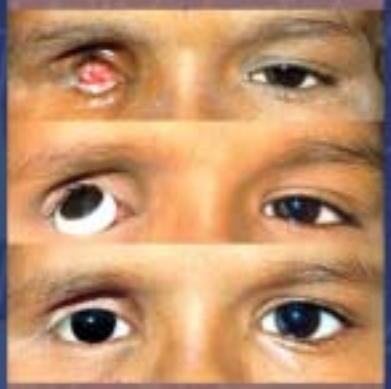

# DR. G. VENKATASWAMY EYE RESEARCH INSTITUTE

Aravind Medical Research Foundation

# REPORT 2008-09

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## Aravind Medical Research Foundation

# REPORT 2008-09

*The Meenakshi temple was not started and finished by one ruler. It was a work of love and faith and vision that spanned a whole succession of rulers and several generations. And yet it has maintained its integrity. Hundreds of years since its beginning it draws more and more barefoot pilgrims with each passing year. Temples are not built for individuals or by individuals. They are created for all humanity by a band of skilled and dedicated workers. And the result is a living, timeless gift to the world. And it can be the same with institutions . . .*

DR. G. VENKATASWAMY EYE RESEARCH INSTITUTE
Aravind Medical Research Foundation

## MISSION

*To eliminate needless blindness by providing evidence through research and evolving methods to translate existing evidence and knowledge into effective action*

# INTRODUCTION

The inauguration of the Dr.G.Venkataswamy Eye Research Institute on 1st October 2008 by Dr.A.P.J. Abdul Kalam, Former President of India, is a major landmark event in the annals of Aravind Eye Care System. This integral institute will have the state-of-the-art infrastructural facility to understand the basic biological mechanisms of eye diseases at Genome, Transcriptome, Proteome, Cytome and Histome levels apart from the clinical and research activities of the various components of Aravind Eye Care System – Aravind Eye Hospitals, Aravind Medical Research Foundation, Lions Aravind Institute of Community Ophthalmology and Aurolab.

The new research building houses an advanced facility with GLP compliance for translational research for utilization of adult stem cells in vision-related illness. The advances in the laboratory have been translated into clinical benefits with our achievements in the transplantation of tissue-engineered buccal epithelial stem cells for reconstruction of corneal surface and socket.

The department of Ocular Pharmacology created during this year has been involved in the development of newer drugs and understanding the Pharmokinetics/Pharmaco dynamics of drugs meant for ocular use. Aravind Eye Hospital has been recognised as a centre of National Retinoblastoma Registry by Indian Council of Medical Research. In this context, a major study on Molecular Biology of Retinoblastoma has been initiated to understand the mechanism of chemo-resistance by using in vitro models. Newer surgical initiatives and instrumentation have been incorporated to facilitate the results of research into actual clinical practice.

Aravind Eye Care System is a recognized centre for Diabetic Retinopathy by TIFAC-CORE, Department of Science and Technology, Government of India. Following our definitive finding that diabetic retinopathy is an inflammatory disease, our present studies carried out in collaboration with University of Belfast indicate the importance of RAGE (Receptor for advanced glycation end product) in modulating the expression of inflammatory cytokines and Vascular Endothelial Growth Factor in human retinal pigment epithelial cells. In this context, we have observed significant association of single nucleotide polymorphism in RAGE gene in diabetic retinopathy patients.

Other highlights during this year were the identification of the causative agents (Eye fluke) in the formation of anterior chamber granuloma and the demonstration of molecular mimicry between leptospiral and human lens proteins in the rapid maturation of cataract in leptospiral uveitis patients.

The Indian eye research group (IERG) meeting was conducted at our institution from July 26 – 27, 2008. While the Bireswar Chakrabarti memorial oration was given by Dr. Anant Swaroop, Dr. Fielding Hejtmancik of National Eye Institute gave the inaugural Dr.G.Venkataswamy memorial oration .

We continue to be driven by our quest to reduce needless blindness and we believe that this new institution, which will integrate the basic and clinical research will aid in achieving this mission.

# CONTENTS

# BASIC RESEARCH

## Molecular genetic analysis of corneal endothelial dystrophies

Principal Investigator : P. Sundaresan, Aravind Medical Research Foundation (AMRF) - Madurai
Co-Investigators : M. Srinivasan, Aravind - Madurai
J. Arun Kumar, Aravind - Madurai
Research Scholar : B. Hemadevi
Funded by : Department of Science and Technology
Duration : 2007 - 2010

Congenital Hereditary Endothelial Dystrophy (CHED) and Fuchs Endothelial Corneal Dystrophy (FECD) are categorised under the corneal endothelial dystrophies, affecting corneal transparency and refraction, leading to visual impairment and blindness. FECD is usually a sporadic condition but familial forms showing autosomal dominant inheritance are also recognised. COL8A2 which encodes the alpha-2 chain of type VIII collagen was identified as a candidate gene for FECD.

Objective is to screen for mutations in COL8A2 gene in Fuchs' Endothelial Corneal Dystrophy (FECD). Eighty patients with Fuchs' dystrophy and hundred normal individuals were recruited for the study. Genomic DNA was isolated from peripheral blood leukocytes. Mutations in COL8A2 coding regions were screened using Polymerase Chain Reaction, SSCP analysis and Bi-directional sequencing. RFLP analysis was used to identify the previously reported mutations in COL8A2 in association with FECD.

Screening of COL8A2 gene revealed the previously identified pathogenic mutation Arg155Gln (c.464G>A). Two novel polymorphisms, Asn548Ser, Asp537Asn and the two reported silent variations Gly495Gly, Ala35Ala were also identified. However all the variations identified in the gene were also present in unaffected controls.

This is probably the first study analysing COL8A2 gene in Indian patients having FECD. Ala35Ala and Gly495Gly, which are synonymous substitutions, showed statistically significant association with FECD. However the previously reported mutations (Leu450Trp, Arg304Gln, Arg434His, and Gln455Lys) presumed to play a pathogenic role in cases of FECD were not identified and no other pathogenic mutations were identified in COL8A2, suggesting that it may not be the cause for defect in the FECD patients examined in this study.

## Identification of genetic defects occurring in Indian oculocutaneous (OCA) and ocular albinism (OA) families

Principal Investigator : P. Sundaresan, AMRF - Madurai
Co-Investigators : P. Vijayalakshmi, Aravind - Madurai
Asim Kumar Sil, Vivekananda Mission Ashram Netra Niramay Niketan, West Bengal
Research Scholar : K. Renugadevi
Funded by : Department of Biotechnology, New Delhi
Duration : 2006 - 2009

Albinism is a congenital hypopigmentary disorder characterised by partial or total lack of melanin pigment. Albinism results from inheritance of recessive alleles. The most significant clinical problem in human albinism is the loss of visual acuity associated with deficient melanin pigment in the developing eye and optic system. Patients with albinism have vision impairment; the retina does not develop correctly if melanin pigment is not present during eye development. There are two main categories of albinism in humans: In Oculocutaneous Albinism (OCA) pigment is lacking in the eyes, skin, and hair; in Ocular Albinism (OA) only the eyes lack pigment. People who have OA generally show normal skin and hair color, and many even have a normal eye appearance.

The objective of this study is to screen for mutations in all the known genes (TYR, P, TYRP1, MATP and GPR 143). Thirty five albinism patients from twenty three families with positive history of albinism were recruited and their DNA samples were analysed by bi-directional sequencing for the exonic regions of the known candidate genes using ABI 3130 genetic analyser. Among the 35 samples, one reported mutation R239W in TYR gene and one novel mutation G485R in OCA 2 (P gene) were identified (Presented in Asia ARVO-2009). Seventy five samples from sporadic cases of albinism will be screened for the same candidate genes in future studies.

Albinism patient sample

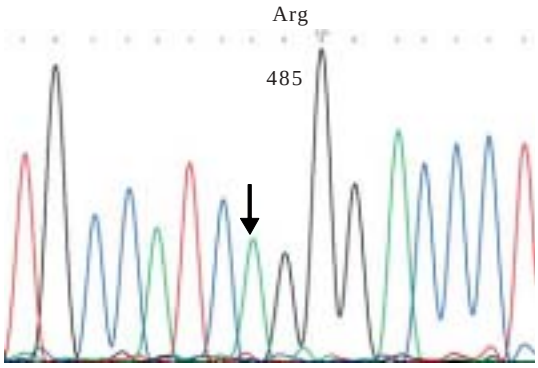



*Fig- A. Shows the chromatogram of OCA patient showing the mutated sequence at codon 485 in P gene*

Control sample

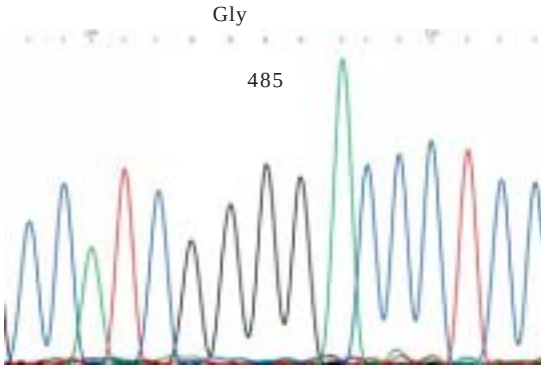



*Fig- B. Chromatogram of control individual showing normal sequence at same position*

## Association studies on diabetic retinopathy with type 2 diabetes in South Indian population

| | | |
|---|---|---|
| Principal Investigator | : | P. Sundaresan, AMRF - Madurai |
| Co-Investigators | : | P. Namperumalsamy, Aravind - Madurai<br>R. Kim, Aravind - Madurai<br>Anand Rajendran, Aravind - Madurai |
| Collaborator | : | J. Fielding Hejtmancik, NEI / NIH, Bethesda, USA. |
| Research Scholar | : | B. Suganthalakshmi |
| Funded by | : | TIFAC-CORE in DR, CSIR & NIH Visiting Fellowship, National Institute of Health, Bethesda, Maryland, USA. |

Diabetes is one of the most common non-communicable diseases globally. Diabetic retinopathy is the prevalent cause of blindness worldwide. This microvascular complication of the retina due to hyperglycemia, displays a remarkable complexity in its pathogenesis due to the interplay of genetic, environmental and biochemical factors, resulting in mild non-proliferative diabetic retinopathy or severe sight threatening proliferative diabetic retinopathy. Genetic factors have been reported to influence the pathogenicity of diabetic retinopathy in various ethnic groups worldwide. However, detailed investigation pertaining to Indian population is limited.

Hence, this study proposes to investigate the association of various candidate genes and look into its association with diabetic retinopathy in South Indian cohort. The candidate genes reported to be associated with Diabetic Retinopathy in different ethnic groups were selected for the present study.

Ten candidate genes (RAGE, PEDF, ALR2, IGF, CFH, ARMS2, EPO, HTRA1, ICAM and HFE) coupled with different biochemical pathways, hypoxia and oxidative stress mechanisms descriptive to diabetic retinopathy were chosen for the study. The possibility of association between polymorphisms of ten candidate genes and diabetic retinopathy was examined by genotyping 13 single nucleotide

polymorphisms and two dinucleotide repeat polymorphism in 211 diabetic patients with retinopathy and 237 diabetic patients without retinopathy for more than 15 years. The alleles and genotypes were evaluated using the following techniques: Direct sequencing, sequencing using M13 labeled primer by ABI3100 genetic analyser, TaqMan SNP genotyping assay using ABI 7900HT Fast Real-Time PCR System (Figure1) and SNaPshot PCR by ABI3130xl genetic analyzer (Figure2). Statistical analysis was performed to analyse the genotype and allele frequencies by Exemplar program.

Among 15 polymorphisms, one SNP rs2070600 in RAGE gene, which leads to a change of amino acid Gly82Ser showed significant association with diabetic retinopathy, when compared with diabetes without retinopathy (ASIA-ARVO 2009). The other SNPs did not show significant association with diabetic retinopathy in our population. A Gly82Ser polymorphism in RAGE is potentially interesting since it occurs at a predicted N-linked glycosylation motif in the AGE binding site, thereby influencing the AGE-RAGE interactions. Therefore, our results suggest that SNP rs2070600 in RAGE gene may play a role in the development of retinopathy in diabetes in the South Indian population.

SNaP shot PCR analysis for RAGE, ICAM and HFE gene polymorphisms

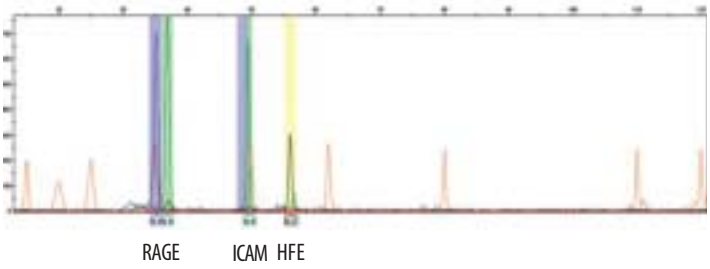



*Figure 1*

Taq Man SNP Geneotype assay for EPO gene polymorphisms

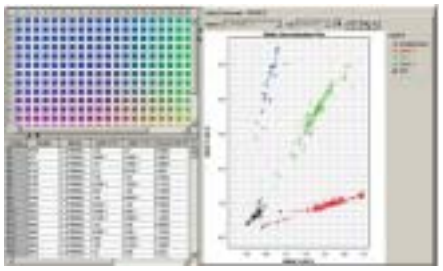


*Figure 2*

## Genetic study on congenital hereditary cataract

| | | |
|---|---|---|
| Principal Investigator | : | P. Sundaresan, AMRF - Madurai |
| Co-Investigator | : | P. Vijayalakshmi, Aravind - Madurai |
| Research Scholar | : | Ramya Devi and Amala Rajasundari |
| Funded by | : | Aravind Medical Research Foundation, India |
| Duration | : | 2005 - 2008 |

Paediatric cataract is the most common and major eye abnormality that constitutes 12% of the child-hood blindness and 50% were due to genetic causes. Systematic screening of candidate genes such as Crystallin and connexin for mutation followed by genome wide scanning in a large panel of samples collected from South Indian families with inherited cataract were carried out. We found 7 novel mutations (3 - crystallins; 4 – connexin). We had also reported for the first time, association of human cataracts with a gene change in the BFSP1 gene through linkage analysis where we found the deletion of exon6 entirely. (Ramya et al., Published in Hum Genet, 2007).

Totally 34 loci have been mapped to associate with cataracts, of them more than 20 have been associated with mutations in specific genes. Half the mutations have been reported in crystallins, about quarter in connexins and remaining has been split between genes for aquaporuin AQPO, LIM2, HS and BFSPF2. As the previous study has screened for crystallins and connexins in the patients with family history, the present study aims to screen for the other candidate genes such as aquaporin (AQP0) and Lim2 which are the second major membrane intrinsic protein of lens.

## A genetic component to the INDEYE study of cataract in India

Aravind Medical Research Foundation in collaboration with AIIMS, New Delhi and London School of Hygiene and Tropical Medicine

| | | |
|---|---|---|
| Principal Investigator | : | Astrid Fletcher, London School of Hygiene & Tropical Medicine, London |
| Co-Investigators | : | D. Nitsch, L Smeeth<br>London School of Hygiene & Tropical Medicine, London<br>R.D. Ravindran, Aravind - Pondicherry<br>P. Sundaresan, AMRF - Madurai |
| Research Scholar | : | Ashwini Shanker |
| Junior Technicians | : | V. Saravanan, J. Radha, G. Hema Meenakshi |
| Funded | : | Wellcome Trust |
| Duration | : | 2008 - 2010 |

### Aims of the project

- To investigate genetic variants as possible contributors to high rates of cataract in India, complementing the ongoing research on environmental factors being undertaken in the INDEYE study.
- To enrich the samples acquired in the INDEYE study of environmental factors for cataract in India with cases from the same geographical location in order to achieve adequate power needed to test for disease associations in genetic studies.
- To build local capacity for high throughput genotyping in Madurai, TamilNadu.

### Progress on the INDEYE genetic study

- Out of 6000 samples, we have extracted 3988 DNA samples (2588 from North India and 1400 samples from South India).
- Allelic discrimination assays were performed for 140 INDEYE feasibility study samples to determine mutant vs. wild type for the C-Reactive Protein gene. Three SNPs were found to have homozygous and heterozygous mutations (T/G, G/A, C/T).
- Sequencing aquaporin gene for 25 samples (12- north and 13- south) is being done. Based on the results, we will be able to derive adequate tagging of SNPs for high throughput genotyping.
- High throughput genotyping for 40 tagging SNPs will be done for the four genes of interest - galactokinase, aquaporin, C-reactive protein, and complement Factor H using Real Time PCR.

## Molecular genetics of leber congenital amaurosis in South Indian population

| | | |
|---|---|---|
| Principal Investigator | : | P. Sundaresan, AMRF - Madurai |
| Co- Investigator | : | P. Vijayalakshmi, Aravind - Madurai |
| Research Scholar | : | Anshuman Verma |
| Funded By | : | UGC CSIR (Fellowship) |
| Duration | : | 2008 – 2010 |

Leber congenital amaurosis (LCA) is the most severe form of retinal dystrophy. People with the LCA condition are born with severe visual impairment or develop vision loss early in childhood usually before the age of 1 year. It is a rare disorder with occurrence of 2 to 3 per 100,000 live births but it accounts for 5% of all inherited retinal dystrophies and 20% of children attending school for the blindness mainly in Europe. LCA is clinically and genetically heterogeneous disorder. Clinically it is characterised by features like sensory nystagmus, amaurrotic pupils, high refractive error and absence of electroretinogram (ERG) responses.

So far 14 candidate genes have been identified, mutation in which accounts for approximately 70% of all LCA cases, the candidate genes for LCA can be grouped in five functional categories (A) Phototransduction - (AIPL1, GUCY2D) (B) Retinoid cycle (RDH12, LRAT, RPE65) (C) Photoreceptor development and structure (CRX, CRB1) (D) Transport across the photoreceptor connecting cilium

(TULP1, RPGRIP1, CEP290, Lebercilin) (E) Miscellaneous (IMPDH1, MERTK, RD3). The proposed researches involve the population-based studies focusing on the molecular genetics of LCA susceptible genes, and identification and analysis of candidate genes and perform a genotype and phenotype analysis.

Currently we are targeting CRX gene mutation screening in 45 LCA samples using PCR, SSCP and sequencing analysis. The conditions for these techniques have been optimised. Such study will help in clinical and molecular characterisation of Indian cohort of patients affected with LCA. The study will devise a general approach to study inherited heterogeneous eye disorders and is an essential step in the development of possible effective therapy (Gene therapy).

## Screening of LOXL1 gene mutations in exfoliation glaucoma patients

| | | |
|---|---|---|
| Principal Investigator | : | P. Sundaresan, AMRF - Madurai |
| Co-Investigators | : | S.R. Krishnadas, Aravind - Madurai |
| | | G. Haripriya, Aravind - Madurai |
| | | R. Sharmila, Aravind - Madurai |
| Research Scholar | : | Sushil Kumar Dubey |
| Funded by | : | ALCON Anterior Segment Research Grant |
| Duration | : | 2008 - 2011 |

Glaucoma is the second most common cause of blindness world-wide. The disease is clinically and genetically heterogeneous characterised by optic nerve damage usually associated with a high intra-ocular pressure. Exfoliation syndrome (XFS) is an age-related disorder of the extracellular matrix characterised by the rapid production and progressive accumulation of abnormal microfibrillar material on the aqueous bathed surfaces of the anterior segment of the eye. The average world wide prevalence of XFS is 10%-20% of the general population over the age of 60 yrs. XFS is most common identifiable cause of open angle glaucoma which is due to accumulation of exfoliative material.

