Multifocal IOLs

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The conventional monofocal IOL gives maximum visual acuity only at a distinct distance. With improvements in phacotechnology, natural vision with spectacle independence is the kind of visual rehabilitation we aim for in cataract patients today.

Though bifocal glasses achieve *Pseudoaccomm-odation*, the user must learn to cope with loss of distance vision with down gaze and poor near vision except in down gaze. *Monovision* that is when one eye is made emmetropic and the second eye purposely made myopic by 2.5 to 3.0 D for near vision has also been accepted to restore multifocality but has the inherent limitation of loss of stereopsis, which is not well accepted in most patients.

Phacoemulsification surgery combined with the latest in intraocular lenses, namely multifocal lenses, brings about the possibility of good quality vision for distance, near and intermediate distance too. Expectations following cataract surgery today are not limited to just restoration of vision alone but wanting vision close to what a young normal patient has, in other words qualitative emmetropia.

History of multifocal IOLs: Hoffer in 1982 was the first to hit upon the idea of a multifocal IOL after observing a patient who had 6/6 vision in spite of an IOL that was decentred by more than 50% of the pupillary area. Logistic problems prevented him from being the first surgeon to implant bifocal IOL. The credit goes to Dr. John Pierce in 1986 who was to implant the bull's eye style of the multifocal IOL.

However due to old surgical techniques and lens designs there was a lot of surgical astigmatism and decentration of lens leading to poor visual results. Dedicated research into optical designs along with the development of new surgical techniques have resulted in more effective multifocal implants.

Type of Multifocals

There are mainly 3 types of multifocal

1. Refractive
2. Diffractive
3. Combination of diffractive & refractive

All MIOLs cause a loss of contrast sensitivity due to light distribution through different focal points. Studies done by Stienart et al[17], Merdedes at al[12], Bleckman et al[4] Gimble at al[3] have also reported a small amount of glare and halos experienced by the patients due to the lens optics, as there is some scattering of light at the dividing line of the different zones.

The first MIOL product to be granted Food and Drug Administration investigation status was the center surround or the *bull's eye lens* manufactured by Precision Cosmet and later acquired by IOLAB corporation. This is a refractive type of PMMA bifocal IOL with central add surrounded by distance optical power (fig.1). The rays of light get refracted through it and form two foci – one for near and one for distance. However the zone principle has the shortcoming of being dependent on the pupil size for full effect. There is a sudden loss of vision in bright sunlight since constricted pupil blocks the distance segment of lens. It is poorly tolerated by persons who enjoy outdoor sports in which clear vision is required and by those with a small pupil. As a modification in the bull's eye IOL another lens was introduced as a 3-zone bull's eye lens with a central distance zone, second-near zone and third again distance zone (fig.1b).

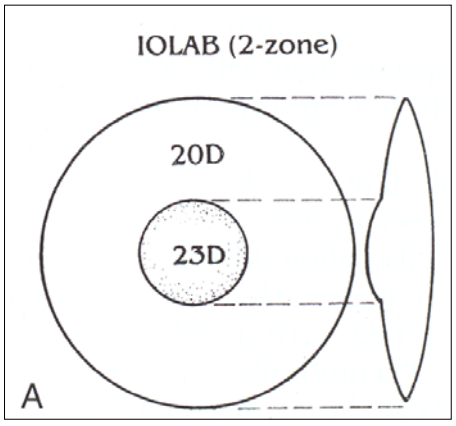

Fig.1(a): Bull's Eye Lens (2 zone)

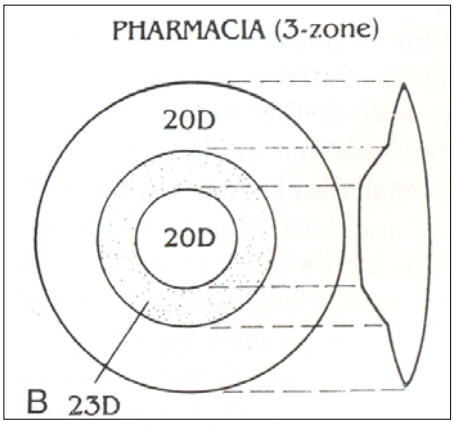

Fig.1(b): Bull's Eye Lens (3 zone)

The first *diffractive MIOL* which was introduced by the 3M corp called as the 3M diffractive MIOL (fig.2). This IOL utilizes the principle of diffraction in conjunction with refraction to create two foci. The basic refractive power is provided by the anterior aspheric surface and the diffractive power comes from the multiple grooves on its posterior surface. 41% of light is focused for distance vision and another 41% is focused for near vision. The remaining portion of light is distributed to higher orders

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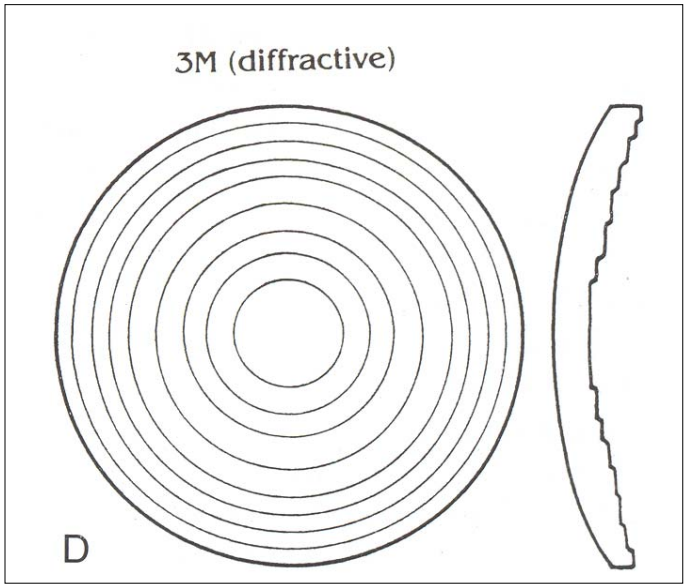

Fig.2: 3M Diffractive Multifocal IOL

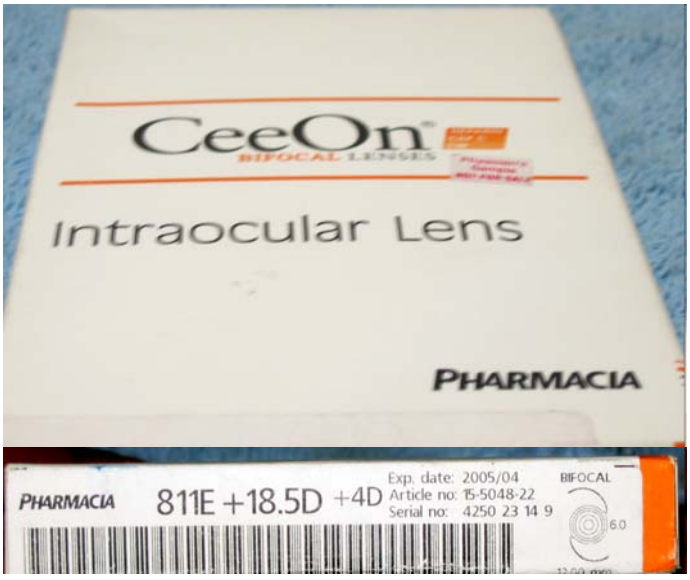

Fig.3: Pharmacia diffractive PMMA Multifocal IOL (6mm optic dia)

of diffraction. The Pharmacia 808,811E (fig.3) and 3-M diffractive IOLs are PMMA diffractive lenses. Since this lens has a diffractive optical effect present at all points of the lens, even if the lens is decentred or the pupil is eccentric or deformed, lens will always supply power for distance and near vision. Thus diffractive IOLs are pupil independent. However there is still loss of contrast sensitivity due to light division. Glare & halos may also disturb the vision due to the concentric annular zones. Wallace et al[11] and Simpson concluded loss of contrast sensitivity and glare and halos with the implantation of this lens.

Foldable Multifocals

All these lenses were designed in the right direction

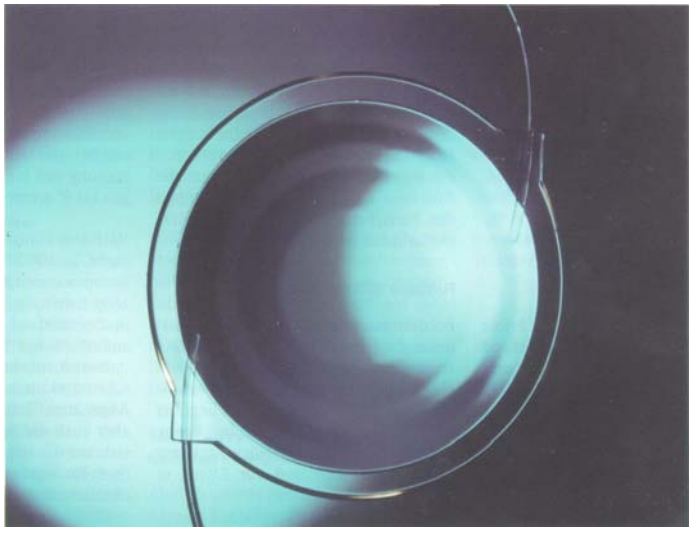

Fig.4: AMO Array lens Sa40

aiming for a good pseudo-accommodative effect. But in the pre-phaco era the surgical results were not that reproducible and postoperative decentration was commonly encountered. Today in this era of highly advanced cataract surgery the surgical results are now predicatable and reproducible. The need for a good foldable multifocal IOL was fulfilled by the first FDA approved **foldable MIOL** which was the silicone **AMO Array** lens. It is divided into 5 concentric zones on its anterior surface with varying optical powers such that light distribution with a typical pupil size is approximately 50% for distance 37% for near and 15% for intermediate vision (fig.4). The ability to insert the foldable Array through a small incision has been a real asset for this lens. Unwanted astigmatism does not occur as does with the large incision created for implantation of PMMA lenses. This lens had a near additions of 3.5D at the IOL plane and 2.1D at the spectacle plane. The lens had a major limitation of being pupil dependent (ideal size- about 3-3.5 mm). The average pupil size in Indian eyes is small, specially when associated with senile miosis. So the Array lens did not suit the Indian eyes very well. The Array lens was associated with halos & glare which were more common under mesopic conditions. In a study by Sen H.N. et al to study the quality of vision after AMO array multifocal IOL implantation, 33 were compared with the eyes having a monofocal implant. In all the eyes with multifocal implant contrast sensitivity was significantly lower in comparison to the monofocal group. But at the same time the near visual acuity was much better than the unaided monofocal group. The study highlighted that lower contrast sensitivity and increased perception of halos by the subjects with the multifocal IOLs appear to be an acceptable compromise to enhance near and distant vision.

It is important to note that one should ideally aim for emetropia or sight hypermetropia post-operatively. The

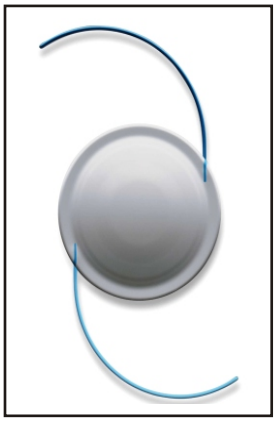

Fig.5(a): AMO ReZoom Multifocal

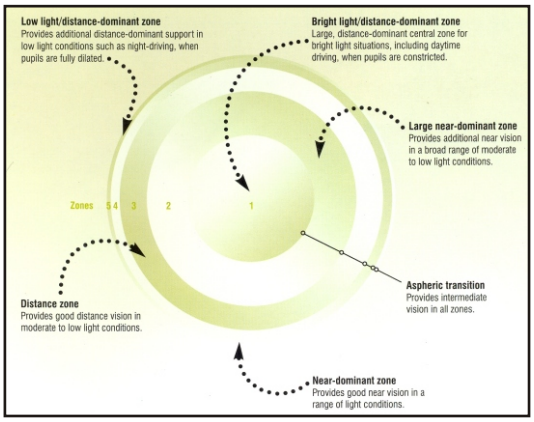

Fig.5(b): AMO ReZoom Multifocal-Modified zone to 1 & 3 for distance

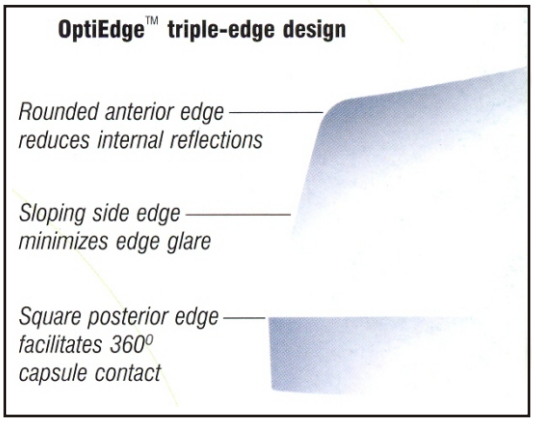

Fig.5(c): Square Posterior edge & sloping side edge in ReZoom multifocal

cases should never be made myopic post-operatively as the symptoms of glare and halos will be more in such a condition. This is because the blur circle falls directly on retina in a myopic eye (Diagram-1b), where as in the hypermetropic eye the distant image appears a little blurred but the halo formed around it get less diffuse (Diagram-1c) and thus the patient is more comfortable.

We, at Sir Ganga Ram Hospital conducted a prospective study on refractive multifocal in 30 eyes. Refractive IOLs (AMO Array) were implanted bilaterally in 20 eyes and unilaterally in 10 eyes with the other eye having a previously implanted monofocal IOL. We observed that 90 % of eyes had an unaided visual acuity of $\geq$ 6/9 which was comparable to a monofocal IOL. 70% of eyes with MIOL had a near vision of $\geq$ N/9 without correction, this was significantly more when compared to 20% in the monofocal eyes. 90% of patients with bilateral implantation neither complained of contrast sensitivity loss nor were bothered by glare and halos. Infact they were happy to carry out all usual activities independent of glasses. Although on examination with Pelli Robson contrast sensitivity chart there was a decrease in contrast sensitivity compared to the monofocal IOL, with bilateral implantation this decrease was not statistically significant.

Though this was the first foldable multifocal to be widely used, the need for reading glasses, pupil dependency and presence of glares/haloes limited the popularity of this IOL.

Micro-R et al showed that Array multifocal IOL with its center distance design is distance biased. Distance contrast sensitivity shows marked deficits at higher spatial frequencies under mesopic conditions. Near contrast sensitivity obtained with multifocal array IOL is below that which can be achieved by an appropriate monofocal near correction. These limitations led to the further research and modification of the design in the form of the ReZoom lens.

The *Rezoom lens* (fig.5a) is a foldable acrylic MIOL from AMO. It has zones similar to Array, zone 1, 3 and 5 are

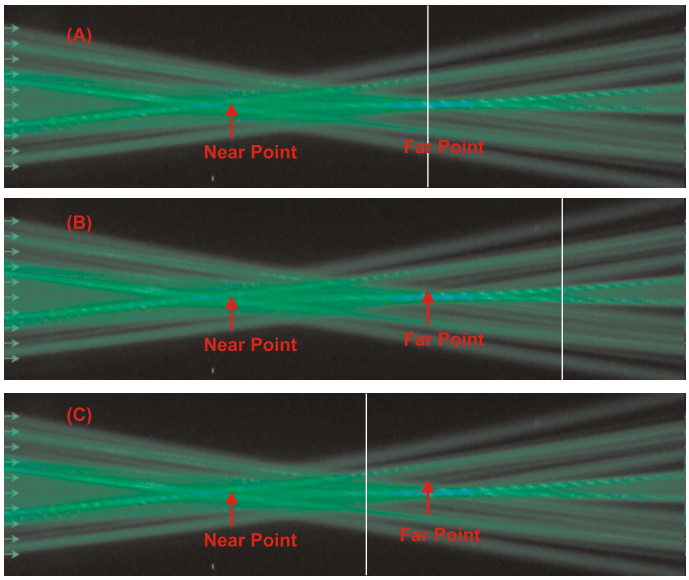

Diagram (1a): Point of focus as formed in an emetropic eye, Far point falling on the retina. **(1b):** Point of focus as formed in a myopic eye, far point in front of the retina, creating a blurr circle on the retina. (**1c):** Point of focus as formed in a hypermetropic eye, far point behind the retina, decreasing the blurr circle.

distant dominant and zones 2 and 4 are near dominant (fig.5b). This lens has been modified by expanding the first and third zones for distance such that 60% of incoming light is for distance and 40% for near and intermediate distances. The near add has been increased. Most of the patients with Rezoom have a good distance and intermediate vision but still may require an additional near aid for gaining vision of N/9 or better. Most studies show the 80% patients are J-3 or better thus reducing the need for near glasses but may not totally eliminate the need for the same. It gives good distance visual acuity for both day and night time. It has a triple edge design with rounded anterior edge which reduces internal reflection, sloping side edge which minimizes edge glare and square posterior edge which facilitates 360º capsule contact (Fig.5c). Aspheric transition between the 5 zones provides a better intermediate vision and also reduces glare and

Fig.6: Acry.Sil multifocal 737D-distance dominant, 733D near dominant

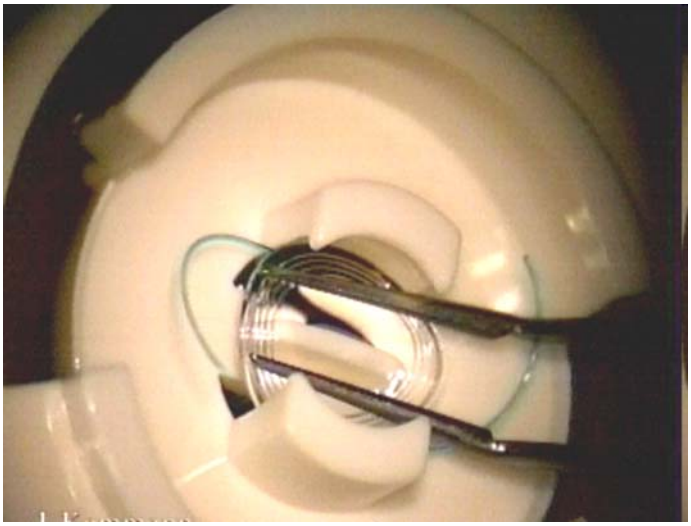

Fig.7: Acry.Sil differactive multifocal

halos which were compartively more with the Array lens. Therefore, it theoretically reduces glare and visual aberration and minimizes PCO formation. It is less pupil dependant and gives better intermediate distance vision and near vision than the Array.

Thus this lens is a very good choice for a combination implantation with a diffractive multifocal to provide a good intermediate vision specially in computer professionals.

The main limitation of multifocals are the presence of glare/halos and reduced contrast sensitivity, which is seen to improve with bilateral implantation, because of "a bilateral summation" effect. Based on the idea of bilateral summation the Acri-Tec foldable intraocular lens was introduced. This is a foldable silicone, bifocal diffraction IOL. There are two models – one is near dominant (733 D) (fig. 6) with 70% of light for near and 30% of light for distance focus and the second is distant dominant (737D fig.6) with 70% of light for distance focus and 30% for near focus. With their implantation there is nearly 100% of light for near and distance bilaterally therefore a considerable improvement in contrast sensitivity. This lens gives a very good distance/near correction with promising results and spectacle independences. Due to specific edge design of the lens with fresnel structure contributing to the total refractive power, this lens is extra thin. The anterior surface of the multifocal lens contains the diffractive optic providing the lens with a near addition of +4.0 diopters.

A study was conducted in Sir Ganga Ram Hospital, New Delhi where 40 eyes of 20 patients were implanted with Acri.Twin diffractive bifocal IOL. With the distance dominant 737D Acri.Twin 65% of total patients had visual acuity better than 6/9. Binocularly 90% had visual acuity better than 6/9. With near dominant Acri.Twin 733D 100% of patients had near vision better than N8. Out of these 60% were N6 Binocularly all patients were better than N8 out of these 75% were N6. In contrast sensitivity measured by Pelli Robson chart 45% of patients were better than 1.8 log unit with both 737D Acri.Twin as well as with 733D Acri.Twin. None of the patients had less 1.65 log unit contrast sensitivity. Binocularly 65% were better than 1.8

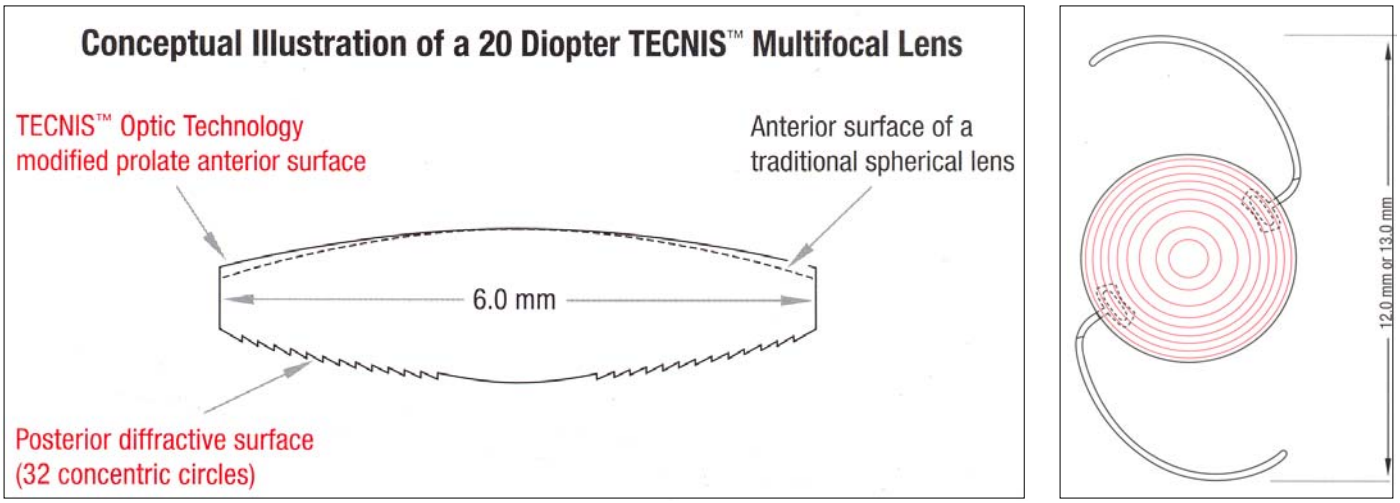

Fig.8: Tecnis multifocal Zm900 IOL

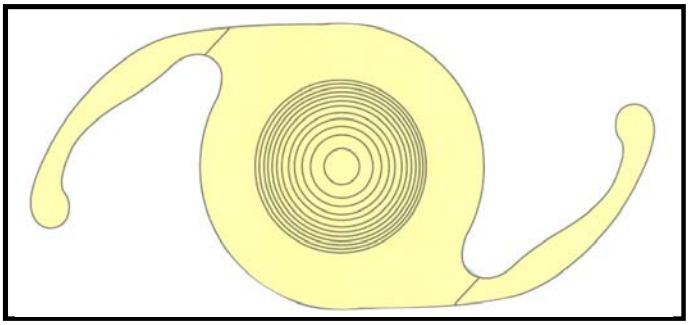

Fig.9: AcrySoft ReSTOR SA60D3 apodized diffractive IOL

log units. Indicating a minimal loss of contrast. To conclude, these diffractive bifocal IOLs out perform monofocal IOLs by providing good near vision and at the same time giving functionally useful distance vision. Also due to asymmetrical distribution of IOL there is not much loss of contrast sensitivity as compared to other bifocal IOLs.

The diffractive technology seems some what more promising with a better performance. The latest IOL in the multifocal armamentarium are Tecnis IOL (AMO) and the ReSTOR IOL (Alcon).

The Tecnis IOL (Advanced Medical Optics, Inc., Santa Ana, DA) represents the first IOL that has a wavefront-designed, modified prolate, anterior-surface optic that neutralizes the positive spherical aberration of the human cornea.[1] Its design is based on the average corneal-surface wavefront-derived spherical aberration in a group of patients, and the optic neutralizes this aberration.[2] Spherical aberration is the human optical system, and it increases throughout life to continually decrease visual quality. Implanting conventional spherical IOL optics not only fails to address this problem but also contributes to it. The implantation of the Tecnis IOL can significantly reduce spherical aberration in postoperative cataract patients.[1,9]

Most of the undesirable optical side effects of any single-optic bifocal IOL are due to spherical aberration. Using the highly successful and stable Tecnis platform, optical engineers added a diffractive multifocal optic to the posterior surface of the lens. The result is the modified prolate Tecnis Multifocal (fig.8).

A prospective studies conducted at Augenklinik, Bad Hersfeld, and Gutenberg University, Mainz, Germany, was conducted to evaluate reading performance with 3 types of multifocal IOLs under different lighting conditions based on reading acuity and reading speed tests, where they implainted, the SA40N IOL (AMO) in 20 patients, Tecnis ZM001 IOL (AMO) in group 2 (20 patients) and AcrySof ReSTOR SA60D3-IOL (Alcon) in group 3. They concluded that under bright light conditions second generation multifocal IOLs (group 2&3) provided better reading performance than the Array SA40N IOL. When tested

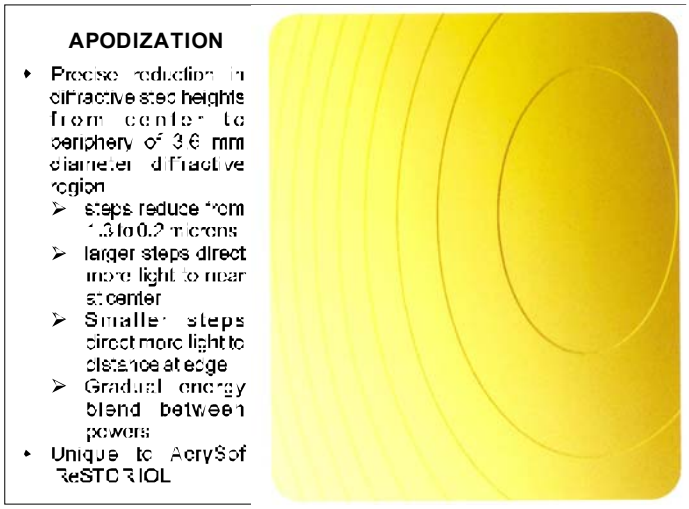

Fig.10: Apodization (Original magnification 80X)

under low light condition, patients with Tecnis 2M001 IOL had the best reading acuity and reading speed.

The most recently introduced is the AcrySof ReSTOR apodized diffractive IOL (fig.9) This IOL has 2 separate optical regions to provide quality vision at various distances A central aprodized diffractive region is 3.6mm wide and the peripheral refractive region contributes to distance focal point for larger pupil diameter and is thus dedicated to distance vision. The central apodized diffractive region (fig.10) consists of 12 concentric steps of gradually decreasing (1.3-0.2 microns) steps heights provide a good range of vision for different distances. This lens incorporates +4.0D of additional power in lenticular plane for near vision, resulting in +3.2D at the spectacle plane. Apodisation, which is a gradual reduction or blending of the diffractive steps heights is a special fecture of AcrySot ReSTOR IOL. This technology optimally manages light energy delivered to the retina, because it distributes the appropriate amount of right to near and distant focal points, regard less of the lighting situation, resulting a better quality of vision.

Pre-operative Considerations

Apart from our honest intention to provide the best surgical outcomes some of the key considerations for Multifocal Implants are listed below.

The Patient should have a strong desire to be spectacle independent. This is the single most important indication for multifocal lens surgery. After all it is futile to place a multifocal lens in a patient who is reluctant to give up wearing glasses!!

Age- By and large, for the first 100 cases, it would be better to operate within the age group 35 to 75.

Functional & Occupational Requirements- A detailed history on this point is most crucial. Does the patient have any

hobbies like painting, playing the piano, playing cards or billiards or is he just the unusual avid reader? Patients often complain of the difficulty in MULTI TASKING post IOL surgery with monofocal lens implant .This category of patients are the ones to target for.

Pre-existing Ocular Pathologies-One has to rule out the possibility of pre-existing ocular diseases like ARMD,GLAUCOMA etc. more so in these cases as these are visually and surgically demanding cases where the real benefits of multifocality may not be produced or appreciated by the patients. Secondly a partial contrast loss due to the multifocal lenses may add on the visual handicap of the patient.

