ciliary muscle functioning by pointedly changing refraction. IOP can be regulated physiologically by ciliary muscle modulation which results in IOP decrease. Optimally, mild hyperopic refraction (0.5 D) should be planned.

Elastic IOL activates hydrodynamics due to iris-lens diaphragm and anterior hyaloid membrane movements as well as ciliary body excursion and ciliary muscle stimulation. As a result, aqueous humor outflow increase and IOP lowers. Hence, IOL selection can also have an influence on post-op IOP levels. Further studies are needed to develop a customized approach to IOL selection in OHT patients.