A recent genome-wide association study in the Icelandic population identified multiple SNPs in the lysyl oxidase like-1 (LOXL1) gene on chromosome 15q24.1 to be significantly associated with XFS and XFG. The three SNPs are, allele T of rs2165241 in the first intron and allele G of rs1048661 (R141L) and allele G of rs3825942 (G153D) in exon 1 of LOXL1.

The objective of the study is to screen LOXL1 gene mutations in Indian patients with exfoliation syndrome (XFS) and exfoliation glaucoma (XFG). DNA samples of 30 XFS and 140 for XFG patients have been collected. Studies are underway to screen for the LOXL1 SNPs through restriction fragment length polymorphism and through bi-directional sequencing using ABI 3130 genetic analyser. Identification of genetic markers may allow early detection of individuals at risk of glaucoma and prevention of needless blindness from glaucomatous optic nerve damage.

## Biophysical characterisation of human myocilin and its deletion mutants

| | | |
|---|---|---|
| Principal Investigator | : | S. Krishnaswamy, Madurai Kamaraj University - Madurai |
| Co-Investigators | : | P. Sundaresan, AMRF - Madurai |
| | | S.R. Krishnadas, Aravind - Madurai |
| Research Scholars | : | Prasanthi Namburi, Eswari P, Rangachari K |
| Funded by | : | Department of Biotechnology, New Delhi |
| Duration | : | 2006 - 2009 |

Trabecular meshwork (TM), a specialised tissue located at the anterior chamber angle of the eye, is believed to be responsible for the development of glaucoma. *Myoc* gene is directly linked to both juvenile and primary open-angle glaucomas and encodes myocilin, a secreted glycoprotein. Myocilin (55 kDa mol wt, 504 aa, Swissprot Q99972) is localised both intracellularly and extracellularly at multiple sites and may exert diverse biological functions. Therefore, it is proposed to characterise the human myocilin protein.

Based on a model of myocilin built by us, four regions (N-term, coiled coil, hinge and C-term) have been identified (Kanagavalli et al, 2003). Constructs with the deletion of these individual regions

and in combinations have been made, over expressed in Rosetta (DE3) pLysS and purified in order to study the structural features of myocilin and structural functions of individual domains. C6H-Myoc has been characterised using spectroscopic and light scattering studies and the results suggest the presence of beta sheet region and the tendency to aggregate.

### Aggregation studies by using DLS (Dynamic Light Scattering) data

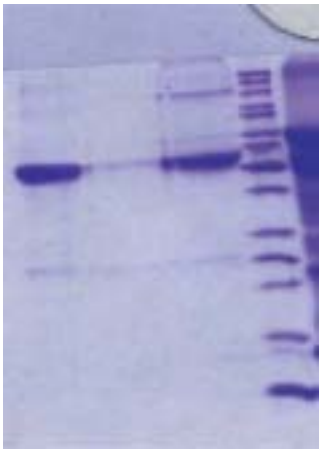
Table 1:DLS data of dimer population at 1mg/ml concentration of C6H-Myoc

| PK | %Area | Rh (nm) | Position | Std Dev | %RSD | MW (kD) |
|---|---|---|---|---|---|---|
| 1 | 76.9 | 4.64 | 4.37 | 0.42 | 9.1 | 124.59 |
| 2 | 23.1 | 2252 | 18.62 | 9.84 | 437 | 5196.52 |

Table 2:DLS data of dimer population at 0.5mg/ml concentration of C6H-Myoc

| PK | %Area | Rh (nm) | Position | Std Dev | %RSD | MW (kD) |
|---|---|---|---|---|---|---|
| 1 | 91.0 | 3.57 | 3.55 | 0.20 | 5.7 | 67.06 |
| 2 | 9.0 | 25.42 | 22.91 | 4.37 | 17.2 | 6914.42 |

Fig: Dimer formation of C6H- Myoc on SDS PAGE




*Boiling the sample in presence of SDS disturbs dimer formation*

C-term deleted myocilin (CTD-Myoc) has been subjected to gel filtration and shows that it dimerises. Future studies involve the aggregation and crystallographic characterisation of the C6H-Myoc and the deletion mutants.

## Molecular genetics of keratoconus

Principal Investigator : P. Sundaresan, AMRF - Madurai
Co-Investigators : M. Srinivasan, Aravind - Madurai
N.V. Prajna, Aravind - Madurai
Research Scholar : P. Mohanapriya
Funded by : ALCON - Anterior Segment Research Grant
Duration : 2008 - 2011

Keratoconus is a bilateral, non-inflammatory, chronic, and asymmetric thinning of the cornea. Keratoconus reported in most cases are sporadic and 6% to 23.5% of the cases had a positive family history. In familial keratoconus, the inheritance pattern is autosomal dominant with incomplete penetrance and variable expressivity. The significant clinical problem in keratoconus is the loss of visual acuity, leads to progressive myopic and irregular astigmatism. It leads to steepening and distortion of cornea, also thinning of apical cornea and corneal scarring. Genome wide linkage analysis of affected patients has

shown evidence of disease susceptibility genes, mapping to several putative chromosome loci, including 16q22.3-q23.1, 20q12, 21q22, 15q22.23-q24.2, and 5q14.3-q21.1 and 2p24. Though keratoconus is a genetically complex disease, two genes were so far reported to be involved in the pathogenesis for keratoconus.

The objective of the study is to screen for the mutations in VSX 1 (20q12) and SOD1 (21q22) in 100 keratoconus patients. In addition we are also looking for other candidate genes responsible for keratoconus. The mutational change will be identified through bi-directional sequencing using ABI 3130 genetic analyser. These studies will provide further insight for the genetic basis of keratoconus.

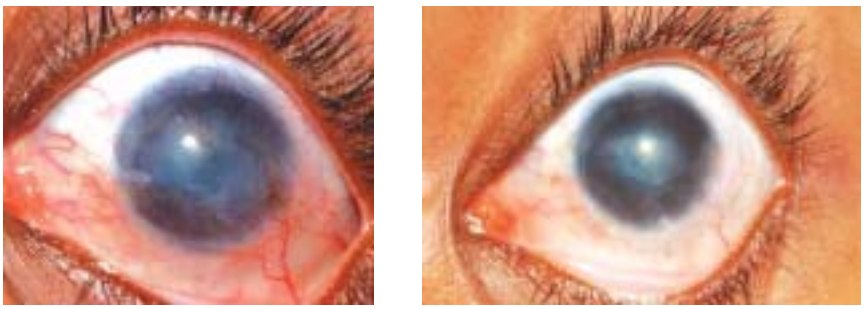
## Corneal surface reconstruction using cultured human limbal epithelial cells

| | | |
|---|---|---|
| Principal Investigator | : | VR. Muthukkaruppan, AMRF - Madurai |
| Co-Investigators | : | M. Srinivasan, Aravind - Madurai |
| | | N. Venkatesh Prajna, Aravind - Madurai |
| | | Gowri Priya Chidambaranathan, AMRF - Madurai |
| Research Scholar | : | P. Prabhu |
| Funded by | : | National Association for Blind (NAB) |

The objective of this study is to culture autologous limbal biopsy from unilateral stem cell deficient patients and to transplant such *ex vivo* generated epithelial sheet for reconstruction of the corneal surface.

Limbal biopsies were obtained from 12 patients with unilateral stem cell deficiency due to grade IV chemical injury. The limbal epithelium was expanded as explant cultures for 12-15 days. Analysis of the cultured epithelial cells revealed a ten-fold increase in the total number of limbal epithelial stem cells by two parameter analysis (p63 and N/C ratio). After transplantation of such *ex vivo* expanded epithelium, the patients were followed up for a maximum of 15 months. Success of transplantation was defined as anatomical (clear cornea, reduction in blood vessels and conjunctivalisation) and/or visual success (improvement of at least three lines in Snellen's visual acuity measurement). Visual improvement was observed in four patients and anatomical success in six patients.

### Clinical appearance before and after transplantation of *ex vivo* expanded autologous limbal epithelial stem cells



*Pre-OP (Vn-1/60)* *One year post-OP (Vn-6/9)*

*The above pictures show that the best corrected visual acuity has improved by more than 3 lines at the last follow-up visit. Post operatively, the corneal surface showed complete epithelialisation with no peripheral vascularisation*

## Characterisation of corneal epithelial stem cells

| | | |
|---|---|---|
| Investigators | : | VR. Muthukkaruppan, AMRF - Madurai |
| | | Gowri Priya Chidambaranathan, AMRF - Madurai |
| Fulbright fellow | : | Paul Phelps |
| Funded by | : | Fulbright Program |
| Duration | : | 2008 - 2009 |

Paul Phelps is fourth year medical student at Drexel University College of Medicine who was awarded a nine month Fulbright Fellowship to conduct medical research at AMRF. The goal of Paul's project is to determine p63 isoform expression patterns of human limbal epithelial stem cells. Our earlier studies have shown that two-parameter analysis, based on mean amplitude of p63 and nucleus to cytoplasm ratio, can identity stem cells. There are three isoforms of p63-÷ Np63∇, η and ν and among them ÷Np63∇, is highly expressed in limbal stem cells. In order to understand the functional roles of these isoforms in relation to stem cells identified on the basis of two-parameter analysis, *in situ* Hybridisation (ISH) with specific non-isotopic RNA probes will be carried out.

To date, Paul has prepared the RNA probe specific for the alpha isoform of p63 using RNA isolated from limbal tissue. His future plans include creating riboprobes for the other isoforms of p63. ISH will be carried for all the isoforms of p63 along with two parameter analysis.

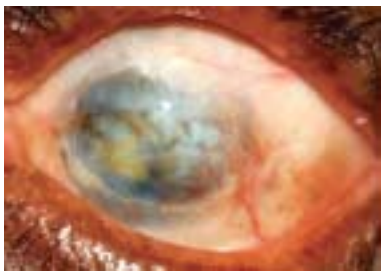
## Identification, characterisation and quantification of human buccal epithelial stem cells for corneal surface reconstruction

| | | |
|---|---|---|
| Principal Investigator | : | VR. Muthukkaruppan, AMRF - Madurai |
| Co-Investigators | : | N. Venkatesh Prajna, Aravind - Madurai<br>Gowri Priya Chidambaranathan, AMRF - Madurai<br>Usha Kim, Aravind - Madurai |
| Research Scholar | : | S. Vaishali |
| Duration | : | 2006 - 2009 |
| Funded by | : | Defence Research and Development Organisation (DRDO) |

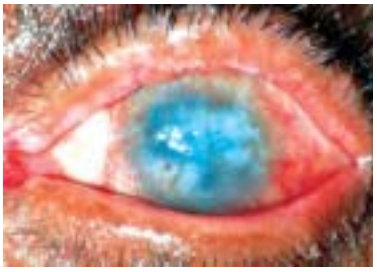
In patients with bilateral limbal stem cell deficiency, autologous buccal mucosal epithelium forms an alternative source for corneal surface reconstruction. The objectives of the current study are to characterise the cellular profile of this alternative source, to determine the presence of stem cells in bio-engineered epithelium and to study the clinical outcome after transplantation.

*Close up view of the face from a 65 year old male with chemical injury (Grade IV), corneal opacities, vision restricted to hand movement*

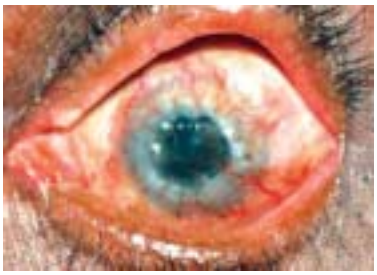
Confocal analysis of buccal epithelial cells identified a distinct population of small cells (5%) expressing high levels of p63 with greater N/C ratio. These cells were negative for Cx43, positive for melanoma-associated chondroitin sulfate



*View of the left eye showing corneal opacity with vascularisation and no distinct limbal area*



*View of the left eye, three months after transplantation of bio-engineered buccal epithelial sheet. Superficial vessels are limited to the periphery and limbal barrier is established: however, vision has not improved*



*View of the left eye, 6 months after penetrating keratoplasty (PK) showing both anatomical and visual improvement from hand movement to 6/60*

proteoglycan (MCSP) and they showed the ability to form holoclones with the colony forming efficiency of 0.2%. Thus, the method of identifying buccal epithelial stem cells on the basis of two parameters (p63 and N/C ratio) confirms our earlier observations in limbal epithelium (Arpitha *et al.*, 2005;2008).

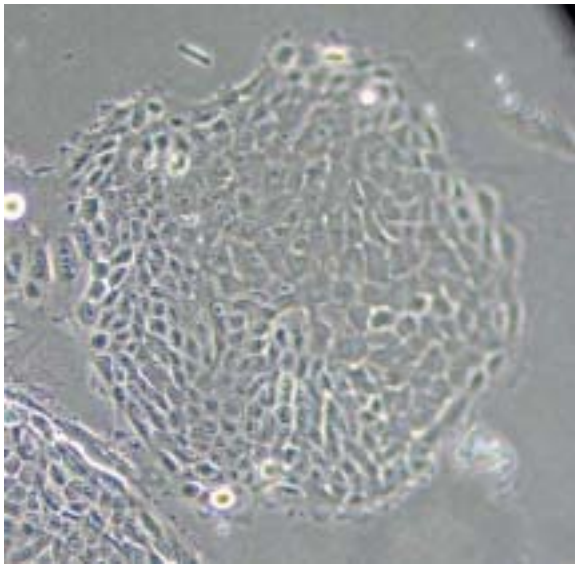
The isolated buccal epithelial cells when cultured for 15 - 20 days on human amniotic membrane with 3T3 as feeder layer showed a five fold increase in the total number of stem cells. Such *ex vivo* expanded buccal epithelium was transplanted to six patients with bilateral LSCD due to chemical injury (Grade IV). In two cases, the limbal barrier was established and PKP was carried out at 3-4 months. Eight months after PKP, there was no vascularisation over cornea and the vessels were limited to the limbus with the visual improvement from hand movement to 6/60 (Figure). Thus the transplantation of such bio-engineered autologous buccal epithelium under xenobiotic free condition, followed by PKP is a strategy for reconstruction of the corneal surface in bilateral LSCD.

## Developing xenobiotic-free culture conditions to generate stem-cell rich epithelium for corneal surface reconstruction

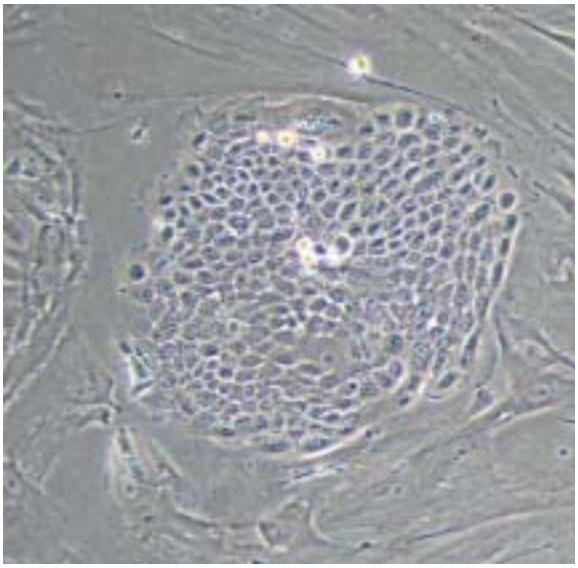
| | | |
|---|---|---|
| Investigators | : | Gowri Priya Chidambaranathan, AMRF - Madurai<br>VR. Muthukkaruppan, AMRF - Madurai<br>N. Venkatesh Prajna, Aravind - Madurai<br>Usha Kim, Aravind - Madurai |
| Research Scholars | : | Vaishali, Prabhu |
| Duration | : | 2008 - 2011 |
| Funded By | : | ALCON Anterior Segment Research Grant<br>Champalimaud - Aravind Research Grant |

The most commonly used method for corneal surface reconstruction involves *in vitro* expansion of stem cells with the use of a growth-arrested murine (3T3) fibroblast feeder layer and Fetal Bovine Serum (FBS) supplemented culture medium. With growing concerns regarding the potential transmission of adventitious agents such as prions and animal viruses, this study aims to culture cells for human transplantation under xenobiotic-free conditions, while preserving the proliferative potential and stem cell characteristics and to validate the new culture condition by quantifying the stem cell content on the basis of two parameter analysis established earlier (IOVS, 2005; Cornea, 2008) or by using other putative stem cell markers.

Holoclone in 3T3 fibroblast



Holoclone in human limbal fibroblast



*The picture shows the buccal epithelial stem cell-derived holoclone colony in the presence of feeder layer*

In this regard, we are now developing a culture condition devoid of cholera toxin and FBS, components of microbial/animal origin. Optimal culture conditions with high proportion of stem cells are selected on the basis of the method of identifying and quantifying stem cells using two parameter (high expression of p63 and greater N/C ratio) analysis as well as on the basis of clonal analysis. To achieve the objective we have developed human limbal fibroblast cell line which has been shown to support the growth of stem cells similar to the murine fibroblasts (Figure). Studies are underway to identify a substratum for culturing the epithelial cells and media components like growth factors that are associated with stemness of stem cells. Thus establishment of a better method will facilitate *ex vivo* expansion of stem cells under conditions of good laboratory practices (GLP) for transplantation/clinical application.

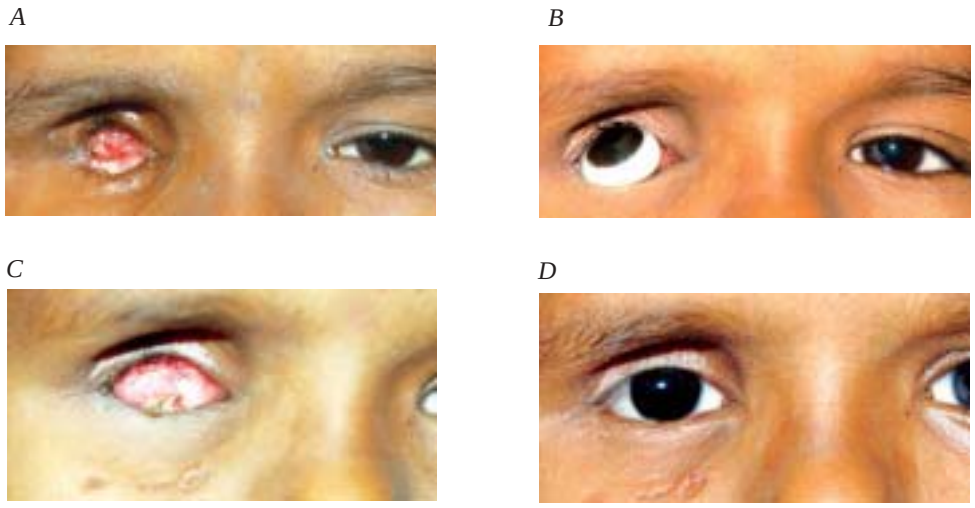
## Socket reconstruction using bio-engineered autologous oral mucosal epithelium


Principal Investigator : Usha Kim, Aravind - Madurai
Co-Investigators : Gowri Priya Chidambaranathan, AMRF - Madurai
VR. Muthukkaruppan, AMRF - Madurai


A contracted socket, an aesthetic concern, poses a major management challenge for the ophthalmologist as well as the patients who may undergo multiple reconstructive surgeries and may still be unable to retain a cosmetically acceptable ocular prosthesis. This is due to extensive loss of conjunctival surface area, deep cicatrix formation, atrophy of the orbital fat, and fornix contraction.

Successful reconstruction of the contracted socket requires a stable fornix with adequate depth by increasing the surface area with the use of grafts. Several graft materials, such as dermis-fat, oral mucous membrane, and nasal mucosal grafts have been previously described for use in socket reconstruction. While all these grafts may be adequate in cases with less severe contracture or single forniceal involvement, it is sometimes difficult to obtain sufficient graft material to recreate both the palpebral and bulbar surfaces of both upper and lower fornices.