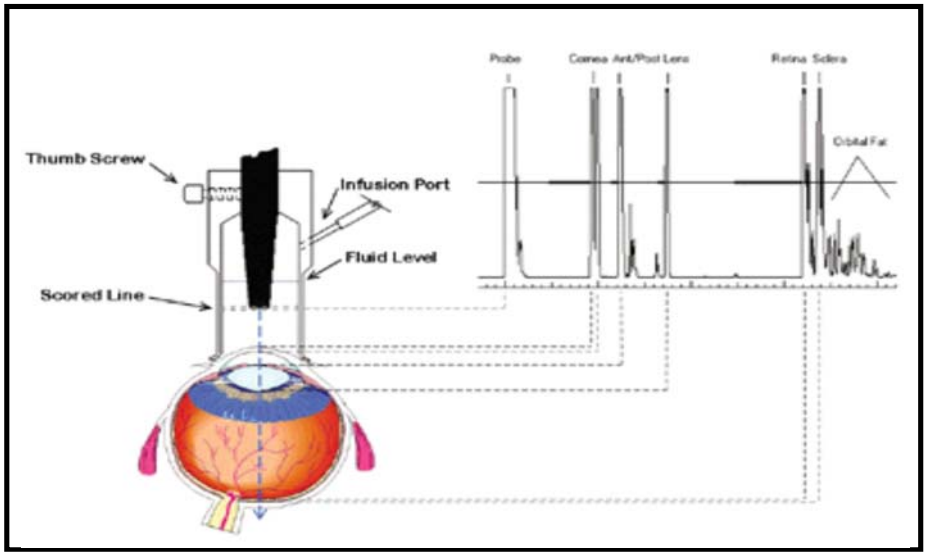

Fig.11: Immersion Biometry

Hypercritical & Demanding Patients-This class of patients should be strictly avoided. One should prefer to operate on those patients who trust their surgeon's skills and capability. In other words, patients with whom there is a comfort level. It is better to avoid proving ourselves to a cynical and suspecting patient who remains unhappy no matter how best we perform. Such are the patients who will remain more bothered with the halos and mild transient glare which may be present initially.

Strong urge for near reading without glasses –These avid readers will be very happy with the apodised diffractive multifocal which has very good unaided near vision especially in bilateral lens implants.

Occupational night drivers –For all these patients even a short term glare or halo effect will be intolerable. Counseling these patients and explaining them about potential side effects and also the fact that they are easily tolerable with binocular summation and lessen with time is very crucial. After all we know that the brain perceives what it wants to!!

Medical Exclusion

Apart from the psychological profile of the patients, there are certain clinical pointers to suitability for mulfifocals.

1. *Patients with more than 1.0 D of corneal astigmatism*-Since we are aiming for emmetropia, post op astigmatism is undesirable. Fashioning the wound around the steeper meridian or combining an LRI or double CCI with normal phaco surgery may help in tailoring the astigmatism.

Pre-existing ocular pathology-Especially those with retinal problems which may have already decreased the contrast sensitivity, may not be ideal candidates.

Individuals with a monofocal lens in one eye- It is recommended to avoid these patients. Symmetry and binocular summation since play an important note in the final adaptation of the patient.

History of previous Refractive Surgery-Although these patients are the most strongly motivated ones to have multifocal lens implants they may be unsuitable. If K readings are less than 40 one should suspect this possibility. Biometry accuracy is not always possible in these patients and clinical correlation with previous or present spectacles along with the pre-refractive surgery keratometry is important if a multifocal IOL is planned.

Intra-operative Exclusion Criterias

The following intra-operative factors can have a negative impact on long-term IOL performance. All these situations can affect lens centration and support which are the key factor for target surgical outcome for all these multifocal lenses.

- Significant vitreous loss during surgery
- Pupil trauma during surgery
- Zonular damage
- Capsulorhexis tear
- Capsular rupture

Keys for Successful Multifocal IOL Implantation

Patient Selection- The right patient is to be selected

Accurate Biometry- IOL master strongly recommended as optical biometry (IOL Master) is approximetely 10 times more exact. Use of immersion biometry (fig.11), would be better choice than applanation biometry. Cross-checking by 2 technicians, clinical correlation with present or past refractive error and comparison with fellow eye is suggested.

Power Calculation- Maximize visual outcomes by calculating for a post-operative refractive spherical equivalent from Plano to <+0.25. Use of newer formulae like SRK-T and Holladay are helpful.

Surgical Technique- The following are helpful in achieving good results-Round, centered CCC completely overlapping the Lens Optic, removal of all viscoelastic from behind the lens and proper positioning of lens in capsular bag. In other words the surgery must be a work of art. A combination of perfect surgery and right selection of patients results in a happy patient who becomes the all important flag bearer for other eager but hesitant patients.

The amount of our chair time spent with the patient prior to surgery greatly reduces chair time spent afterwards. However this great technological leap forward is setting the bar just one step higher in the ladder of surgical quest and ambition. With the encouraging results obtained with Multifocals implants in cataract patients, this may well be the answer to the non-cataractous presbyopes who are unwilling to wear glasses. In fact many surgeons worldwide are using these high quality multifocals for clear lens extractions with encouraging results.

Combining Refractive & diffractive IOLs

Refractive IOLs such as the AMO ReZoom lens offer excellent intermediate and distance vision as well as 100% transmission of light. Incoming light is directed across the entire focal plane of the lens to provide vision at all distances. However, near vision is not as strong with these lenses as with some other technologies, so patients may have more difficulty reading up close. These lenses are also pupil dependent, so there may be mild night-vision symptoms.

Refractive lenses are ideal for light to moderate readers who drive mostly during the day. Patients who play sports, use a computer frequently, or enjoy activities such as playing cards activities that all rely heavily on intermediate vision will benefit from refractive lenses.

Diffractive IOLs such as Alcon's ReSTOR lens and Advanced Medical Optics' Tecnis Multifocal IOL offer excellent near and distance vision as well as good reading speed. They are pupil independent, so patients experience fewer problems with night vision. However, there is a, gap in intermediate vision as well as a loss of transmitted light and therefore, a loss in contrast sensitivity with these lenses. Diffractive lenses are ideal for patients who spend a lot of time reading or doing detailed craft-work. Those who like to go to the movies and those who often drive at night are also good candidates for these lenses because they function independently of pupil size.

However, not all patients fit neatly into one category. Some individuals love sports and movies. Others aren't big readers but often drive at night. Studies have been done compare the results of bilateral implants of the same IOL to a mix-and-match diffractive/refractive.

Mixing and matching different IOLs allows the surgeon to combine the advantages of both refractive and diffractive lens technologies, according to Brazilian ophthalmologists Pedro Paulo Fabri, M.D. and Leonardo Akaishi, M.D. They presented data comparing refractive outcomes, reading speed, spectacle independence, and quality of vision using various multifocal IOL approaches during the February World Ophthalmology Congress in Sao Paulo, Brazil.

In the study, four groups of patients were compared: 100 patients with bilateral ReSTOR implants, 100 patients with bilateral ReZoom implants, 88 patients with ReSTOR in the non-dominant eye and ReZoom in the dom-inant eye, and 15 patients with a Tecnis multifocal implant in one eye and ReZoom in the other.

Study Results

Most notably, patients in both of the mixed lens groups achieved 100% spectacle independence, compared to 75%-89% in the bilateral implant groups.

Distance acuity was weakest in the bilateral ReSTOR patients but very good across all the study groups. Intermediate vision was best with the ReZoom/Tecnis. Multifocal combination but also was excellent in the bilateral ReZoom group. Average near vision in the patients with at least one ReSTOR lens was J 1.40-1.50. However, the ReZoom / Tecnis Multifocal group achieved even better near visual acuity of J 1.10. Additionally, they find that the ReZoom/Tecnis Multifocal combination offers good bilateral near vision in lower light situations. The typical reading distance is a more comfortable one, and there is greater bilateral contrast sensitivity than when ReSTOR and ReZoom are combined. Finally, having a Tecnis Multifocal IOL in at least one eye reduces spherical aberration (Table 1).

Conclusion

Every patient's visual needs and expectations are unique. Mixing and matching refractive and diffractive IOL styles can offer patients binocular vision that is excellent at all distances: near, intermediate, and far. This approach, provides a greater chance of spectacle independence and fulfills all the patient's lifestyle expectations.

The newer generation multifocal IOLs have now established superiority over monofocal IOLs in many situations. The patient counseling and evaluation play an important role in the eventual success. Further work such as addition of cylinder, need to be done to provide custom-made IOLs for all types of patients.

Table 1: Comparison at Bilateral vs. Mix-and-Match Results				
	Bilateral ReSTOR	***Bilateral ReZoom***	***ReSTOR+ReZoom***	***Tecnis MF+ReZoom***
No. Patients	100	100	88	15
Mean follow up Near VA*	4 mos.	4 mos.	2 mos.	1 mo.
(reading distance	J 1.40 (30cm)	J 2.30 (38 cm)	J 1.50 (39 cm)	J 1.10 (42 cm)
Intermed VA*	J 3.85	J 2.15	J 2.30	J 2.10
Distance VA*	20/25	20/20	20/20	20/20
Reading speed (wpm with a 3.5-mm pupil)	165	125	155	185
Spectacle Independence	89%	75%	100%	100%
Halos/glare	1+	2+	1+	1-
**Visual acuity was measured binocularly*				

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Improving Outcomes in Retinoblastoma

Anita Sethi MD, DNB, FRCS

Retinoblastoma (RB), as we all know, is the commonest intraocular malignancy in children. Though this is not a common condition, it is one of the few life-threatening conditions that present to an ophthalmologist. A timely diagnosis could thus save the life of the child. From being considered universally fatal at one time, there is now a reported 75-90% survival rate. With the advent of newer therapeutic modalities like laser, primary neo-adjuvant chemotherapy and plaque radiotherapy, the use of combination therapy can result in preservation of vision thus avoiding enucleation. The emphasis is now on multi-disciplinary treatment for the best possible outcome.

Epidemiology of Retinoblastoma

The incidence of RB appears to be similar as reported from studies from all over the world at 1/ 17000- 18,000 live births/year. This provides a strong evidence that environmental factors don't have a significant role to play. Other factors that have been linked to a higher risk are advanced paternal age and excess cancer in relatives.

Family history and genetics: RB is said to be familial in 25-30% but in Indian conditions we are not always able to elicit a positive family history. One should look for regressed lesions in the parents of bilateral cases and ask for a history of deaths in early childhood in the family. Also, screening of siblings (aged less than 5 years) of all cases should be done, whether unilateral or bilateral. Though the genetic abnormality is identifiable in some cases, chromosomal analysis may not be practical in our scenario since it is expensive and the results take a long time.

Clinical Features of Retinoblastoma

The commonest presentation of retinoblastoma is leucocoria in a child aged 1-5 years. In a typical case it may not be so difficult to make the diagnosis. However, given the grave consequences of a missed or delayed diagnosis, it is prudent for us ophthalmologists to maintain a high index of suspicion so as to pick up the all the cases at the earliest. The clinical features together with appropriate investigations can correctly establish the diagnosis in most cases.

Age: Though RB commonly presents between 18-24months, in our country we often find children presenting at a later age (Fig.1). Rarely, it may present in the first year of life (Fig.2).

Leucocoria: Leucocoria, unilateral or bilateral , is by far the commonest presentation of RB. There may be overlying engorged vessels or calcification visible (Fig.3). There is a long list of differential diagnosis of leucocoria usually clubbed a 'pseudoglioma'. The ones likely to cause a diagnostic dilemma are PHPV, organized vitreous haemorrhage, Advanced Retinopathy of Prematurity, endophthalmitits and Coats disease in older children. The associated anterior segment findings may help, in the form of microcornea in PHPV and a low tension in endophthalmitis. In any case of leucocoria, a dilated examination of the fellow eye is mandatory. Raised IOP, ectropion uveae, rubeosis and pseudohypopyon are all pointers to a tumour in the eye.

Squint: Any squint in a child warrants a fundus examination with dilated pupils. A macular tumour causing the squint can be picked up even with a cursory indirect ophthalmoscopic examination so there is no excuse for telling the parents to bring the child back for squint surgery later, without seeing the fundus.

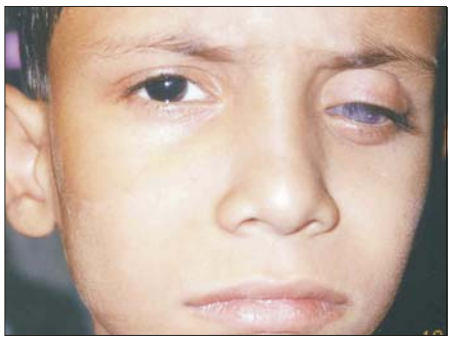

Fig.1: Retinoblastoma in a 8 year old boy

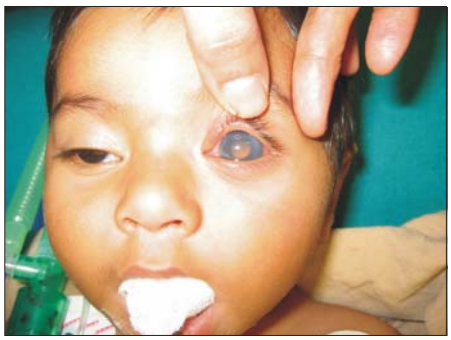

Fig.2: RB at age 4 months, Note the hazy enlarged cornea.

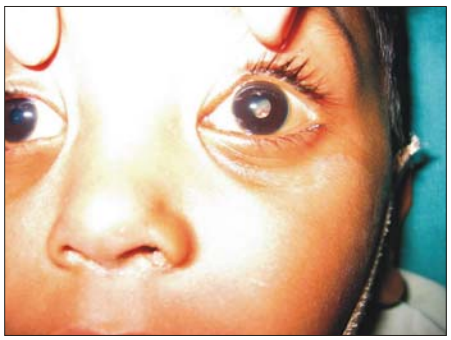

Fig.3: Leucocoria demonstrating vessels

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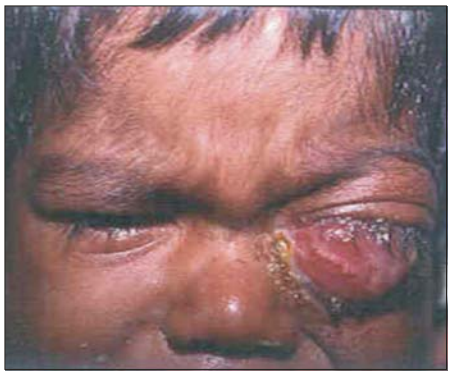
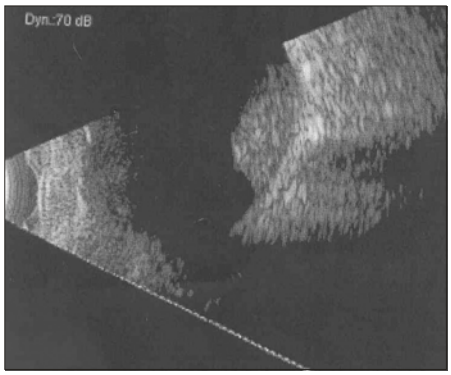


Fig.4: Proptosis due to extensive growth of tumor



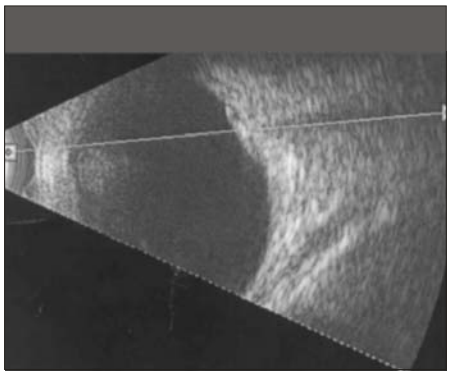


Fig.5: USG showing decrease in lesion after 3 cycles of chemotherapy

Secondary Glaucoma: If the parents miss the initial leucocoria, RB can present as secondary glaucoma with an opaque cornea. Therefore, one should rule out a tumor in these cases by examining the other eye and doing an ultrasound, if possible.

Pseudohypopyon and endophthalmitis: Though infections are rare in RB, it can present as pseudohypopyon in an inflamed eye and/or masquerading as endophthalmitis. One needs a high index of suspicion in these cases especially if seen in older children.

Proptosis: Unfortunately in India, there are still a large number of children presenting with proptosis (Fig. 4). A history of leucocoria may sometimes be forthcoming. Though orbital cellulitis is still the commonest cause of proptosis in children, tumors like orbital RB and rhabdomyosarcoma should be kept in mind.

How to investigate a case of suspected RB

Investigations in RB are aimed at confirming the diagnosis and establishing extent of disease both for the prognosis and therapy decisions.

Ultrasonography: USG is an important tool in establishing the diagnosis of RB. RB is usually seen as a mass lesion of moderate- high internal reflectivity, arising from the retina. There maybe an overlying detachment visible. Calcification, characterized by spikes of 100% reflectivity, is seen in 90% cases and is diagnostic of RB. Optic nerve involvement and scleral infiltration may also be picked up. USG monitoring of tumor height is important when the patient is on chemoreduction (Fig. 5).

CT Scan: On CT Scan, RB is seen as a moderately attenuating mass lesion with calcification (Fig.6). Extraocular spread in the form of optic nerve or scleral infiltration and/or intracranial extension is well demonstrated. CT Scan is required for radiotherapy planning as well.

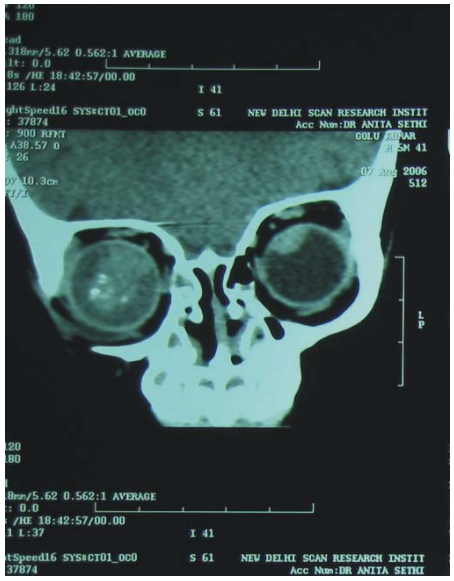


Fig.6: CT Scan showing mass lesion with calcification in the right eye. The left eye shows a smaller tumor at the posterior pole with no calcification.

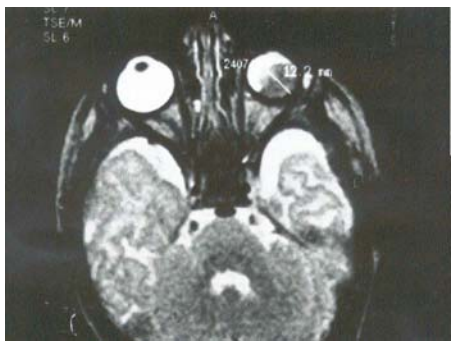


Fig.7: MRI & RB.

MRI : MRI is not as useful in the diagnosis of RB except in cases where vitreous haemorrhage/ exudative retinal detachment is suspected (Fig.7). MRI is especially useful in demonstrating fluid in case of suspected Coats disease. Though calcification is not so well demonstrated, the soft tissue visualization is better especially in case of chiasmal involvement or trilateral Retinoblastoma.

Special Investigations

In most cases the diagnosis can be clinched with the above-mentioned clinical features and investigations. In certain cases where the diagnosis is difficult, like leucocoria without calcification, older age groups etc some special investigations may be indicated. One such investigation is Fine needle aspiration biopsy (FNAB). FNAB done under indirect opthalmoscopic guidance and with an experienced cyto-pathologist can be a useful diagnostic tool.

Investigations for metastasis

The investigations for determining the spread of RB are CSF

examination and Bone marrow biopsy. Bone scanning may be done if metastasis is suspected.

Staging of RB

As in all cancers, staging of the disease is essential both for prognostication and for planning the treatment. A thorough examination of both eye, preferably under anesthesia is advisable. The Retcam 120 digital imaging system is extremely useful in documenting the lesions and for monitoring the therapy.

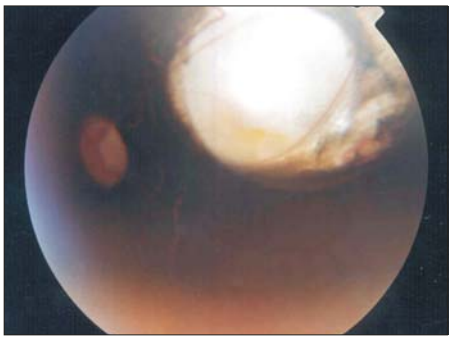


Fig.8: Regrened RB following cryotherapy.

The age-old *Reese-Ellsworth* classification, though still followed in a number of centers, may not be so relevant today. For one, it is only an intraocular classification and secondly, anterior lesions, which today can easily treated with cryotherapy, have been assigned a worse prognosis. Other recent classifications like the St Jude's Hospital classification have included both extraocular and intraocular disease. The RPC-IRCH classification also lays the basis for combined modality (local therapy, radiotherapy and chemotherapy) treatment. A newly proposed classification is based on the likelihood of salvaging the eye when chemotherapy is used as the primary treatment of the intra-ocular malignancy. There are 6 groups from Group A-Group F.

Management of RB

The emphasis in RB management has now shifted from enucleation to the use of combination therapy in an effort to preserve vision and salvage the globe. For this multimodality therapy to work, good co-operation is *essential* between the ophthalmologists, pediatric oncologists and radio-therapists. The therapy of each child needs to be carefully planned with active involvement of the concerned doctors if optimum results are to be obtained.

The therapeutic options available are

1. *Local treatment:*
   Cryotherapy
   Laser therapy
   Thermotherapy
2. *Surgical:*
   Enucleation with implant
   Exenteration
3. *Chemotherapy:*
   Chemoreduction with various drugs-Etopside, Carboplatin, Vincristine, Cyclophosphamide
4. *Radiotherapy:*
   Brachytherapy with radioactive plaques
   External beam radiotherapy

Local treatment

Local treatment is directed at small lesions away from the fovea and optic nerve that are accessible either with laser or cryotherapy. It may either be the primary therapy or used after chemoreduction-this has been described as serially aggressive local therapy (SALT).

Cryotherapy

The lesions which are upto 2-3DD in size and extend upto just beyond the equator are usually amenable to cyrotherapy.

Technique: This is done by elevating the lesion on a cryoprobe and applying the triple freeze-thaw technique. The endpoint of the cryo is when the reaction reaches the surface of the tumour into the overlying vitreous. Patient should be reviewed after 2-3 weeks and cryo may be repeated if required. The lesion usually regresses to a flat scar (Fig. 8). On subsequent follow up the edges of the scar need to be carefully examined for recurrence.

Laser

Laser treatment is suitable for small lesions (1-1.5 disc diameter with minimal elevation). Here contiguous laser spots are applied around the lesion to cut off the vascular supply. These lesions then may regress completely without any scarring.

All patients treated with local modalities need to be carefully followed up at monthly intervals initially.

Thermotherapy

The principle behind this is that gentle warming of the tumour (by 6-10^0) helps in the uptake of platinum based chemotherapy. The Diode laser is used with a large spot size (upto 2mm) and long duration (9s). The entire tumor is covered over 10-15min. Intravenous Carboplatin is given on the same day.

Surgical treatment

Most children present with the eye full of tumor, leaving enucleation as the only option. During enucleation, one should take care to obtain a long stump of the optic nerve and also subject the globe to histo-pathological examination to confirm the diagnosis and determine the extent of infiltration of the intra-ocular structures; (Fig.9) information that has a bearing on the overall prognosis. All attempts should be made to give a good cosmetic result in the form of an implant and a good fitting prosthesis (Fig.10).

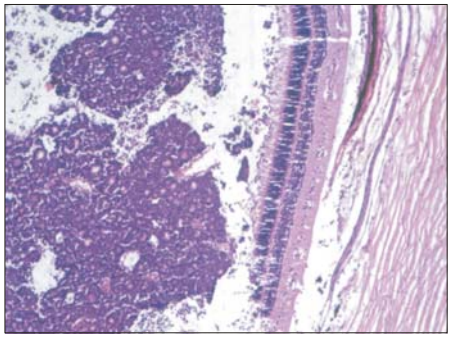


Fig.9: Slide showing histo-path of RB. Note the Flexner-wintersteiner rosettes.

Fig.10: Post-operative (1 week) picture of child in whom enucleation with implant was done for RB.

Orbital retinolastoma is treated with exentration followed by radiotherapy. However, once the tumor breaches the sclera and extends to the orbit, the prognosis for life is very dismal.

Chemotherapy

The newer chemotherapeutic drugs with better ocular penetration like Carboplatin and Etoposide, Tenoposide, Cyclosporin A etc have revolutionized RB therapy. Chemotherapy is no longer used as just adjuvant therapy but as primary neo-adjuvant therapy. Chemotherapy is started as primary therapy for intra-ocular RB to decrease the size of the lesions so as to make them amenable to local therapy i.e. chemoreduction. The smaller size of the tumour post-chemoreduction means that there is less damage to the retina and thus better chances of preserving vision. It has been seen that there are specific features of intra-ocular RB that may affect the response to chemotherapy and this has been incorporated into the new classification.

Chemotherapy (Platinum based) has also been seen to enhance the effects of radiotherapy, i.e. lower doses, less side effects, and should be given within 6 months of chemotherapy.

Adjuvant therapy: Adjuvant therapy is defined as CT given to prevent metastasis in patients at high risk for extra-ocular spread. Six-twelve cycles of chemotherapy are given in cases with poor prognostic factors (Optic Nerve involvement, massive choroid/ scleral infiltration or evidence of systemic spread) as it has been seen to improve the prognosis. Carboplatin has also been tried as peri-ocular injections with limited success.

Side effects of chemotherapy: Most of the side effects are dose related and of short duration. Though these drugs are comparatively less toxic than those previously used (Vincristine, Cyclophophamide, Adriamycin) there is still a risk of leukemia when the child grows.

Radiotherapy

External beam radiotherapy has been the standard conservative modality used with good effect in RB. The use of therapy planning systems, lens sparing methods and fractionation of doses have minimized the complications namely radiation retinopathy, cataract, dry eye and socket contraction. The risk of secondary non-ocular tumors is decreased by avoiding EBRT in infancy, especially in familial cases. EBRT is presently available at the IRCH, AIIMS, Batra Hospital and Rajiv Gandhi Cancer hospital, Anand Hospital, Preet Vihar.

Brachytherapy involves the placement of radio active plaques such that the dose is concentrated around the tumor. The advantage is that the rest of the eye receives a lower dose and thus the complications are less. Iodine 125 is one of the commonly used radio-isotopes. In India, these plaques are now available in LV Prasad Eye Institute, Hyderabad and Sankara Nethralaya, Chennai.

Multi-modality therapy now ensures that we have a number of therapeutic options for children with RB. However, the onus is still on the ophthalmologist for early diagnosis and timely referral if we are to save the life and the eye.

Suggested Reading

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Imaging Modalities in Glaucoma: OCT/HRT II/ GDx-VCC

Parul Sony, MD

Glaucoma is characterized by the optic nerve head (ONH) changes leading to irreversible visual field loss. The commonly accepted parameters that are used for glaucoma diagnosis are raised intraocular pressure (IOP), visual field defects (VFD) on white on white perimetry (WOW), and optic disc changes. It is a well established fact that 50% of the patients have an IOP within normal range at the time of first presentation, and VFD defects are picked up by standard automated perimetry (SAP) when an irreversible loss of 40-50 % retinal nerve fibre layer has already occurred. Thus in most of the cases when a confirmative diagnosis of glaucoma is established, the eye has already had some irreversible changes, owing to the disease.

Another important aspect in glaucoma patient is establishing the progression of disease process. Detection of VFD progression is one of the most challenging aspects of glaucoma management. It may take years to show a definitive progression on the basis of WOW perimetric changes. Decision of whether to change therapy or to operate often requires confirmation of the disease progression with certainty. Now days everyone is concerned about early detection of the disease process so that a diagnosis is made before appearance of any irreversible loss.

The upcoming technologies and newer diagnostic modalities may enable us to make a pre-perimetric diagnosis of glaucoma and pre-empting the progress of the disease. These include technologies such as confocal scanning laser ophthalmoscopy (HRT), scanning laser polarime-try (GDxVCC), and Optical Coherence Tomography (OCT). All these provide quanti-tative, reproducible, and objective measurements of optic nerve head and RNFL thickness. These methods may especially be helpful in eyes with increase IOP and normal VF (ocular hypertension; OHT) where these may help us to identify and treat those patients who are at risk of developing glaucoma. These imaging machines are being increasingly used in diagnosing and assessing the progression in a case of glaucoma but none of them have achieved a global acceptance. Major factors preventing there wide spread use is the lack of normative data, longitudinal data and phenomenal cost of these instruments. This article will be briefly discussing the application of these modalities in glaucoma.

Fig.1.1: OCT3 Stratus

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Optical Coherence Tomography

Optical coherence tomography is based on the principle of Michelson interferometry. Low-coherence infrared (830nm) light coupled to a fiberoptic travels to a beam-splitter and is directed through the ocular media to the retina and to a reference mirror, respectively. Light passing through the eye is reflected by structures in different retinal tissue layers. The distance between the beam-splitter and reference mirror is continuously varied. When the distance between the light source and retinal tissue is equal to the distance between the light source and reference mirror, the reflected light from the retinal tissue and reference mirror interacts to produce an interference pattern. The interfer-ence pattern is detected and then processed into a signal. The signal is analogous to that obtained by A-scan ultrasonography using light as a source rather than sound. A two-dimensional image is built as the light source is moved across the retina. One can think of the image as a series of stacked and aligned A-scans to produce a two-dimensional cross-sectional retinal image that resem-bles that of a histologic section. This imaging method thus can be considered a form of in vivo histology. An infrared-sensitive charge-coupled device video camera documents the position of the scanning beam on the retina.