The use of a cultured mucous membrane in socket reconstruction may be an alternative approach to reconstruction of severely contracted fornices to enable retention of an ocular prosthesis. For this, autologous buccal mucosal tissues of 4-5mm$^2$ were obtained from eight patients with contracted socket. The buccal biopsies were cut into 2mm pieces and cultured as explants containing buccal epithelium along with stroma. After culturing for 15-20 days in DMEM: Ham's F12 medium containing 10% autologous serum, insulin, EGF and amphotericin, the epithelial sheet of 35mm diameter along with




*The patient in figure A had undergone multiple socket reconstructive surgeries using the known methods in right eye. However, she failed to retain prosthesis (Figure B). The same eye (Figure C) six weeks after transplantation of cultured buccal epithelium shows adequate surface lining and fornices. At 6th month of observation, custom fit prosthesis is well retained as in Figure D*

buccal tissue was transferred onto human amniotic membrane and used for transplantation. Under general anesthesia, the cultured epithelium on amniotic membrane was sutured to the host conjunctiva. The patient underwent custom prosthetic fitting 6 weeks after the surgery. Of the 8 patients, 6 retained the prosthesis for 6 months and the patients are being followed further. Thus the use of bioengineered autologous buccal mucosal epithelium is a good alternative method for socket reconstruction in patients with contracted socket.

## Cytokine profile in aqueous humor of parasitic granuloma

Principal Investigator : Gowri Priya Chidambaranathan, AMRF - Madurai
Co-Investigators : SR. Rathinam, Aravind - Madurai
VR. Muthukkaruppan, AMRF - Madurai
Duration : 2008 - 2011
Funded by : ALCON Anterior Segment Research Grant

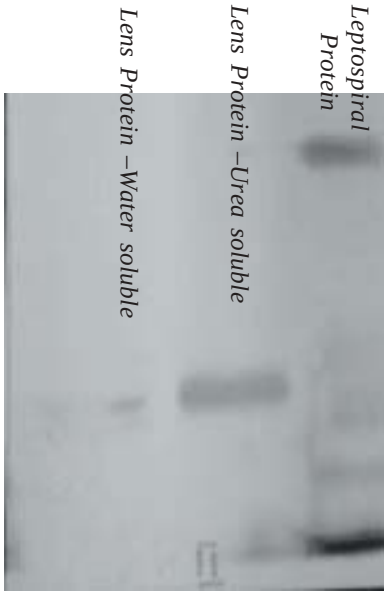
Granulomatous anterior uveitis caused by a water-borne trematode accounts for one third of the paediatric uveitis cases. These patients were exposed to village pond or river water in various districts of Tamil Nadu and Kerala. Uveitis due to a trematode infection was identified by the presence of a tegument of trematode in the granuloma (Am. J. Ophthalmol, 2002). In order to understand the associated pathogenesis, the current study aims to study the profile of infiltrating cells and cytokines in the anterior chamber (AC) fluid. In this project aqueous humor and serum samples have been collected from 13 patients clinically diagnosed as trematode-induced granulomatous uveitis. Analysis of AC fluid by Giemsa staining revealed the presence of eosinophils indicating parasitic infection, along with predominant infiltration of neutrophils and lymphocytes in these patients. Further, to confirm the aetiology in patients and to establish the aetiology in relation to the environmental source, cercaria released by snails collected from village ponds by patients will be analysed by PCR along with patient's sample (AC granuloma/sub-conjunctival scleral nodule/AC fluid) in collaboration with Dr. Veena Tandon, North Eastern Hill University, Shillong.


*Pictures of a snail (A) collected by a trematode infected patient from his village pond and the cercaria (B) released by the snail on exposure to light in the laboratory*

## Antigenic mimicry between leptospiral and human lens proteins

Principal Investigator : Gowri Priya Chidambaranathan, AMRF - Madurai
Co-Investigators : SR. Rathinam, Aravind - Madurai
VR. Muthukkaruppan, AMRF - Madurai
Duration : 2008 - 2011
Funded by : ALCON Anterior Segment Research Grant

Rapid maturation of cataract in young patients is one of the important anterior segment findings in leptospiral uveitis. Antigenic mimicry between leptospiral proteins and ocular antigens (equine cornea




*Western blot analysis of human lens proteins and leptospiral proteins using sera from a leptospiral uveitis patient*

and lens) has been suggested as a possible cause for recurrent uveitis in horses. Hence the objectives of this study are to identify cross-reacting proteins between leptospiral and human lens antigens by *in-silico* analysis and to experimentally confirm the antigenic mimicry between leptospiral and human lens proteins. For this study, aqueous humor and serum samples were collected after getting informed consent from 8 leptospiral uveitis patients without cataract, 20 leptospiral uveitis patients with cataract, 8 non-leptospiral uveitis patients and 10 age related cataract patients.

Our studies indicate the presence of cross-reactive proteins in human lens (21kDa) and leptospira (36kDa) on the basis of Western blot analysis using leptospiral uveitis patient's sera (Figure). Absorption of serum by lens protein followed by Western blot analysis showed a reduction in the intensity of the 36 kDa protein. Control sera (non-leptospiral uveitis and cataract) did not detect these proteins. Further studies are being carried out to confirm the nature of cross reactivity between these proteins by peptide analysis using LC-MS/MS. *In silico* analysis will also be performed to identify additional cross reacting proteins.

## Pathogen host interactions in mycotic keratitis

| | | |
|---|---|---|
| Principal Investigator | : | N. Venkatesh Prajna, Aravind - Madurai |
| Co – Investigator | : | K. Dharmalingam, Madurai Kamaraj University, Madurai |
| | | S. Lalitha, Aravind - Madurai |
| Research Scholar | : | S. Ananthi |
| | | P. Narmatha Devi |
| Funded by | : | Department of Biotechnology, New Delhi |
| Duration | : | 2007 - 2009 |

Infectious keratitis is a major public health problem worldwide. In India and other developing countries, fungi are the most common causes of infectious keratitis. However, not much is known about the nature of inflammatory response associated with this disease. In order to understand the pathogenesis of this condition, we will be using a proteomics approach involving profiling of control and infected tear samples. The objectives of our study are:

1. Examination of the proteome of a selected fungal pathogen and its comparison with the lab strain.
2. Examination of virulence factors particularly toxins of selected pathogens.
3. Study of host response to the fungal invasion in various stages of the disease by;
    a. Characterisation of cytokines by ELISA
    b. Characterisation of tear proteome.

In order to study the differential expression, the first step was to optimise solubilisation and other parameters for proteome analysis of tear sample. Towards this, tear samples were collected from healthy individuals and subjected to three different precipitation methods, Trichloroacetic acid (TCA), TCA/acetone, Deoxycholate and Ultrafiltration and Albumin depletion.

Two-dimensional (2D) electrophoresis was used for separation of fractionated tear proteins and subjected to Nanoscale LC – Nanospray Tandem Mass spectrometry and MALDI TOF based detection of selected protein spots from the gels (1D or 2D).

## Secretome of a clinical isolates of *A.flavus*

*A. flavus clinical isolate 40h*


*IEF* : *18cm, pH 4-7, Active Rehydration, VHS- 71081*
*2nd Dimension* : *12% gel*
*Staining* : *Glutaraldehyde Silver*

Ultrafiltration and TCA precipitation resulted in more number of protein spots compared to TCA/acetone, Deoxycholate and Albumin depletion. Further, in tear samples, precipitation with TCA and ultrafiltration results in efficient sample concentration and desalting for proteomic analysis. In addition, we have shown that the inclusion of a wetting agent to the rehydration solution, markedly improves the quality of 2D gels.

The differential expression of tear protein profile was seen in fungal keratitis patients and controls. Glutaredoxin related protein is a fungal protein and it was present only in infected patients and absent in controls. (Molecular Vision 2008; 14:500-507).

Corneal scraping was collected from fungal keratitis patients and cultured on potato dextrose agar to isolate *A.flavus*. Clinical isolates were grown in solid state fermentation conditions and extra cellular proteins were extracted at different times (30 hours and 40 hours) and separated by 2D electrophoresis. Proteins that showed differential expressions were identified using LC- MS/MS.

Difference in the expression of proteins at 30 and 40 hours of solid state fermentation was observed. We found that 40 hours of culture yields more number of extracellular proteins. Many known proteins, such as alkaline proteins, glucoamylase, taka amylase, endo-1,4-alpha-glucosidase, alpha-L-arabinofuranosid, serine/threonine protein kinase, pyrroline-5-carboxylate reductase, oryzin precursor, cellobiohydrolase C, enoyl reductase and xylanase were identified as shown in the figure.

### Further studies

1. To examine the virulence factors particularly toxins
2. To understand the pathogenesis of fungal keratitis in the late stage, we are using the fungal keratitis infected corneal button for proteomic studies.

## Proteomic profiling of serum in proliferative diabetic retinopathy

Investigators : VR. Muthukkaruppan, AMRF - Madurai
K. Dharmalingam, Madurai Kamaraj University, Madurai
R. Kim, Aravind - Madurai
Research Scholar : M. Valar Nila
Funded by : TIFAC-CORE in Diabetic Retinopathy

Diabetic retinopathy is the most frequent microvascular complication in the retina and the leading cause of blindness. There are diabetic patients (Type II) who do not develop retinopathy even for 15 years. However, some diabetic patients develop retinopathy much earlier. Therefore, the purpose of this study is to elucidate the serum protein profile of these two populations of diabetic patients, using promising proteomic approaches, with the hope of identifying a marker for retinopathy.

Serum samples from eleven Proliferative Diabetic Retinopathy (PDR) patients and eleven diabetic patients without retinopathy for 5-10 years were collected and used for proteomic analysis. All patients were subjected to eye and blood examination.

Neat or Albumin depleted Sera (using biorad, aurum serum kit) was analysed using SDS-PAGE and 2D Gel Electrophoresis. The protein spots were excised and digested overnight using trypsin and dried to obtain peptides. Tryptic peptides were analysed using Liquid Chromatography; Tandem mass Spectrometry (LC-MS/MS – Dionex nano LC Ultimate 3000 – Bruker MicroTof Q MS) or MALDI-TOF (Schimadzu). Further, proteins were identified using MASCOT (matrix science) search engine.

The protein profiling of the PDR serum differed from that of diabetic patients without Retinopathy (Fig-1). Among the identified proteins, Ceruloplasmin, Alpha-1B-glycoprotein precursor, Serotransferrin precursor, Ig mu chain C region, Isocitrate dehydrogenase, Apolipoprotein A-IV precursor, Haptoglobin precursor, Haptoglobin ∇2 chains were upregulated in PDR serum. Alpha-trypsin chain 1; Alpha-trypsin chain 2, Heamoglobin ∇ and η chain were downregulated. 1-alpha-1-antitrypsin did not show any difference. Interestingly, Haptoglobin ∇2 chain - isofrom ∇2M, is significantly upregulated in PDR (Fig-2). Further experiments are in progress to confirm this result and to identify additional proteins that could be useful as biomarker.

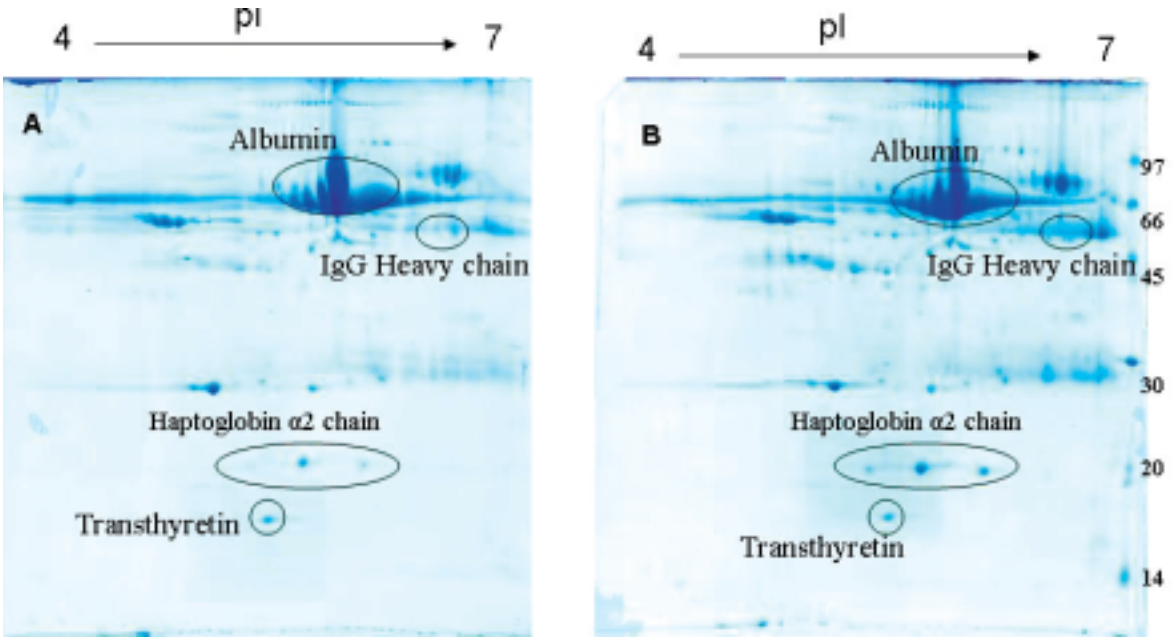



*Figure 1: 2D protein profile of serum sample*
*(A) Diabetes without Retinopathy (B) Proliferative Diabetic Retinopathy*

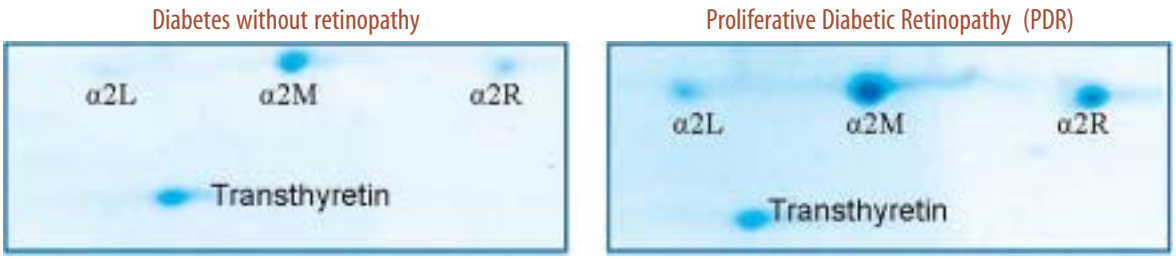



*Figure 2: Coomassie stained 2D gels (Partial view) showing Haptoglobin isoforms.*
*Spot 2L, 2M and 2R indicate Haptoglobin a2 chain isoforms, upregulated in PDR. This is reproducible in eight cases of each group*

## Identification of biomarkers for primary open angle glaucoma

Principal Investigator : Dr. S.R. Krishnadas, Aravind - Madurai
Co-Investigators : Dr. P. Sundaresan, AMRF - Madurai
Prof. K. Dharmalingam- Madurai Kamaraj University, Madurai
US Collaborator : Dr. John W Crabb, Cole Eye Institute, Cleveland, USA
Funding Agency : Department of Biotechnology, New Delhi

Development of routine diagnostic technology for use in clinical medicine to predict POAG susceptibility and to monitor therapeutic efficacy. The long term objective of the proposed research is the development of routine diagnostic technology for use in clinical medicine to predict POAG susceptibility, essentially as serum cholesterol measurements are used today for risk management for cardiovascular disease. A pilot project is proposed with the following specific aims.

1. Test the hypothesis that oxidative protein modifications from hydoxynonenal, iso[4] levuglandin2 and/ or argpyrimidine are elevated in POAG plasma and provide diagnostic biomarkers of POAG. Preliminary results show that these adducts are abundant in POAG trabecular meshwork. ELISA will be used in a case control study to probe plasma for these protein adducts as diagnostic biomarkers for POAG. We will determine whether such immunological measurements may be useful indicators for POAG therapeutic efficacies and / or POAG susceptibility.
2. To test the hypothesis that plasma mass spectrometric peptidomic patterns provide diagnostic biomarkers for POAG and examine the qualitative (post translational modifications) and quantitative changes in the plasma and serum of the study groups using MALDI TOF and ESI MS/MS approaches. Quantitative proteomics approach will utilise DIGE technology as well. High resolution MALDI TOF/TOF and QTOF mass spectrometry will be used to screen POAG and control plasma and serum for proteome and peptidomic changes. Analysis of post translation modification will be employed as an alternative approach to detect diagnostic biomarker in primary open angle glaucoma.

It is hypothesised that the biomarkers exist in blood of the individuals susceptible to developing POAG that will allow identification of those at risk prior to clinical evidence of the disease. It is expected to identify optimised POAG plasma peptide signature and, with the availability of MALDI TOF TOF MS/MS and QTOF MS/MS, we expect to determine the sequence of the peptides in the patterns. We expect optimised signature to be composed of relatively small number of peptides (<20). Optimised peptides signature will be identified through retrospective analysis in which plasma donors will be substratified with regard to POAG family relatedness, visual field mean deviation, associated diseases, medical therapies and other ocular treatment. To eliminate possible interference from demographic, statistically significant number of gender and age merged healthy control will be analysed in the major ethnic groups available to our clinics. In the long term, as optimised peptide signatures are identified for the “definite POAG” donors, we will select (i.e., predict) patients from the less severe disease categories based on peptide profiles to follow for the development of definite POAG. Additional plasma samples will also be obtained from patients undergoing treatments for POAG and peptidomic analysis performed to evaluate the impact of treatments on the peptide profiles. We expect this process to continue beyond the two year grant period and ultimately, to validate the clinical utility of POAG peptide biomarkers for predicting susceptibility and monitoring therapeutics. This pilot project will attempt to minimise the impact of confounding factors by selecting test samples from donors without significant confounding issues.

## Evaluation of a suitable in vitro model for diabetic retinopathy

Principal Investigator : S. Senthilkumari, AMRF - Madurai
Source of Funding : Champalimaud Research Grant
Duration : 2008 - 2009

Diabetic retinopathy is an important cause of blindness and it is estimated that approximately 2% of people become blind and about 10% develop severe visual impairment after 15 years of diabetes. Recently, there is mounting evidence suggesting that functional and structural changes in the retinal pigment epithelium (RPE) occur in experimental and clinical diabetes. It is also the site of advanced glycosylation end product formation, growth factor expression, and accelerated apoptosis. In the recent years, it is observed that targeting polyol pathway (Aldose reductase enzyme (AR) system) for preventing or delaying the progression of microvascular complications is a possibility in treating diabetic retinopathy. It is proposed that the aldose reductase is getting upregulated when the RPE cell is cultured under high glucose or galactose *in vitro*. Therefore, the object of the present proposal is to evaluate a suitable *in vitro* model for diabetic retinopathy using ARPE-19 – a spontaneous human retinal pigment epithelial cell line. This could provide a suitable *in vitro* model for examining the biochemical changes associated with the polyol pathway.

Objective is to characterise ARPE-19 cell line under high glucose culture condition and to evaluate AR inhibitors for diabetic retinopathy. Primary RPE culture from cadaver donor has been established in our laboratory (Murugeswari et al, 2008).

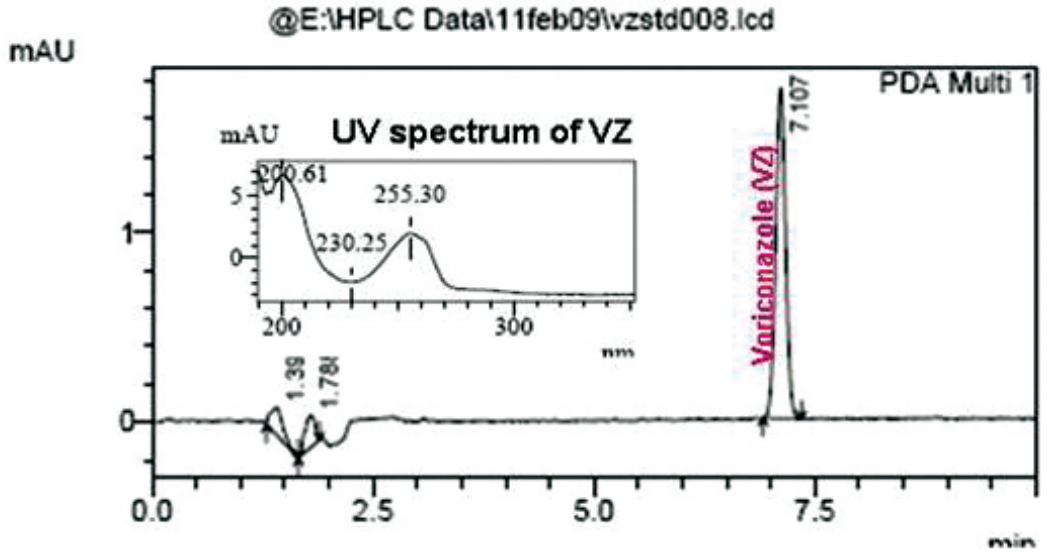
ARPE-19 cell line purchased from ATCC is established. Work is in progress to characterise the cell line using epithelial markers as well as RPE specific makers.

## Topical kinetics of voriconazole (1% and 0.1%) in humans

| | | |
|---|---|---|
| Principal Investigator | : | S. Senthilkumari, AMRF - Madurai |
| Co-Investigators | : | N. Venkatesh Prajna, Aravind - Madurai |
| | | Lalitha Prajna, Aravind - Madurai |
| | | Haripriya Aravind, Aravind - Madurai |
| Source of Funding | : | Champalimaud Research Grant |
| Duration | : | One year (January 2009 – 2010) |

Fungal keratitis is a leading ocular morbidity which may be caused by ocular trauma with the involvement of organic matter. New generation triazoles have been introduced in treating fungal infections due to the limited number of broad spectrum antifungal agents, emergence of resistance and its poor tissue penetration. Voriconazole is a new triazole anti-fungal agent with the broadest spectrum of activity against *aspergillus species, blastomyces dermatitidis, candida species, paecilomyces lilacinus, coccidioides immitis, cryptococcus neoformans, histoplasma capsulatum, penicillium species, scedosporium species, curvularia* species and others *in vitro*. Topical voriconazole instilled every 2 hrs (multidosing) reaches

Chromatogram showing the separation of standard voriconazole



sufficient concentration in aqueous as well as vitreous humor in inflammed and non-inflammed eyes. However, the topical kinetics following single instillation has not been studied yet.

Therefore in the present study, it is proposed to elucidate the topical kinetics of voriconazole following single drop in patients undergoing cataract surgery at different time intervals. A highly sensitive "High Performance Liquid Chromatograhy (HPLC) method is optimised with both photo-diode array detector and fluorescence detector for measuring the voriconazole concentration in the aqueous humour samples from patients. This information would be crucial for us in deciding the dosing regimen for effective management of fungal infection in sight saving attempts. Schimadzu Prominence HPLC system with quaternary pump, autosampler and PDA detector was used.

## Standardisation and application of multiplex PCR as a rapid diagnostic test for the detection of infectious agent in the intraocular fluids of clinically suspected retinochroiditis patients

| | | |
|---|---|---|
| Principal Investigator | : | Lalitha Prajna, Aravind - Madurai |
| Co-Investigators | : | Rathinam Sivakumar, Aravind - Madurai |
| | | Kim Ramasamy, Aravind - Madurai |
| Research Scholar | : | Lalan Kumar Arya |
| Funding Agency | : | ICMR |
| Duration | : | 2006 - 2009 |

### Introduction

Retinochoroiditis is the inflammation of the retina and choroid, it may be due to many factors including various infectious agents. The primary agents of infectious retinochoroiditis are Herpes simplex virus, Varicella zoster virus, Cytomegalovirus, and Toxoplasma gondii. Retinochoroiditis is a vision threatening condition both in immunocompetent as well as immunocompromised patients. In ocular infections the vitreous and aqueous fluid used for diagnosis is available in very small volume not sufficient for culture or serology. In order to start the therapy the exact diagnosis is important. The Polymerase Chain Reaction (PCR) is one of the techniques which is highly sensitive and can be employed in very small volume of specimen where as multiplex PCR provides the advantage of detecting multiple organisms at the same time.

### Objectives of this study

1. To standardise and apply PCR for the detection of Herpes simplex virus, varicella zoster virus, cytomegalovirus and Toxoplasma gondii, in the intraocular fluids of patients diagnosed with infectious retinochoroiditis
2. To standardise and apply multiplex PCR technique for the rapid identification of the viral agents.

### Outcome

During this project, aqueous and vitreous were collected from 110 patients (aqueous-43 and vitreous humor-67), who were clinically diagnosed with retinochoroiditis and also equal number of control samples were collected from patients undergoing vitrectomy for indications other than infection. The DNA was extracted using the qiagen DNA extraction kit and subjected for the Multiplex PCR and Uniplex PCR using published primers which is specifically targeting the Glycoprotein D gene, MTR gene, immediate early gene 63, and B1 gene of the HSV-1, CMV, VZV, and toxoplasma gonddi respectively.

### PCR results of the patients (110)

| PCR | Uniplex | | Multiplex | |
|---|---|---|---|---|
| | Case +ve | Percentage | Case +ve | Percentage |
| HSV | 10 | 9 | 10 | 9 |
| CMV | 4 | 4 | 4 | 4 |
| VZV | 6 | 5 | 6 | 5 |
| Toxo | 1 | 1 | 1 | 1 |

Analysis of the samples revealed that 17% were positive for one or more infectious agents by both uniplex and multiplex PCR. The sensitivity and specificity of both uniplex and multiplex were found to be similar. Multiplex PCR is more promising in terms of detecting multiple pathogens in shorter duration and less expensive, than the uniplex PCR.

## Molecular insights into the etiology of infectious uveitis

Principal Investigator : Lalitha Prajna, Aravind - Madurai
Research Scholar : K. Nithya
Funding Agency : Department of Biotechnology, New Delhi
Duration : 2008 - 2011

Uveitis is an ocular inflammation that causes debilitating pain and can lead to serious and permanent visual loss due to complications like cataract and glaucoma. Infectious Uveitis occurs in greater frequency in developing countries from 11.9% to 50 % of overall cases and are most often due to herpes virus, cytomegalovirus and varicella zoster virus, parasites like Toxoplasmosis, and bacteria like syphilis, tuberculosis, and leprosy. For the diagnosis, the ocular fluids like aqueous humor and vitreous humor are analysed by gold standard techniques like staining and culture, but they suffer the drawbacks of lack of sensitivity and are time consuming. By employing the molecular biology tools like Polymerase Chain Reaction (PCR) rapid as well as more accurate results can be obtained. The recent advent of Real Time PCR can be used for the specific diagnosis of the Uveitis, which is more sensitive than the conventional PCR. Moreover there are many entities where the etiology is unknown. The objective of this study is to develop diagnostic test for bacterial, viral and parasitic cause of uveitis using the aqueous and vitreous humor of patients with uveitis by Real Time PCR.

## Elucidating the virulence genes involved in the pathogenesis of corneal ulcers by *Aspergillus*

Principal Investigator : Lalitha Prajna, Aravind - Madurai
Co-Investigators : N.V Prajna, Aravind - Madurai
K. Dharmalingam, Madurai Kamaraj University - Madurai
Research Scholar : Siva Ganesa Karthikeyan
Funding Agency : ALCON Anterior Segment Research Grant
Duration : 2008 - 2011

*Aspergillus* spp are one of the common opportunistic pathogens of the eye causing mycotic Keratitis. Not much information is available on the pathogenesis of mycotic Keratitis. Disruption of the corneal epithelium is the predisposing factor for establishing the infection. The main factors involved in the pathogenesis include the adherence of the fungal conidia to the corneal surface, followed by invasiveness of the hyphae into the corneal stroma, and other factors include toxins, enzymes and secondary metabolites.

### Objective

1. Elucidate the genes associated with conidial surface, cell wall, pigment biosynthesis and Cyclic AMP signalling pathways in aspergillus fumigatus isolated from corneal ulcers
2. Elucidate the genes associated with toxin production from the species of *Aspergillus*

The sample used for the studies includes the strains of *A. fumigatus* and, *A. flavus* isolated from patients with corneal ulcers and corneal scrapings from patients with fungal corneal ulcers.

Ten isolates of *Aspergillus fumigatus* were obtained from infected corneal tissue, which was confirmed by microbiological gold standard methods. A *fumigatus* ATCC strain and one environmental strain isolate were used as a reference control. Total RNA was extracted from seven of the clinical isolates and converted to cDNA. The PCR condition for the virulence gene-Gliotoxin was optimised and studies are underway to characterise other virulence genes.

## To elucidate the mechanism of neovascularisation in proliferative diabetic retinopathy - Pro-inflammatory Cytokine release from RPE is linked to RAGE signalling

| | | |
|---|---|---|
| Investigators | : | Alan Stitt, Centre for Vision Science, Queen's University, Belfast, UK<br>VR. Muthukkaruppan, AMRF - Madurai<br>R. Kim, Aravind - Madurai<br>P. Namperumalsamy, Aravind - Madurai<br>D. Shukla, Aravind - Madurai |
| Research Scholar | : | P. Murugeswari |
| Duration | : | 2008 - 2009 |
| Funded by | : | Common wealth Split-site Doctoral fellowship, TIFAC-CORE<br>Department of Science and Technology |

Pro-inflammatory cytokines and vascular growth factors play a major role in retinal vascular diseases and these factors are known to be expressed by Retinal Pigment Epithelium (RPE). The pro-inflammatory receptor for the advanced glycation end products (RAGE) is also expressed by RPE. The purpose of this study was to determine the role of S100B (a defined ligand for RAGE) and Lucentis® (Anti-VEGF antibody, Ranibizumab) in the expression of inflammatory cytokines and key growth factors in RPE cells in vitro.Human RPE cell line (ARPE-19) were exposed to S100B or in combination with IFNν for 24 hours. Protein and mRNA expression of a wide range of pro-inflammatory cytokines were determined by ELISA and real-time RT-PCR.

S100B treatment induced significant increase in the expression of TNF-alpha ($p<0.01$), IL6 ($p<0.05$), IL8 ($p<0.01$), and MCP-1 ($p<0.05$) cytokines and also induced upregulation of VEGF. Anti-VEGF antibody (Lucentis®) treatment prevented VEGF secretion. MCP-1 and MIF protein expression were down-regulated on exposure to Lucentis® ($p<0.001$)

The current study shows that S100B has a significant biological effect on RPE, causing an enhanced expression of various growth factors and cytokines. S100B binds to RAGE and in RPE this receptor appears to modulate important pro- inflammatory responses. Further studies are underway to quantify the cytokines in vitreous of Proliferative Diabetic Retinopathy (PDR) and Eales' Disease (ED) using Biochip array technology and investigate the angiogenic potential of this vitreous in retinal endothelial cells.

## Will cytoskeletal drugs prevent posterior capsule opacification?

| | | |
|---|---|---|
| Principal Investigators | : | VR. Muthukkaruppan, AMRF - Madurai<br>Baohe Tian, Department of Ophthalmology and Visual Sciences,<br>University of Wisconsin - Madison (UW), USA |
| Co-Investigator | : | Haripriya, Aravind - Madurai |
| Research Scholar | : | S. Jeyalakshmi |
| Funded by | : | National Eye Institute, NIH, USA |
| Duration | : | 2006 - 2009 |

The objective of the project is to determine if the perturbation of the actin cytoskeleton induced by latrunculin B (LAT-B) or H-7 / Y-27632 facilitates clearance of residual lens epithelial cells (LECs) during lens surgery and/or inhibits proliferation and migration of the residual LECs in cultured human lens capsules. Human donor eyes (n=30) underwent extracapsular lens extraction and the eyes were treated with LAT-B (2µM), DMSO (0.25%), Y-27632 (200µM), and BSS (1%). After the drug treatment, capsular bag was dissected out and the lens capsules were fixed and stained with Haematoxylin and photographed. The cell free area was measured. Y-27632 and LAT-B treatment at this concentration during surgery had no significant effect on the clearance of LECs.

Following cataract surgery with donated human eyes (n=38), lens capsules were prepared and cultured by the standard technique and they were treated with H-7 (300µM, 100µM, 50µM, 25µM), BSS (1%), LAT-B (2µM, 5µM), and DMSO (0.25%) in culture. The capsule cultures lasted 4 weeks and PCO formation was photographed and scored by a 4-point scale. All 5 capsules receiving H-7 (300µM)

treatment showed no capsule wrinkling, in vitro equivalent of PCO, while the capsules receiving H-7 (100µM, 50µM, 25µM) did not completely inhibit the PCO formation. The capsules receiving BSS, DMSO or LAT-B treatment showed capsule wrinkling. Lens capsule culture on treatment with H-7 prevented PCO formation probably by inhibiting proliferation and migration of LECs. This study indicates that perturbation of the actin cytoskeleton pharmacologically may inhibit PCO.

### Drug treatment in culture

| Group No. | Drug / Vehicle Treatment | Concentrations | No. of eyes | Highest grade of PCO at week 3 or 4 |
|---|---|---|---|---|
| I | H-7 | 300µM | 5 | 0 |
| | | 100µM | 2 | 1 |
| | | 50µM | 2 | 2 |
| | | 25µM | 1 | 2 |
| II | LAT-B | 2µM | 3 | 3 |
| | | 5 µM | 5 | 0* (in 2 eyes)<br>3** (in 3 eyes) |
| III | H-7 + LAT-B | 50µM H-7 + 2µm LAT- B | 1 | 2 |
| | | 25µM H-7 + 2µm LAT- B | 1 | 2 |
| IV | BSS | 1% | 9 | 3 |
| V | DMSO | 0.25% | 9 | 3 |
| | Total eyes done | | 38 | |

* indicates the grade of PCO in 27 yrs and 62 yrs old donor capsule

** indicates the grade of PCO in 3yrs, 57 yrs and 75 yrs old donor capsule.
In the 3 yr old donor capsule, there was aggressive proliferation of lens epithelial cells as early as day 3.

# PUBLICATIONS

## J MED VIROL

**2008: 80: 536-546**

Thanapal Amala Rajasundari, Periasamy Sundaresan, Perumalsamy Vijayalakshmi, David WG Brown and Li Jin.

- *Laboratory confirmation of congenital rubella syndrome in infants - an eye hospital based investigation*

## MOL CELL ENDOCRINOL.

**2008; 30:282(1-2):2-11**

Moumné L, Batista F, Benayoun BA, Nallathambi J, Fellous M, Sundaresan P, Veitia RA.

- *The mutations and potential targets of the forkhead transcription factor FOXL2*

## MOLECULAR VISION

**2008; 14:500-507**

Sivagnanam Ananthi , Thangavel Chitra , Ramachandran Bini , Namperumalsamy Prajna, Prajna Lalitha, Kuppamauthu Dharmaligam

- *Comparative analysis of the tear protein profile in mycotic keratitis patients*

## MICROSCOPY RESEARCH AND TECHNIQUE

**2008; 71(6):469-76**

Parthasarathy Arpitha, Namperumalsamy V Prajna, Muthiah Srinivasan, and Veerappan Muthukkaruppan

- *A method to isolate human limbal basal cells enriched for a subset of epithelial cells with a large Nucleus/ Cytoplasm ratio expressing high levels of p63*

## RETINA

**2008;28(6):817-824**

D. Shukla, Anand Rajendran, R. Kim, P. Namperumalsamy, P. Murugeswari, VR.Muthukkaruppan

- *Pro-inflammatory cytokines, angiogenic and anti-angiogenic factors in vitreous of patients with Proliferative Diabetic Retinopathy and Eales' disease*

## ARCH OPHTHALMOL

**2008 May; 126(5):700-8**

Boomiraj Hemadevi, Reiner A Veitia, Muthiah Srinivasan, Jambulingam Arunkumar, Namperumalsamy Venkatesh Prajna, Corinne Lesaffre and Periasamy Sundaresan

- *Identification of mutations in SLC4A11gene in patients with recessive Congenital Hereditary Endothelial Dystrophy*

## HUM MUTAT.

**2008 May 16. [Epub ahead of print]**

Jeyabalan Nallathambi, Paul Laissue, Frank Batista, Bérénice A. Benayoun Corinne Lesaffre, Lara Moumné, PJ Eswari Pandaranayaka, Kim Usha, Sankaran Krishnaswamy, Periasamy Sundaresan, Reiner A. Veitia

- *Differential functional effects of novel mutations of the transcription factor FOXL2 in BPES patients*

## CORNEA

**2008;27(10):1164-70**

Parthasarathy Arpitha, Namperumalsamy V Prajna, Muthiah Srinivasan, and Veerappan Muthukkaruppan

- *A subset of human limbal epithelial cells with greater Nucleus/Cytoplasm ratio expressing high levels of p63 possesses slow-cycling property*

## CLINICAL AND VACCINE IMMUNOLOGY

**2008; 15:1019–1023**

Ashutosh Verma, S.R.Rathinam, C. Gowri Priya, V.R. Muthukkaruppan, Brian Stevenson, John F. Timoney

- *LruA and LruB antibodies in sera of human cases of leptospiral uveitis*

## WORLD J MICROBIOL BIOTECHNOL

**2008; 24:903–907**

P. J. Eswari Pandaranayaka . Kanagavalli J, S. R., Krishnadas P. Sundaresan, S. Krishnaswamy

- *Over expression and purification of recombinant human myocilin*

## MOLECULAR VISION

**2008; 14:1157-1170**

R. Ramya Devi, Wenliang Yao, P. Vijayalakshmi, Yuri V. Sergeev, P. Sundaresan, J. Fielding Hejtmancik

- *Crystallin gene mutations in Indian families with inherited pediatric cataract*

## INVEST OPHTHALMOL VIS SCI

**2008; 49(12):5419-24**

CG Priya, Rathinam SR, Muthukkaruppan VR

- *Leptospiral endotoxin as a causative factor for human ocular inflammation*

## HUMAN MOLECULAR GENETICS

**2009; 18:1110-1121**

Asai-Coakwell M, French CR, Ye M, Garcha K, Bigot K, Perera AG, Staehling-Hampton K, Mema SC, Chanda B, Mushegian A, Bamforth S, Doschak MR, Li G, Dobbs MB, Giampietro PF, Brooks BP, Vijayalakshmi P, Sauvé Y, Abitbol M, Sundaresan P, van Heyningen V, Pourquié O, Underhill TM, Waskiewicz AJ, Lehmann OJ.

- *Incomplete penetrance and phenotypic variability characterize Gdf6-attributable oculo-skeletal phenotypes*

## INDIAN JOURNAL OF PEDIATRICS

**(In press)**

Neethirajan G, Solomon A, Krishnadas SR, Vijayalakshmi P, Sundaresan P

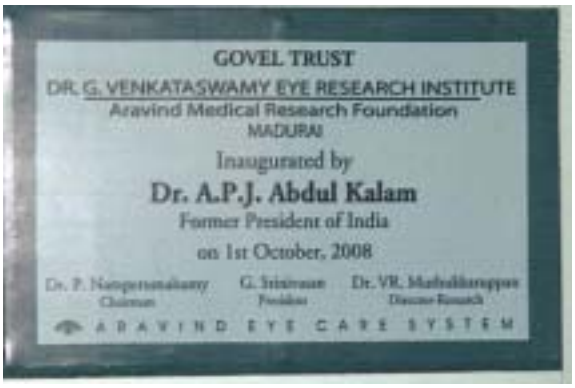
- *Genotype / phenotype association in Indian congenital aniridia*

# INAUGURATION OF DR.G.VENKATASWAMY EYE RESEARCH INSTITUTE

A state-of-the-art facility, Dr. G. Venkataswamy Eye Research Institute, was inaugurated on October 1, 2008 by the former President A. P. J. Abdul Kalam. He emphasized the importance of finding solutions to the unique problems of eye diseases faced in India, by way of developing effective medicines at affordable cost.