The OCT image can be displayed on a gray scale where more highly reflected light is brighter than less highly reflected light. Alternatively, it can be displayed in color whereby different colors correspond to different degrees of reflectivity. On the OCT scanners currently commercially available, highly reflective structures are shown with bright colors (red and yellow), while those with low reflectivity are represented by darker colors (black and blue). Those with intermediate reflectivity appear green.

Current com-mercial scanners employ a low coherence super luminescent diode source (820 nm). The presently available model Stratus OCT (OCT 3, figure 1.1) has a theoretical axial resolution <10 mm. Ultra-high resolution research OCT scanners use a titanium sapphire laser that has an ultrabroad spectral bandwidth centered at approximately 800 nm. With these light sources, axial resolution can be

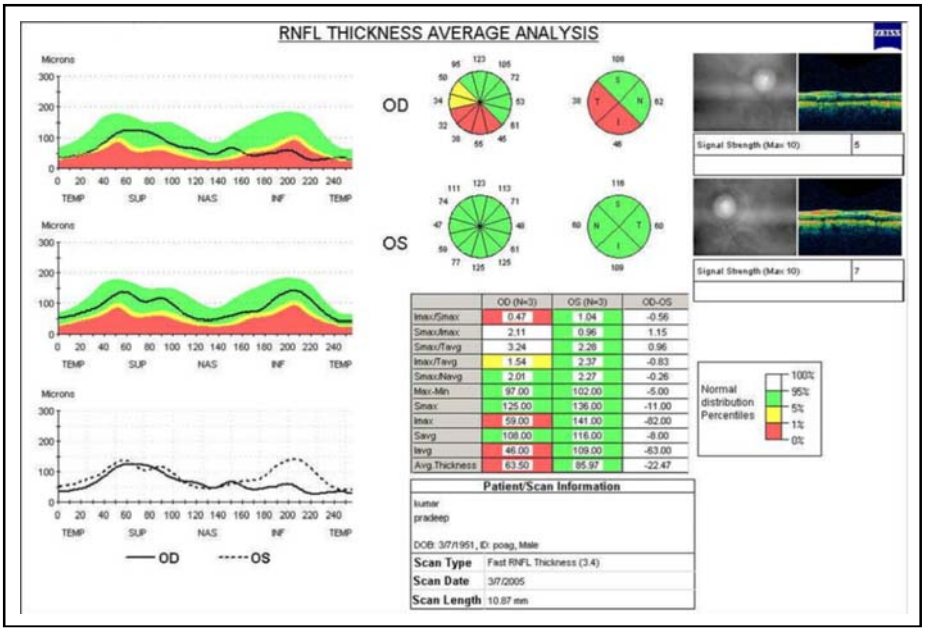

Fig.1.2: RNFL thickness analysis printout

increased to 2 mm to 3 mm but these light sources are expensive and have a limited role in routine clinical applications.

OCT is used for evaluation of the RNFL thickness, macular thickness and the ONH parameters in eyes with glaucoma.

RNFL image acquisition

The newer Stratus OCT(OCT 3; Carl Zeiss Inc, Dublin, California, USA) can be used in the absence of dilation in many individuals, and usually requires a 3-mm pupil for adequate visualization. Still, Image is acquired preferably under a dilated pupil with a diameter of 5 mm (with tropicamide 1% before recording the images). The internal fixation is preferred owing to its higher reproducibility.An operator-determined circular or linear path centered around the optic disc is scanned, to generate a series of 100 axial reflectance profiles. From these, a real-time two-dimen-sional tomographic image is constructed. The first reflection measurement is the vitreous-internal limit-ing membrane interface. The highly reflective interface posterior to this is the retinal pigment epithelium-photo-receptor interface. Retinal thickness is measured using the location of the vitreo-retinal interface and the retinal pigment epithelium defining the inner and outer boundaries of retina respectively.

Mean RNFL thickness is calculated using the inbuilt RNFL thickness average analysis protocol. The boundaries of RNFL are defined by first determining the thickness of the neuro-sensory retina. The location of posterior boundary of RNFL is determined by evaluating each A-scan for a threshold value chosen to be 15dB greater than the filtered maximum reflectivity of the adjacent retina. Average measurements are given for 12 30-degree sectors. The depth values of the scans are independent of the optical dimensions of the eye, and no reference plane is required.

Clinical Interpretation of RNFL Thickness Average analysis

OCT 3 offers a variety of RNFL thickness measurement and analysis protocols (figure 1.2, 1.3).

- *RNFL thickness protocol (3.4mm):* Acquires a scan with radius 1.73mm, centered on the optic disc.
- *Fast RNFL thickness protocol (3.4mm):* Acquires three fast circular scans. This is time efficient scan alignment and placement is required only once.
- *Proportional circle:* This protocol allows measurement of RNFLT around the optic disc along a circular scan, the

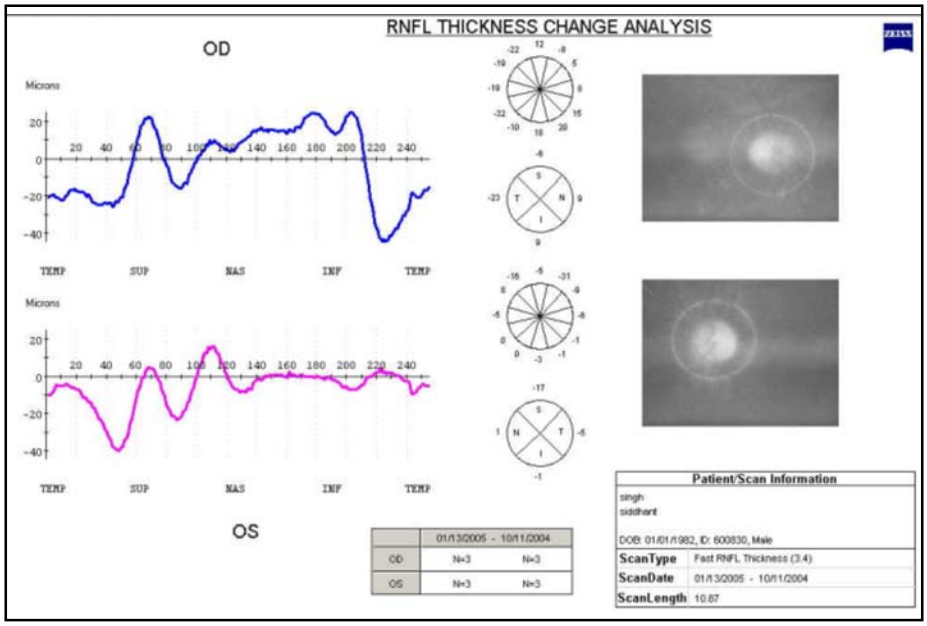

Fig.1.3: RNFL serial analysis

size of which can be tailored as per individual's need taking into account the size of optic nerve head.

- *Concentric 3 rings:* This protocol enables us to measure RNFLT along three equally placed default circular scans of 0.9mm, 1.81mm and 2.71mm radii. However the scan radius can be altered according to the need.
- *RNFL thickness (2.27Xdisc):* This circular RNFLT scan size is 2.27times the radius of the optic nerve head. This may help us to measure RNFLT with accuracy is various disc sizes.
- *RNFL map:* This protocol comprises of six circular scans of 1.44mm, 1.69mm, 1.90mm, 2.25mm, 2.73mm, and 3.40mm radii. This gives an overlay view of the RNFLT, around the peripapillary area.

Retinal nerve fibre layer measurement with a circular scan of 1.34 mm radius, centered on the optic nerve head has been shown to have a maximum reproducibility.

Mean RNFL thickness is calculated using the inbuilt RNFL thickness average analysis protocol. For understanding purpose the RNFL thickness average analysis print out can be divided into various zones that include:

1. ***Zone 1:*** Patient ID data.
2. ***Zone 2:*** Individual TSNIT curves for each eye presented in comparison with the age matched normative database.
3. ***Zone 3:*** Overlap of TSNIT curve showing a comparison of two eyes.
4. ***Zone 4:*** Circular diagram (4) showing quadrant wise and clock hour wise distribution of average RNFL thickness in both eyes.
5. ***Zone 5:*** Data table; this table shows various ratios, quadrant averages, and difference among the quadrants and between the two eyes. Each value is marked in color to show its level of deviation from the normal values.
6. ***Zone 6:*** Red free photograph; B&W photographs of two eyes taken with the infrared camera are available on the printout. These denote the position of scan circle on the fundus.
7. ***Zone 7:*** Precentile distribution color coding; A small box denoting the color coding of percentile distribution of normative database is provided. White and green color representing the distribution within 95%, yellow color representing the areas of RNFL thickness below 5th percentile, and red color representing the areas of RFNFL thickness below 1 percentile. Similar color coding is applicable for the individual TSNIT curves also.

Average thickness: The average RNFL thickness along the entire circular scan.

Savg & Iavg (Superior average and inferior average): The Average RNFL thickness in the respective 90^0 of the circular scan

Smax & Imax(Superior maximum and inferior maximum): Maximum RNFL thickness recorded in the respective 90^0 quadrant of the scan

Max-Min: Difference between the maximum and minimum RNFL value along the circular scan.

The four ratios provided in the data table are self-explanatory.

Optic nerve head analysis

The newer version of the OCT, OCT 3 allows a detailed quantitative evaluation of the optic nerve head. It is provided with two scan protocols

- *Optical disc scan* consists of equally placed line scans 4 mm in length, at 30^0 intervals, centered on the optic disc. The number of lines can be adjusted between 6-24 lines.
- *Fast Optical disc scan* compresses six optical disc scan into one scan and acquire scan in short time of 1.92 seconds.

The optic nerve head (ONH) analysis and various ONH parameters are calculated using the inbuilt ONH analysis protocol (Figure 1.4). This analysis detects the anterior surface of the retinal nerve fibre layer (RNFL) and the retinal pigment epithelium (RPE). The cup perimeter is determined by automatic detection of the reference points. The inbuilt algorithm detects and measures all the features of disc anatomy based on anatomical landmarks, (disc reference points), on each side of the disc where the RPE ends. It locates and measures the disc diameter by tracing a straight line between the disc reference points. The cup diameter is measured on a line parallel to the disc line and offset anteriorly by 150 microns and various optic nerve head parameters are automatically calculated. These parameters include optic disc tomography included average disc area, cup area, rim area (disc area minus the cup area), vertical integrated rim area (VIRA), horizontal integrated rim width (HIRW), cup volume, average cup-disc ratio and horizontal and vertical cup-disc ratios.

Vertical integrated rim area (Volume): This estimates the total volume of RFNL tissue in the rim.

Horizontal integrated rim width (Area): This estimates the total rim area.

Rest all other measurements are self explanatory.

The ONH analysis print out can be divided into various zones that include

Zone 1: Patient ID data.

Zone 2: Gives the overview of ONH head analysis along with the composite image figure, contructed from all scans

and all the important ONH parameters.

Zone 3: Individual radial scan analysis, along with scan image it gives the disc diameter, cup diameter, rim area, and rim length in that particular meridian.Overlap of TSNIT curve showing a comparison of two eyes.

Zone 4: Red free photograph; B&W photograph of the optic disc taken with the infrared camera is also available on the printout

Hypotonous maculaopathy: OCT being non-contact and noninvasive and fast scan acquisition can be easily used in post-operative eyes. *Hypotonous maculopathy* OCT in eyes with hypotonous maculopathy shows an increased macular thickness when compared to the fellow eye

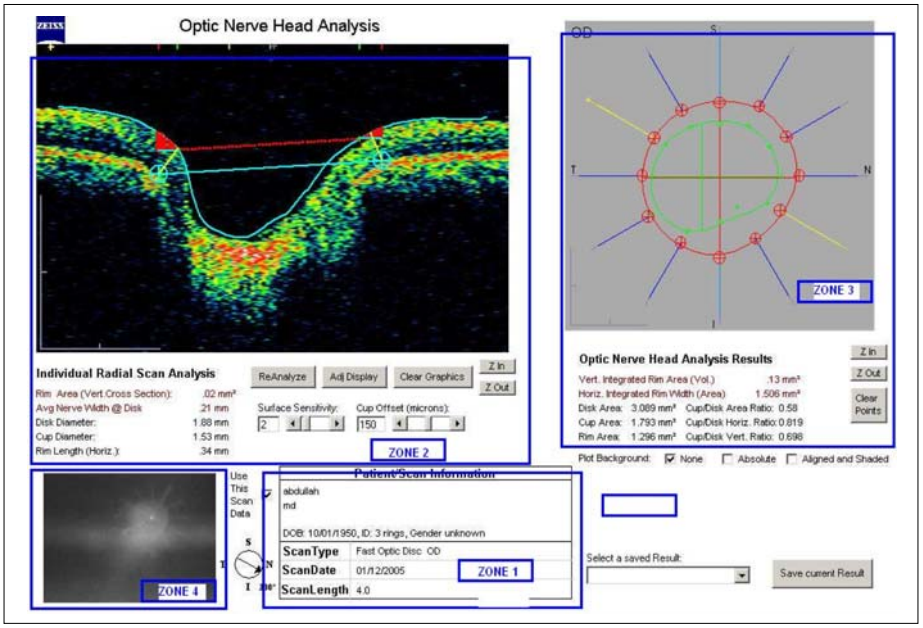

Fig.1.4: The ONH analysis on OCT3

Cystoid macular edema: OCT also serves as a useful diagnostic tool in eyes that develop postoperative and drug induced (travaprost or xalatan0 cystoid macular edema (CME).

Advantages

- Objective, quantitative, reproducible measurements of the retina and RNFL thickness.
- Measure-ments are not affected by refractive status, axial length of the eye, or the presence of early-to-moderate nuclear sclerotic cataracts.
- Structural information is independent of any arbitrarily defined reference plane.

Limitations

- High cost
- Requirement of pupillary dilation
- Posterior subcapsular and cortical cataracts impairs performance
- OCT images contain significantly fewer pixels than both SLP and CSLO.

Scanning Laser Polarimetry (GDx-*VCC*)

Retinal nerve fibre layer analyzer (NFA-GDx) measure the thickness of peripapillary RNFL. NFA-GDx works on the principle of scanning laser polarimetry. *Birefringence* is the splitting of a light wave by a polar material into two components. Polarized light is selectively retarded by a polarizing/ birefringent structure with alignment perpendicular to the incident rays of light. When a polarized light (near infrared 780nm) is projected on to the retina, the incident ray and the reflected ray double pass the RFNL before emerging. The RFNL has the property of birefringence thus causes change in the polarization of the light. This is called *retardation*.

Fig.2.1: GDx-VCC

The NFA GDx (figure 2.1) uses this retardation to measure the RFNL thickness over an15^0X15^0 retinal area around the disc. The amount of retardation is captured by a detector, and converted into thickness (in microns).The image is color coded from yellow to red to blue representing areas from high to low retardation. Bright color show thicker RFNL. The images of blood vessels are excluded by the built in software. It does not require pupillary dilatation; the image acquisition and processing takes around 30 seconds. For analysis a ring is placed along the margins of the optic disc and measurement is automatically performed at 1.75 disc diameter away. It gives RFNL measurements in four quadrants of 120^0 superiorly and inferiorly, 50^0 temporally and 70^0 nasally. It instantly compares the values with normative database provided in the computer and shows the level of significance. The parameters outside normal range are flagged in red. It also gives an index number the higher the number the higher the probability that the patient has glaucoma.

Anterior Segment Birefringence: The cornea and lens are also polarizing structures; the latest version of GDx-*VCC* has a variable

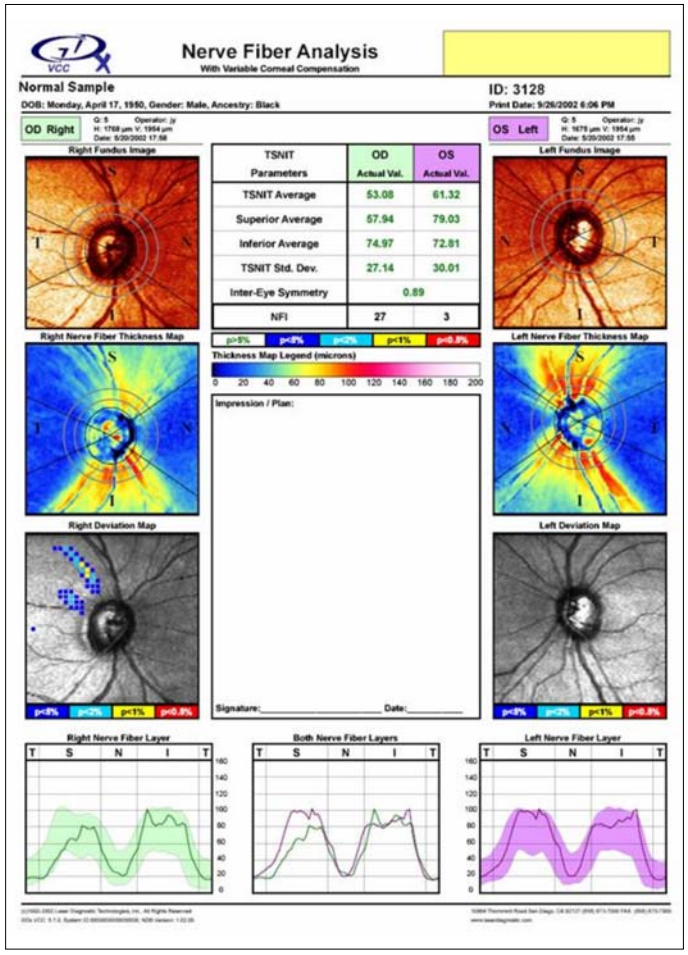

Fig.2.2: RNFL analysis

corneal compensator incorporated into the machine. Compensation of anterior segment birefringence is necessary to isolate RNFL birefringence. GDX VCC measures and individually compensates for anterior segment birefringence for each eye. This is determined by analyzing the macular region birefringence which is uniform and symmetric. Once the anterior segment birefringence axis and magnitude values are determined, the retardation signal from the anterior segment can be compensated. In cases of macular pathology, an alternative method is available that accurately compensates for the anterior segment birefringence.

Clinical Interpretation of the GDX VCC Printout (fig. 2.2)

For each GDX VCC scan, an age-matched comparison is made to the normative database and any significant deviations from normal limits are flagged as abnormal with a p value.

Quantitative RNFL evaluation is provides various elements including the

- *Thickness Map* shows the RNFL thickness in a color-coded format with the color spectrum going from blue to red. Thick RNFL values are colored yellow, orange, and red while thin RNFL values are colored dark blue, light blue, and green.
- The *Deviation Map* reveals the location and magnitude of RNFL defects over the entire thickness map. The Deviation Map analyzes a 128 x 128 pixel region (20° x 20°) centered on the optic disc. To reduce variability due to slight anatomical deviations between individuals, the 128 x 128 pixel thickness map is averaged into a 32 x 32 square grid, where each square is the average of a 4 x 4 pixel region (called super pixels). For each scan, the RNFL thickness at each super pixel is compared to the age-matched normative database, and the super pixels that fall below the normal range are flagged by colored squares based on the probability of normality. Dark blue squares represent areas where the RNFL thickness is below the 5th percentile of the normative database. This means that there is only a 5% probability that the RNFL thickness in this area is within the normal range, determined by an age-matched comparison to the normative database. Light blue squares represent deviation below the 2% level, yellow represents deviation below 1%, and red represents deviation below .05%. The Deviation Map uses a grayscale fundus image of the eye as a background, and displays abnormal grid values as colored squares over this image.
- The *TSNIT* map stands for Temporal-Superior-Nasal-Inferior-Temporal map and displays the RNFL thickness values along the calculation circle starting temporally and moving superiorly, nasally, inferiorly, and ending temporally. In a normal eye the TSNIT plot follows the typical 'double hump' pattern, with thick RNFL measures superiorly and inferiorly and thin RNFL values nasally and temporally. The TSNIT Graph shows the curve (or function) of the actual values for that eye along with a shaded area which represents the 95% normal range for that age. In a healthy eye, the TSNIT curve will fall within the shaded area. When there is RNFL loss, the TSNIT curve will fall below this shaded area, especially in the superior and inferior regions. In the center of the printout at the bottom, the TSNIT graphs for both eyes are displayed together. In a healthy eye there is good symmetry between the TSNIT graphs of the two eyes and the two curves will overlap. However, in glaucoma, one eye often has more advanced RNFL loss and therefore the two curves will have less overlap. A dip in the curve of one eye relative to another is indicative of RNFL loss.
- The *parameters* are displayed in a table in the center of the printout. The TSNIT parameters are summary measures based on RNFL thickness values within the calculation circle. These parameters are automatically compared to the normative database and are quantified in terms of probability of normality. Normal

parameter values are displayed in green, abnormal values are color-coded based on their probability of normality. The *calculation circle* is a fixed circle (a fixed size band) centered on the ONH. The band is 0.4 mm wide, and has an outer diameter of 3.2 mm and an inner diameter of 2.4mm.

TSNIT Average: The average RNFL thickness around the entire calculation circle.

Superior Average: The average RNFL thickness in the superior 120° region of the calculation circle

Inferior Average: The average RNFL thickness in the inferior 120° region of the calculation circle

TSNIT SD: This measure captures the modulation (peak to trough difference) of the double-hump pattern. A normal eye will have high modulation in the double-hump RNFL pattern, while a glaucoma eye will typically have low modulation in the double-hump pattern.

Inter-eye Symmetry: Measures the degree of symmetry between the right and left eyes by correlating the TSNIT functions from the two eyes. Values range from –1 to 1, where values near one represent good symmetry. Normal eyes have good symmetry with values around 0.9.

The Nerve Fiber Indicator (NFI): The NFI is a global measure based on the entire RNFL thickness map. It is calculated using an advanced form of neural network, called a Support Vector Machine (SVM). It utilizes information from the entire RNFL thickness map to optimize the discrimination between healthy and glaucomatous eyes. The output of the NFI is a single value that ranges from 1-100 and indicates the overall integrity of the RNFL. Output values range from 1 –100, with classification based on the ranges: 1-30 -> normal,31-50 -> borderline,51+ -> abnormal.

Detecting Progression of RNFL loss: Serial Analysis (figure 2.3)

The Serial Analysis printout can compare up to four exams. The first exam is the baseline or reference exam, and all follow-up exams are compared to this baseline exam. The Deviation from Reference Map displays the RNFL difference with different color coding, pixel by pixel, of the follow-up exam compared to the baseline exam..A colored rectangle to the left of the Thickness Map contains the date and quality score of each exam.

Advantages

- Does not require pupillary dilatation
- Good reproducability
- Does not require a reference plan

Limitations

- Does not measure actual RNFL thickness (inferred value)

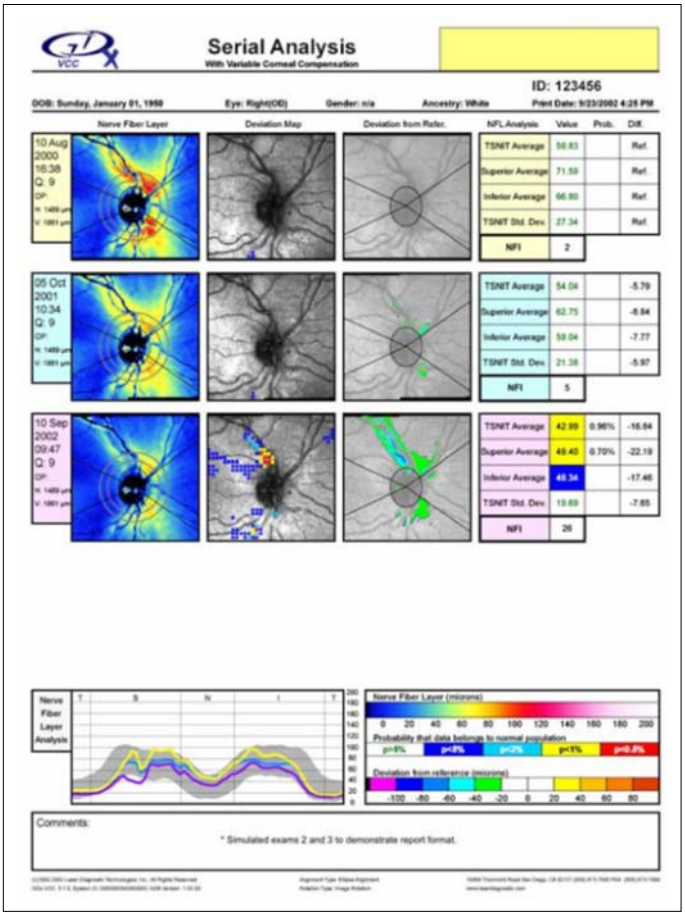

Fig.2.3: RNFL serial analysis

- Measures RNFL at different locations for each patient
- Does not differentiate true biological change from variability
- Requires a wider data base from the Indian Population
- Affected by anterior and posterior segment pathology including Ocular surface disorders, Macular pathology, Refractive errors (false positive in myopes), Peripapillary atrophy (scleral birefringence interferes with RNFL measurement)

Heidelberg Retinal Tomography (HRT Figure 3.1)

HRT is a Confocal Laser Scanning ophthalmoscope (CSLO). It helps in acquisition and quantitative analysis of three-dimensional images of the posterior segment. It describes the topography of retina and optic nerve head. The HRT uses a diode laser with a wavelength of 670 nm. A three-dimensional image is acquired as 32 consecutive and equidistant optical section images, each consisting of 256 × 256 picture elements. The size of the field of view is set to 10° × 10°, 15° × 15°, or 20° × 20°. Pupil dilation is not necessary. Topography images are computed from the acquired three-dimensional images. A topography image consists of 256 × 256 individual height measurements which are absolutely scaled for the individual eye

examined and have a reproducibility of the height measurements of approximately 20 microns at each point. The topography image is colour coded, dark colors represent elevated structure and light color represents depressed areas. After image acquisition the optic nerve head analysis is performed by defining the disc margins manually. Following the definition of the disc contour, the software computes and provides a set of stereo metric parameters useful for the description of the shape optic nerve head (classify it as being normal or outside normal limits) for contributing to the diagnosis of glaucoma, and for follow-up of glaucomatous progression.

Fig.3.1: HRT II

HRT II gives around 23 stereo-metric parameters, like Disc area, cup area, cup depth, mean RFNL thickness etc (figure 3.2). It uses *Moorefield regression* analysis for classifying the different sectors of optic nerve head. *Green tick* mark denoting a *normal* area and a *red cross* an *abnormal* area. It correlates well with WOW perimetry. HRT has high sensitivity and specificity thus allowing it to have a very high precision in early diagnosis and allowing us to pick up pre-perimetric glaucoma and detect early progression. Its practical application is in cases where disc picture is doubtful like with large physiological cups, when there are no VFDs. Though HRT has very high reproducibility the definition of the optic disc is conducted manually by tracing a line along the disc margin and thus it any produce substantial variability regarding the final assessment of the optic nerve head.

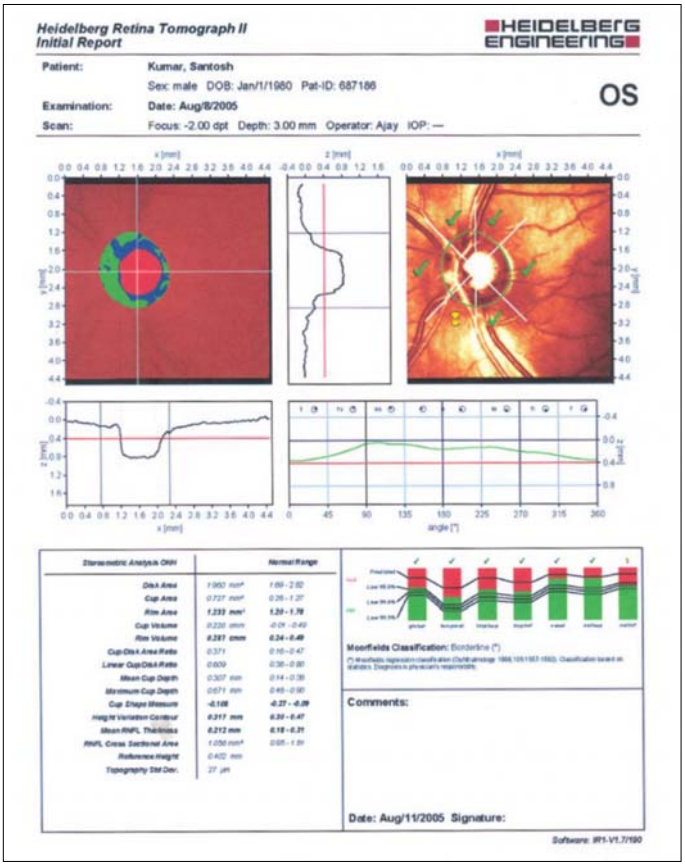

Fig.3.2: HRT print out.

Limitations

- Requires reference plane for all measurements
- Reference plane can be tricked by tilted discs, optic nerve drusen, bean pot cupping, and physiological cupping.
- Indirect measure of RNFL thickness
- Moorfields regression analysis (normative database) is based on 80 caucasian patients.