M. Natarajan, Principal Scientific Advisor to Defence Minister, Defence Research & Development Organisation, Wallace J. Lee Alward, Professor of Ophthalmology, University of IOWA, Pararajasekaram, former World Health Organisation consultant from Sri Lanka, P. Namperumalsamy, Chairman, Aravind Eye Care System, and VR. Muthukkaruppan, Director, Research participated in the inaugural function.

The new institute has Immunology, Molecular Genetics, Genetic susceptibility, Stem cell biology, Proteomics and translational research as thrust areas. The Rs.29-crore facility would supplement efforts to eliminate needless blindness in the World. The facility would be an umbrella organisation to integrate research in all fields of ophthalmology.



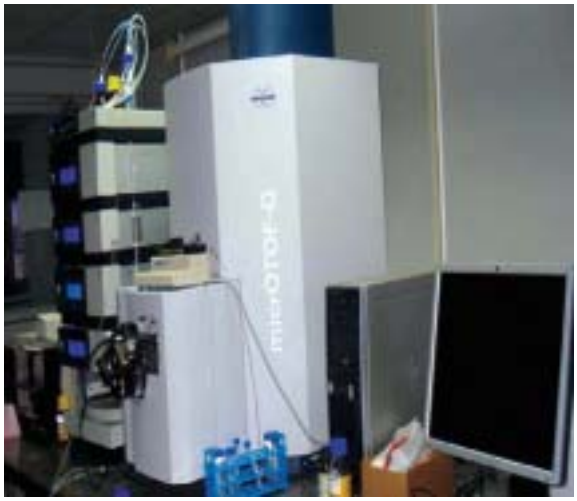

## FACULTY

| | | |
|---|---|---|
| VR. Muthukkaruppan | Director-Research | Immunology and Cell Biology |
| P. Sundaresan | Scientist | Molecular Genetics |
| A. Navaraj | Scientist | Molecular Biology and Functional Genomics |
| C. Gowripriya | Scientist | Immunology and Cell Biology |
| S. Senthilkumari | Scientist | Ocular Pharmacology |

# MAJOR EQUIPMENT

*Leica Confocal Microscopy*

*Flowcytometry –FACS CALIBUR*



*LC MS/MS: Dionex Nano LC ultimate 3000 – Bruker MicroToF Q MS*

*Liquid Handling*

*ABI 7900 HT Fast Real Time PCR System*

*ABI 3130 Genetic Analyser*

*Shimadzu High Pressure Liquid Chromatography (HPLC) system*

# AWARDS

B. Suganthalakshmi, Senior Research Fellow was awarded Pre doctoral Fellowship (2007-08) under Dr. Fielding Hejtmancik at National Eye Institute – "Genetics of diabetic retinopathy"

S. Vaishali, Junior Research Fellow received "Best scientific paper presentation award" at the Indian Eye Research Group meeting held in July, 2008 (Identification of stem cells in cultivated buccal mucosal epithelium and clinical outcome after transplantation in patients with bilateral LSCD)

S. Jeyalakshmi, Junior Research Fellow received "Best scientific paper presentation award" at the ASIA ARVO meeting held in January 2009 (Characterisation of human epithelial cells and epithelial-mesenchymal transition cells in relation to PCO formation in culutre)

P. Murugeswari, Junior Research Fellow was awarded UK Commonwealth Split-Site doctoral scholarship 2008 to carry out part of Ph.D – Centre for Vision Science, School of Bio medical Science, Queen's University, Belfast under the guidance of Dr.Alan Stitt - (October 1, 2008 to September 2009)

## PH.D AWARDED

Ms. R. Ramyadevi
October 2008
Understanding the molecular genetics of cataract

Mr. J. Nallathambi
October 2008
Involvement of transcription factor genes PAX6/FOXL2 in various ocular anomalies

# CONFERENCES & WORKSHOPS HELD AT ARAVIND

## Indian eye research group meeting

July 26-27, 2008

In this 17th Annual meeting 120 delegates from all over the country participated and discussed latest trends and developments in research in Stem cell, Genetics, Proteomics, Cell biology and Ocular pharmacology.

Dr.G.Venkataswamy Memorial Oration Award was given to Dr. Fielding Hejtmancik, Chief,

molecular ophthalmic genetics section, ophthalmic genetics and visual function branch, National Eye Institute, NIH, Bethesda, USA. The title of the oration. "The barbados family study of open angle glaucoma: recent progress".

The Bireswar Chakrabarti memorial oration award was given to Dr.Anand Swaroop, senior investigator & Chief, neurobiology neurodegenration & repair laboratory (N-NRL), National Eye Institute, National Institutes of Health, USA. The

title of oration "Retinal development and degeneration: treatment paradigms from basic biology".

R. Ramya Devi
- *Crystalline gene mutation in Indian families with inherited paediatric cataract*

S. Vaishali
- *Identification of stem cells in cultivated buccal mucosal epithelium and clinical outcome after transplantation in patients with bilateral LSCD*

C. Gowri Priya
- *Leptospiral serogroups prevalent among animals and humans in and around Madurai*

S. Senthilkumari
- *Evidencing the effect of P-Glycoprotein modulation at blood-ocular barriers using gamma scintigraphy*

S. Ananthi
- *Differential expression of mammoglobin B precursor in healthy male and female tears*

B. Hemadevi
- *Screening COL8A2 gene variation in Indian fuchs endothelial dystrophy patients*

S. Jeyalakshmi
- *Cytoskeletal drugs prevent Posterior Capsular Opacification in human lens capsules in vitro*

K. Renugadevi
- *Screening of oculocutaneous albinism and ocular albinism candidate gene variants in Indian albinism patients*

P. Murugeswari
- *Retinal pigment epithelium secretes pro-inflammatory cytokines, angiogenic and anti-angiogenic factors in vitro*

Lalan Kumar Arya
- *Nested PCR-A diagnostic tool for the detection of infection agents in the intraocular fluids of retinochloriditis patients*

P. Prabhu
- *Ex vivo expansion of limbal epithelial stem cells and corneal surface reconstruction*

## TIFAC-CORE workshop on flow cytometry and its application in ophthalmic research

February 17-21, 2009 (Partly supported by International Society for Analytical Cytology)

### Faculty

- *Dr. Attila Tarnok, University of Leipzig, Germany*
- *Dr. James F. Leary, Purdue University, USA*
- *Dr. Robert M Zucker, US Environmental Protection Agency, USA*
- *Dr. Susann Muller, Helmholtz centre for Environmental Research UFZ, Germany*
- *Dr. Henning Ulrich, University of Sao Paulo, Brazil*
- *Dr. VR.Muthukkaruppan*
- *Dr. Gowri Priya*

## PARTICIPATION IN CONFERENCES AND WORKSHOPS

### ARVO – Fort Lauderdale

Florida, April 27-May 1, 2008

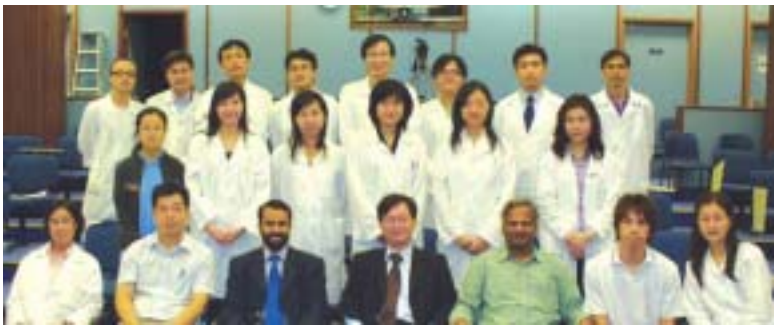
- VR.Muthukkaruppan made a poster presentation on "The isolated human limbal basal cells with high levels of p63 expression and large N/C ratio possess slow cycling property".
- P. Sundaresan made a poster presentation on "Low prevalence of known disease causing mutations in South Indian Leber Congenital Amaurosis patients".

### World ophthalmology congress

Hong Kong, June 26-28, 2008

P. Sundaresan

- *Invited lecture on "Genetic eye diseases in Indians and he also participated as the chairperson for the on "Molecular studies on eye disease genes session"*



### 9th Indo-US cytometry workshop

Bangalore, July 21-25, 2008

C. Gowri Priya, Scientist attended this workshop.

### Asia ARVO-2009

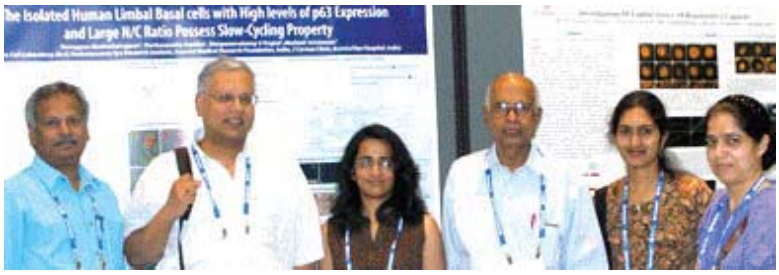
Hyderabad, January 15-18, 2009

Ms. B.Hema devi

- *COL8A2 and SLC4A11 gene variants in Indian patients with fuchs endothelial corneal dystrophy*

Ms. S.Ananthi

- *Development of an effective sample preparation method*




*for the tear proteome analysis using 2-D gel electrophoresis*

Ms. K. Renuga Devi
- *Genetic analysis of Indian oculocutaneous albinism patients*

Ms. S. Jeyalakshmi
- *Characterization of human epithelial cells and epithelial-mesenchymal transition cells in relation to PCO formation in culture*

B. Suganthalakshmi
- *Lack of EPO gene promotor SNP rs1617640 and association of RAGE gene 3 SNP Rs.2070600 with type 2 diabetic retinopathy in South Indian population*

Ms. S.Vaishali
- *Evaluation of adult human limbal fibroblasts as a feeder layer for ex vivo expansion of buccal mucosal epithelial cells*

Ms. P. Narmathadevi
- *Proteomic analysis of secretome of aspergillus flavus isolated from fungal keratitis patients*

Mr. P. Prabhu
- *Ex vivo expansion of human corneal epithelial stem cells in limbal explant culture*

Dr. C. Gowri Priya
- *A New method to identify human corneal epithelial stem cells on the basis of ABCG2 expression combined with a large N/C ratio*

Dr. S.Senthil Kumari
- *Demonstrating the effect of P-glycoprotein (P-gp) modulation at blood ocular barriers using gamma scintigraphy*

Invited talk in ASIA ARVO 2009

VR.Muthukkaruppan
- *Ex vivo expansion of human corneal epithelial stem cells and transplantation for ocular surface reconstruction*

P. Sundaresan
- *Genetic studies of corneal endothelial dystrophy*
- *Genetic and functional analysis of myocilin, a protein associated with primary open angle glaucoma*

## GUEST LECTURES

- Micro RNA – A new therapeutic strategy by Dr.K.V.Venkatachalam, Professor of Biochemistry, College of Medical Sciences, Nova Southeastern University, Fluorida on 29th May 2008
- Is Basic transcription factor 3 (btf3) regulates pigmentation? by Dr.S.Mathavan, Research Scientist, Genome Institute of Singapore on 7th July 2008
- Immunotherapy of Human B cell Malignancies by Dr.S.Baskar, Associate Investigator, ETIB, CCR, National Cancer Institute, National Institutes Health, Bethesda, MD on 21st July 2008
- Modelling an inherited human vascular malformations in mice: Hereditary hemorrhagic telangiectasia by Dr.Sudha Srinivasan, Medical writer, Envision Pharma, South port, Conncticut, USA on 28th July 2008
- Regulatory Issues Associated with Biotherapeutics by Dr.S.Muthukumar, Senior Scientist, Division of Monoclonal Antibodies, Office of Biotechnology products, Centre for Drugs, Bethesda on 4th Aug. 2008
- Drug Discovery: Where to start and how to lead? by Dr.Thirumurthi Velpandian, Assistant Professor & head, Department of Ocular Pharmacology & Pharmacy, Dr.R.P.Centre, All India Institute of of Medical Sciences, New Delhi on 8th Sep. 2008
- "Regenerative medicine and stratified human epithelia" by Dr.Graziella Pellegrini, Associate Professor of Cell Biology, Head of Cell Therapy Program of Center

for Regenerative Medicine in the Department of Biomedical Sciences, University of Modena and Reggio Emilia, Italy

- The Future of IOP Lowering Therapy in Glaucoma by Dr. Paul Kauffman, Professor and Chair, Department of Ophthalmology, University of Wisconsin, USA.

### Fulbright research fellow

Paul O. Phelps is a fourth year medical student from Drexel University College of Medicine in Philadelphia, USA.
**Fulbright Fellowship**: 2008-09

**Project Title:** Characterisation of corneal epithelial stem cells.

### Lectures by Dr.VR.Muthukkaruppan

- Meenakshi Medical college, Kanchipuram - STEM CELLS in regenerative Medicine
- PSG College of Pharmacy, Coimbatore – Mouse Corneal model to test for the angiogenic and anti-angiogenic factors in relation to tumor growth and regression
- Lady Doak College, Madurai - STEM CELLS in regenerative Medicine

## VISITORS

Dr. Wallace L.M. Alward, Prof. of ophthalmology, Service Director, Glaucoma clinic, University of IOWA, Iowa city, USA visited Aravind Medical Research Foundation on 2nd October 2008 to have discussion with Dr. P. Sundaresan and Research scholars.

**Dr. Graziella Pellegrini**, Associate Professor of Cell Biology, Head of Cell Therapy Program of Center for regenerative medicine in the department of Biomedical sciences, University of Modena and Reggio Emilia, Italy visited Aravind Medical Research Foundation to have discussion on corneal epithelian stem cells from 19th - 20th January, 2009. She gave a lecture on “Regenerative medicine and stratified human epithelia”.

# CLINICAL RESEARCH

## VISION REHABILITATION SERVICES

### The study of low vision children in blind school

Investigators : Dr. K. Ilango, Aravind - Madurai
Ms. Jeyaseeli Flora, Aravind - Madurai
Dr. P. Vijayalakshmi, Aravind - Madurai

Department : Vision rehabilitation centre and paediatric ophthalmology services

#### Background

There are 1.4 million visually impaired children in the age group of 0 – 14 yrs. The vast majority of visually impaired children with low vision condition in developing countries like India are sent to the blind schools despite having usable vision because they do not have access to vision rehabilitation services that would enable to integrate them into regular schools. With this background in mind the vision rehabilitation centre and paediatric ophthalmology services at Aravind Eye Hospital planned the Madurai study of low vision children in blind schools.

#### Objectives

- To identify children having low vision with potential sight under curriculum for the blind.
- To provide appropriate low vision devices.
- To facilitate and transfer low vision children from the curriculum for the blind to normal curriculum with support of assistive devices and counselling to parents and teachers.

#### Results

The first phase of study for the year 2008 was conducted in 5 schools for the blind around Madurai. The following results were obtained. Out of the 360 children who were screened 5 children had BCVA of 6/6 – 6/18 and 39 children had BCVA of <6/18 – 6/60. 44 out of 360 (12.2%) children can study in the normal school with the help of assistive devices. They were counselled to be transferred to normal schools. These results emphasise the greater need for participation by the ophthalmic professionals not only in the prevention of blindness but also in providing compassionate care, guidance and appropriate education to these unfortunate children.

### Impact of the low vision devices and rehabilitation services on the quality of life

Investigator : Dr. K. Ilango, Aravind – Madurai
H. Jeyaseeli Flora, Aravind – Madurai
Mr. R.D. Thulasiraj, Aravind – Madurai

Department : Vision Rehabilitation centre, Aravind – Madurai

#### Background

Visual impairment is devastating in the developing world where it has a profound impact on the quality of life for the visually impaired person and his or her community. Clinical evaluation can help to quantify the extent of vision loss, but understanding the impact of vision loss on one's functional

ability and its relation to the use of low vision devices and rehabilitation services are also useful in providing proper services for the visually impaired. Keeping this in mind, the Vision Rehabilitation centre at Aravind Eye Hospital, Madurai planned the study "Impact of low vision devices and rehabilitation services on the quality of life".

### Objective

- To assess the impact of low vision devices on the quality of life of the visually impaired
- To assess the impact of rehabilitation services on the quality of life of the visually impaired

### Current status

This study is currently underway testing the questionnaire with a pilot following which the study will be conducted.

## GLAUCOMA SERVICES

### Safety and efficacy of manual small-incision cataract surgery combined with trabeculectomy: comparison with phacotrabeculectomy

Investigator : Dr. Saurabh Mittal, Apoorva Mittal, Aravind - Madurai
Dr. Rengappa Ramakrishnan, Aravind - Tirunelveli

### Aim

To determine the safety and efficacy of mitomycin-C-augmented manual small-incision cataract surgery combined with trabeculectomy and to compare the procedure with phacotrabeculectomy.

### Methods

In this retrospective review, 55 eyes undergoing mitomycin-C-augmented manual small incision cataract extraction combined with trabeculectomy were compared with 52 eyes undergoing phacotrabeculectomy. Visual acuity, intraocular pressure and postoperative complications were analysed.

### Results

There were no significant differences in age, sex, laterality, glaucoma type, cataract type, preoperative intraocular pressure and follow-up duration between the 2 groups. After an average 39.8 months (SD, 18.5 months) follow-up, the intraocular pressure decreased from a baseline of 19.9mm Hg (SD, 7.47mm Hg) to 13.9mm Hg (SD, 3.81mm Hg) in the manual small-incision cataract surgery group and from 18.0 mm Hg (SD, 6.45mm Hg) to 13.9mm Hg (SD, 3.54mm Hg) in the phacotrabeculectomy group ($p<0.05$ for both groups). Surgical success in terms of intraocular pressure <21mm Hg, with or without antiglaucoma medication, at the end of the follow-up period was 89.1% for the manual small-incision cataract surgery group and 92.3% for the phacotrabeculectomy group. Intraocular pressure reduction was significantly better following mitomycin-C-augmented manual small incision cataract extraction combined with trabeculectomy for open angle glaucoma (7.4mm Hg). Best-corrected visual acuity improved to 6/12 in 43 eyes (78.2%) undergoing manual small-incision cataract surgery and in 44 eyes (84.6%) undergoing phacotrabeculectomy ($p = 0.357$). The incidence of complications was numerically greater in the manual small-incision cataract surgery group but this was not statistically significant ($p = 0.32$). The most common complication was posterior capsule opacification, in 44.5% of eyes.

### Conclusion

Mitomycin-C-augmented manual small-incision cataract extraction combined with trabeculectomy is safe, effective, and of equal efficacy in terms of intraocular pressure reduction, visual rehabilitation, and complications when compared to phacotrabeculectomy.

## Surgical outcome of phacotrabeculectomy in eyes with small pupils – A prospective study

Investigator : Dr. Vidhya, Aravind - Madurai
Dr. George V Puthuran, Aravind - Madurai
Dr. Karan, Aravind - Madurai
Dr. Manju, Aravind - Madurai
Jijo, Aravind - Madurai

### Objective

A prospective study was carried out to compare the outcome of the intraocular pressure control, visual acuity and intraoperative and postoperative complications among patients undergoing combined phaco-trabeculectomy procedures as indicated for their disease condition.

### Methods

Patients were divided into two groups viz., those with small pupils (<4mm) even after maximal pharmacological dilatation and the others with pupils larger than 4mm. A total of 91 eyes of 91 patients (43 small pupils, 48 larger pupils) were studied from November 2006 to June 2007 with a minimum follow up of 3 months, recruited from the patients attending the glaucoma services of Aravind Eye Care System during this period. Standard surgical techniques for phacoemulsification and trabeculectomy were employed as well as the pupils were enlarged using the previously tested methods for the same, including, stretch pupiloplasty, iris hooks etc.

### Results

48 eyes with small pupils subject to trabeculectomy with phacoemulsification after stretch pupilloplasty or use of iris hooks were compared with 43 eyes which had glaucoma triple procedure with well dilated pupils. There was no statistically significant difference in IOP between the two groups on day one and the first and subsequent three months following surgery. There were no significant differences in the incidence of preoperative complications between the two groups, except, excessive bleeding in the group with well dilated pupils.

### Conclusion

It was concluded that pupil stretch during phacoemulsification was not associated with a statistically significant difference in BCVA, IOP control, inflammation or other complications postoperatively compared with the results in the well dilated group without pupil stretch. It was also seen that pupil stretch improves visualisation during all steps of intraoperative manipulation and may in fact avoid many disastrous complications associated with small pupil cataract surgeries.

### Annexure: Charts and tables

### Preoperative patient demographics

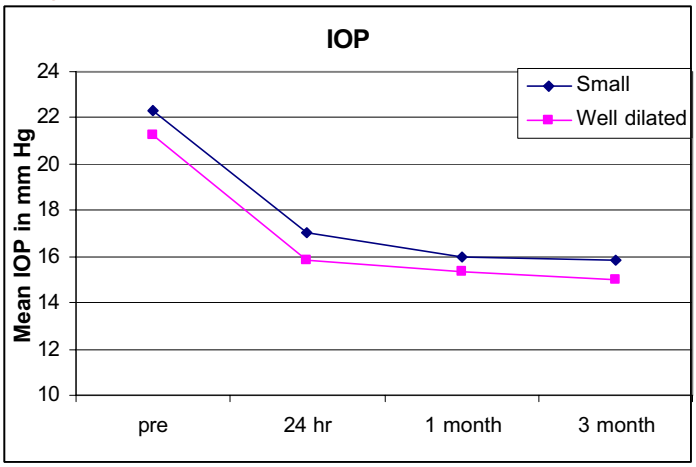
| | **Pupil diameter** | **N** | **Mean ± SD** | **P - value** |
|---|---|---|---|---|
| Age | small | 48 | 63.92 ± 9.88 | 0.179 |
| | well dilated | 43 | 64.77 ± 8.59 | |
| Visual acuity (logMAR) | small | 48 | 0.64 ± 0.63 | 0.239 |
| | well dilated | 43 | 0.54 ± 0.43 | |
| IOP | small | 48 | 22.29 ± 9.70 | 0.573 |
| | well dilated | 43 | 21.23 ± 9.64 | |

There is no significant difference in preoperative characteristics between the 2 groups.

### Postoperative results

| | Small | | | Well dilated | | |
|---|---|---|---|---|---|---|
| Parameter | 1 Day | 1 Month | 3 Month | 1 Day | 1 Month | 3 Month |
| Visual Acuity (logMAR) | | | | | | |
| Mean ± SD | 0.46 ± 0.63 | 0.30 ± 0.60 | 0.23 ± 0.47 | 0.39 ± 0.45 | 0.18 ± 0.30 | 0.18 ± 0.30 |
| P- value | 0.436 | 0.244 | 0.554 | | | |
| IOP | | | | | | |
| Mean ± SD | 17.02 ± 6.37 | 15.98 ± 5.37 | 15.87 ± 4.54 | 15.83 ± 5.95 | 15.33 ± 4.46 | 14.98 ± 5.21 |
| P- value | 0.363 | 0.532 | 0.393 | | | |

### Postoperative results chart




### Preoperative complications

| Complications | Pupil diameter | |
|---|---|---|
| | small | well dilated |
| DM strip | 0 | 1 |
| PCR | 0 | 1 |
| Zonular Dialysis | 1 | 0 |
| vitreous loss | 0 | 1 |
| Excessive Bleeding | 1 | 4 |
| Others | 1 | 0 |

## Correlation of central corneal thickness and retinal nerve fibre layer in POAG

Investigator : Dr. Prateek Agarwal, Aravind - Madurai
Dr. Manju R Pillai, Aravind - Madurai
Dr. Prashanth R, Aravind - Madurai
Dr. Jijo, Aravind - Madurai
Dr. Krishnadas, Aravind - Madurai

### Purpose

To correlate the retinal nerve fibre layer thickness (RNFL) and optic nerve head (ONH) parameters measured by optical coherence tomography (OCT) with central corneal thickness (CCT) measurements in POAG suspects and POAG (primary open angle glaucoma) patients.

### Materials and methods

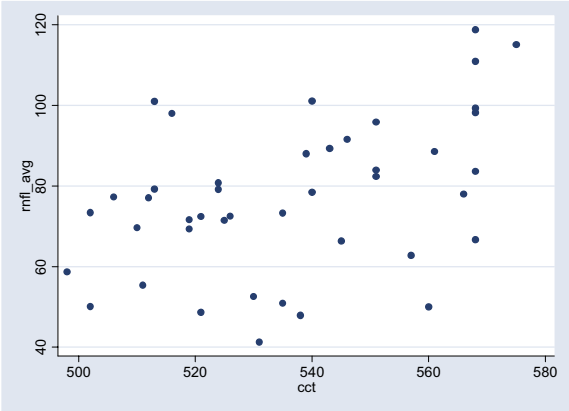
Observational cross –sectional study in a tertiary eye care institute. 128 eyes of POAG SUSPECTS and 46 eyes of POAG patients were included in the study. Both the groups were stratified into three subsets thin (CCT <520), medium (CCT 526-555) and thick (CCT >555) corneas. RNFL thickness (Smax, Imax and average) and ONH parameters (cup to disc area ratio, rim area, vertically integrated rim area) were measured by OCT. CCT was measured by ultrasound pachymetry. The outcome measures were analysed as correlation between each subset of CCT and OCT measurements of RNFL and ONH parameters.

### Results

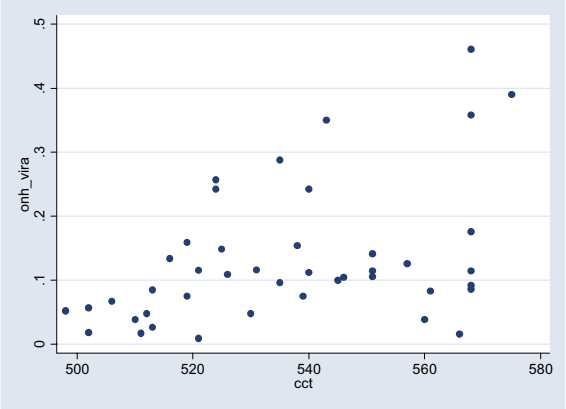
- In the POAG suspect group there was significant correlation with all the three ONH parameters (cup to disc area ratio, rim area, vertically integrated rim area; r=-0.238, r=0.222, r=0.306) but none with the three RNFL measurements (Smax, Imax and average)
- In POAG patients there was significant correlation with all the three ONH parameters (cup to disc area ratio, rim area, vertically integrated rim area; r=-0.380, r=0.463, r=0.423), as well as all the three RNFL measurements ( Smax , Imax and average; r=0.354, r=0.332, r=0.438). The RNFL in POAG suspects as well as POAG patients was significantly thinner in CCT <555 microns as compared to thick corneas (p<0.01).

### Conclusion

Retinal NFL thickness seems to positively correlate with central corneal thickness in POAG. POAG suspects with CCT <555 microns have either very early undetected glaucoma or inherent structural predisposition to glaucomatous damage. Thus these patients need early screening to prevent irreversible damage.




*CCT Vs average RNFL thickness in POAG. r=0.438, p value=0.003*




*CCT Vs vertical rim area in POAG r=0.432, p=0.004*

## Comparison of intraocular pressure measured by Pascal dynamic contour tonometry and Goldmann applanation tonometry

Investigator : Dr. Sharmila, Aravind - Madurai
Dr. Nidhi Gupta, Aravind - Madurai
Ms. Nithya Neelakanth, Aravind - Madurai

### Aim

To compare the intraocular pressure (IOP) measurements obtained using the pascal dynamic contour tonometer (PDCT) with the standard Goldmann applanation tonometer (GAT) and to correlate these with central corneal thickness (CCT).

### Methods

This is a cross sectional, observational clinical study of 170 eyes from patients attending glaucoma clinic. All eyes underwent IOP measurement by GAT and PDCT followed by measurement of central corneal thickness.

### Results

A clear co-relation was found between PDCT and GAT (r=0.66; p <0.001). The mean IOPs recorded by GAT and PDCT were 20.8+/- 8.3mmHg and 19.7+/- 5.0mmHg respectively. There was no statistically significant difference between the mean IOPs recorded by the two instruments. There was a good agreement in the PDCT and GAT when the IOPs were less than 21mm HG; this means that the average

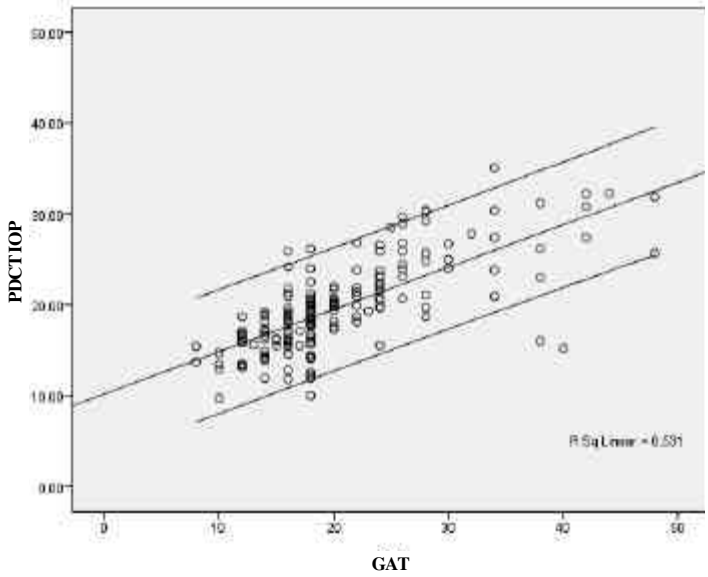
difference between measurements of the two devices varied as the IOP increased. Dividing the eyes into three groups on the basis of CCT, the mean IOP recorded in the thicker corneal range by GAT showed a poor agreement with IOP recorded by PDCT. However PDCT measurements showed no significant differences with different CCTs (p=0.96).

## Conclusion

The two tonometers (PDCT and GAT) showed good agreement with each other. Demonstration of the relative independence of PDCT IOP measurements from CCT supports a potential clinical role for this instrument over conventional Goldmann applanation tonometer for screening and management of patients with glaucoma.

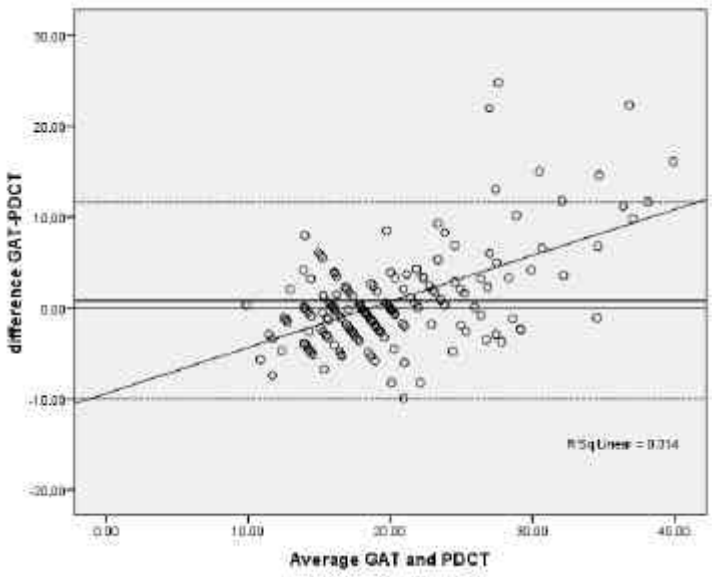
**Scatter plot of IOP measurement by GAT and PDCT**

ICC= 0.66 (0.56, 0.73), p=0.000




## Bland-Altman plot

- Kappa 0.51 (p value=0.000)
- When IOP equal or >than 21mm Hg, GAT IOP tend to be more than PDCT



## Comparison of intraocular pressure rise in the early postoperative period between phacoemulsification with intraocular lens implantation and phacotrabeculectomy in patients with primary open angle glaucoma and pseudoexfoliative glaucoma

Investigator : Dr. Brahadeesh Subramaniam, Aravind - Madurai
Dr. George V Puthuran, Aravind - Madurai
Dr. Krishnadas, Aravind - Madurai
Dr. Sharmila, Aravind - Madurai
Dr. Roy, Aravind - Madurai

### Objective

To compare the intraocular pressure rise in the early postoperative period between phacoemulsification with intraocular lens implantation and phaco - triple procedures in patients with primary open angle glaucoma and pseudoexfoliative glaucoma.

### Patients and methods

91 consecutive patients with moderate glaucoma and visually significant cataract were assigned to clear corneal phacoemulsification or trabeculectomy with phacoemulsification and PCIOL implantation, to compare the relative IOP rise immediately following surgery in each group. Individuals with moderate glaucoma, who were on 1 medication and IOP <=21 mmHg prior to surgery were assigned to phacoemulsification with PCIOL implantation alone (N=38). Individuals on more than one medication or IOP >=21mmHg were assigned to trabeculectomy with phacoemulsification with PCIOL implantation (N=53). IOP was measured as 6 hours and 24 hours postoperatively using a Perkins hand held applanation tonometer by single observer in all patients.

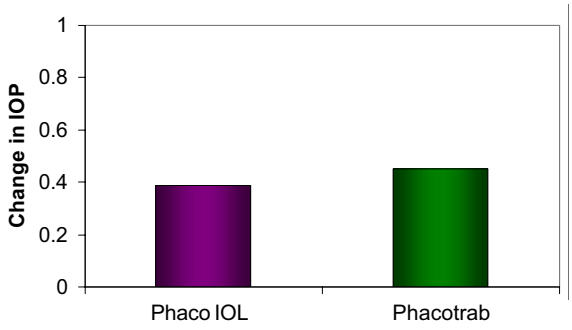
### Results

In phaco IOL group, mean increase in IOP at 6 hrs was 0.39±4.08mm Hg SD (range - 10 to 7, P value=0.277). In phaco TRAB group, mean increase in IOP at 6 hrs was 0.45±3.38mm Hg SD (range -8 to 8, P=0.167). In Phaco IOL group, the increase in IOP was not statistically significant at 24hrs from the preoperative IOP (mean IOP increase -0.40±4.42mm Hg SD, range -10 to 11, p = 0.293). In Phaco TRAB group, the increase in IOP was not statistically significant at 24hrs from the preoperative IOP (mean IOP increase -0.77±3.72mm Hg SD, range -10 to 7, p=0.068). There was no statistically significant difference between the two groups at 6hrs (p = 0.941) or 24hrs postoperative (p=0.660) period.

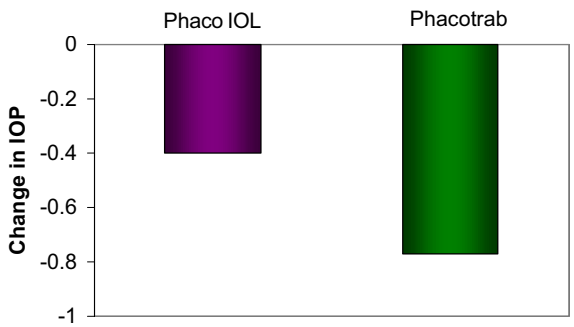
### Conclusion

In a defined patient population with moderate primary open angle and exfoliative glaucoma, there was no statistically significant difference in post operative IOP rise following phacoemulsification and posterior chamber IOL implantation alone as compared to glaucoma triple surgery.

Change in IOP at 6hrs




Change in IOP at 24hrs




There was no statistically significant difference between the two groups at 6hrs postoperative (p = 0.941) and 24hrs postoperative (p=0.660) period.

## Mitomycin C augmented trabeculectomy combined with single site manual small incision cataract surgery-A retrospective analysis.

Investigator : Dr. Rengaraj Venkatesh, Aravind - Pondicherry
Dr. Sabyasachi Sengupta, Aravind - Pondicherry
Dr. S. Kavitha, Aravind - Pondicherry

### Purpose

To analyse the outcome of Mitomycin C (MMC) augmented trabeculectomy combined with manual small incision cataract surgery (MSICS/Trab) at 6 months.

**Design :** Retrospective analysis of case records of patient who underwent MSICS/Trab.

### Participants and methods

Records of 103 MSICS/Trab augmented with MMC (two minutes of 0.2mg/ml) performed from January 2006 to May 2007, by a single, experienced surgeon, were reviewed by an independent investigator. MSICS was done through a superior straight scleral tunnel and after implantation of PCIOL; a Kelly's punch was used to make the internal ostium of the trabeculectomy. Peripheral iridectomies were performed and scleral tunnel was closed with two 10'0 nylon suture.

### Main outcome measure

Intraocular pressure (IOP) reduction and achievement of target IOP (<18mm Hg) at 6 months.

### Results

The minimum follow up was 6 months for all patients. Out of the 103 patients, 64 (62.1%) had primary open angle glaucoma (POAG), 23 (22.3%) had secondary open angle glaucoma (SOAG) due to pseudoexfoliation (PXF) or pigment dispersion (PD) and 16 (15.5%) had chronic angle closure glaucoma (CACG). The demographics and mean IOP at the time of surgery (30.4±10.3mmHg) were comparable in all three groups. A significant reduction in IOP levels (16.64±4.75 and 16.59±4.01 mm Hg) was observed at 3rd and 6th month follow up (p=0.035) using the paired T-test, irrespective of the type of glaucoma. Subgroup analysis showed that there was a significant difference in IOP levels of CACG group compared to the SOAG group (p=0.015) at 6 months follow up using the Mann-Whitney test for statistical significance. However, no statistically significant difference was observed in the IOP comparisons between POAG and CACG groups or POAG and SOAG groups. Intraoperative as well as postoperative complications were similar in all the three groups. About 10.7% patients needed one antiglaucoma medication to achieve target IOP at 6 months and 2 patients needed 2 antiglaucoma medications.

### Conclusion

MMC augmented MSICS/Trab is a safe and effective method of tackling coexistent glaucoma and cataract. Results in CACG seem to be better than SOAG; however POAG and CACG results are comparable.

## Pars plana vitreous tap combined with manual small incision cataract surgery for management of phacomorphic glaucoma

Investogator : Dr. Rengaraj Venkatesh, Aravind - Pondicherry

### Abstract

Phacomorphic glaucoma patients have an extremely shallow anterior chamber and high intraocular pressure. And this condition is not uncommon in the developing world owing to delay in having cataract surgery. Cataract extraction is the only definitive treatment for phacomorphic glaucoma. There is an increased risk of complications like peripheral capsulorhexis tears, iris prolapse, descemet's membrane detachment and expulsive suprachoroidal hemorrhage during surgery. We evaluated pars plana vitreous tap as an aid to facilitate manual small incision cataract surgery in eyes with phacomorphic glaucoma.