Clinical Studies

The RNFL thickness values measured by each of these machines show a good correlation with each other however the *absolute values* show a *marked variation*. This is attributed to the difference in the site of measurement and the

Table 1: Comparative evaluation of OCT3, HRT II and GDx-VCC

	OCT 3	*HRT II*	*GDX VCC*
	All three machines are non- contact, rapid, scanning time few seconds		
Light source	830nm Diode	670nm Diode	780nm Diode
Resolution	8-10	30	-
Pupillary dilatation	Y	N	N
Reproducibility Repeatability	Reproducibility Repeatability high for all 3		
SensitivitySpecificity	95%89%	96%84%	89%98%
Normative database	328 normals	112 normals	540 normals & 262 glaucoma patients

technique thickness calculation of the RNFL around the peripapillary area.

There are numerous studies in literature showing that all three machines have high *reproducibility and repeatability*. The parameters measured by OCT3, HRTII and GDx-VCC show good *correlation with visual field indices* as measured on standard white on white automated perimetry (SAP) and short wave automated perimetry (SWAP) also. They also possess high *sensitivity and specificity* for differentiating normal eyes from glaucomatous eyes and even in early stages of glaucoma. All three have provision for serial analysis of the scans to detect changes in ONH or RNFL over a period of time.

Role in pre-perimetric diagnosis: Various studies evaluating the role of OCT, HRT and GDx-VCC generated RNFL and optic nerve head parameters have valuable role in identifying glaucoma suspects and differentiating them from normal eyes. However there is a considerable overlap amongst the normal and early glaucoma eyes. Therefore exact role of these imaging modalities in preperimetric diagnosis still remains undefined. And till date there are not well defined guidelines that can enable an ophthalmologist to choose whether a patient requires initiation of treatment or simply a follow-up still undefined

A study of comparative evaluation of three machines i.e. OCT, HRT II and GDx-VCC to to discriminate eyes with ocular hypertension (OHT, 26 eyes), glaucoma-suspect eyes (GS, 55 eyes) with glaucomatous disc without visual field loss or early glaucomatous eyes (EG, 76 eyes) from normal eyes. Most parameters in GS and EG eyes showed significant differences compared with normal eyes. However, there were few significant differences between normal and OHT eyes. No significant differences were observed in area under the curve (AUC) between SLP and OCT. In EG eyes, the greatest AUC parameter in OCT had a higher AUC than that in CSLO. In GS, the greatest AUC parameter in OCT (average RNFL thickness) and SLP (nerve fiber indicator [NFI]; 0) had higher AUC than that in CSLO (vertical cup/disc ratio; 0.720). The authors concluded that all the three instruments were useful in identifying GS and EG eyes. For glaucomatous eyes with or without early visual field defects, SLP (GDx-VCC) and OCT performed similarly or had better discriminating abilities compared with CSLO (HRT II).

Suggested Reads:

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5. Medeiros FA, Zangwill LM, Bowd C, Weinreb RN. Comparison of the GDx VCC scanning laser polarimeter, HRT II confocal scanning laser ophthalmoscope, and stratus OCT optical coherence tomograph for the detection of glaucoma. Arch Ophthalmol. 2004 Jun;122(6):827-37.

Importance of Sample Size and p-value in Clinical Research

Rajiv Nath

All the clinicians have to be conversant with epidemiological methods as well as statistics in order to achieve "good clinical practice" which includes the practice of evidence based medicine. Many a times, ophthalmologists are heard saying: "I don't need to struggle with all that stuff. I am happy with my patient work". However, they forget that even if they are not doers of research, they still always shall be the users of research. All clinicians have to critically interpret research publications, as well as conference presentations, and modify their clinical decisions according to recent recommendations thereof. If consumers are not cautious, they get taken for a ride by the scrupulous industries. Similarly, if doctors can not differentiate between good and bad research, they get misguided by vested interests; which may cause abandoning of good therapies, or adoption of bad ones, and expose the patients to the hazards of inappropriate management. Therefore there is now a growing need to have a satisfactory working knowledge of biostatistics.

Uses of Statistics in Clinical Research

The use of statistics should start at the stage of planning of research protocol, because prevention of errors is better than finding excuses for errors later on. The aim of this planning is to ensure:

(a) Sample Size Estimation , so that the researcher becomes aware of the number of subjects required in that study. This will in turn reflect on the time and money required to complete that work. The researcher will be able to introspect his/her capabilities and time frame and take an informed decision whether that study would be worthwhile and doable. The data will also not get wasted due to lack of sufficient power in that study (if sample is small), nor will the efficiency be compromised (as happens with very large studies).

(b) Selection of Subjects, in a manner that they represent the reference population (that group of human beings to whom the researcher wants the results to be applied to e.g. a new type of glaucoma surgery evaluation will have its reference population as all the patients of glaucoma in that state or country or globally). This will be possible only if the selection is free from all types of biases, and is done in a random manner, which is a statistical exercise.

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(c) Allocation of Study Subjects to treatment groups in an unbiased manner, so that the treatment groups remain similar to each other except the difference in their treatment regimes. If they are not similar they can not be compared, and therefore the allocation is best done in random manner, taking statistical help.

(d) Measurement of all the Variables (study variable, outcome variable as well as all the confounders) should be done by precise, valid and reproducible methods, and statistical evidence should be generated to demonstrate that this was actually done. For example if the researcher can not have intraocular pressure measured in a precise and valid manner, there is no point in accepting his work on glaucoma.

(e) Method of Statistical Analyses should be appropriate. How will the data generated by that study will be summarized, presented, and analyzed to test the hypothesis & get acceptable conclusions at the end of the data collection should be planned in advance, so that no allowance is there for playing around with the data for finding a way to analyze and misuse, or waste it later on.

Sample Size Estimation and Power of the Study

The power of a research study is defined as the probability that this study will be able to pick up a difference between two or more groups if that difference truly exists in the reference population. It is needless to say that the truth referred here is unknown at the beginning, which is why the research is being undertaken. Therefore, one has to prepared with sufficient strength in the power not to miss a true difference, only then it will be proper to conclude a no difference if the results do not show a difference.

Suppose a new anti-glaucoma treatment is expected to produce a 10% lowering of intraocular pressure (as demonstrated in experimental animals). If the researcher starts with a small sample, he / she may not be able to pick up this small 10% difference between the IOP of patients receiving that new drug and those not receiving the new drug. In other words, the difference shall be missed even if truly there. On the other hand, if a drug is expected to produce a 30% lowering of IOP, even a small sample will be able to reveal that difference. Thus the appropriate sample size varies inversely with the expected effect size.

The power of the study assumes more importance when a negative result is being reported (no difference in the IOP of treated and untreated groups of glaucoma patients), because readers of that publication will want to know whether the researchers had started with a sufficient

sample size; while the latter can not be changed now at the end of the data collection.

Sample size of all research study should be estimated beforehand. Bio-statistical text books include various formulae for this calculation. These formulae need estimates such as mean/proportion & standard error of the mean/ proportion (which is generally available by literature search), expected effect size (generally available from previous animal studies or pilot trials), desired power of the study (which can be traded according to the resources available or efficiency desired) etc. There are different formulae for different types of study designs, and sampling techniques, and method of analysis expected to be used. Soft wares are also available for this purpose.

Test of Significance (p-value)

The *probability (p-value*) represents the possibility (in a fraction of 1.0 which is another way of expressing up to 100%) that the results which a researcher has obtained has been obtained by chance (chance here is a proxy for reasons unknown at present or luck in other words). By and large, all the biological variables follow the laws of nature, and barring some exceptions they show consistently similar observations. For example, the off springs of a myopic couple are likely to be myopic, while those of hypermetropic couple are likely to inherit hypermetropia. However, sometimes by chance (due to genetic mutation or otherwise) this inheritance may not take place. If few exceptions are seen, this shall be called as chance; but if a large number of off springs do not show that pattern, this event shall be termed as a happening above possibility of chance. It is up to the researcher(s) and user(s) of research to set a deadline to demarcate possibility of chance and beyond chance. Generally in most of the biological research (though not all) a p-value of 5% (i.e. 0.05) is taken as the cut off point. Thus if the possibility of the result as they are, having arisen by chance is less than 0.05, then the results of the study are considered acceptable, and the hypothesis of the researcher is accordingly dealt with. However, if the p-value if higher than 0.05, the results are considered not significant. This is also known as the test of significance.

This p-value can be arrived at by various methods of testing significance. The method which is considered most appropriate for the given hypothesis, study design, type of data is selected at the planning stage to avoid data fabrication and fishing. Some of these tests are: t-test for testing difference between means of a variable between two groups, ANOVA for testing difference between means of a variable of more than two groups, test of two proportions, X-square test for strength of association between two variables, regression analysis for testing strength of association between two variables after controlling the effect of possible confounders etc. All of these tests provide estimates of a test statistic (which is different for the different tests), the value of which is used to read out the p-value from pre-existing charts or soft wares. It is pertinent to remember that all these statistical tests have certain rules and in-built assumptions and their usage will be appropriate only if these assumptions are met with by the study methodology, which necessitates planning at protocol stage itself.

It is to be cautioned that if the techniques of measurements are inappropriate (invalid or imprecise), then these tests of significance will give misleading results. In above example, if the method of diagnosing type of refractive error is not correct, then some of hypermetropics shall get classified as myopics and vice versa. This contamination will give misleading data and results, for which the blame should go to the researcher, not to the statistics. The statistics will give as sound conclusions as the data collection is. Therefore, researcher should be conversant with the epidemiological methods and measurements techniques also. The users of research should judge the conclusions on over all merit rather than p-value alone.

Recent Advances in Management of Optic Neuritis

Rohit Saxena MD, **Ankur Sinha** MD, **Swati Phuljhele** MD, **V Menon** MS

Optic neuritis is an acute inflammatory, infective or demyelinating disease affecting optic nerve. It is characterized by sudden loss of vision in affected eye, often accompanied by pain. Morphologically optic neuritis is classified in to Papillitis (Associated with disc edema) (figure 1a), Retrobulbar neuritis (no disc edema) (figure 1b) or Neuroretinitis (papillitis associated with inflammation of nerve fiber layer and macular star in late stages.

Etiology is unknown in majority of cases but it could be associated with demyelinating lesion, of which most common cause is multiple sclerosis. Other diseases known to cause optic neuritis are:

Viral infections (e.g. chicken pox, measles, mumps etc.)

Granulomatous infections such as tuberculosis, cat scratch fever, syphilis, lyme disease or cryptococcal meningitis

Autoimmune diseases such as SLE, Wegner's Granulamatosis or sarcoidosis

Contagious inflammation from orbit, meninges and sinuses

Intraocular inflammation involving retina, uvea, sclera

Clinical Features

A typical patient often presents with sudden painless loss of vision that may be associated with retro bulbar pain, which worsens on eye movement. Some patients may complain of photopsia. . Majority of cases are female, aged between 20-50 years.

On examination Relative Afferent Pupillary Defect is present in all the cases and is the most useful clinical sign. The vision ranges from mild reduction in visual acuity to no light perception. It is accompanied by a parallel reduction in contrast sensitivity with a reduction in color vision that is out of proportion to the visual loss. Disc swelling is noted in cases of papillitis and the fundus is normal in retro bulbar neuritis. The inflammation in the vitreous is usually minimal and a severe inflammation should trigger a search for another etiology. The macular exudates, along with disc oedema, are present in case of neuroretinits. Retinal venous sheathing associated with optic neuritis indicates increased risk of developing of MS. The visual field can show any pattern of visual loss with generalized field loss being most common. Fellow eye abnormalities are quite common and include defects in color vision, contrast sensitivity, visual fields and VER.

Optic neuritis can be typical or atypical classified on the basis of clinical features and course of disease. The features of typical and atypical forms of optic neuritis are given in table 1.

Differential Diagnosis

An *ischaemic optic neuropathy* is characterized by lack of pain, pallid disc swelling with hemorrhages and sometimes segmental disc swelling is also noted. The visual field loss is in form of altitudinal changes. There is no leak in fluorescein angiography in ischaemic optic neuropathy unlike a profuse disc leak in cases with optic neuritis (figure2).

A steadily progressing visual loss or lack of improvement with standard therapy is unusual in optic neuritis and such features may indicate a compressive or infiltrative optic neuropathy. Chronic optic neuritis is a diagnosis of exclusion.

Leber's optic neuropathy may have a confusing presentation particularly when the vision starts improving. However a lack of pain, circumpapillary telangiectatic microangiopathy, absence of leak on fluorescin angiography as well as a maternal pattern of inheritance would point to the diagnosis.

Sarcoidosis may also cause optic neuritis. The visual loss improves with steroid therapy but recurrence on tapering steroids is characteristic. This feature is distinctly unusual in demyelinating optic neuritis.

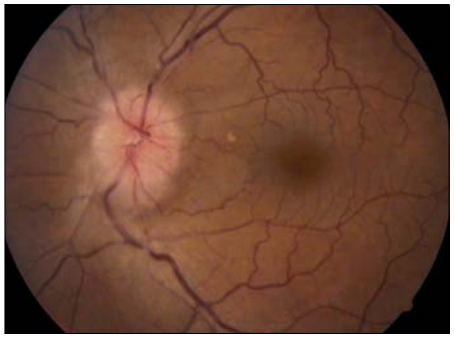

Fig.1a: Papillitis

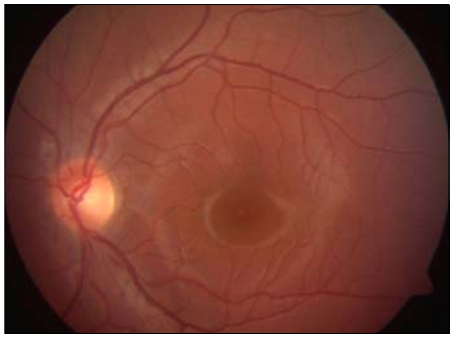

Fig1(b): Retro-bulbar neuritis

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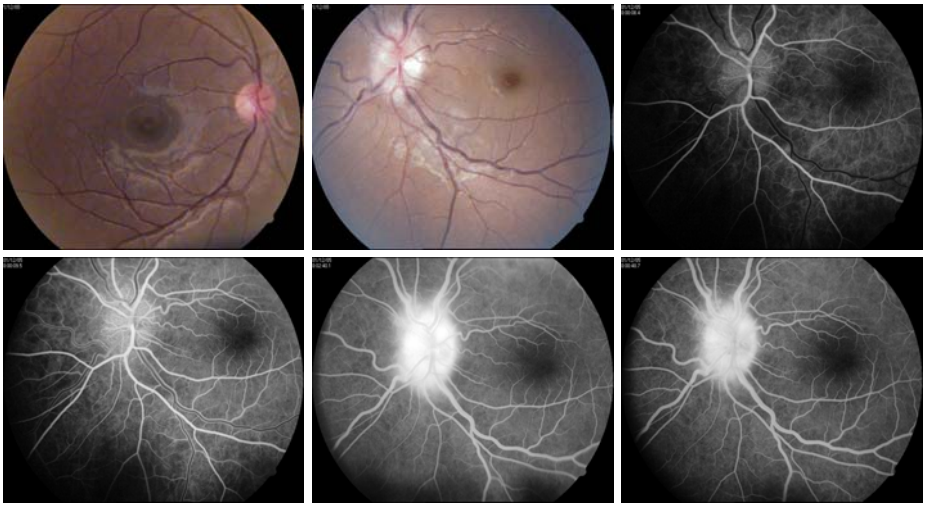

Fig.2: Fluorescein Angiography-Papillitis

Syphilis and other infections (e.g. Lyme disease, Borreliosis) may cause optic neuritis. But the optic nerve inflammation is usually associatedwith other signs of the disease and rarely the sole finding.

Devic's disease may initially present as optic neuritis but paraplegia follows. Cavitation is seen in neuroimaging unlike the gliosis in multiple sclerosis. Also cerebellar involvement is unusual when compared to optic neuritis.

Sailent Features of Some Prominent Causes of Optic Neuritis

Optic neuritis in case of sarcoidosis: it is a well documented manifestation of sarcoidosis. Vision declines slowly and optic disc may or may not be swollen. Systemic signs of sarcoidosis may be subtle or even absent. Vision improves with steroids and recurrences are common. Bilateral retrobulbar neuritis is reported as the initial manifestation of systemic sarcoidosis, in which on detailed evaluation, systemic investigations were positive for sarcoidosis and patient responded to oral prednisolone. Optic neuropathy in sarcoidosis occurs in 5% of patients but it is not generally identified as sarcoid disease. Optic nerve disease appears as papilledema, atrophy, papillitis, infiltration or retrobulbar neuritis. Ocular abnormalities may be an initial finding in sarcoidosis.

Chronic relapsing inflammatory optic neuropathy (CRION) There is a report of 15 patients over 10 years in which patients presented with Clinical characteristics and early natural history of a form of inflammatory bilateral optic neuropathy, which was often painful and having relapses and remissions. Blood investigations and CSF was normal MRI scans of the brain are normal and those of the optic nerves often, but not always, show high signal abnormalities. The symptoms and signs respond well to corticosteroid treatment, but relapsed on steroid withdrawal although long-term immunosuppression is often necessary. This disorder was named as chronic

Table 1. Features of typical and atypical optic neuritis

Features of Typical optic neuritis	*Features of Atypical optic neuritis*
Predominantly affects females 5:1	No gender predeliction
Retrocular pain made worse with eye movements	Painless visual loss
Common in the age group of 15 to 45	Old patients
Uniocular	Bilateral
Peak visual loss within 2 weeks	Progression of visual loss beyond 2 weeks
Acute often painful visual loss over hours to days RAPD is often associated	
Visual loss may be subtle to complete Starts improving thereafter	Patients fail to improve with treatment
Poor colour vision and contrast sensitivity	
Fundus is normal in retrobulbar neuritis, Rarely Disc edema, vitreous cells, hemorrhages and cotton wool spots can occur.	Disc hemorrhage and cotton wool spots can occur
Any visual field defect may be seen, generalized depression is most common	Same as typical optic neuritis
VER shows prolonged latency with normal or depressed amplitude	

relapsing inflammatory optic neuropathy (CRION).

Optic neuritis in multiple sclerosis Optic Neuritis occurs in about 50% of patients with MS and is presenting feature in about 20%. Recurrent ON is more common with MS which may involve same or fellow eye. ONTT has shown that female gender, one or more brain lesions seen on MRI, history of non specific neurological symptoms (usually transient numbness), prior optic neuritis in fellow eye or Retro bulbar optic neuritis are positive risk factors for development of multiple sclerosis. Similarly negative risk factors are male gender, no lesions on MRI, optic disc swelling, absence of pain and ophthalmoscopic findings of severe optic disc edema, peripapillary hemorrhages, or retinal exudates. ONTT has shown that 10-year risk of development of multiple sclerosis is 38%. Patients having one or more typical lesions on the baseline MRI had a risk of 56% as compared to those with no lesions having a risk of 22%. With higher numbers of lesions the risk of development of MS does not increase appreciably. In patients having optic neuritis without CDMS, 10 to14 years after enrollment in the ONTT, at least one T2 lesion 3 mm or larger was observed on follow-up MRIs in 44% with normal baseline MRIs and additional lesions (3 mm) were present on follow-up MRIs in 74% patients with abnormal baseline MRIs and thus a subset of patients with monosymptomatic optic neuritis manifest neither clinical signs nor MRI evidence of demyelination after more than 10 years of follow-up. In a different study patients having recurrent ON without intervening symptoms of a disseminated demyelinating condition were followed and they found the 5-year conversion rate to MS is 14.4%

Atypical forms of optic neuritis in multiple sclerosis has also been reported in which all patients had severe bilateral eye disease with no or incomplete recovery.

In any case of disc oedema, papilloedema should be ruled out, the points of difference between optic neuritis and papilloedema are given in table 2.

Table 2: Differentiating points between Papilloedema and optic neuritis

	Papilloedema	*Optic Neuritis*
Disc edema	Present	Present in 30%
Visual acuity	Normal till late stages despite sever disc edema	Usually decreased
Color vision and contrast	Normal till late stages	Severely decreased
RAPD	Present only if optic atrophy sets in	Always present
MRI	Shows causative lesion and enlargement of ventricles	Shows demyelinative lesions in periventricular region

Investigations

Routine investigations are not required in a typical case of optic neuritis (ONTT). MRI brain is helpful to prognosticate the development of multiple sclerosis. Investigations are indicated in following conditions:

- Atypical presentation
- Recurrent optic neuritis
- Acute optic neuritis in children

Table 3: List of investigations in case of optic neuritis

S No	*Systemic Investigation*
1	Routine hemogram
2	X-ray (Chest)
3	Mantoux
4	FTA-ABS & VDRL for syphilis
5	serology and culture for bartonella
6	Markers of viral infection
7	Serum electrolytes and fasting blood sugar
8	MRI
9	Lumbar puncture and CSF tap (IgG index and oligoclonal bands)
10	Blood culture
11	ANA,dsDNA
12	Serology for toxoplasmosis

Table 4. List of ophthalmic investigations in a case of optic neuritis.

S No	*Ophthalmic Investigation*
1	Refractive error and BCVA of both eyes (to rule out hypermetropia)
2	Colour vision of both eyes
3	Contrast sensitivity of both eyes
4	Visual evoked response of both eyes
5	Coloured fundus photography and Fluorescien angiography
6	USG orbit
7	Optical coherence tomography (if available)

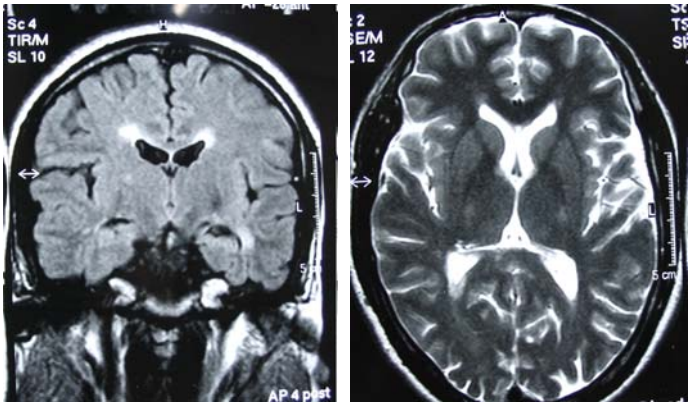

Fig.3: Periventricular Demyelination

- Presence of systemic inflammatory disease
- Various systemic and ocular investigations which can be done are listed in table 3 and 4 respectively

Role of MRI (Neuroimaging)–MRI is always to be preferred to CT scan in prognosticating the disease due to its excellent ability to show demyelinating lesions (figure3). It can also detect infections of the Para-nasal sinuses. The ONTT found it to be the strongest predictor for the development of clinically definite multiple sclerosis. More recently it has emerged as a guideline for initiating therapy with interferon alpha-1a to delay onset of multiple sclerosis. The CHAMPS study group has found that a weekly dose of 30-microgram i.m of interferon alpha-1a (avonex) reduces the development of multiple sclerosis in patients with lesions in MRI at presentation. While this is the only test in which some Multiple Sclerosis lesions can be seen, it cannot be regarded as conclusive; because, all lesions do not register on MRI scans and many other diseases can produce identical MRI images. MRI shows the size, quantity and distribution of Lesions larger than 2mm, and together with supporting evidence helps in diagnosis of MS MRI Criteria for diagnosing MS

At least 3 Lesions and two of the following:

- Lesions abutting the Lateral ventricles
- Lesions with diameters greater than 5mm
- Lesions present in the Posterior Fossa (infratentorial)

MRI is also helpful to rule out any compressive or demyelinating lesion and to prognosticate the case

Role of CSF analysis: ONTT has concluded that no patients had their diagnosis or management altered as a result of CSF findings. Except for oligoclonal bands, few patients showed any abnormalities on CSF tests, and no tests correlated with the 2-year development of CDMS. Thus CSF analysis may not be necessary in the routine evaluation of patients presenting with a typical clinical profile of acute ON.

The diagnosis of a classic case is usually straightforward and can be made clinically. Investigations help to prognosticate the disease and in atypical cases. Usual systemic and ophthalmic investigations done in cases of optic neuritis are listed in table 3 and table 4 respectively.

Treatment

The main stay of treatment is corticosteroids. They have been used by the oral, retrobulbar and parenteral route. The results of ONTT have provided the guidelines for the management of a typical optic neuritis. A pulse therapy of intravenous Methylprednisolone in dose of 250mg QID for 3 consecutive days followed by oral prednisolone 1mg/kg body weight for 11 days is given. In our centre we give dexamethasone in dose of 3-5 mg per kg in 5% of dextrose, instead of methylprednisolone, intravenous infusion over an hour or two, and no taper dose of oral steroids is required. The ONTT study and studies from this centre are elaborated later.

Clinical Course

The natural history is to worsen over several days to 2 weeks and then to improve. The ONTT found that among patients who received placebo 79% began to improve within 3 weeks of onset and 93% improved within 5 weeks. For most patients visual acuity recovered completely within 5 weeks. Less than 10% have a visual of less than 20/40.Persistent defects in color vision, contrast, Stereopsis and visual fields were noted. Recurrences occurred in 11-24% of patients in various studies. Multiple sclerosis has been noted to develop in 75% of women and 34% of men after 15-20 years of follow up.

The Optic Neuritis Treatment Trial

The ONTT was a multi-center randomized trial involving 454 patients from 1988-1991 to evaluate the efficacy of steroids in the treatment of optic neuritis.

Study Objectives: To evaluate the efficacy of corticosteroid treatment of acute optic neuritis To investigate the relationship between optic neuritis and multiple sclerosis

Conclusions: Intravenous Methyl Prednisolone followed by Oral prednisolone speeds the recovery of Visual Loss due to Optic Neuritis and results in slightly better vision at six months. Oral Prednisone alone, as prescribed in this study, is an ineffective treatment in standard doses and increases the risk of new episodes of optic neuritis. Intravenous followed by oral steroids decrease the 2 year incidence of multiple sclerosis. Brain MRI should be considered to assess the risk of future neurological events of MS. Most patients retained good to excellent vision (20/25 or better in 87%) in the 5 years following an attack of optic neuritis, even if the optic neuritis recurred.

Recurrences were more frequent in patients with multiple sclerosis and in those treated with oral prednisone alone. Neurological impairment 10 Years after Optic Neuritis was mild, with 65% of patients having an Expanded Disability Status Scale score lower than 3.0.and the degree of disability appeared to be unrelated to whether the baseline magnetic resonance imaging scan was lesion-free or showed lesions. Dyschromatopsias, Defective stereo acuity, RAPD, Delayed latencies on VER, Pulfrich and Uhtoff phenomenon and persistent field defect remain as residual defects after an attack of optic neuritis.

Champs Study

The Controlled High Risk Avonex Multiple Sclerosis Trial

Study Objective: Whether interferon beta la (Avonex) treatment would benefit patients who had experienced a first acute demyelinating event involving the optic nerve, brain stem/cerebellum, or spinal cord, and who displayed MRI brain abnormalities that have previously predicted a high likelihood of future MS-like events. All patients received intravenous methylprednisolone 1 g per day for three days within days of the onset of their neurologic symptoms. This followed by an oral prednisone taper beginning with 1mg/kg for 11 days and ending with 4-day oral taper. Then patients were divided in two groups

Group 1 once-weekly intramuscular injection of interferon beta 1-A

Group 2 placebo injections

Primary outcome measured was development of CDMS and change in demyelinating lesions on serial brain MRI scans

Conclusions: At the end of three years, the probability of CDMS was 50% in the placebo-treated group and 35% in the interferon 1-A-treated group There was no difference in treatment among patients presenting with optic neuritis, brain stem/cerebellar, or spinal cord events. Patients on active treatment had a lower T2 lesion reduced number of gadolinium-enhanced lesions. Treatment with Avonex significantly reduces the two-year likelihood of future neurologic events and worsening of the brain MRI in patients with a first acute CNS demyelinating event.

ETOMS

Early Treatment Of Multiple sclerosis Study

Study objective: to determine whether an early treatment with interferon b 1b is effective in delaying thedevelopment of CDMS after the first attack.

The ETOMS study entered 308 first-attack patients, ages 18 to 40 years, with unifocal or multifocal (39%) CNS presentations and abnormal brain MRI.[36] The MRI was required to show 4 T2 white matter lesions, or 3 T2 white matter lesions if 1 was enhancing or infratentorial. Patients were assigned to receive IFN beta-1a 22 mcg SC weekly or placebo, and were followed for 2 years.

Champions Study

Controlled High Risk Avonex Multiple Sclerosis Prevention Surveillance

Objective: Compared outcomes in those who had given drug from the start of the CHAMPS study (Immediate treatment" or IT group) versus those who had switched from placebo after about 30 months ("delayed treatment" or DT group).

Results: IT group had significantly fewer relapses and fewer MRI brain lesions than the DT group and that significantly fewer of its members converted to definite MS.

Contributions from RPC

A pilot study in RPC showed dexamethasone to be equally effective and a cheaper alternative to methyl prednisolone in treating optic neuritis.