## Safety and efficacy of using off label bevacizumab versus mitomycin C to prevent bleb failure in a single site phaco trabeculectomy by a randomised controlled clinical trial

Investigator : Dr. Sabyasachi Sengupta, Aravind - Pondicherry
Dr. Rengaraj Venkatesh, Aravind - Pondicherry
Dr. S. Kavitha, Aravind - Pondicherry
Champalimaud Award Project

### Abstract

#### Aims and objectives

To analyse the safety and efficacy of Bevacizumab (Avastin) versus 0.03% Mitomycin C (MMC) for preventing bleb failure following single site combined phacoemulsification and trabeculectomy (Phacotrab).

**Study type** : Interventional

**Study design** : Prospective, three armed, randomised, double blind, active control, parallel assignment, safety / efficacy study

#### Materials and Methods

In this study, 75 consecutive patients presenting to glaucoma specality clinic at Aravind Eye Hospital, Pondicherry with POAG or CACG requiring phacotrab will be randomised for the study into 3 groups. One group will receive 0.03% MMC for 3 minutes; second group will receive subconjunctival Avastin (1.25mg in 0.05ml) immediately postoperatively, and on day 7 and the third group will receive Avastin soaked in a sponge intraoperatively (1.25mg/1ml) on the sclera like MMC regimen for 3 minutes. Patient will be followed up on day 1,7,14, 30, 90 and 180.

#### Results

The primary outcome measure will be treatment success and bleb morphology in the study eye at the 6 month follow-up. Complete success will be defined as an IOP <18mm Hg without anti- glaucoma medications at 6 months follow up after surgery or at least a 20% reduction from baseline IOP. Qualified success will be defined as an IOP of <18mm Hg with one anti-glaucoma medication. Bleb morphology will also be considered in the primary outcomes using the Indiana Bleb Appearance System (IBAS). Any adverse event either intra or post operative will be recorded.

#### Statistical analysis

Univariate comparisons between treatment groups will be made by the two-sided student t test, $\chi^2$ test, or Fisher exact test. The association of surgical complications with treatment outcome and vision loss will be assessed for statistical significance with the $\chi^2$ test or Fisher exact test. A p value of .05 or less will be considered statistically significant.

## Central corneal thickness changes after combined (trabeculectomy and phacoemulsification) surgery

Investigator : Dr. S. Kavitha, Aravind - Madurai
Dr. Rengaraj Venkatesh, Aravind - Pondicherry

### Project summary

#### Major objectives

To evaluate changes occurring in central corneal thickness (CCT) immediately after uneventful combined (trabeculectomy and phacoemulsification) surgery.

#### Methodology including inclusion and exclusion criteria

Fifty consecutive patients with uneventful combined (Trabeculectomy and Phacoemulsification) surgery by the same experienced surgeon will be taken up for the study. CCT will be measured 1 hour

preoperatively and 1 day, 1 week and 2 weeks postoperatively. The unoperated eye will also have CCT measurements simultaneously on all occasions and will serve as a control. For all patients an informed consent will be taken. Patients with approximately grade 2 or 3 nuclear sclerotic age related cataract associated with POAG and who will benefit from a combined surgery will be included in the study. Mono-ocular patients and patients with corneal pathology, including evidence of endothelial abnormality will be excluded. Patients, who had an unexpected intraoperative course, including prolonged phacoemulsification time, will also be excluded. Precise CCT measurements will be performed with the ultrasonic pachymeter.

### Sample collection

Assuming pre-OP CCT is 550 and post-op is 565 (difference of 15 microns) we would need 106 patients at a confidence interval of 0.05 levels.

### Expected outcome

Previous reports say that changes occur in CCT in the immediate period after cataract surgery and that the changes are reversible, resolving to near baseline levels within 1 week. The change in the CCT can give a falsely elevated IOP reading during the first postoperative week. This might partially account for the IOP spikes recorded in the first postoperative week. So our study can see whether similar changes in CCT occur in combined surgery also.

### Ethical issues

CCT is done for all glaucoma patients; the only change is that we will be measuring postoperative CCT which is not done as a routine.

## Comparative study of safety and efficacy of rigid PMMA and foldable lenses in glaucoma triple procedures

Investigator : Dr. Sailaja Ketineni, Aravind - Madurai
Dr. Sharmila, Aravind - Madurai
Dr. Royce, Aravind - Madurai
Dr. Krishnadas, Aravind - Madurai

### Aim

To compare the surgical outcome of phacotrabeculectomy with implantation of polymethyl methacrylate intraocular lens and phacotrabeculectomy with implantation of acrylic intraocular lens.

### Methods

One hundred consecutive patients were randomised to receive either a PMMA IOL or a foldable acrylic IOL. Visual acuity, intraocular pressure, bleb characteristics, complications and interventions were examined at intervals upto 3 months.

### Results

There was no significant difference between the two groups with respect to visual acuity, intraocular pressure control, bleb survival, complications and interventions. However, at 1 month after surgery, the mean IOP in acrylic group (16.3± 5.5) was slightly more than that in the PMMA group (15.8±4.6) which was statistically insignificant ($p = 0.871$).

### Conclusion

Trabeculectomy combined with rigid PMMA or foldable intraocular lenses were effective in reduction of IOP after glaucoma triple procedures in this short term study. The two groups did not differ significantly in magnitude of IOP reduction, improvement in visual acuity or incidence of adverse events post operatively.

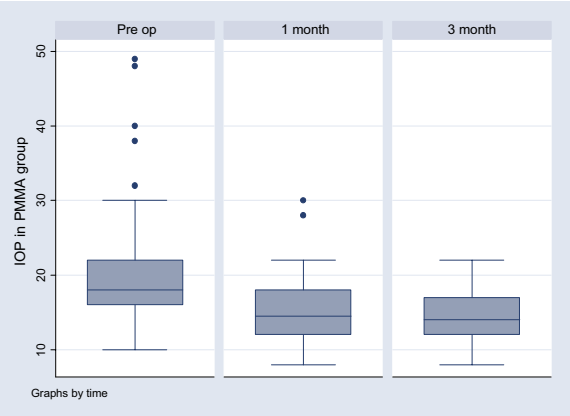



*Figure – 1*

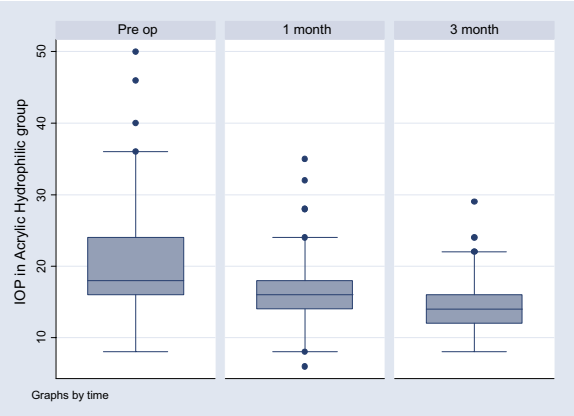



*Figure – 2*

Table - 1: Intraocular pressure (IOP)

| IOP | PMMA | | Acrylic Hydrophili | |
|---|---|---|---|---|
| | Mean± SD | Range | Mean± SD | Range |
| At Pre-op | 20.9± 8.2 | 10-49 | 21.0± 8.8 | 8-50 |
| At 1 month | 15.8± 4.6 | 8-30 | 16.3± 5.5 | 6-35 |
| At 3 month | 14.7± 3.1 | 8-22 | 14.6± 4.2 | 8-29 |

*SD- Standard Deviation*

There was a statistically significant reduction in IOP over time (P-value<0.001). But there is no statistically significant difference between the two groups in reduction on IOP over time (P-value=0.871).

## Results of repeat trabeculectomy with MMC 0.02% in POAG

Investigator : Dr. Rohan Daniel, Aravind - Coimbatore
Dr. Ganesh V Raman, Aravind - Coimbatore
Dr. Anoop Thomas, Aravind - Coimbatore
Dr. P. Sathyan, Aravind - Coimbatore

### Aims

**Primary aim:** To assess the reduction of IOP (success) after repeat trabeculectomy in POAG patients at 1 year.

**Secondary Aim:** To report changes in the visual acuity, number of medications used before and after surgery, complications following surgery.

### Methods

Retrospective review of case records of 27 eyes of 27 patients with 1 year follow-up, with POAG who underwent repeat trabeculectomy at Aravind Eye Hospital, Coimbatore between 1996 to 2007 was done. All patients underwent a fornix based triangular scleral flap trabeculectomy with mitomycin – C 0.02% for 4 minutes. At the end of 1 year success was defined as IOP < 18mmHg without medication, Qualified success as IOP < 18 with medication or IOP between 18 – 21 with or without medication, and failure IOP > 21mmHg with or without medication. Visual acuity was recorded based on Snellen's test types and was scored as follows 1 = 6/6-6/9, 2 = 6/12-6/18, 3 = 6/24-6/36, 4=6/60-4/60, 5 = 3/60-2/60, 6 < 1/60 for statistical purposes.

### Results

The mean age of the patients was 53.8 years and 88.9% of patients were males. The mean preoperative IOP was 24.1mmHg (range 26.2 to 22.0mmHg) and the mean postoperative IOP was 17.4mmHg

(range 19.4 to 15.4mmHg) (P=0.000). At the end of 1 year success was achieved in 29.6% of cases, qualified success in 48.1% of cases, and failure in 22.2% of cases. Preoperative visual acuity was better than 6/18 in 77.8 % of patients, and worse than 3/60 in 14.8% of patients. The visual acuity deteriorated to less than 6/18 in 9.5 % of patients at the end of 1 year, although the number of patients who had very poor visual acuity remained constant at the end of 1 year (14.8%). The number of medications used preoperatively was 1.62 per patient, and this was reduced to 0.6% at the end of 1 year. Of the 27 eyes which underwent repeat trabeculectomy only 4 eyes had prior surgery elsewhere, the other eyes had undergone surgery in our centre. Sixteen of the 27 eyes had releasable suture application. Of those 16 eyes only 1 patient had transient shallowing of the anterior chamber which resolved with conservative medical management. 2 patients (hyphaema-1, choroidal detachment-1) required surgical intervention. Four patients had very low visual acuity (score 5 and 6) because of advanced glaucomatous optic neuropathy (marked disc pallor-1, cataract-1, Retinitis Pigmentosa-1).

### Conclusion

Repeat trabeculectomy with Mitomycin – C is an effective procedure in failed filters not controlled in primary open angle glaucoma patients. The procedure is successful and carries similar safety profile as that of primary trabeculectomy in experienced hands. The low IOPs without medications are achieved in only approximately 30% of cases but the procedure helps to reduce the number of medications per patient in the long term.

## Assessment of consensual ophthalmotonic reaction (COR) following diode laser cyclophotocoagulation (DLCP) for advanced / refractory glaucoma


Investigator : Dr. P. Bendele, Aravind - Coimbatore
Dr. G. V. Raman, Aravind - Coimbatore
Dr. S. J. Prasanna, Aravind - Coimbatore
Dr. F. Francis, Aravind - Coimbatore
Dr. R. Daniel, Aravind - Coimbatore
Dr. P. Sathyan, Aravind - Coimbatore


### Objectives

**Primary outcome:** to assess the difference between the pre-op IOP and post-op IOP of treated eye, and the difference between the pre-op and post-op IOP of the untreated better eye.
**Secondary outcome:** response to diode laser treatment and pre-op IOP.

### Material and methods

Retrospective charts of forty one patients were included in the study. All patients underwent transscleral DLCP between October 2007 to March 2008. In the Glaucoma Clinic, Aravind Eye Hospital, Coimbatore. Standard parameters of DLCP were used in all the patients such as duration of 2000ms, Power 2000-2500 W, 12-40 spots.

### Results

**Table 1: Demographic data of 41 patients**

| | |
|---|---|
| Eyes | 41 |
| Patients | 41 |
| Sex | |
| Male | 25 |
| Female | 16 |
| Race | South Asian |
| Age (SD) | 60.63 years (18.12) |
| (Range) | (19-111 yrs.) |
| Eye | |
| Right | 51 % |
| Left | 49 % |

The mean preoperative IOP in the treated group was 45.02±10.6 mmHg. The mean postoperative IOP in the treated eye after 1 month was 19.80 +/- 13.5 mmHg and 21.27±12.79 mmHg at 3 months. The mean preoperative IOP in the untreated eye was 16.90±6.9 mmHg and the mean postoperative IOP in the untreated eye was 14.88±4.7 mmHg at 1 month and 16.44±4.34 mmHg at 3 months. Significant reduction of IOP was observed in the treated eye at one month (p-value = 0.0000) and at 3 months (p = 0.0002) (Wilcoxon signed-rank test). No significant reduction in IOP was observed in the untreated eye at one ($p<0.05$) and three months ($p<0.73$). There was a positive correlation ($r=0.283$) observed between preoperative IOP of the treated eyes and number of DLCP spots. However, this was not statistically significant (P-value = 0.08).

### Conclusion

This small retrospective analysis did not show any consensual ophthalmotonic reaction following DLCP. It may be that the untreated eye (1) did not have IOP high enough to show changes, (2) being the better eyes were on maximum medical therapy (3) did not have similar type of glaucoma (4) may have undergone various surgical procedure. Further prospective studies are needed to establish the clinical effect of COR glaucoma patients blind in one eye because of absolute/ refractory glaucoma should undergo aggressive treatment for both eyes as some patients may benefit from the COR.

## Optical coherence tomography measurement of the retinal nerve fibre layer in normal and juvenile glaucomatous eye

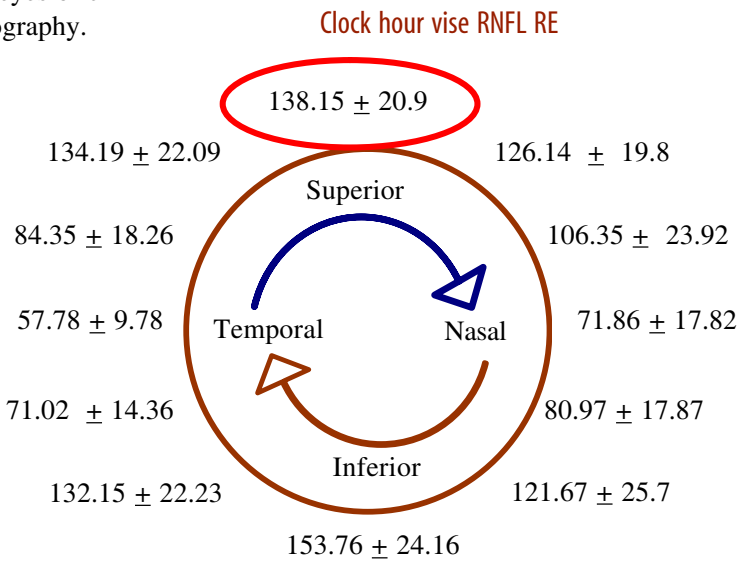
Investigators : Dr. Devendra Maheswari, Aravind - Tirunelveli
Dr. Rama Krishnan R., Aravind - Tirunelveli
Dr. Mohideen Abdul Kadar, Aravind - Tirunelveli

### Aim

To quantitatively assess and compare the thickness of the peripapillary retinal nerve fiber layer (RNFL) in normal and glaucomatous eyes of children using the optical coherence tomography.

### Method

The mean RNFL thickness of normal paediatric eyes (n=28) was compared to that of paediatric glaucomatous eyes (n=28). The eyes were classified into diagnostic groups based on conventional ophthalmologic examination, stereoscopic optic nerve head evaluation by experienced glaucoma specialist and optical coherence tomography by stratus OCT.3. The mean RFNL was significantly thinner in glaucomatous eyes than in normal eyes: 75.72±11.92µm, respectively. More specifically, the RNFL was significantly thinner in glaucomatous eyes than in normal eyes in the inferior quadrant: 90±25.6 and 135.74±14.72µm, respectively.




### Results

The mean and inferior quadrant RFNL thickness as measured by the optical coherence tomography showed a statistically significant correlation with glaucoma.

| | Mean | SD |
|---|---|---|
| Superior | 131 ± | 16.37 µm |

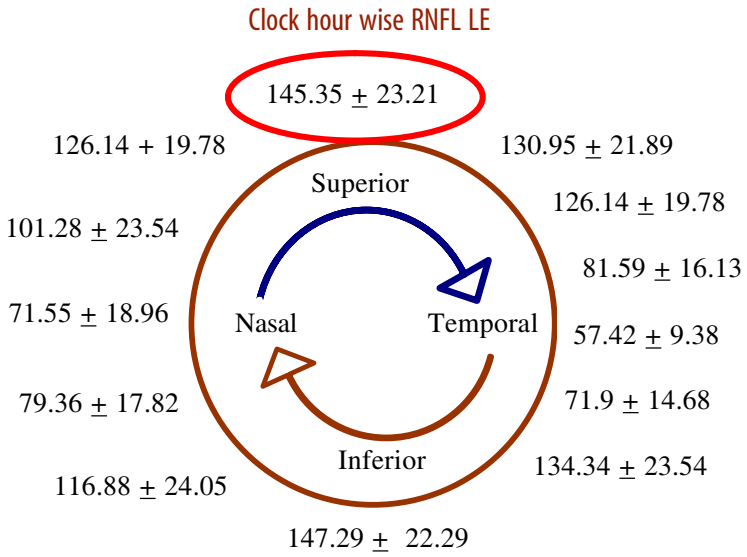
### Conclusion

Optical coherence tomography may contribute in detecting early RNFL loss in Juvenile open angle glaucoma.

### RNFL thickness by quadrants

| | | |
|---|---|---|
| Nasal | 83.88 ± | 18.68µm |
| Inferior | 135.8 ± | 16.87µm |
| Temporal | 73.00 ± | 9.67µm |

- I>S>N>T (I >S, P<0.05; N>T, P<0.0001 Student - t test)
- Average RNFL thickness 107.9 ± 9.2µm (Range, 82.26-140.33)




## Study of diode laser cyclophotocoagulation in refractory glaucoma in South Indian population

Investigator : Dr. Mohideen, Aravind - Tirunelveli
Dr. Rama Krishnan R, Aravind - Tirunelveli
Dr. Vishal Kishore, Aravind - Tirunelveli
Dr. Devendra Maheswari, Aravind - Tirunelveli
Dr. Rita Singh, Aravind - Tirunelveli

### Aims & Objectives

To study the effect of diode laser cyclophotocoagulation on IOP, vision, number of medication and complications in South Indian population of patients with refractory glaucoma.

**Design :** Prospective, non randomised, interventional study.

### Material and method

We enrolled 47 patients for treatment but 5 subjects were excluded from the study on the basis of exclusion criteria, hence final sample size was 42 patients. Patients were subjected to thorough pre-treatment examination and then underwent diode laser cyclophotocoagulation. Regular review on 1st day, 1st week, and 6th month posttreatment. Detailed examination done on all follow ups. The study parameters namely vision, intraocular pressure, posttreatment complication, addition/ omission of any anti-glaucoma drugs and any additional procedure were noted on all follow up visits. (Statistical analysis was done by ANOVA and paired t test.)

### Result

Intraocular pressure decreased during posttreatment visit and this was statistically highly significant in all follow up visits ($p<0.001$), there was decrease in the number of anti-glaucoma drops administered during pretreatment and 6 month posttreatment. ($p<0.05$), no deterioration in vision was noted. Post DLCP only few complications were noted on first few visits. No complications were noted in 3rd and 6th month follow ups.

### Conclusion

DLCP is effective, repeatable and relatively complication free procedure for adequate and sustained intraocular pressure (IOP) reduction in eyes with refractory glaucoma in a South Indian population.