Objective: To evaluate the role of Intravenous dexamethasone in optic neuritis. In an observational case series, 40 patients of acute optic neuritis (age group of 15-50 years) were included and treated with intravenous dexamethasone (100 mg in 250 ml of 5% dextrose over 1-2 hours daily, for3 days). Results and conclusions: best corrected visual acuity of 20/40 or better at 6 months and 2 years was seen in 82.14% cases. 21.4% of patients regained normal contrast sensitivity, 75% regained normal color vision after 3 months. Treatment with intravenous pulsed dexamethasone led to rapid recovery of vision in acute optic neuritis, without any serious side effects.

Another study is compared the efficacy of standard dose (100mg dexamethasone i.v for 3 days) vs. high dose (200mg dexamethasone i.v for 3 days) for the treatment of optic neuritis. This did not reveal significant benefit of high dose of steroids over the standard dose.

The *newer modalities* of treatment that can modify the disease course and are being tried:

- Copolymer-1
- T-Cell Receptor Peptide Immunization
- Anti-CD4 Monoclonal Antibody
- Azathioprine (Imuran)
- Cyclophosphamide (Cytoxan)
- Oral Myelin
- Methotrexate
- Cladribine
- Intravenous Immunoglobulin G

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Paralytic Squint

Kanak Tyagi DOMS, DNB, **Gaurav Kakkar** MS, **Abhishek B. Dagar** MS, DNB, FICO, FPOS

Paralysis is complete loss of muscle force. Paresis denotes partial / incomplete paralysis. Palsy and paralysis are synonyms.

Classification

Neurogenic

Supranuclear Nuclear Infranuclear

Congenital Traumatic, ischemic inflammatory, neoplastic, toxic demyelination,idiopathic

Myogenic

Myasthenia gravis

Absence/Malinsertion of muscle or musulofascial anomalies

Traumatic laceration / disinsertion

Inflammatory (Myositis)

Orbital myopathic (Dysthyroid)

Dystrophies (CPEO)

Paralysis of cranial nerves

According to most recent study which includes 4373 acquired muscle paralysis cases the most frequently nerve involved is sixth nerve 43.8%, followed by third nerve28% and fourth nerve 15%. In stabismic clinic the most common nerve palsy seen is fourth nerve, followed by sixth and third nerve

Clinical Characteristics Which Distinguish Incomitant from Comitant Strabismus.

Limitation of the movement in the field of action of muscle. However, examination for ductions may mask paresis and more revealing is the examination of versions in these patients.

Incomitance – Variable ocular deviation in different eye position. Larger deviation when the affected eye fixates and larger deviation in the field of action of affected muscles defines incomitance.

Primary Vs Secondary deviation – according to the Herring's law of equal innervation, innervation flowing to the yoke muscles of both eyes is always determined by the fixating eye. When sound eye fixates the deviation measured is the primary deviation and with paralytic eye fixating the deviation is secondary deviation which is always greater than primary deviation.

Stages of paralytic Squint

Stage I – Characterized by weakness of paralyzed muscles

Stage II – over action of direct antagonist of paralyzed muscle

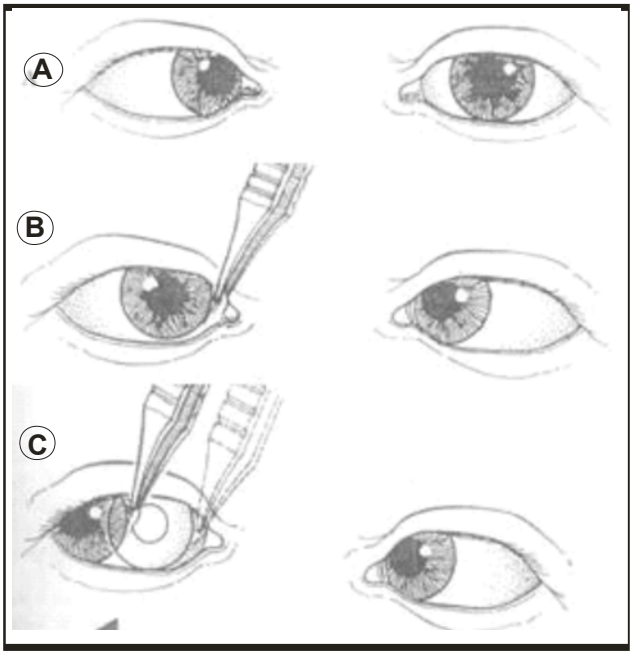
Overtime, overacting muscles undergo process called as contracture and is characterized by shortening or reduction in muscles elasticity.

Stage III – under action of the yoke muscle of antagonist of paretic muscle, designated as inhibitional palsy of contralateral antagonist. During this stage there is spread of comitance and may no longer be possible to detect paretic muscle.

Examination of Paralytic Case

History

- Age of onset
- Fever,
- Headache, vomiting



Forced duction test
(a) Right Esotropia
(b) Resistance to abduction of right eye shows restrictive element
(c) Unapposed abduction of right eye shows paralytic component

Venu Eye Institute & Research Centre,
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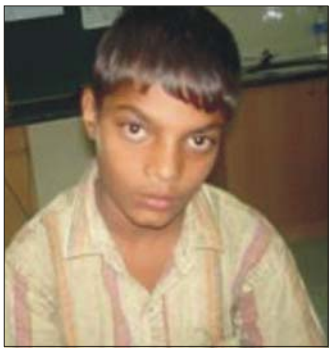
- Head injury
- Other associated neurological signs
- Old photographs, family photographs

Compensatory head posture one should simply remember that there is a head position in which patients avoid diplopia and maintain BSV. Some patients unable to maintain BSV with face turn or by means of head posture will tilt or turn to opposite direction to ensure the distance between the double images.

Past pointing – It is an error of subjective localization caused by disproportion between innervational input and motor output. It occurs only with paralysis of recent onset. Clinical value of this is in distinguishing between congenital and acquired paralysis.

Measurement of the deviation – A quantitative study of the angle of deviation in diagnostic positions of gaze with either eye fixating will reveal more subtle forms of paralysis. This examination is essential in establishing severity of disturbance and in assessing whether deterioration or recovery will take place. There can be subjective or objective (Prism cover test) measurement.



Congenital right SO palsy Left head tilt with slight chin depression with fascial asymmetry

time of progression or improvement but also for medico legal purposes as a record of patient's disability.

Head tilt test – universally k/s Bielschowsky head tilt test. This is applicable in paresis of any of the cyclovertical muscles. Park's popularized the diagnostic scheme. 1. Left or right hypertropia in primary position? 2. Does this deviation decreases in dextro or levoversion? 3. Does it increases with the head tilt to right or left shoulder?

Sensory Anomalies – The fact that most patients are able to maintain simultaneous binocular vision in a direction of gaze, opposite to the field of action of paretic muscle the sensory anomalies are not common in paralytic squint. Sensory anomalies are restricted to patients with congenital paralysis or paralysis of early childhood.

Subjective Measurement (Diplopia Charting)

The deviation is recorded by asking the subject to quantify the separation between the double images which are dissociated with red / green glasses. This is done in all the nine diagnostic position. Points to be noted are-

Maximum separation is in the quadrant in field of action of muscles.

Image that appears farthest belongs to deviating eye

The image is shifted in the direction of action of paralyzed muscle

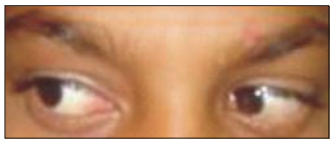
Hess charting / Lees' charting based on haploscopic principle. Hess chart uses red green colour dissociation, the eye with the red filter fixates and the other eye with green filter is charted. In case of under action of muscles smaller square are covered and more squares in cases of overactions. Less charting method utilizes dissociation by mirror septum.

Binocular fields of vision – This is very important test to evaluate the field of binocular fixation and the field of diplopia with the help of perimeter. Such records are invaluable not only for documenting subtle changes in

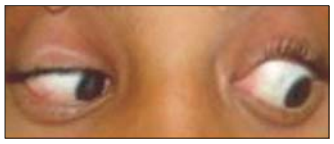
Differential Diagnosis		
	Congenital/ old paralysis	***Recent Paralysis***
Diplopia	Rare but may occur suddenly with decompensation	Always present but may be limited to paretic field
Image tilting	Absent	Common with cranial nerve IV palsies
Amblyopia	May be present	Absent
Comitance	Spread of comitance may obscure original paresis	Characteristically incomitant
Abnormal head posture	May persist on covering paretic eye because of secondary scoliosis and contracture of neck muscles	Disappears on covering paretic eye
Facial asymmetry	Common with torticollis of long standing	Absent
Contracture of antagonist with positive forced ductions	May be present	Absent
Past-pointing	Absent	Present
Old photographs	May show anomalous head posture	Negative

Right hypertropia in primary gaze

Left gaze shows inferior oblique overaction



Normal motility in Right gaze



In left down gaze underaction of right SO

Amblyopia in paralytic strabismus occurs only in patients unable to maintain binocular vision in any direction of gaze.

Forced Duction Test -It is simple and most useful method for diagnosing the presence of mechanical restriction of ocular motility. Conjunctiva is anaesthetized properly with topical anesthetic drops. The eyes are moved with two toothed forceps applied to conjunctiva near the limbus in the direction opposite to which mechanical restriction is suspected. If no resistance is encountered the mobility defect is due to paralysis if resistance is encountered mechanical restriction exist. It is important not to press the globe into the orbit during the test since it may become false negative.

Exaggerated force duction test-Described by Guyton. It is to estimate the tightness of oblique muscle .For this test eye must be put in the orbit (retro pulse the globe) as it is then rocked back and forth by extorting and intorting the globe around the tendon to check the oblique muscle tightness.

Differential Intraocular Pressure

Helveston and co-worker suggested that the generated muscles force could be estimated by comparing intraocular pressure in various positions of gazes and pressure increase may be as high as 50mmhg in cases of restrictive elements.

Eye Movement Velocity

May be useful only as an auxiliary diagnostic method, in evaluating the paralytic squint. The eyes are capable of making saccades /fast eye movements up to the velocity of 200-700^0/sec. In cases of paralysis this normal saccades being replaced by slow drifting eye movements. Restrictive squints have normal saccadic velocity till the restriction comes into effect.

Management of Paralytic Strabismus

To determine whether a patient with paralytic squint will require therapy depends upon diplopia in the practical field of fixation (occupational visual requirements) and inability to maintain single binocular vision without a conspicuous anomalous head posture.

Non Surgical Therapy

While surgery is necessary to achieve the goal of binocular single vision in most instances conservative methods should be considered in suitable cases.

Prisms

When deviation is less than 10 PD prismatic corrections is most effective in deleting diplopia. In some cases the segmental Fresnel prisms may be considered**.**

Occlusion In desperate situation in which BSV cannot be restored by any means occlusion of one eye preferably the sound eye is a last resort. However, occlusion of good eye may lead to disorientation. Alternate occlusion to be done to prevent secondary contracture of ipsilateral antagonist.

Chemodennervation

Indication of Botox in the cases of paralytic cases is in recently acquired neurogenic cases. The iatrogenic paralysis induced with Botox counter balances the original paralysis of the antagonist. Botox injection improves the quality of life for patients during the recovery period by providing useful field of binocular vision and it prevents the contracture of muscles.

Surgical Management

Six months after onset of acute nerve palsy the chances of spontaneous recovery is generally reduced. A surgical strategy for nerve paresis and total palsy are different. Pre operative evaluation of the following parameters should be done i.e. deviation in primary gaze, face turn, binocular diplopia free field.

Mainly aim to weaken the ipsilateral antagonist and in some cases contralateral antagonist. In paresis cases recession and resection are the best procedures although more than normally suggested surgical amounts are required.

In complete paralysis cases transposition procedures are used.

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Anterior Segment Optical Coherence Tomography and its Application in Clinical Ophthalmology

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Optical coherence tomography (OCT) is a cross-sectional, three-dimensional, high-resolution imaging modality that uses low coherence interferometry to achieve axial resolution in the range of 3-20 μm. It can overcome many of the limitations of the current techniques used to image the anterior segment of the eye. OCT is similar to ultrasound except that light is used instead of sound. It is a completely noninvasive technique. As it uses interferometry for depth resolution it can have a long working distance and a wide field of transverse scanning compared to confocal microscopy. OCT has predominantly been used so far for posterior segment imaging of the eye because of various reasons.

Anterior segment imaging using OCT was first demonstrated in 1994 by Izatt et al using light with a wavelength of 830 μm. Not much attention was paid to anterior segment applications until Lubech group described OCT imaging of Laser thermokeratoplasty lesion in 1997 and Maldonado et al reported imaging of LASIK flap in 1998.

The primary limitation of OCT imaging of the anterior segment is speed and penetration. The OCT systems used in commercial retinal scanner thus far have used 830 nm wavelength, with image acquisition time of 1 to 5 seconds. The wavelength higher than 830 nm in posterior segment had more dissipation in vitreous hence was discarded from posterior segment use, but it found its solace in anterior segment. Wavelength 1310 nm allowed deeper penetration even through sclera and cross-sectional imaging of the anterior chamber, including visualization of the angle.

Very recently, ophthalmic OCT in 1310 nm wavelength has been described, with an acquisition time of 3.3 seconds. All of these systems require image-processing technique to remove artifacts caused by patient motion during data acquisition.

A system capable of faster data acquisition would not be affected by involuntary eye movement and would allow real time display.

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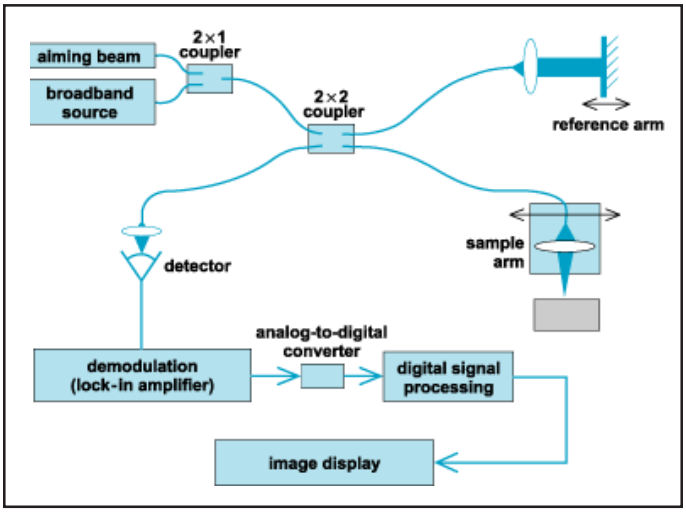
Principle of Optical Coherence Tomography

In a typical optical coherence tomography system (see illustration), light from a broadband, near-infrared source and a visible aiming beam is combined and coupled into one branch of a fiber-optic Michelson interferometer. Broadband sources include super luminescent diodes, fiber amplifiers, and femtosecond pulse lasers in the wavelength range of 800-1550 nanometers. The light is split into two fibers using a 2×2 coupler, one leading to a reference mirror and the second focused into the tissue. Light reflects off the reference mirror and is recoupled into the fiber leading to the mirror. Concurrently, light is reflected from index-of-refraction mismatches in the tissue and recoupled into the fiber leading to the tissue. Reflections result from changes in the index of refraction within the structure of the tissue, for instance between intercellular fluid and collagen fibers. Light that has been back-reflected from the tissue and light from the reference arm recombine within the 2×2 coupler.

Because the broadband source has a short coherence length, only light which has traveled very close to the same time (or optical path length) in the reference and tissue arms will interfere constructively and destructively. By changing the length of the reference arm, reflection sites at various depths in the tissue can be sampled. The depth resolution of the optical coherence tomography system is determined by the effectiveness of this time gating and hence is inversely proportional to the bandwidth of the



High-speed corneal and anterior segment optical coherence tomography at 1.3 μm wavelength

Fig.1: The Visante AS-OCT (Carl Zeiss Meditec, Inc, Dublin, CA, USA)

source. An optical detector in the final arm of the Michelson interferometer detects the interference between the reference and tissue signals. During optical coherence tomography imaging, the reference-arm mirror is scanned at a constant velocity, allowing depth scans (analogous to ultrasound A-scans) to be made. Either the tissue or the interferometer optics is mounted on a stage so that the beam can be scanned laterally across the tissue to build up two- and three-dimensional images, pixel by pixel.

Majority of the studies published on anterior segment OCT applications used commercially available retinal scanners. The majority of these studies focused on corneal imaging, with regard to AC angle imaging, however these OCT systems were suboptimal for tissue delineation because 0.8 μm light cannot penetrate the sclera, there by preventing visualization of the underlying angle structures.

In contrast, OCT at 1.3μm wavelength of light is better suited for AC angle imaging due to two significant properties. First, the amount of scattering in tissue is lower at this wavelength. This enables increased penetration through scattering ocular structures such as the sclera and the iris so that more detailed AC angle morphology is visualized. Second, 1.3μm wavelength is strongly absorbed by water in ocular media and therefore, only 10 % of the light incident on the cornea reaches the retina. The reason being that absorption and scattering in most tissue constituents decreases with wavelength in the near infrared spectrum whereas absorption in water (the primary constituent of vitreous humor) increases sharply, being approximately an order of magnitude higher at 1.3μm than at 0.8μm. The improved retinal protection allows for the use of high power illumination that, in turn, enables high-speed imaging. The permissible exposure level at 1.3μm wavelength is 15 mW according to the current standard set by the American Laser Institute and the American National Standard institute (ANSI 2000). This level is 20 times higher than the 0.7mW limit at the 0.8μm wavelength. The high-speed imaging eliminates motion artifacts, reduces examination time, allows for rapid survey of relatively large areas and enables imaging of dynamic ocular events.

Recently an anterior segment OCT system (The Visante AS-OCT, Figure 1) has been launched (Carl Zeiss Meditec, Inc, Dublin, CA, USA). In brief, this system uses a semiconductor optical amplifier light source capable of emitting 22mW of low coherence light with a central wavelength of 1.3μm wavelength and as spectral bandwidth of 68mm full width at half maximum. The optical power incident on the eye is 4.9 mW that is well within the permissible levels. The scanning speed is 4000 axial scans per image, giving an image acquisition rate of 8 frames per second. The lateral resolution is 8 μm. The scan geometry is telecentric (rectangular) allowing wide field capability, which is essential for corneal and anterior chamber studies.

Slit lamp adaptation of AS-OCT has also been described which use a charged couple device (CCD) camera to visualize the scan area in real time. This can be an ideal device for the immediate postoperative evaluation of filtering blebs and the morphologic features of chamber angle region as it allows non-contact measurements. It may improve detection, documentation and follow up examination of iris and ciliary body pathological conditions and enable monitoring of ciliary body changes during accommodation.

Potential applications of anterior segment Optical Coherence Tomography

1. Laser assisted in situ keratomileusis and other refractive surgeries

Imaging of the corneal layers with high speed OCT provide useful information relevant to keratorefractive surgery, especially in laser in situ keratomileusis (LASIK). Many useful anatomic features can be identified in the image (Figure 2).

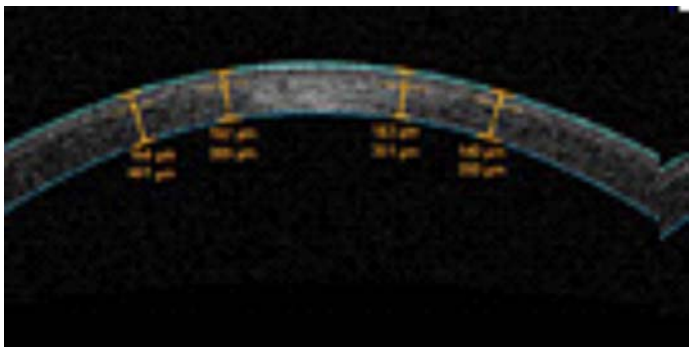


Fig.2: Post LASIK ASOCT outlining the flap

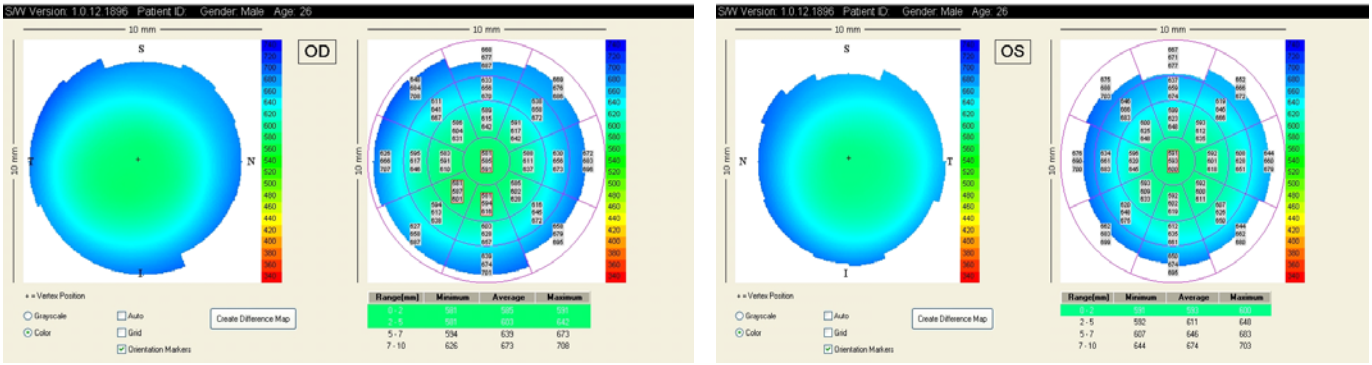


Fig.3: Optical Pachymetry map of normal cornea as provided by ASOCT

Corneal flap thickness is an important parameter in LASIK because it determines the amount of residual stroma available for ablation. Currently there is no technique that directly measures corneal flap thickness and it has been demonstrated that there are noteworthy discrepancies between intended and actual thickness values. By directly measuring corneal flap thickness intraoperatively, it can potentially improve the predictability of LASIK. It can also potentially determine ablation rates, and factor causing variation in this parameter such as stromal hydration can be taken into account, thereby minimizing the differences between planned and actual ablation depths. Owing to superior resolution of morphological features, it can also be used for postoperative assessment of the anatomical correlates of the refractive outcome. It can also provide the comprehensive pachymetry map of the entire cornea and helps in the detection of normal (figure 3) from abnormally thin corneas in which subtractive refractive surgery like LASIK may need to be avoided.

The anterior surface reflection is strong at the perpendicular incidence and produces a vertical flare that marks the corneal apex. Finer features, such as the epithelial-Bowman and the flap lamellar boundaries, are best visualized with a slight off-normal beam incidence angle in the midperiphery.

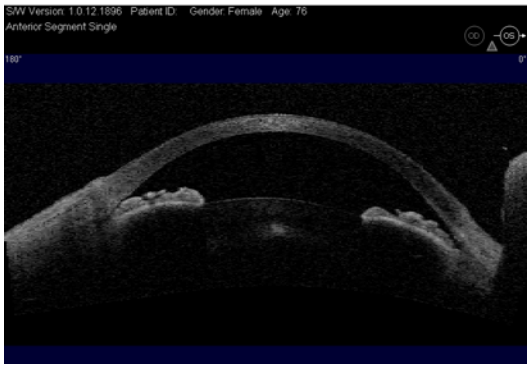
2. *Screening of Angle Closure Glaucoma*

Primary angle closure glaucoma is highly prevalent in certain regions of the world. Treating anatomically narrow angles with a laser peripheral iridotomy may prevent development of angle closure. Therefore, early detection of anatomically narrow angle is important. Currently, Gonioscopy is the gold standard for evaluating the anterior chamber angle; however it is subjective, semi quantitative and requires specialized training. Also there are no uniform criteria for identifying angles that require treatment. Cross sectional imaging of the anterior chamber can provide quantitative data and may prove to be less subjective than gonioscopy (Figure 4).

Ultrasound biomicroscopy and Schiempflug photography have been used for quantitative angle evaluation. OCT can provide with the added advantage of being non-contact, devoid of artificial opening of angle and easy to perform.

AS-OCT can be used to assess angle width. The images obtained are processed using computer to correct image distortion arising from 2 sources. First, the fan shaped scanning geometry of the OCT beam and second, the effect of refraction at he cornea air interface. Due to lower scattering loss at 1.3µm, highly detailed AC angle imaging is possible, and angle structures including the iris root, the angle recess, the anterior ciliary body, the scleral spur, and, in some eyes, the canal of Schlemm can be visualized. Scleral spur particularly is highly reflective and can be easily identified on OCT. Objective assessment of the angle characteristics can also be made from the OCT images.

In addition to the AOD (Angle opening distance) and



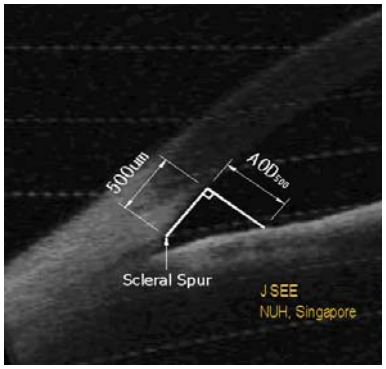


Fig.4: AS-OCT image showing chronic PACG with closed angles.
Fig.5: Quantitative assessment of the angle using the AS-OCT: Angle opening distance at 500µm from the scleral spur (AOD_{500})

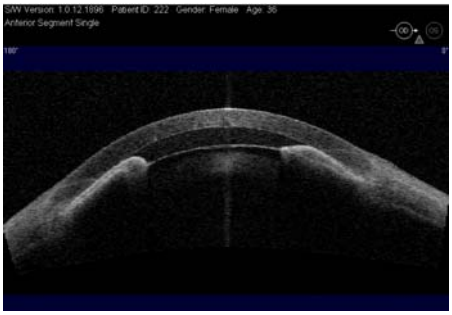


Fig.6: AS-OCT image showing a case of malignant glaucoma with flat anterior chamber

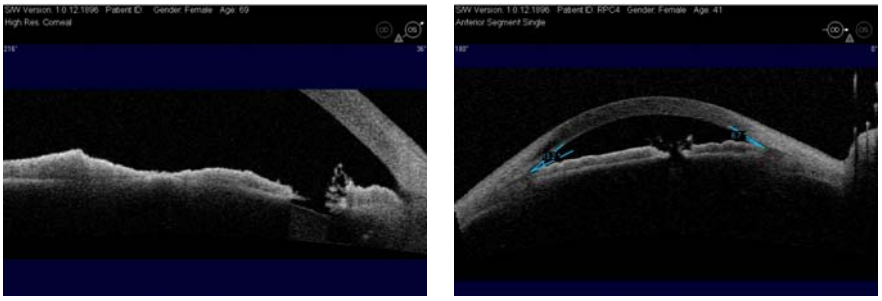


Fig.7: AS-OCT images showing patency of laser peripheral iridotomy

the ARA (Angle recess area), which have been described previously in UBM studies, two new parameters: the TISA (Trabecular-iris space area) and the TICL (Trabecular-iris contact length) are described for defining AC angle anatomy. (Figure 5) The TISA differs from the ARA in that it only measures the filtering area in front of the scleral spur whereas the ARA also includes the nonfiltering angle recess. Thus, the ARA may be less sensitive in identifying a narrow angle in eyes with a relatively deep angle recess. In OCT imaging, another advantage of the TISA over the ARA is that identification of the scleral spur is more reliable than the angle recess. This is because the scleral spur is highly reflective and appears bright on the OCT image whereas the recess is less reflective and may be less precisely defined in some eyes.

3. Other Applications of AS-OCT in Glaucoma

Evaluation of the structural causes of angle closure glaucoma such as plateau iris syndrome, malignant glaucoma, and pupillary block glaucoma can be performed.

Study of alterations in anatomical configuration of angle structures in response to light and accommodation can be performed. This may help detection of conditions such as plateau iris syndrome, pigmentary glaucoma, malignant glaucoma (Figure 6) and primary angle closure glaucoma.

Real time imaging is possible during performance of provocative tests for assessment of angle occludability, such as the dark room and the prone provocative tests.

Other applications of the AS-OCT includes its use in the evaluation of the efficacy of various treatments, such as laser peripheral iridotomy (Figure 7), laser iridoplasty or cataract extraction, where the angles may be shown objectively to open after such treatment. The patency of iridotomy can be judged well on the ASOCT by viewing the anterior lens capsule behind the full thickness defect created because of PI.

The AS-OCT may also be helpful in the assessment of tube patency or position of the glaucoma drainage device in cases of corneal opacity.

Non-invasive nature of the OCT allows its safe use in situations where ocular tissue has been lacerated or punctured - in which gonioscopy cannot be performed because of the danger of aqueous leak.

4. Anterior chamber width and other biometric parameters

Use of phakic intraocular lenses (IOLs) for the treatment of high myopia and hyperopia is increasing. For low to moderate myopia and hyperopia, excimer laser refractive surgery currently is the accepted procedure of choice. However for eyes with high ametropia surgical complications like ectasia may preclude any corneal surgical intervention. Placement of phakic IOL retains accommodation and is better choice than Clear lens extraction. Of the various styles available angle-supported phakic IOLs offer ease of implantation, but require proper sizing to minimize complications. Pupil ovalization, iris atrophy, and iritis occur when the IOL is too large. Undersized IOLs may become mobile and result in endothelial damage, iritis, peripheral anterior synechiae, and secondary glaucoma.

A properly sized angle supported AC IOL, has haptics sitting on the scleral spur or gently within the angle recess, and the IOL vault places it approximately midway between the iris and cornea. Traditionally, external white-to-white (WTW) corneal diameter has served as a substitute for AC depth because practical methods of internal AC width measurement were not available. Measurement of the external corneal diameter, however, depends on external limbal landmarks and may not correlate well with internal landmarks. External measurements are also significantly influenced by pannus, arcus and other anatomical variations. OCT is a promising method for accurate anterior segment biometry owing to its high spatial resolution and non-contact nature (Figure 8) and can improve sulcus supported phakic IOL sizing also. In cases of iris fixated anterior chamber phakic IOLs (eg. Verisyse IOL) a minimum of 3.0 mm ACD must be present prior to undertaking the surgical procedure and the minimum IOL crystalline vault in the pupillary area should be atleast 0.5mm besides creation of 2 Nd: YAG iridotomies before undertaking the procedure. Both these measurements can be accurately provided by the ASOCT.

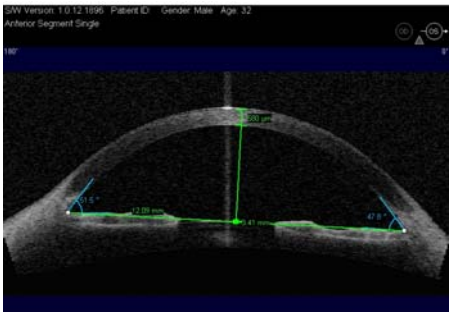


Fig.8: Angle width, AC width and depth measurement

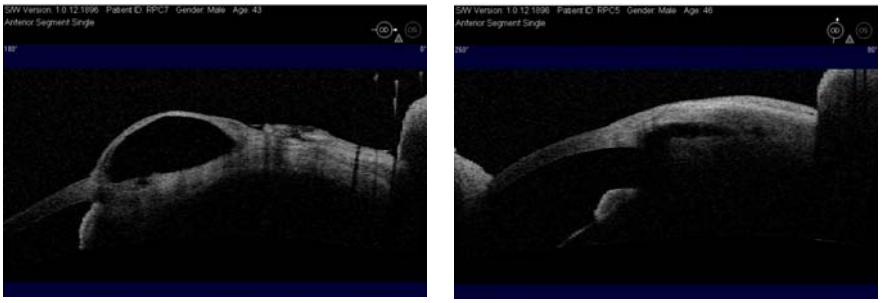


Fig.9: ASOCT images showing a successful bleb

5. Application in Imaging Trabeculectomy Blebs

Bleb morphology is an important clinical parameter in filtering surgery. It indicates function of the filtration shunt created by the trabeculectomy procedure and guides the ophthalmologist in performing interventions such as needling and suture lysis in order to optimize shunt function. AS-OCT has been used to image trabeculectomy blebs to provide information about internal structure that is not available at the slit lamp. It is able to provide clear images of the bleb wall, cavity, flap and ostium as displayed below (Figure 9&10).

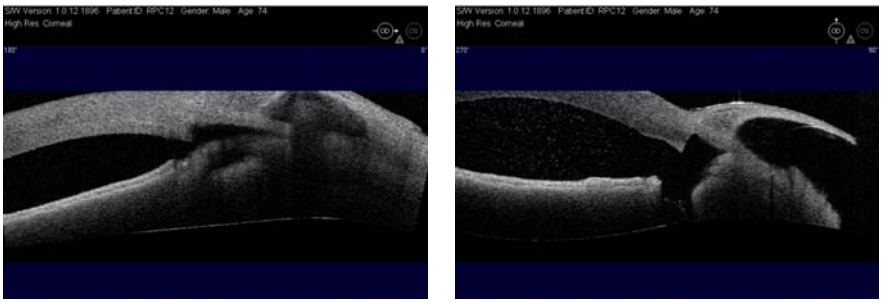


Fig.10: ASOCT image of a bleb showing the intrascleral course of the aqueous and a patent surgical PI.

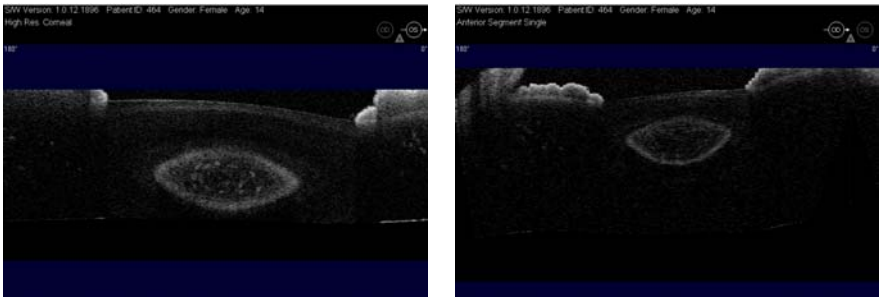


Fig.11: ASOCT image displaying developmental cataract.

Successful blebs display conjunctival thickening as a hallmark of success, regardless of degree of bleb elevation. This reflects facility of transconjunctival aqueous flow. Highly elevated blebs sometimes display marked conjunctival thickening and only a small cavity.

In failed blebs, AS-OCT is particularly useful in imaging failed blebs to demonstrate the level of failure. Ostial closure, flap fibrosis and presumed episcleral fibrosis in the absence of the former two situations are all clearly demonstrated. In the early postoperative period, a failing bleb with a closely apposed scleral flap may be resuscitated by suture lysis, resulting in a more expanded bleb.

Hence AS-OCT is a useful tool to image trabeculectomy blebs and may aid the clinician in postoperative bleb management. It can also image the intrascleral lake and implant used in non-penetrating glaucoma surgery (deep sclerectomy) and glaucoma drainage devices.

6. Assessment of tumors of iris and ciliary body

Accurate localization, measurement of the tumor size, and evaluation of factors such as the depth of penetration and extrascleral extension is a potential application of ASOCT which is still undergoing evaluation.

7. Others

AS-OCT can image upto posterior capsule of lens. Thus it can also show the morphology of lens and its abnormality like developmental cataract (Figure 11), posterior capsular dehiscence in case of posterior polar cataract and subluxated crystalline lenses (Figure 12). It can also be of use in delienating the anterior segment anatomy in cases of opaque corneas (Figure 13), failed grafts (Figure 14), adherent leucomas (figure 15) and help in the surgical planning prior to keratoplasty by preoperatively documenting the potential areas of iris adhesion for which the surgeon should be extra cautious during surgery in order to avoid potential iris trauma during trephination, dissection etc. to the glaucoma filtering surgeon it can

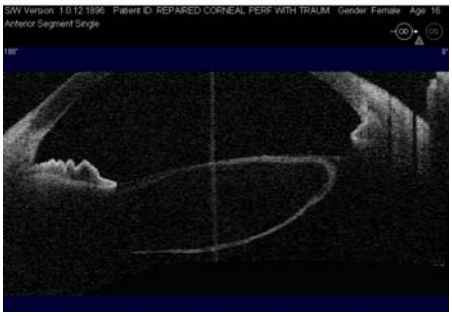


Fig.12: Subluxated crystalline lens with broken zonules

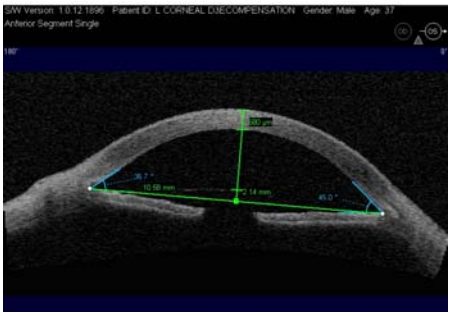


Fig.13: PBK with angle supported ACIOL

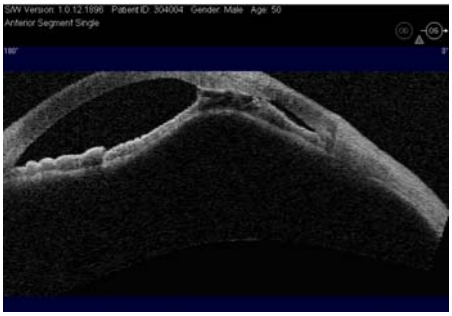


Fig.14: PAS with graft host junction synechia in post PK glaucoma

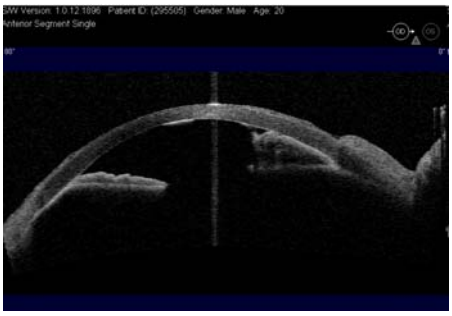
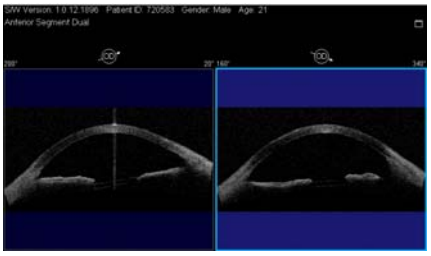


Fig.15: Post traumatic adherent leucoma



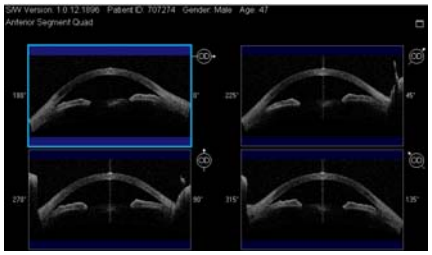


Fig.16: Dual scan and Quad scan of ASOCT

provide useful information with regard to sites of AC entry during trabeculectomy as well as placement of tube shunts away from the areas of iris adherence.

Future developments

The aim of future studies should be an increase of scleral transmission, which may be achieved by pressure to the scleral surface, or use of glycerin, which may increase the transparency of the sclera. Future advancements will also have to take into consideration ways to enhance penetration through the iris pigment epithelium for making structures posterior to the iris like ciliary body, zonules etc to be better visualized.

Comparison of ASOCT versus UBM

Ultrasound biomicroscopy provides high-resolution images (50-µm lateral resolution in the commercially available system) of the AC angle region, has a depth of penetration of 5mm in tissue, and is able to image through opaque media. However, it has several limitations. A coupling medium is required such that scanning must be performed through an immersion bath. The procedure is time-consuming and requires a highly skilled operator to obtain high-quality images. There is a risk of infection or corneal abrasion due to the contact nature of the examination. Finally, inadvertent pressure on the eye cup used while scanning can influence the angle configuration, as demonstrated by Ishikawa et al using a small UBM eyecup. Since the patient is in a supine position, the iris

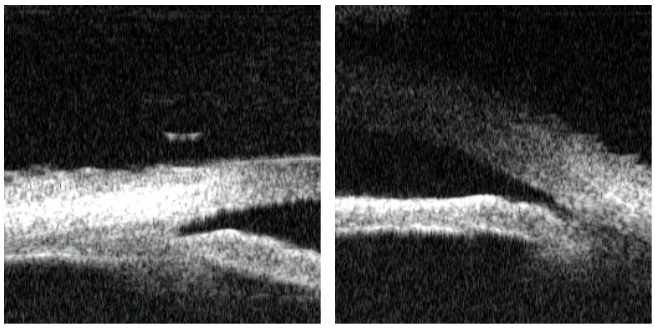


Fig.17: UBM image of superior angle and inferior angle in two different images

lens diagphragm falls back due to effect of gravity and may lead to artifactual opening up of the angle.

Optical coherence tomography is a light-based imaging modality that has several advantages over the other techniques used for objective assessment of the AC angle. It has a higher image resolution than UBM, is totally noncontact, and is easily performed with minimal expertise. The noncontact nature of OCT not only enhances patient comfort and safety but also makes it especially suitable for ocular biometry and AC angle assessment since there is no mechanical distortion of the tissue being imaged. Simultaneous two or four quadrant can be scanned by dual scan and quad scan mode by AS-OCT (Figure 16) while in UBM only one angle can be imaged at a time (Figure 17).

Advantages of the AS-OCT

- It is a non-contact method therefore do not cause indentation of the angle by placement of the scleral

cup on the eye (which is required to maintain the water bath in UBM) Also, no possibility of corneal abrasion or punctuate epithelial erosions (possible with UBM).

- It is a more physiological examination as patient is imaged sitting upright. (Lying supine may artificially widen the anterior chamber angle as the iris-lens diaphragm moves posteriorly due to gravity.)
- Shorter imaging time. (Patient setup in UBM takes longer. Also, only one angle is imaged at a time with the UBM.)
- Rapid image acquisition. Eight frames can be captured per second, allowing operator to choose the best centred image.
- Requires less expertise to perform- small learning curve for the operator.
- Target may be used to induce accommodation in the eye being imaged. (This is especially useful in the evaluation of accommodative intraocular lenses.)
- More comfortable for the patient, due to non-contact technique, upright position and rapid imaging acquisition.
- Less interoperator variability, due to non-contact technique.

Disadvantages of the AS-OCT

At present unable to image structures posterior to the iris as the optical beam cannot penetrate the iris pigment adeqately except in Albinos. Ciliary body imaging cannot be performed unlike the UBM which allows imaging of structures posterior to the iris, in particular, the ciliary body and peripheral retina. In addition, the upper and lower lids come into the field of view and obstruct imaging of the superior and inferior angle, requiring the examiner to manually lift up the eyelids for obtaining a proper view

Summary

Thus ASOCT using 1.3 μm wavelength is a very helpful tool for non contact anterior segment evaluation. Its measurements correlate well with ultrasound biomicroscopy with various advantages over UBM like non-contact technique, short time, patient friendly, and ability to view dynamic changes. Amongst the limitations of ASOCT are its inability to obtain clear images through opaque media and the iris, obstruction by the eyelids making imaging of the superior and inferior angles difficult and it provides limited visualization of the ciliary body. It may be used as the standard modality for anterior segment imaging in clinical practice. Further long term studies are required to elucidate the full potential of this exciting new imaging modality which might leave a mark in the fields of refractive surgery, glaucoma and other ophthalmic specialities.

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Modified Technique of Intravitreal Injection

Pradeep Venkatesh MD, **Raju Sampangi** MD, **Satpal Garg** MD

Intravitreal injections commonly used for treating endophthalmitis are now increasingly utilized in the management of various ocular conditions like retinal detachment (pneumatic retinopexy), choroidal neovascular membrane and diabetic macular edema. Intravitreal injections are given under topical anaesthesia with appropriate pre and peri-injection asepsis[1]. Reflux during withdrawal of the needle after injection commonly occurs and is prevented by rolling sterile cotton tipped applicator over the injection site. We describe a simple modification in the injection technique to decrease the reflux by a two plane, valvular needle entry technique.

Conventional injection technique: Site of pars plana injection is in the inferotemporal quadrant 3.5mm (pseudophakic) to 4 mm (phakic) from the limbus. The needle is inserted perpendicular to the sclera into the vitreous cavity aiming toward the center of the globe. While withdrawing the needle, cotton tipped applicator is used to prevent reflux of injected contents.

Modified injection technique: Site of entry is as for the conventional technique, however the needle (27G, 5/8 inches) is initially directed parallel to the limbus at 30 (figure 1a) degree angle for a very small distance intrasclerally (about 40 to 50% depth) (approximately half the bevel length) and then the direction changed towards the center of the globe (figure 1b, figure 1c). Firm fixation of the globe using a lim's or fixation forceps to avoid torsion of the globe is necessary during the entire procedure. In this manner a two plane entry with a valve like effect is made and this decreases risk of regurgitation.

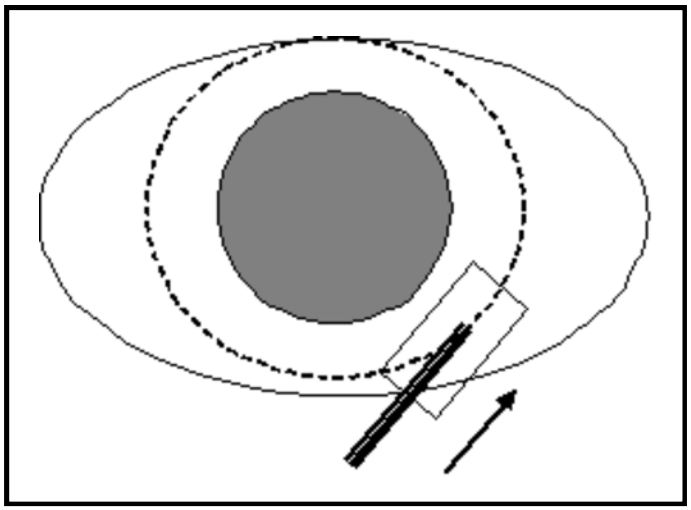

Fig.1a: Initial direction of needle (parallel to the limbus)

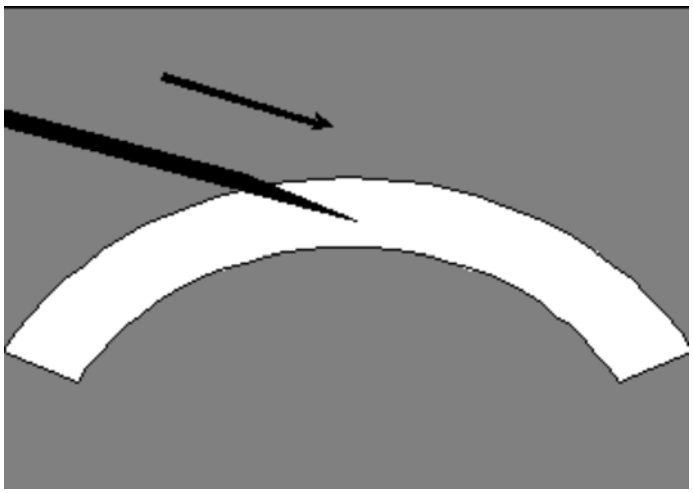

Fig.1b (Modified technique): Angle of needle entry at 30 degrees

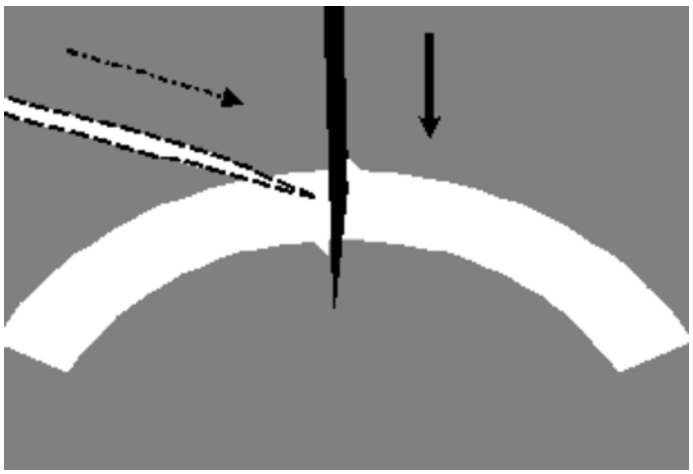

Fig.1c: (Modified technique): Final needle direction just before intravitreal entry

Discussion

Intravitreal injections are an important route of administering ocular medications, as the drug is directly delivered into the vitreous cavity. Role of this route of drug delivery is ever expanding and is being increasingly used to treat conditions other than endophthalmitis. Intravitreal triamcinalone has been used for managing conditions such as diabetic macular edema and macular edema from other causes. Newer indications for this route of drug delivery include intravitreal anti-VEGF agents (ranibizumab and

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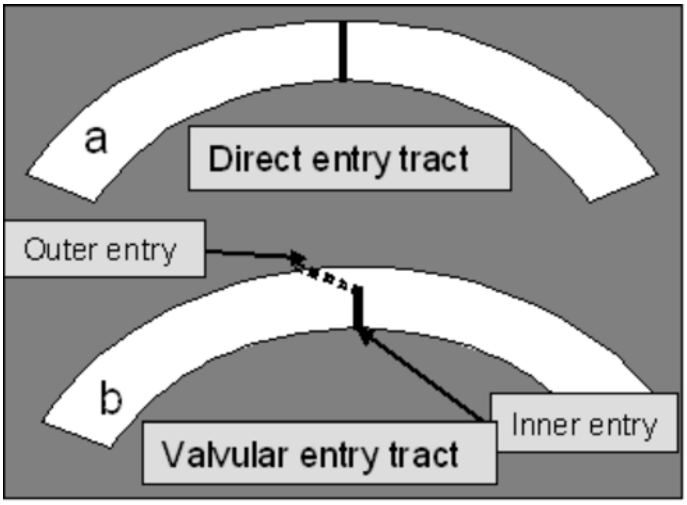

Fig.2: Cross section of entry tract. Conventional injection technique (a); Modified injection technique (b)

bevacizumab) for choroidal neovascular membranes (CNVM) and diabetic macular edema. These newer indications deliver very small quantities of medications into the vitreous hence it is all the more important to deliver the right quantity without any loss of drug.

Reflux during needle withdrawal occurs frequently when injecting by the regular technique as the needle makes a direct tract in the sclera. A simple modification in the injection technique that is similar to the technique of entry port for 23G vitrectomy, results in a valvular entry. A diagrammatic comparison of the cross-section across the needle track using the conventional and modified methods is shown in figure 2.

Reduced regurgitation of the gas (during pneumatic retinopexy) or of the drug, enhance the likelihood of delivering the exact dosage of the drug or gas intravitreally. In addition this modification is also likely to decrease vitreous herniation through the needle tract and minimize the potential for 'posterior vitreous wick' syndrome and endophthalmitis.

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Presbyopic LASIK

S.K. Narang MS, **Sapna Jain**, MS

Management of refractive errors has seen vast changes in the last decade from radial keratotomy to photorefractive keratectomy and laser assisted insitu keratomiliuesis. Myopia, hypermetropia, astigmatism are now being successfully managed with further refinement through the newer techniques.

The challenge to all ophthalmologist has been management of presbyopia. Presyopia is a gradual progressive age related loss of accomadation which starts around 40 years of age.

Mechanism of presbyopia as stated by von Helmholtz postulates that when the ciliary muscle contracts, it releases the resting zonule tension, which otherwise pulls on the lens equator and keeps it in a relatively flattened, unaccommodated state. The release of zonular tension enables the lens to "round up" to a more accommodative configuration due to the forces of the capsule on the lens.

There are many contributing factors to the progression of presbyopia, but perhaps the most important factor is failure of crystalline lens to changes its form in the presbyopic eye during accommodation.

The aim of any corrective procedure for presbyopia has been maintenance of distant vision and restoration of progressively changing near vision.

Treatment options till few years back have been spectacles and contact lenses but today's prosperous, appearance conscious patients ask for other methods which could make them less dependent on glasses.

Present day other treatment modalities available to manage presbyopia are surgery on the cornea (lasik, conductive keratoplasty), on the lens (multifocal IOL) and the sclera (scleral expansion -PMMA bands and relaxation - anterior scleral sclerectomy).

LASIK(laser-in-situ keratomileusis) procedure in treatment of presbyopia can be aimed at providing monocular or binocular vision.

Creating monocular vision

In this procedure dominant eye is maintained for distance and the nondominant eye is treated by LASIK for near vision.

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The biggest problem with monovision is getting the patients'acceptance. The ophthalmologist should give a trial of monovision contact lens to check the acceptance of such surgical procedure. It should be emphasized to the patients clearly that adapting to monovision after surgery will take three to four weeks and that dependence on glasses will be reduced rather than completely eliminated.

Creating binocular multifocal vision

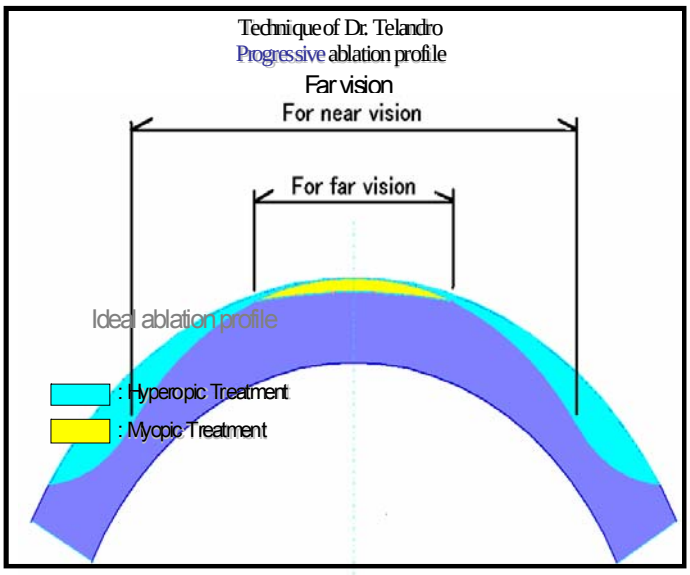
The idea of ablating a multifocal pattern on the cornea to treat presbyopia has been around for a number of years

- Sectoral ablation (T. Anschütz 1991);
- Concentric central near zone (B&L; L. Ruiz 1998)
- Inferior off center ablation (JM. Blauberg 1999)
- Concentric peripheral near zone (A. Telandro 2001)

The Central Distance Approach

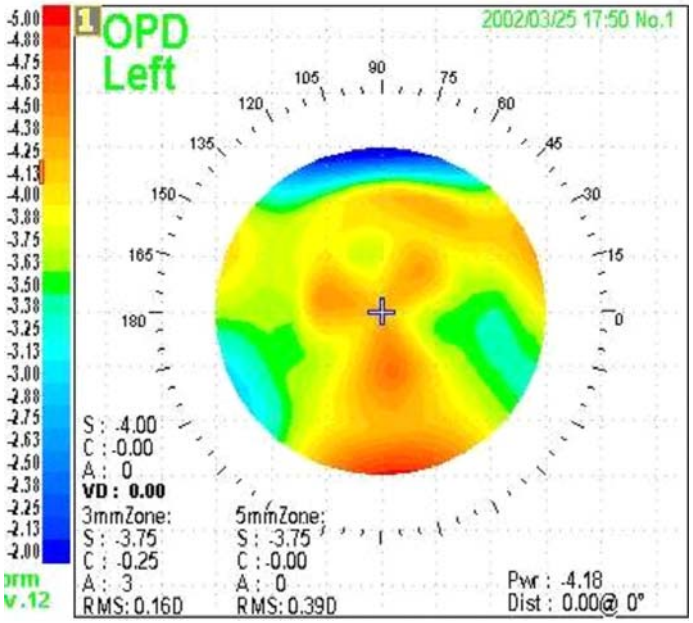
Alain Telandro, MD, who practices in Cannes, France, has worked extensively with multifocal ablation using the Nidek EC5000 excimer laser system, favors use of the center zone for distance.

Dr. Telandro, has created PAC [Pseudo Accommodative Cornea] software to make this correction when using the Nidek laser.

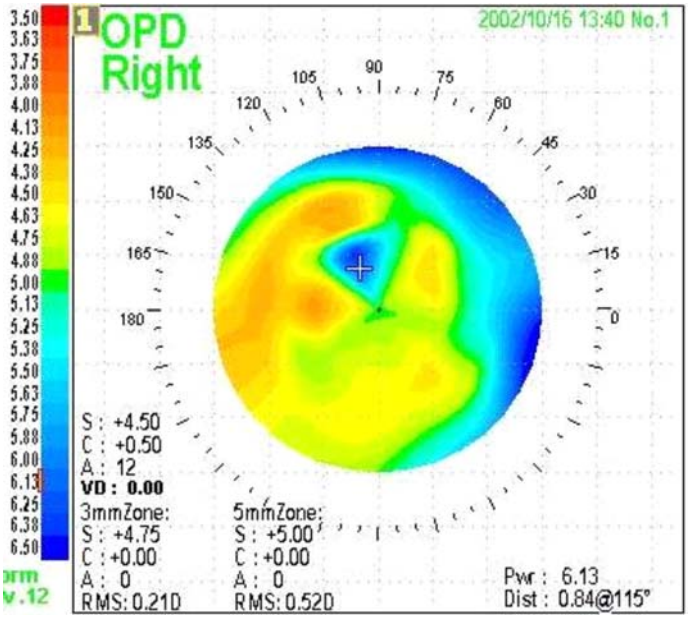


The basic aspect of PAC technique are

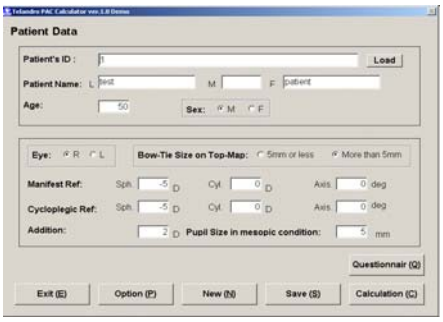
1. to create emmetropia at the central of visual axis of 3.5 mm optic zone
2. to create an annular transition area from the central

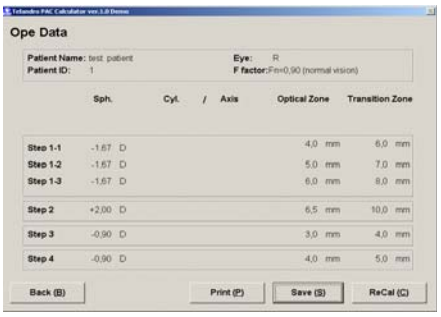


Myopic presbyopic patient's OPD maps compare 3mm and 5mm refractive error



Hypermetropic presbyopic OPD map. Compare 3mm, 5mm refractive error





PAC programme example of mypic presbyopic correction

Results				
S.No	*Characteristics*	*Group A Hyprmetopia*	*Group B Myopia*	*Group C Emmetropia*
1.	No. of patients	26	28	8
2.	Sex male female	9 17	10 18	1 7
3.	Age (years)	40-52	40-57	40-44
4.	Refractive error(D)	+1.00 to +4.00	-0.75 to -4.0	Nil

optic zone moving more peripherally into near vision zone

3. to create a third zone of near vision at the periphery of cornea (starting 3.5mm of the visual axis)

Different optic zones and transition zones are combined with variable diameters to correct presbyopia with or without associated refractive error like myopia , hypermetropia with or without astigmatism.

The procedure is carried out in 3basic stages which are further divided intosubstages depending on the primary refractive error

Stage 1: correction of the refractive error for distance

Stage 2: treatment of presbyopia

Stage 3: demyopization of myopia induced by presbyopic hyperopic correction induced .At this stage an F factor is introduced depending on patients predominant visual needs

Technique

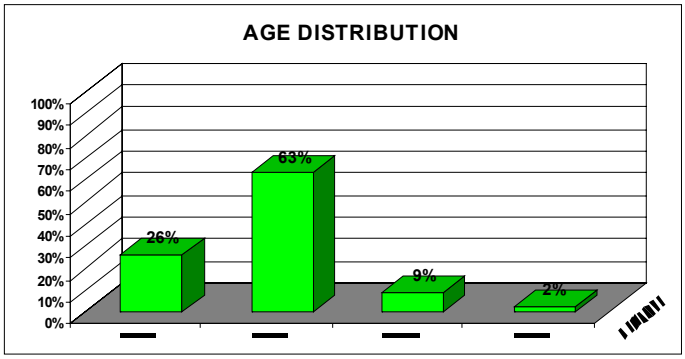
Case selection

Age - 40 years and above

Detailed questionnaire especially regarding the reason for presbyopic surgery and the dominant visual need whether distant, intermediate or near. Simultaneously patients motivation and realistic expectations are assessed Routine preoperative evaluation which should include a cycloplegic refraction, aberrometry , topography.

Corneal topography detailed study of the maps especially the OPD maps : check the refraction in 3mm and 5mm zone to see the accommodation

Cycloplegic refraction and OPD maps help to decide the near addition correction for these patients



Example 1: Emmetropic Presbyopic Correction

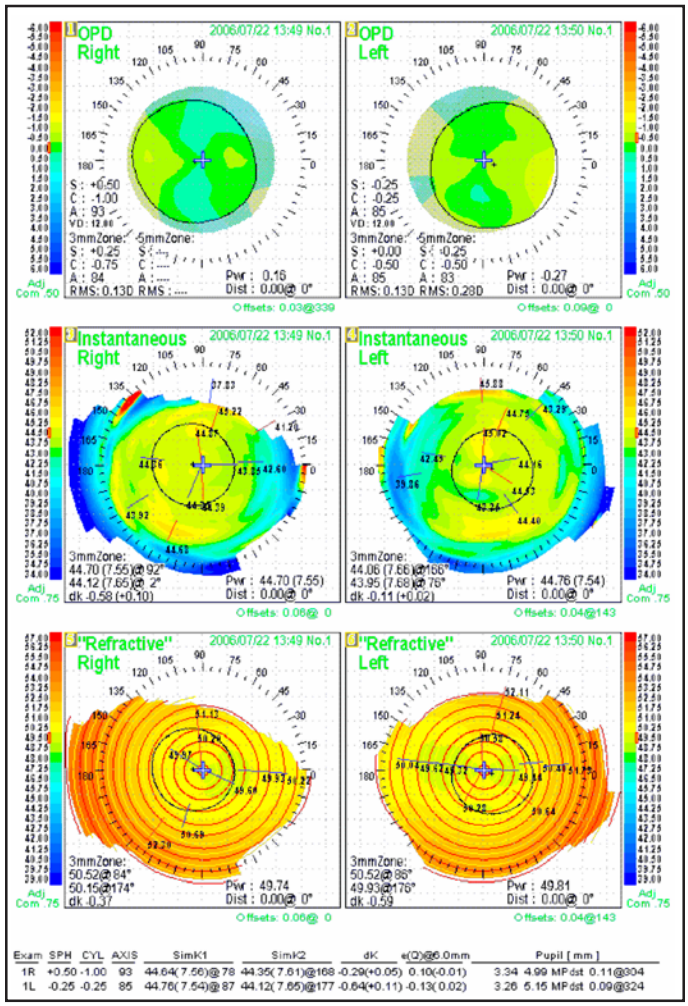


Fig.1: Emmetropic Presbyopia Pre-operative

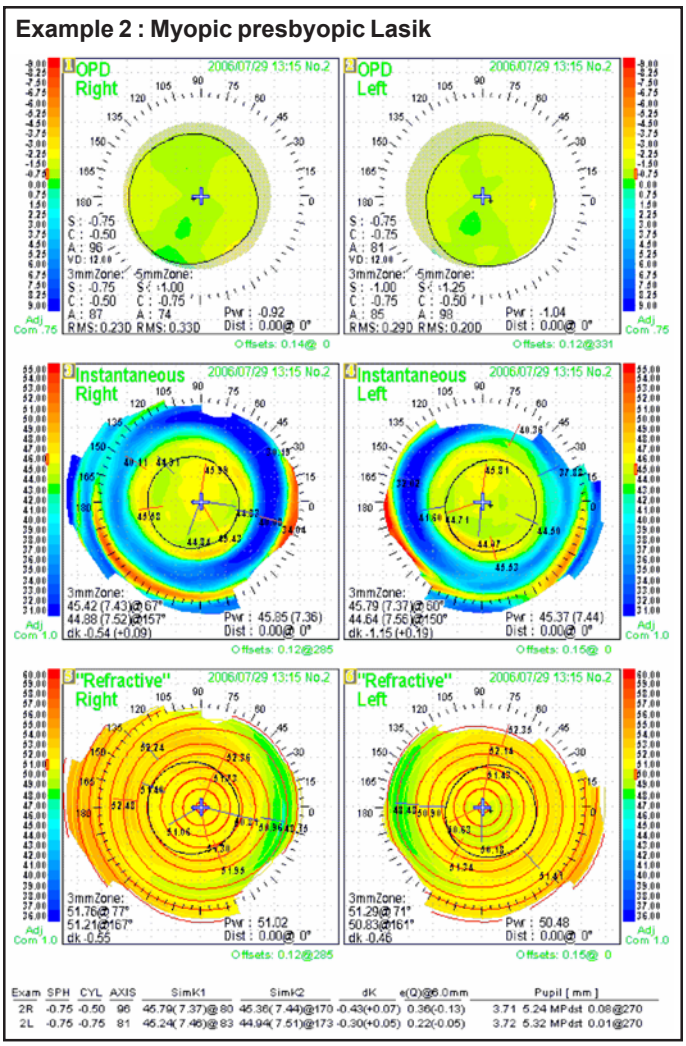


Fig.2: Post-operative Emmetropic Presbyopic Maps Show Multifocal Cornea ,seen Clearly in Instantaneous Maps

Contraindications for the procedure are as for any LASIK - keratoconus, severe dry eyes , uncontrolled diabetes mellitus or glaucoma

Surgery

Bilateral LASIK in the same sitting

We create a superficial corneal flap with Moria microkeratome of 110 micron head. The corneal flap performed with the microkeratome must be between 9.5 to 10.0 mm. Once the flap has been created lasik ablation is carried out in various stages.

Step 1 central emmetropization

Step 2 hyperopic ablation in a zone of 6.5 -10.0 mm is done.

step 3 induced myopia is treated in two steps of optic zone (OZ)/transition zone (TZ) -3.0/4.0 and 4.0 /5.0.

The flap is now cleaned and replaced back in position.

Example 1: emmetropia with presbyopia

Example 2: hyperopia with presbyopia

S.No	*Characteristics*	*Group A*	*GroupB*	*Group C*
1.	Refractive error distance	-0.75 to +0.25D	-0.75 to .12D	-0.25 to-0.50
	near	+0.25D	+0.25D	+1.50D
2.	Satisfaction level	Satisfied	Satisfied	Variable

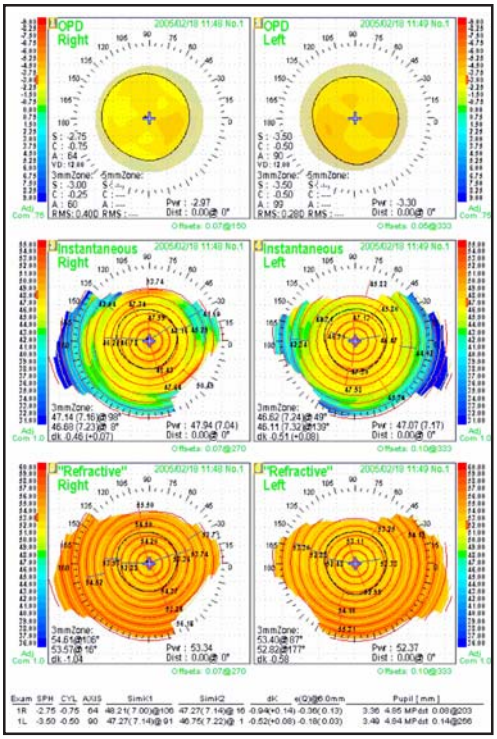


Fig.3: preoperative

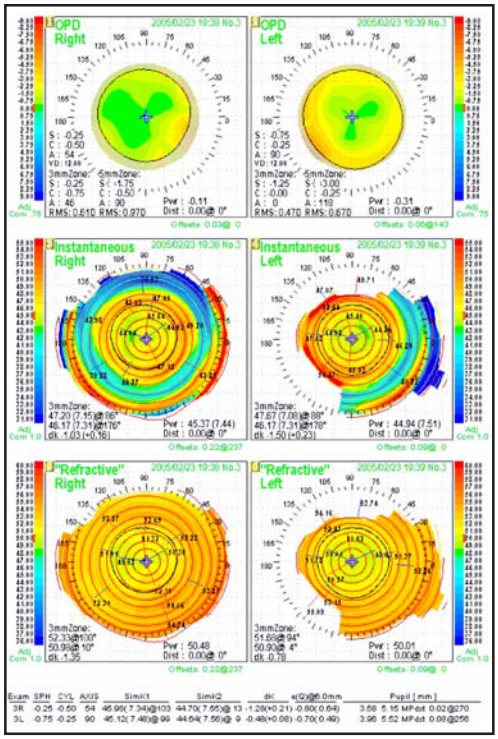


Fig.4: Postoperative Multifocal Cornea seen Clearly in Instantaneous Maps Hypermetropic Presbyopic Correction

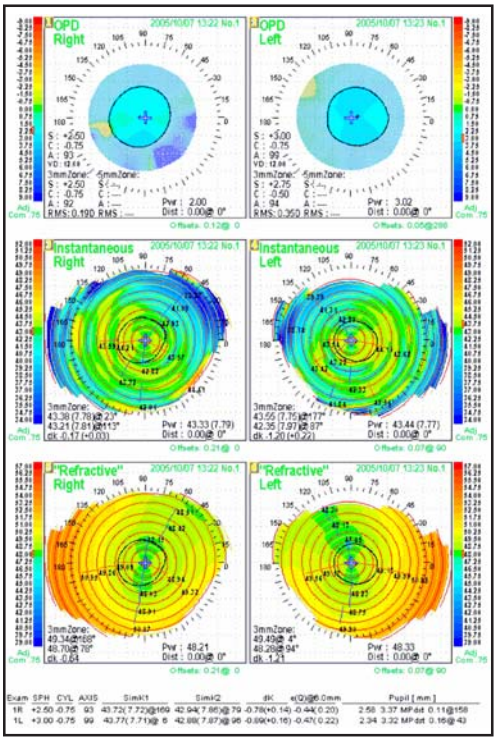


Fig.5: Preoperative Maps

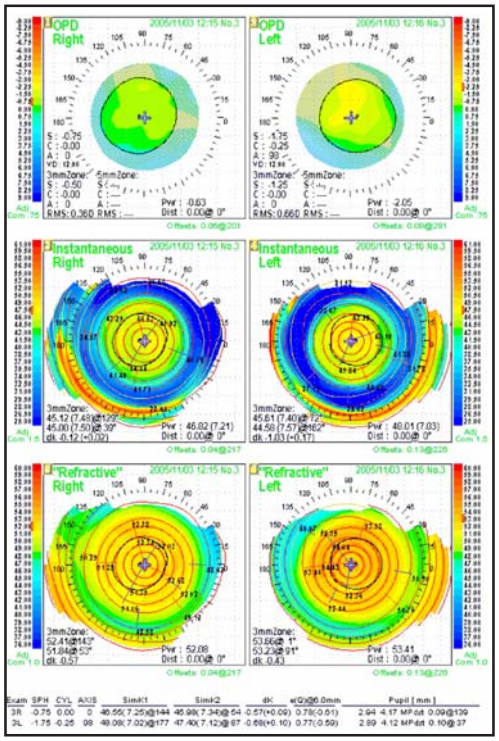


Fig.6: Post-operative Hypermetropic Presbyopic Correction

Example 3: myopia with presbyopia

For the last 2.5 years (june 2004 to dec 2006) we have done 62 patients and here we present our results of presbyopic correction using PAC technique (of Dr.Alan Tolendro)

We required enhancement of the lasik in three cases of the sixty two done so far. All were for distance correction which was done in 3mm - 4.5 mm optic zone

Distance vision usually settles by 2 months post LASIK where as near vision settles within first post operative week

There is no over correction of near vision in presbyopia.

We aim to correct distant vision to -0.50D spherical, that is slightly undercorrect myopia and overcorrect hypermetropia our concern during the presbyopic correction is -

1. it needs a large ablation zone preferably 10.5 mm which is presently difficult to achieve using Moria microkeratome , so we have modified the nomogram with 9.5 mm hyperopic zone

2. there should be no loss of distant vision especially so in the emmetropic group. In this group our results are less predictable (60%).The programme needs further modification at our hands for treatment of emmetropic presbyopia

3. results of near vision are stable with good predictability . 80% for the hypermetropic presbyopic group, 65-70% for myopic and emmetropic group.

Conclusion

Presently we evaluate the patient post-operatively by the OPD and instantaneous maps , by the subjective acceptance for near and distant vision and most importantly by the patient satisfaction.

PAC software for treatment of presbyopia shows promising results though still requiring further refinement so as to give us more predictable results.

Femtosecond Laser in Corneal Surgery

M.Vanathi MD, **Sanjay Kai** MD

Unlike excimer laser which works on the principle of photoablation, the femtosecond laser works on the principle of photodisruption. Photodisruption begins with laser-induced optical breakdown (LIOB), when a strongly focused and short duration laser pulse generates a high intensity electric field, causing the formation of a mixture of free electrons and ions that constitute the plasma state.[1] The optically generated hot plasma expands with supersonic velocity displacing surrounding material.As the plasma expansion slows down, the initial supersonic displacement propogates through the surrounding tissue as a shock wave.[2,3] During propogation, the shock wave loses energy and velocity, eventually converting to a biologically harmless sound wave.[4,5] The rapid expansion of generated plasma quickly decreases its temperature, and the vapourized tissue forms a cavitation gas bubble in the focal of laser beam.[6]The cavitation gas bubble consist mainly of Co_2, N_2 and H_2o, which can diffuse out from the tissue through normal mechanism.[7]

The Intralase femtosecond mode laser was designed to address most limitations of current systems. This laser system uses 1053 nm (infrared) wavelength (Nd:Glass).The focused cavitation spots produced in the corneal stroma are theortically predictable upto ±4 μm. Although performed since the early 1980s, ophthalmic photodisruption has been limited to intraocular procedures because of relatively large energies needed to initiate LIOB with available nanosecond pulse duration Nd:YAG lasers.[8] The resulting large shock waves and cavitation bubbles produced results in significant collateral damage and do not permit contigous pulse-to-pulse placement.Reducing either spot size or the pulse duration of the laser decreases the threshold energy for LIOB. Although there is a lower limit for the focal spot diameter of a few microns (imposed by focusing optics, laser wavelength and propagation effects), the lower limit of laser pulse duration has decreased by as much as six orders of magnitude to the femtosecond (10^{-15} second) range.[9]

The pulse duration dependence of LIOB and photodisruption has been investigated down to approximately 20fs, revealing that near minimal threshold can be obtained with pulses of several hundred femtosecond duration[10,11,12,13]. Because of their large optical bandwidth and high peak intensities, pulses shorter than few hundred femtoseconds are significantly more difficult to generate at required surgical energies and are prone to pulse broadening and nonlinear phenomenona, such as self focusing.[14] These findings suggest that the optimal pulse duration for surgical photodisruptive lasers resides in the hundred femtosecond pulse duration range.

Although the various surgical techniques currently being used for laser in situ keratomileusis (LASIK) have attained a high level of clinical effectiveness and safety, outcome variability and patient anxiety remain a cause of concern. The initial step of flap creation is still responsible for most of the intraoperative and postoperative complications.[15,16,17] The various microkeratome related flap complications such as decentered and free flaps, irregular edges and surface, epithelial abrasions, button hole perforations, cap lacerations, and inadequate diameter for a given correction still prevail. Most systems are limited to producing a single hinge location and create hinge sizes that are highly variable. Preoperative thin and/or steep corneas can limit the use of most systems.[18] Current microkeratomes systems produce variable flap thickness with a standard deviation (SD) greater than ± 25 to ± 40 μm [19,20,21]. Moreover the current microkeratome systems are limited in their ability to create flaps in eyes with different corneal and/or orbital configuration.[22]

Femtosecond lasers offer an alternative to the mechanical cut and can provide additional features regarding the flap morphology [23]. Laser in situ keratomileusis (LASIK) complications are mainly attributable to imperfect cutting with the mechanical microkeratome. The femtosecond laser can provide extremely precise cutting beginning at any corneal point. The optomechanical control of the impact position has been supposed to provide more effective intrastromal cutting than the blade. For LASIK surgery, femtolaser cutting can offer greater safety, reproducibility, predictability and flexibility. The risk of incomplete or irregular cutting and the free cap risk are greatly reduced. Striae, epithelial defects and interface deposits should be minimized. A better flap congruence also limits the risk of secondary displacement and epithelial ingrowth. The results of making thinner flaps are more predictable. Other than the high cost of the procedure, laser cutting has very few disadvantages. The FS laser produces greater corneal stromal inflammation than the microkeratome in the early postoperative period without any increase in apoptosis and stronger flap adhesion late postoperatively.

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Therefore, need for stronger anti-inflammatory drugs to be administered exists [24].

Advantages over microkeratomes

1. Ability to create predictable flap diameter and thickness as compared to mechanical microkeratome
2. Ability to create flaps in eyes with different corneal and/or orbital configuration.
3. It can create variable hinge locations and sizes according to requirement in a case.
4. It is free from complications like decentered and free flaps, irregular edges and surface, epithelial abrasions, button hole perforations, cap lacerations, and inadequate diameter for a given correction
5. Reoperation can be done after waiting period of 45 minutes unlike microkeratome systems which requires atleast 3 months before reoperations can be attempted.
6. Can perform in opaque corneas.
7. It has less incidence of induced optical aberration as compared to microkeratome created flaps

Lamellar keratoplasty and femtosecond laser: Lamellar keratoplasty has increased in popularity in the last few years due to several advances in surgical techniques. Anterior lamellar keratoplasty (ALK) involves dissection of the host cornea to the deep stroma, followed by transplantation of donor corneal tissue sans Descemet's membrane and endothelium. Ramon Naranjo-Tackman [25] has used the femtosecond laser for ALK to cut both the donor and host corneas. His one year results show a mean BCDVA was 20/70 prior to surgery and 20/40 after ALK. The mean final corneal thickness increased from 252 micrometers (mcm) to 538 mcm. The Intralase femtosecond laser (IntraLase Corp, Irvine, California) was used to perform lamellar dissections on 28 donor corneas in a study by Ezra Maguen [26]. A mean deviation of - 9.5 ± 8.6 mcm was found for programmed thicknesses and ranged from 225 to 500 mcm. The usefulness of the femtosecond laser (Intralase) for dissecting a thin, uniform thickness posterior lamellar disk of donor tissue to be used for endothelial transplantation has also been studied. Sikder and Snyder [27] investigated the use of the Intralase to dissect the donor cornea from the posterior side for obtaining a thin and uniform lamellar disk in human donor bank corneas. They have described the technique of using a viscoelastic "cushion" to protect endothelial cells from damage during posterior laser dissection prior to transplantation as providing promising results. The manual dissection technique for deep lamellar endothelial keratoplasty (DLEK) surgery is technically difficult and may not be smooth enough for consistently optimal postoperative vision. Terry et al [28] and Sarayba et al [29] evaluated the feasibility and efficacy of using a femtosecond laser to perform the dissections in the DLEK procedure in cadaver corneas.

Penetrating Keratoplasty and Femtosecond Laser [30, 31]: Trephination of the donor and host corneas using a femtosecond laser in penetrating keratoplasty (PKP) is being described. Gerd U. Auffarth [30] used the 20/10 PerfectVision Femtec femtosecond laser (20/10 Perfect Vision, Heidelberg, Germany) used in 5 patients to cut the donor cornea to a size of 8.0 to 8.1 mm and the recipient cornea to a size of 7.8 mm. A complete perforating cut was achieved in all cases, and the tissue bridges were easily separated with a spatula. Postoperative healing was uneventful.

IntraLase-Enabled Keratoplasty (IEK) for Laser-Designed, Shaped Incisions: IEK allows creation of customized incisions with advanced edge profiles. This results in secure grafts that require less suture tension. Early clinical experience demonstrates that shaped incisions provide a smooth corneal contour immediately following surgery. These profiles provide clinical benefits such as preservation of the corneal optics, reduction of induced astigmatism, and rapid restoration of functional vision, which have hitherto not been possible with the manual trephine systems. Femtosecond laser has been used to create customized Incisions with advanced edge profiles such as the

(a) Mushroom incision profile

(b) Top-hat incision profile

(c) Zig-zag incision profile

The mushroom-shaped incision preserves more host endothelium than the traditional trephine approach. The top-hat–shaped incision allows for the transplantation of large endothelial surfaces. The zig-zag–shaped incision provides a smooth transition between host and donor tissue and allows for a hermetic wound seal. These help to establish secure graft-host junctions which requiring less suture tension and hence lead to early suture removal and rehabilitation.

Intracorneal Ring Segments for Keratoectasia: Femtosecond laser is also being employed for the stromal lamellar tunnel dissection for insertion of the intracorneal ring segments for management of keratoconus. Channel creation using the femtosecond laser was compared with the conventional mechanical technique by Ramon Naranjo-Tackman [32] The femtosecond laser-assisted technique produced tighter channels with slightly better visual and refractive outcomes than the mechanical technique. Complication rates were similar for each technique. Efekan Coskunseven [33] also found that reducing the channel dimensions programmed into the Intralase resulted in tighter channels and greater postoperative effect.

Surgical Procedure

After alignment and fixation of the eye with low suction, the surgeon applanates the patient's cornea with a flat contact glass located at the tip of delivery system. when the laser beam is focused at the desired corneal depth, laser induced optical breakdown occurs at low energy without creating thermal or shockwave damage to the surrounding tissue.The spots are placed 5 to 12 μm apart; as the microcavitation bubbles expand, the spots coalesce, forming a resection plane. This process does not remove corneal tissue. After the horizontal cleavage plane is created, the pattern changes to vertical one, exiting through Bowman's layer and the epithelium. The computer software controls the attempted flap diameter and thickness, the angle of side cut, hinge size and location, and all the energy setting to create these dimensions.

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Retinal Implants: A Ray of Hope

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Macular degeneration and progressive retinal degeneration as in retinitis pigmentosa (RP) and RP-like dystrophies are the major causes of untreatable blindness.

Though considerable progress has been made in treating vitreoretinal disorders with modern surgical or pharmacological approaches but there are still some untreatable conditions which lead to blindness. It is estimated that worldwide 1.5 million individuals are affected by RP[1]. In both macular degeneration and retinitis pigmentosa, the photoreceptor cell layer of the inner retina (a.k.a. rods and cones) progressively degenerates. When these cells lose their function, the retina cannot convert light signals into electrical signals—causing a break in the visual chain.

A number of treatments have been tried, including immunostimulation[2], vitamin supplementation[3], oxygen therapy[4], scleral resection and combinations of these techniques and others[5, 6]. All these approaches have failed to show a benefit for patients in terms of improvement of visual acuity or visual field. As RP is caused by mutations in genes coding for key enzymes in the primary visual processes, gene therapy has been suggested as a therapeutic option. It has been shown that it is possible to transfer copies of these genes or growth factor encoding genes into retinal photoreceptors using different viral vectors[7]. These approaches have shown promising results but are also possibly associated with severe systemic complications[8]. Retinitis pigmentosa is caused by a variety of mutations so that the substitution of a single gene may not be effective in a large number of cases. Moreover, gene therapy may be useful in preventing the disease from progressing but may be less useful in very advanced cases of atrophy of the outer retinal layers.

To restore this function, research work in the late 1960's suggested that visual perception in blind subjects could be induced by electric stimulation of different levels of the visual system beyond the photoreceptors. . Brindley and his group implanted early cortical stimulators with which he obtained visual sensations in subjects blind from RP[9, 10]

While the concept of artificial vision may seem revolutionary and improbable, technological advances in computers, lasers and microelectronics make this a realistic probability.

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Retinal Implant

A retinal implant is a prosthetic retina, i.e. a manmade device designed to approximately do the job of the retina.

There are two kinds of retinal implants, subretinal and epiretinal.

Subretinal Implant

As the degenerative process in RP starts in the photoreceptors the ideal approach would be to simply replace the abnormal photoreceptors by technical elements such as very small photodiodes which can transform light energy into electrical power which can then be used to stimulate naturally the postsynaptic bipolar and horizontal cells in retina. This idea was followed by Alan Chow and co-workers in USA and Eberhart Zrenner and co-workers in Germany.[11,12] The main advantage of this approach is that the topography of incoming signals is more or less the original one. The implantation of subretinal device can be done either through a transvitreal approach (ab interno) after vitrectomy and retinotomy or through a transchoroidal route (ab externo). The energy released by currently available microphotodiodes is not enough to generate electrical power in the range sufficient to stimulate retinal neurons. Therefore, German researchers working on the subretinal prosthesis are developing a secondary system for an amplification of the incoming signal to provide enough energy for neuronal stimulation.[13](Figure 1)

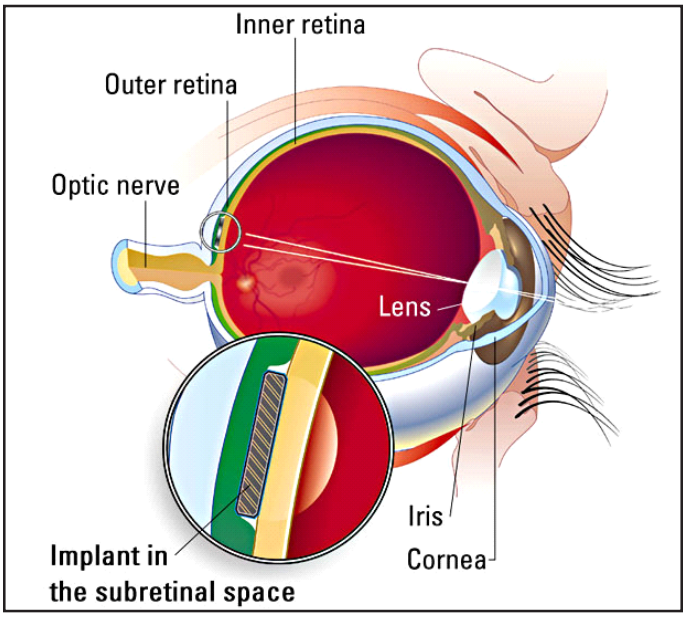


Fig.1: Subretinal Implant *(Source www.Google.com)*

Epiretinal Implant

In this a microelectrode array is fixed onto the retinal surface and the energy for the implant is provided by inductive or optoelectronic pathways.this method was described by Eugene deJuan and co-workers at Wilmers Eye Institute, Baltimore, by Joe Rizzo and co-workers at the MIT, Boston, and by Rolf Eckmiller and the German EPI-RET consortium, and was published as the epiretinal approach towards a retinal prosthesis.[14-16] In the epiretinal approach the scene is captured by a small camera and processed outside the retina before the ganglion cells are stimulated. The camera has to be integrated into the frame of normal spectacles. It can be fabricated as CMOS systems characterized by low energy consumption, small size and efficient on-chip signal processing.[17] The output from the camera is further processed by the retina encoder simulating properties of the target cells. The encoder not only transmits signal to the implant but also the necessary energy to drive the electric circuits of the device. Currently an electromagnetic inductive coupling with a primary and a secondary coil is being fabricated however, an optoelectronic solution which may provide higher data rates is also under construction. The implantation of epiretinal devices is more complex than subretinal implants because a fixation procedure has to be followed for implantation of the receiver part of the implant. Prior to the implantation core vitrectomy with endolaser of the prospective fixation area is done. Alternative is enzyme assisted vitrectomy using plasmin or tPA to separate the posterior vitreous from the retinal surface. It is mandatory that the stimulating electrodes are placed as close as possible to the ganglion cell layer because tissue or any material in between will reduce the effectivity of the stimulation.Further experiments are necessary to demonstrate the behaviour of the interface between the implant and retinal surface.[18-20](Figure 2)

The Subretinal Approach

- In the subretinal approach the retinal stimulator is placed underneath the retina.
- The stimulator consists of thousands of miniaturized photodiodes which transform light into electric power.
- Postsynaptic cells in the retina are the target for stimulation
- Image processing equipment or a camera is not necessary

The Epiretinal Approach

In the epiretinal approach the retinal stimulator is placed onto the retinal surface

- Ganglion cells are the target of epiretinal stimulator
- The image needs to be captured by an extraocular camera

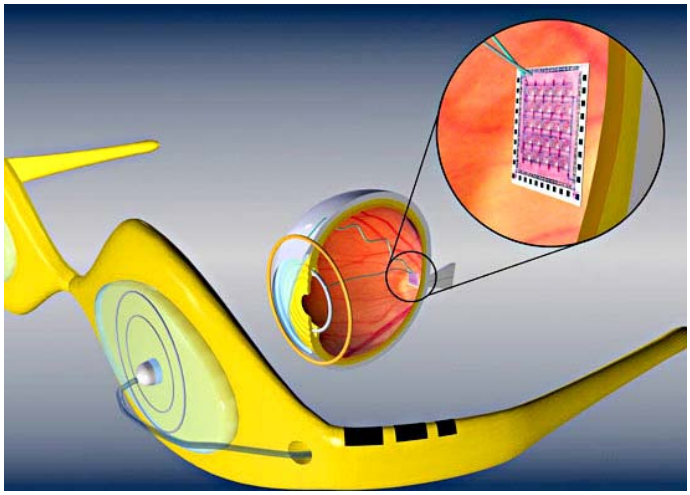


Fig.2: Epiretinal Implant *(Source www.Google.com)*

- The camera signal is further processed by a retinal encoder simulating normal retinal signal processing based on receptive field properties
- The information on the pattern of electrode activity is transmitted via radiofrequency into the eye
- Energy to drive the implant is transmitted via radiofrequency into the eye

Stimulation of retinal implant

Current prosthetic devices use electrical stimulation to excite the neural tissue of interest.Electrical stimulation though,easy to implement is not the most effective method of neural stimulation,Common problems with electrical stimulation include complex circuits, lack of focal stimulation, bio-toxicity and high power requirements.

A solar-powered chip can also be used to stimulate retinal cells by spraying them with neurotransmitters. Unlike other implants under development that apply an electric charge directly to retinal cells, the device does not cause the cells to heat up. It also uses very little power, so it does not need external batteries

The prototype actuator consists of a flexible silicon disc just 1.5 millimetres in diameter and 15 micrometres thick. When light hits a silicon solar cell next to the disc it produces a voltage. The solar cell is connected to a layer of piezoelectric material called lead zirconate titanate (PZT), which changes shape in response to the voltage, pushing down on the silicon disc.

There is some speculation as to whether solar cells can generate an electrical pulse strong enough to be picked up by the brain as an image. Optobionics says 10 years of study and animal trials lead them to believe the solar cells are sufficient. [21]

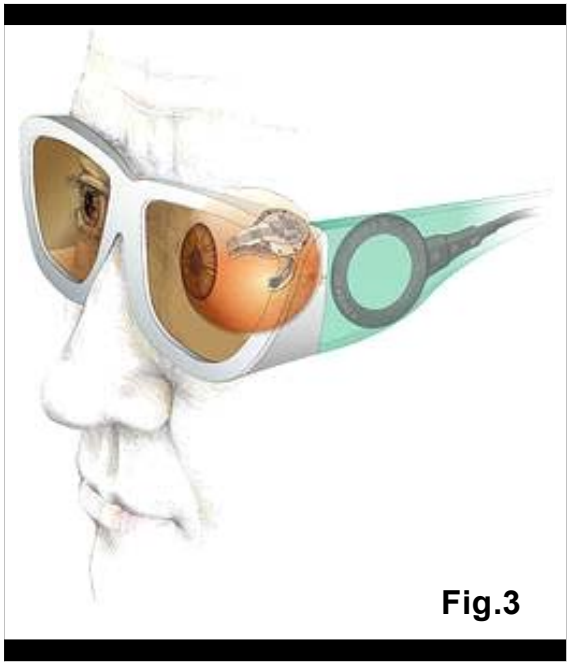
The experiments on Potassium based neural stimulation by Ralph Jensen and Luke Theogarajan on

rabbit retina has indicated that Potassium is a viable alternative to electrical stimulation for the development of retinal implants.

Biocompatibility of Implanted Materials

Polydimethylsiloxane (PDMS), which is also used as a standard material for the fabrication of intraocular lenses, proved to be non-toxic in the studies done for the biocompatibility of implanted material.[22]

The electrodes and wires in current implants are made of platinum and iridium whose electrical conductivity, durability, biological compatibility and oxidation resistance make them perfect for such a role.



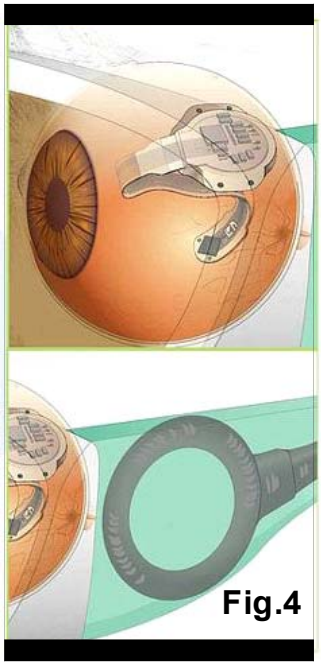


Fig.3: Spectacles containing integrated mini camera *(Source www.Google.com)*
Fig.4: IMI's system *(Source www.Google.com)*

Researchers have developed an ultrananocrystalline diamond (UNCD) film that is guaranteed to be safe, long-lasting, electrically insulating and extremely tough. The coating can also be applied at low temperatures that do not melt the chip's microscopic circuits.[23]

IMI's (Intelligent Medical Implants) Learning Retinal Implant System replaces the signal-processing functions of a healthy retina and provides input to the retinal nerve cells (the ganglion cells) that, in turn, provide input to the optic nerve and the brain.

The System comprises three main components

1. An implant, "The Retinal Stimulator", which is surgically placed into the eye of a patient, who:
2. Wears a pair of spectacles containing an integrated mini-camera and transmitter components for wireless signal and energy transmission ("The Visual Interface"). Via a cable, the spectacles are connected to:
3. "The Pocket Processor" worn at the patient's waist. This device replaces the information processing function of the formally healthy retina.

The use of a high-speed digital signal processor allows the provision of "intelligent information" to the implant (and the nerve cells) by using tuneable software to approximate the information processing normally carried out by the healthy retina. The entire process enables patients to optimize their visual perception during the learning phase. Indeed, using the patient's feedback on perception as an input for the tuning of The Pocket Processor is the unique, patent-protected feature of the System and constitutes the 'learning' capability of the Learning Retinal Implant System.

The system is being tested in patients with Retinitis Pigmentosa.(Figure 3,4)

Clinical Studies

Currently studies are performed with epiretinal implants using the *cochlea implant* approach for signal and energy transfer. In this approach an electrode array is positioned onto the retinal surface using retinal tacks. This array is connected to a cable entering the eye through the sclera with a receiver for signal and energy positioned subcutaneously[24]. The authors reported that in both subjects who were implanted visual perception could be obtained, that surgery was performed without any complications and that the implant was well tolerated. Experiments with subretinal implants were performed by Chow and his group. They found in patients with retinitis pigmentosa that subretinal implants survived for more than 2 years and that patients reported an increase in vision[25].

A retinal transplant is a graft of "good" retina tissue onto a non-working retina. The retinal transplant tissue might originate from another human, perhaps just deceased, or an aborted fetus. Less likely origins of the tissue to be transplanted are human retina tissue which has proliferated in culture; or retina tissue from another animal speciesA handful of laboratories are currently trying to develop retinal transplant technology, or are doing the research on which such technology might eventually be based. Ophthalmic surgeons are still at the stage of testing techniques for placing transplants in the retina. The hope

of some researchers is that if the transplant produces a 2-dimensional pattern of electrical signals in response to light, e.g. in the shape of an alphabetical character projected onto the transplant, the underlying retina which is not light-responsive will still be able to pick up the signal pattern from the transplant and transmit it to the brain.

In order for a retinal transplant to work, several technologies have to be developed:

1. The cells in the transplant must stay alive for a long time, preferably for the life of the recipient
2. Those cells must have, and maintain, the light-sensing activities of normal, healthy retina cells
3. Those cells must transmit electric or electrochemical signals to the brain, which the brain can interpret as the experience of vision.

The other area of investigation is development of a *cortical implant* for patients who would not benefit from a retinal implant. Such patients include those who have lost vision due to a number of conditions, including glaucoma, diabetic retinopathy or trauma to the eye. This prosthetic device will be implanted in the visual cortex of the brain, where sight is interpreted. It, too, will be an extraordinarily tiny device with its own microcomputer. With a cortical implant, information from a tiny digital camera possibly mounted on glasses, could be transmitted to electrodes implanted in the visual cortex, bypassing the non-working retina or optic nerve.

There is research to support this concept. Blind individuals who have received experimental stimulation of the visual cortex with electrodes have experienced localized images of light called "phosphenes." There is some evidence that the brain can learn to relate these different neural signal to previously learned physical and mental knowledge of the world. This would be similar to cochlear implants in the ear for the hearing impaired. These require a learning process for effective use.

While the cortical implant has the potential to help greater numbers of people than the retinal implant, it may require a longer investigation period since it involves implanting a device in the brain and because it has not been studied as much as the retinal implant. Both the retinal and cortical implants represent immense biological and technological challenges. While the substances used for both implants should be inert, meaning that they cannot be absorbed into the body, extensive testing will be necessary during and after their fabrication to make sure that they are safe and effective.[26,27]

Properties of ideal Retinal Implant

- Fully working implant
- Long-term biocompatiility
- Acceptable degree of improvement of ability to see
- Ability to move in space as with a healthy human eye
- Must e simple to implant
- Mustbe easy to deal with by the patient
- Good technical support as well as ongoing training of ophthalmic surgeons responsible for implanting .

Outlook and Perspectives

The last 10 years of visual prosthesis research has demonstrated that the interdisciplinary approach of combining engineering and medical know-how has an important contribution to make in a field where no treatment is available for blind patients. Several research groups have developed prototypes for retinal implants which will be evaluated in terms of safety and efficacy. The quality of vision or visual acuity or visual field properties will depend on a number of factors of the individual patient and not only of the technical implant. However, even if these implants will restore only minor visual functions.But in person with bare light perception,improvement to 20/400 vision could offer the means of getting around in unfamiliar places,recognizing human figures and accessing the public transportation.

A large number of open questions remain, the most important being the long-term stability and function of such a device, the biological behavior of the interface between the electrodes and the target tissue, and the target tissue itself. At present it is not known how in the retina such a coupling between a technical device and the retina itself will function over many years. These questions can only be answered by long term human clinical trials.

Retinal implants are showing promise as replacements for diseased photoreceptor cells, but the work is still in the earliest stages of experimentation and the results are still primitive, allowing the subject to see only areas of light and dark at this time. Still, the progress being made is significant, and probably the best hope so far of restoring at least a semblance of sight to the blind.

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Rebound Tonometry

Jatinder Bali MS, **Yogesh K Gupta** MD

The first prototypes of a rebound type tonometer were developed by Antti Kontiola in 1994. Antti Kontiola's original idea was to "develop a device that would enable IOP monitoring with special patient groups, such as children and demented patients, whose monitoring with existing instruments was nearly impossible" e.g. due to the requirement for absolute immobility. topical anesthetic use hampered monitoring significantly and limited the task to doctors only.

In this concept, an ultra-light probe is made to collide at a very low speed with the surface of the cornea. At this moment the device records the deceleration and motion of the probe during rebound in a time frame of a few microseconds very accurately.

In 1994-95 the first measurements were performed after the prototype was developed. Between 1998 and 2001 a joint development project with a university reseach center in New York, USA was followed by clinical tests.

In July, 2003 CE approval was granted to the commercial product and iCare® rebound tonometer for human medical use was launched. It did not require the use of topical anesthetic.

The device:

Tiolat's iCare® tonometer is a cell-phone sized, lightweight, portable, battery operated instrument. The measuring probe touches the eye so gently that it is barely perceptible. No topical anesthetic is required, making the iCare® even suitable for self-monitoring IOP at home. The instrument is designed to take and calculate the average of six measurements. Each measurement is taken in a fraction of a second. This reduces the influence of factors outside of the eye. The TonoLab is based on the newly patented induction-based-rebound-method which allows intraocular pressure (IOP) to be measured accurately, rapidly, and without using a local anesthetic. This handheld mobile tonometer has the latest IOP measurement technology for the screening of glaucoma. It has a new probe technology that prevents cross contamination. There is no risk of microbial contamination, as one-use probes are used in the measurement. The screening is fast, effective and reliable.

Hindu Rao Hospital,
Bara Hindu Rao,
Delhi

The rebound tonometer consists of a pair of coils coaxial with the probe shaft that are used to propel the lightweight magnetized probe toward the cornea and to sense its movement. Appropriate electronic components allow for the probe movement to be initiated by the solenoid coil and monitored by the sensing coil.

An applied pulse of electrical current induces a magnetic field within the solenoid, causing the probe to be propelled onto the cornea from where it rebounds. Motion parameters of the probe can be determined from movement of the magnetic probe, which generates a voltage in the sensing coil that is readily recorded and analyzed.

The voltage is proportional to the magnetic field induced, which is proportional to the probe speed. Several motion parameters of the probe can be extracted from the sensing coil oscilloscope record and related to the IOP, such as the time of eye contact, the velocity of return, and the deceleration time. The inverse of deceleration time (deceleration time-1) parameter is most closely correlated to IOP.

The probe consists of a magnetized steel wire shaft with a round plastic tip (1 mm diameter) at its front end. This round tip minimizes the possibility of corneal damage from probe impact. Although generally more accurate, lighter probes are more prone to influence by external unrelated magnetic fields, which makes their behavior less predictable.

For measurements the speed before impact is approximately 0.2 m/sec. The deceleration varies depending on the eye pressure.

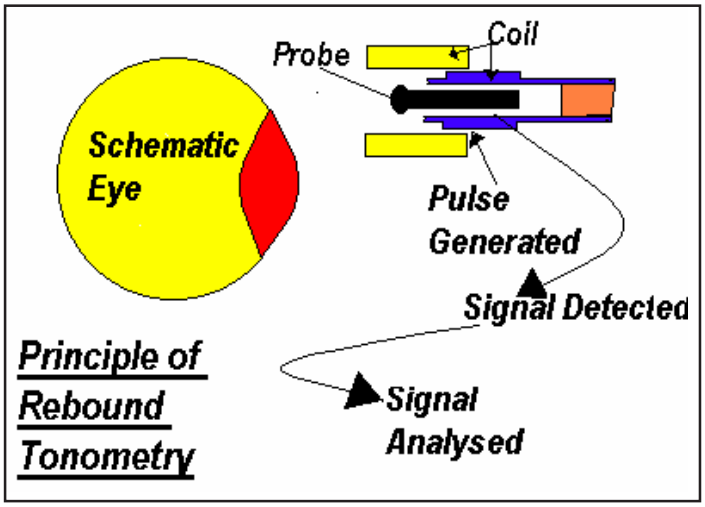
Caliberation

Device calibration was done on enucleated eyes which were cannulated with a 26-gauge needle at 90Â° to the visual axis with the aid of an operating microscope. Cyanoacrylate glue was used around the point of entry of the needle in the anterior chamber to prevent leakage of aqueous humor. IOP was controlled by adjusting the height of a variable column of balanced salt solution (BSS) attached to the cannula (open-stopcock method). IOP was verified and continuously recorded by a pressure transducer (Model TNF-R; Ohmeda, Louisville, CO) connected to the cannula, which was calibrated before eye cannulation by varying the height of the BSS column.

The starting distance of the probe from the corneal surface was approximately 2.4 mm. Only measurements that occurred within a narrow time window (5 ms) 12 ms

subsequent to triggering the tonometer probe were accepted for analysis.

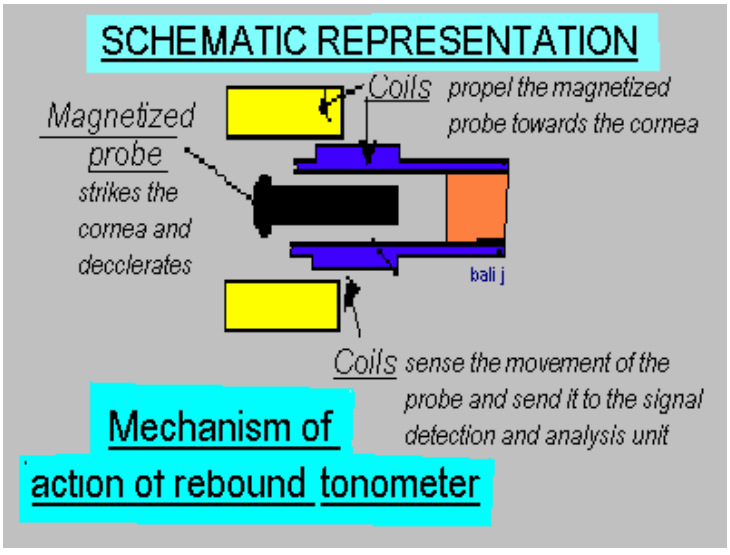
The ratio of probe speed immediately before impact over the deceleration during impact with the cornea was related to manometric (true) IOP. The method was based on impacting a very light probe to the eye at the very low speed (11-13mg, 0.1-0.2m/s) and measuring the motion parameters of the probe during collision to the eye (deceleration, impact time, etc,). The movement energy of the probe was very small (less than 0.25 J) and most of that was rebounded (not absorbed by the eye) so there was no damage to the eye. Several measurements could be made over a long period of time. It is closely related to the principle of vibration tonometry and the earlier Krakau tonometer. It has been applied recently for measuring IOP in large animal eyes ex vivo and clinically in humans.



The advantages of iCare® over existing instruments are its handy size, true portability (no power cords), patient and user-friendliness, and its accuracy. Measuring also does not require the use of topical anesthetics. Corneal thickness and hydration is expected to affect the I/I method of tonometry as it affects most of the other methods (applanation, Mackay-Marg tonometry, pneumatonometry).

Use of a mouse model for studies of glaucoma was more preferable in this calibration as it was easier and more economical to maintain mice than larger animals. Mice have similar eye physiology when compared to human eyes. However, the front chamber of a mouse eye contains only 2-4 l aqueous, making it a challenge to measure IOP.

First measurements were made in 1997 by cannulating the eye of an anesthetized mouse with a very small needle. This method required very deep anesthesia, which in turn, lowered the IOP.



A rebound tonometer device for mouse IOP measurement was adapted from different prototypes. The developed prototype was more accurate than the TonoPen in measuring the IOP of rats. In addition, the goal of measuring IOP from the mouse eye was successful and the prototype was able to measure IOP accurately in vitro and in vivo.

A commercial version of the rebound tonometer is now available. It allows rapid IOP measurements instantly displayed in mm of mercury. The tonometer requires no calibration and features species-specific modes also. The risk of microbiological cross contamination has been eliminated with a single use probe. The time needed from induction to the results of dependable consistent readings is minimal. However, today it is still more of a research tool than an office one. But the advantages offered by the technique make it an appropriate one for large-scale exploitation in office practice. The rebound tonometer readings have been reported to correlate well with goldmann applanation tonometer (GAT) in recent studies. It has been found to be more accurate than the tonopen. Coupled with the advantage of minimal contact and avoidance of anaesthetic use it may be an extremely useful instrument in clinical practice. It can be used in children and even restless patients, as the instrument does not require absolute stillness as for the previous techniques.

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Pascal® Dynamic Contour Tonometry

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Glaucoma is characterized by progressive atrophy of the optic nerve head leading to irreversible loss of vision. Measurement of precise intraocular pressure (IOP) is important for work-up of any glaucoma patient. All the clinical tonometers measure the IOP by relating a deformation of the globe to the force responsible for deformation.

The two basic tonometers are the indentation and applanation tonometers. The shape of deformation by indentation tonometer is a truncated cone. It displaces a large volume of intraocular fluid and measurements are influenced by ocular rigidity, blood volume alterations, corneal biomechanics and Moses effect.

Applanation tonometer produce a simple flattening. It measures the force required to applanate a standard area of corneal surface. The prototype is Goldmann applanation tonometer (GAT) which was introduced in 1954.

The Goldmann applanation tonometer (GAT) is based on the Imbert Fick law which states that an external force (F) against a sphere equals the pressure in the sphere (P) times the area flattened (applanated) by the external force (A) (Fig.1).

$$F = P \times A$$

The validity of the law requires that the sphere be perfectly spherical, dry, flexible and infinitely thin.

The mathematical calculations are based on the presumed average central corneal thickness. Corneal thickness due to edema causes underestimation of IOP whereas in normal corneas, higher pressures are obtained in thicker corneas and lower pressures are obtained in thinner corneas.

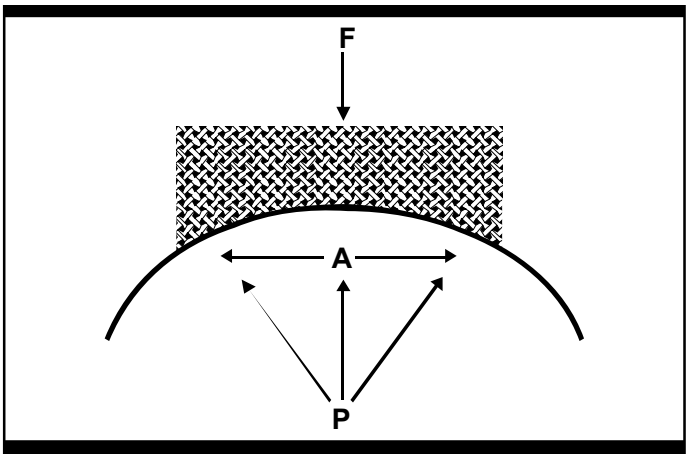

Fig.1: Principle of Applanation Tonometry.

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Ehlers[1] et al published a table in which the average error is 0.7mm of Hg for 10µ of deviation from the mean of 520µ.

Tonopen is a hand-held Mackay-Marg type tonometer which has a strain gauge that creates an electrical signal as the footplate flattens the cornea. A built-in single chip microprocessor senses the proper force curves and averages 4-10 readings to give a final digital readout.

Even the Tonopen has shown to be influenced by CCT with errors of 0.29mm of Hg per 10µ in men and 0.12mm of Hg per 10µ in women[2].

In LASIK patients besides alteration of corneal thickness, there is alteration of corneal rigidity. Patel and Aslanides proposed that the increase in proteoglycans and hyaluronic acid that occurs after excimer laser photoablation causes accumulation of water in stroma which affects corneal rigidity which leads to underestimation of IOP[3]. The association between myopia and chronic open angle glaucoma has been supported by large population based surveys[4,5].

By underestimating IOP in post refractive surgery patients one can miss out on potential glaucoma suspects.

Corneal curvature has also been shown to influence IOP measurements by GAT. There is increase in IOP by 1mm Hg for every 3D increase in corneal power[6].

Irregular corneas distorts the semicircles and interferes with the accuracy of IOP estimates[7].

To circumvent the systematic errors introduced in 'non-standard eyes' the concept of dynamic contour tonometry (OCT) has come up. PASCAL® Dynamic contour tonometer, engineered and manufactured by SMT Swiss Ophthalmic Systems Group Company is marketed by Ziemer Ophthalmic Systems.

The PASCAL® DCT is a digital tonometer that provides direct transcorneal measurement of intraocular pressure and is sensitive enough to detect the ocular pulse amplitude (OPA) due to the patient's heart beat.

PASCAL® DCT is slit lamp mounted (Fig.2). It is a contour tonometry. It makes use of pressure sensors which are accurate and stable devices for measuring the IOP non-invasively. The contour matched tonometer tip has a concave surface which allows the cornea to assume the

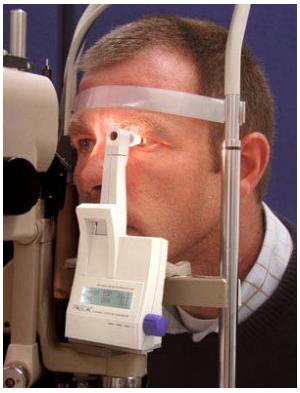

Fig. 2: Slit Lamp mounted Pascal OCT.

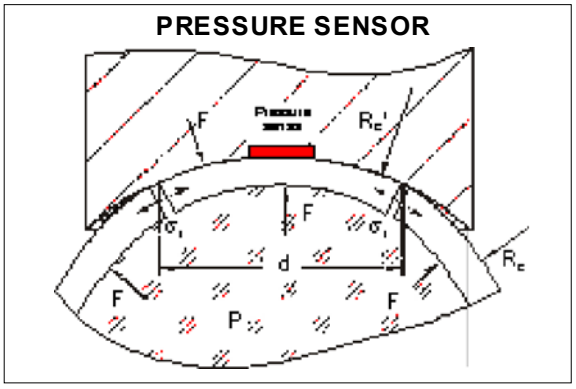

Fig.3: Principle of Contour tonometry.

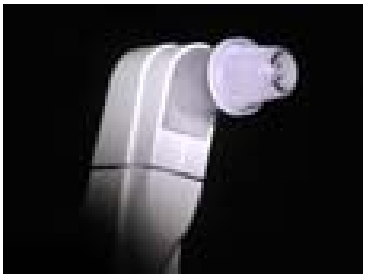

Fig.4: Disposable tip.

Fig.5: LCD

shape which it naturally takes up when pressure on both sides of the cornea are equal and hence no net bending forces are acting on the cornea (Fig. 3).

Contour matching is independent of contact diameter and appositional force. It converts the detected pressure digitally into a numeric result with 12-bit (1/1000mmHg) numerical precision. The results are free from operator bias.

It is easier and faster than conventional tonometers. There is no need for additional pachymetry and conversion of the tonometer estimate.

Pascal sensor cap disposable tip covers are convenient and easy to use (Fig 4). The tip is touched on the eye for a few seconds, the result is read from illuminated LCD.(Fig.5).

Ocular haemodynamics causes lOP to fluctuate, at the patient's cardiac rate, by several mmHg (typically 3mm of Hg, but often upto 9 mmHg). From static lOP measurement, it is not possible to know exactly on pulse pressure curve as to when the measurement was taken.

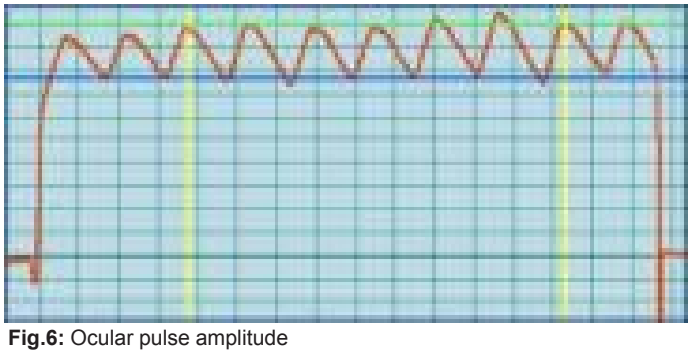

Fig.6: Ocular pulse amplitude

Pascal records the inter pressure curve with a time resolution of 100 data points per second hence captures the full dynamics of lOP (Fig.6). There is a positive correlation between lOP and OP A and negative correlation with Axial length.

Siganos et al compared PDCT with Non contact tonometer(NCT) and GAT. They found that NCT is fairly accurate in 'normal' range of lOP, less accurate in eyes with high lOP and poor fixation. In contrast to PDCT, GAT and NCT tended to underestimate lOP in all patients after LASIK. This could be caused not only by the change in corneal thickness, but most likely by a change in corneal rigidity after LASIK. A decrease in corneal rigidity would facilitate corneal applanation and explain in part, the drop in GAT and NCT readings after LASIK[8].

In conclusion, Pascal tonometry is a precise, contour, and dynamic tonometry which has been introduced with the idea to overcome the factors related to corneal thickness and biomechanics.

More clinical documentation is required for assessing its actual usefulness in diagnosis and follow up of glaucoma patients.

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