### Diagnosis statistics

Table 9: Diagnostic classification of study eyes

| Sl.No | Diagnosis | Number | Percentage (%) |
|---|---|---|---|
| 1. | Neovascular glaucoma | 13 | 30.9 |
| 2. | Primary open angle glaucoma (advanced) | 8 | 19.05 |
| 3. | Glaucoma in pseudophakia | 8 | 19.5 |
| 4. | Primary angle closure glaucoma without papillary block | 3 | 7.1 |
| 5. | Secondary angle closure glaucoma | 3 | 7.1 |
| 6. | Pseudo exfoliation (PxF) glaucoma | 2 | 4.8 |
| 7. | Silicon oil induced glaucoma | 2 | 4.8 |
| 8. | Post keratoplasty glaucoma | 1 | 2.4 |
| 9. | ICE syndrome | 1 | 2.4 |
| 10. | Axenfield - Reiger syndrome | 1 | 2.4 |
| | **Total** | **42** | **100** |

Neovascular glaucoma was seen in 30.9% of the study subjects (most common). Post keratoplasty glaucoma, ICE syndrome and Axenfield – Reiger syndrome were least. Noted in the study eyes with a distribution of 2.4% each, respectively.

## Intraocular pressure and central corneal thickness - A comparison between non-contact tonometry and Goldmann applanation tonometry

Investigators : Dr. Sandeep Reddy, Aravind - Tirunelveli
Dr. Rama Krishnan R., Aravind - Tirunelveli
Dr. Devender Maheswari, Aravind - Tirunelveli
Dr. Sandeep Bachu, Aravind - Tirunelveli
Dr. Venkatrami Reddy, Aravind - Tirunelveli

### Aims and objectives

To study the influence of corneal thickness in measuring IOP in patients using non-contact tonometer and applanation tonometer.

### Introduction

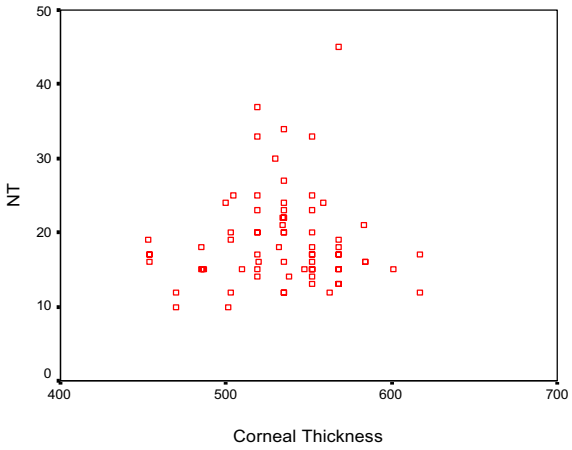
Corneal thickness and deformation seem to have a considerable influence on IOP measurement. Due to difference in corneal deformation in either non-contact tonometer or applanation tonometer, both the methods should be compared in the same group depending on corneal thickness. Study design – A randomised cross-sectional study.

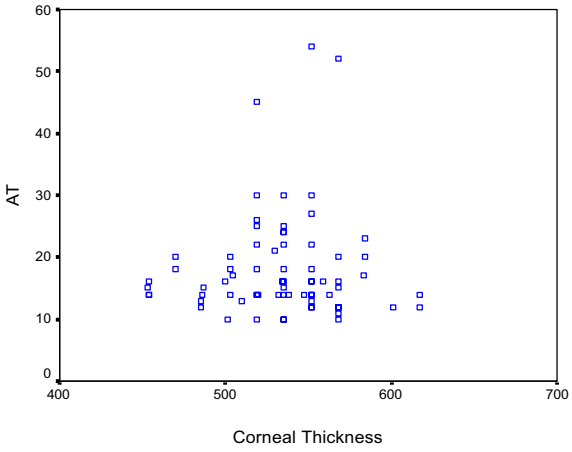
### Material and methods

Study group – all the patients attending glaucoma clinic at our hospital suspected to have glaucoma were included; exclusion criteria – Corneal pathology, previous intraocular surgery and refractive surgery, patients using any ocular medications.

### Methods

100 eyes of 50 patients of suspected cases of glaucoma are taken and their central corneal thickness is measured in each eye by pacscan-300p. IOP is measured in each eye with non-contact tonometer (Topcon CT.80) and 30 minutes later by Goldmann applanation tonometry; Results – Goldmann applanation and non-contact tonometer show good correlation at low central corneal thickness, but NCT gives a higher reading than applanation tonometer at high central thickness.




| | Mean IOP ± SD | | | | |
|---|---|---|---|---|---|
| Corneal Thickness (m) | Non contact Tonometer (mm Hg) | Goldmann Tonometer (mm Hg) | P value | Correlation coefficient | Significance of correlation |
| Entire group | 18.88 ±6.4 | 17.93 ±8.34 | <0.01 | 0.352 | <.01 |
| <513.0 | 18.27 ±4.9 | 17.30 ±3.90 | <0.01 | -0.106 | >.01 |
| 514-539 | 19.14 ±5.81 | 18.27 ±6.27 | >0.01 | -0.345 | >.01 |
| 540-575 | 21.70 ±3.46 | 20.33 ±3.90 | <0.01 | -0.046 | >.01 |
| >575 | 22.40 ±5.00 | 19.47 ±3.55 | <0.01 | 0.634 | <.01 |

## Long term results of mitomycin C enhanced trabeculectomy in young adults

Investigators : R. Ramakrishnan, Aravind - Tirunelveli
R. Singh, D Maheshwari, Aravind - Tirunelveli
MA Kader, Aravind - Tirunelveli

### Purpose

To evaluate long term outcome of trabeculectomy with mitomycin C (MMC) in management of glaucoma in young adults (15-45 years).

### Methods

All patients (15-45years) of glaucoma who underwent trabeculectomy with MMC from January 2004 to December 2006 were included. The medical records of 65 patients (78 eyes) were reviewed .53 surgeries were performed in primary glaucomas, 19 for secondary glaucomas and rest 6 were for developmental glaucomas. Pre and post operative IOP, visual acuity, success rate, surgical failure and complications were main outcomes measured.

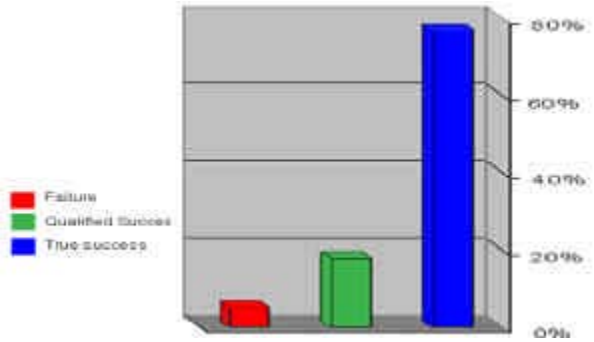
### Results

The mean age of patients was 32.6±8.7 years at the time of trabeculectomy. The IOP reduced from a preoperative level of 32.2±10.5mmHg to a postoperative level of 12.6±5.2mmHg at one year follow up. Complete success was achieved in 76.9%, qualified success in 17.9% and failure rate in 5.2%.

### Conclusion

The success rate of trabeculectomy with MMC was 76.9%, by the end of one year. MMC enhanced trabeculectomy is an effective method of IOP control in young adults.

| **Diagnosis** | **Success** | **Qualified success** | **Failure** | **Total** |
|---|---|---|---|---|
| Primary glaucomas | 39 (73.5%) | 11 (20.7%) | 3 (5.7%) | 53 |
| Secondary glaucomas | 15 (78.9%) | 3 (15.7%) | 1 (11.2%) | 19 |
| Developmental glaucomas | 6 (100%) | - | - | 6 |




| Complications | Number | Percentage |
|---|---|---|
| Bleb failure | 4 | 5.1 |
| Hypotonus maculopathy | 2 | 2.5 |
| **Total** | **6** | **7.6** |

## Long term effect on IOP control after clear corneal phacoemulsification in previous successful trabeculectomies

Investigators : R. Singh, Aravind - Tirunelveli
D. Maheshwari, Aravind - Tirunelveli
MA Kader, Aravind - Tirunelveli
D. Jyoti, Aravind - Tirunelveli
R Ramakrishnan, Aravind - Tirunelveli

### Purpose

To study the effect of phacoemulsification with IOL implantation in previous successful trabeculectomies.

### Methods

60 eyes of 60 patients who underwent temporal clear corneal phacoemulsification after successful filtering surgeries were included. In all patients comparison of preoperative and postoperative IOP, visual acuities, bleb morphology and number of medications were noted. Follow up was done after 1st month, 3rd month, sixth month and one year.

### Results

The mean preoperative visual acuities were 0.98±0.44, and at end of one year postoperative visual acuities was 0.20± 0.21 ( p value less than 0001) 31.7 % of eyes developed fibrosis of the bleb with decrease in the bleb size. The mean IOP before phacoemulsification was 12.42±4.6mm hg and was increased to 14.98, 14.47, 15.44, 15.71 after 1,3,6 and 12 months respectively. At each interval mean IOP was significantly higher than preoperative value (with p value p= 0.000, 0.015, 0.000, and 0.0001 respectively). The mean number of medications before phacoemulsifications was 0.57 and it increased to 0.67 after one year, but difference was not statistically significant.

### Conclusions

This study showed that temporal clear corneal phacoemulsification significantly increases IOP in eyes with pre-existing functioning bleb and alters bleb morphology.

## Retinal nerve fibre layer thickness in normal Indian paediatric population measured with optical coherence tomography

Investigators : Dr. N. Pawar, Aravind - Tirunelveli
Dr. D. Maheshwari, Aravind - Tirunelveli
Dr. R. Ramakrishnan, Aravind - Tirunelveli

### Purpose

To measure the peripapillary retinal nerve fiber layer (RNFL) thickness in normal Indian paediatric population.

### Methods

120 normal children aged 4 to 17 years presenting to Paediatric Clinic at the Aravind Eye Hospital, Tirunelveli, Tamilnadu were included in the study. Retinal nerve fiber layer thickness was measured with optical coherence tomography (Stratus OCT). Patient cooperation and signal strength of the OCT scans were assessed. Slit lamp biomicroscopy was done by a glaucoma specialist in a masked fashion. Children with strabismus or amblyopia with neurological, metabolic, vascular, or other disorders were excluded. Eyes with abnormal optic discs were excluded. One eye of each subject was randomly selected for statistical analysis. The effect of various factors on RNFL thickness was investigated statistically.

### Results

Mean age (±standard deviation [SD]) was 10.8±3.24 years. Mean RNFL thickness (±SD) was (107.9±9.2µm) (range, 82.26-140.33). The RFNL was thinnest inferiorly (135.8±16.87µm) and thinnest temporally (73.00±9.67µm). Age and refraction ($p<0.001$) had a significant effect on RNFL thickness.

### Conclusions

Optical coherence tomography can be used to measure RNFL thickness in children. In normal children, variation in RNFL thickness is large. The normative data provided by this study may assist in identifying changes in RNFL thickness in Indian children.

### Demographics

| | **Normal (n=28)** | **Juvenile Glaucoma (n=28)** |
|---|---|---|
| Age | 5-16years | 9 – 17 years |
| Mean ±SD | 10.32 ± 3.5 | 14.10 ± 2.97 |
| Sex | 13 Males | 18 Males |
| | 15 Females | 10 Females |

### Retinal nerve fibre layer thickness (RFNL by stratus OCT) in µm

| | **Superior** | **Inferior** | **Nasal** | **Temporal** | **Mean RFNL** |
|---|---|---|---|---|---|
| Normal | 131±16.37 | 135.85 ± 14.48 | 83.88± 18.68 | 73.00 ±9.6 | 107.69 ± 9.2 |
| JOAG | 95 ± 19.27 | 91.17±25.96 | 65.82 ± 19.3 | 57.14± 13 | 75.72 ± 16.81 |
| | | *P < 0.001 | | | *P < 0.001 |

*P value < 0.001 student paired t Test

## A comparative study of efficacy, complications and corneal topography following single-site versus twin-site phacotrabeculectomy

Investigators : Dr. Rama Krishnan, Aravind - Tirunelveli
Dr. Mohideen, Aravind - Tirunelveli
Dr. Abhilasha, Aravind - Tirunelveli
Dr. Rita Singh, Aravind - Tirunelveli

### Aims and objectives

- To compare the efficacy of intraocular pressure control and complications in patients treated with single-site versus twin-site phacotrabeculectomy.
- To compare the change in corneal topography in patients treated with single-site versus twin-site phacotrabeculectomy

## Introduction

The decision to perform phacotrabeculectomy through single-site or twin-site remains controversial. The purpose of this study is to compare the results of single-site and twin-site combined phacoemulsification with intraocular lens (IOL) implantation and trabeculectomy surgery with respect to efficacy, complications and corneal topography.

**Design :** Comparative prospective interventional study

## Patients and methods

Results of twin site phacotrabeculectomy (superior trabeculectomy and temporal Phacoemulsification with PCIOL implantation) in 50 eyes of 50 patients are prospectively being reviewed with a minimum follow-up of 1 year. The twin site procedures are being compared with randomly chosen group of 50 eyes of 49 patients undergoing single site phacotrabeculectomy (superior trabeculectomy and phacoemulsification with PCIOL implantation through the same incision), performed by the same surgeon.

## Inclusion criteria

Presence of visually significant cataract in patients with POAG, PACG, PXS and pigmentary glaucoma.

## Exclusion criteria

- Previous ocular surgery
- Any corneal opacity / degeneration
- Previous argon laser trabeculoplasty
- Corneal decompensation
- Secondary glaucoma

## Statistical analysis

The results of both groups will be compared on the basis of efficacy of intraocular pressure control complications, and induced astigmatism by means of corneal topography, using paired student t test.

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# RETINA SERVICES

## Drug Trials

### Efficacy and safety of posterior juxtascleral administrations of anecortave acetate for depot suspension (15mg or 30mg) versus sham administration in patients at risk for progressing to exudative Age-Related Macular Degeneration (AMD)

| | | |
|---|---|---|
| Principal Investigator | : | Dr. R. Kim, Aravind - Madurai |
| Co-Investigators | : | Dr. Anand Rajendran, Aravind - Madurai |
| | | Dr. Sathya J. Kakade, Aravind - Madurai |
| Funding Agency | : | Alcon Research Ltd. |
| Duration | : | Four years and 6 months (2006 - 2010) |

#### Objectives

The primary objective of this study is to demonstrate that anecortave Acetate for depot suspension (15mg or 30mg) is safe and effective in arresting the progression of non-exudative (dry) AMD in patients who are at-risk for progressing to exudative (wet) AMD.

### A Six-month, phase 3, multicenter, masked, randomised, sham-controlled trial (with six-month open-label extension) to assess the safety and efficacy of 700 µg and 350 µg dexamethasone posterior segment drug delivery system (DEX PS DDS) applicator system in the treatment of patients with macular edema following central retinal vein occlusion or branch retinal vein occlusion

| | | |
|---|---|---|
| Principal Investigator | : | Dr. R. Kim, Aravind - Madurai |
| Co-Investigators | : | Dr. Dhananjay Shukla, Aravind - Madurai |
| | | Dr. Naresh Babu, Aravind - Madurai |
| Funding Agency | : | Allergan India Private Ltd. |
| Duration | : | Two years (2006 - 2008) |

#### Objective

To evaluate the safety and efficacy of the 700µg DEX PS DDS Applicator system (700µg dexamethasone) and 350µg DEX PS DDS applicator system (350µg dexamethasone) compared with a sham DEX PS DDS applicator system (needle-less applicator) in patients with macular edema due to branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO).

### A safety and efficacy assessment of vitreosolve® for ophthalmic intravitreal injection for inducing posterior vitreous detachment in non-proliferative diabetic retinopathy subjects

| | | |
|---|---|---|
| Principal Investigator | : | Dr. R. Kim, Aravind - Madurai |
| Co-Investigator | : | Dr. Somnath Chakraborty, Aravind - Madurai |
| Funding Agency | : | Vitreoretinal Technologies Ltd. |
| Duration | : | 2007 - 2008 |

#### Objective

The objective of this study is to evaluate the safety and efficacy of Vitreosolve® Ophthalmic intravitreal injection for inducing a posterior vitreous detachment in non-proliferative diabetic retinopathy subjects.

## A randomised, double masked, active controlled, phase 3 study of the efficacy, safety, and tolerability of repeated doses of intravitreal VEGF trap-eye in subjects with neovascular age-related macular degeneration (AMD)

Principal Investigator : Dr. R. Kim, Aravind - Madurai
Co-Investigators : Dr. Anand Rajendran, Aravind - Madurai
Dr. Umesh Chandra Behera, Aravind - Madurai
Dr. Anuradha, Aravind - Madurai
Funding Agency : Bayer Schering Pharma Ltd.
Duration : 2008 - 2010

### Objectives

#### Primary objective

To assess the efficacy of intravitreally (ITV) administered VEGF trap-eye compared to ranibizumab (in a non-inferiority paradigm) in preventing moderate vision loss in subjects with all subtypes of neovascular AMD.

#### Secondary objectives

- To assess the safety and tolerability of repeated ITV administration of VEGF trap-eye in subjects with all subtypes of neovascular AMD for up to 2 years.
- To assess the effect of repeated ITV administration of VEGF trap-eye in vision-related quality of Life (QOL) in subjects with all subtypes of neovascular AMD, as assessed using the NEI VFQ-25. To describe systemic exposure to study drug.

## A study of featureless retina in diabetic retinopathy: Clinical and angiographic features and therapeutic implications

Principal Investigator : Dr. Dhananjay Shukla, Aravind - Madurai
Co-Investigator : Dr. Somnath, Aravind - Madurai
Dr. Rajkumar, Aravind - Madurai

### Objective

The study aims to put forward guidelines for clinical-investigational clues to diagnose featureless retina in diabetic retinopathy patients and determine its angiographic and systemic associations.

## A retrospective analysis of patients with idiopathic macular telangiectasia (IMT): Natural history, incidence of visual loss and investigations of causes of visual loss

Principal Investigator : Dr. Dhananjay Shukla, Aravind - Madurai
Co-Investigator : Dr. Somnath, Aravind - Madurai
Dr. Sachin, Aravind - Madurai
Dr. Shashank, Aravind - Madurai
Dr. Sumi, Aravind - Madurai

### Objective

To study the natural history, incidence of visual loss and causes of visual loss in IMT

## A retrospective study of the natural history of lamellar macular hole

Principal Investigator : Dr. Dhananjay Shukla, Aravind - Madurai
Co-Investigator : Dr. Praveen. M., Aravind - Madurai

### Objective

To study the natural history of lamellar macular hole, the various etiologies and change in visual and anatomic status.

## A study of polypoidal choroidal vasculopathy: incidence, angiographic and tomographic features

Principal Investigator : Dr. Dhananjay Shukla, Aravind - Madurai
Co-Investigator : Dr. Umesh, Aravind - Madurai
Dr. Praveen M, Aravind - Madurai

### Objective

To study the epidemiology, angiographic and tomographic features of idiopathic polypoidal choroidal vasculopathy

## Atypical manifestations of posterior scleritis: diagnosis and management

Principal Investigator : Dr. Dhananjay Shukla, Aravind - Madurai
Co-Investigator : Dr. Anuradha Dhawan, Aravind - Madurai

### Objective

To describe and document key features of diagnosis and management of patients presenting without classical symptoms or signs of posterior scleritis.

## A restrospective study of anatomic and functional outcome of chronic macula-off rhegmatogenous retinal detachment

Principal Investigator : Dr. Dhananjay Shukla, Aravind - Madurai
Co-Investigator : Dr. Anuradha Dhawan, Aravind - Madurai
Dr. Sathya Kakade, Aravind - Madurai

### Objective

To study the anatomic and functional outcome of chronic macula-off rhegmatogenous retinal detachment and to determine the duration of retinal detachment after which intervention is of insignificant value.

## A prospective study of transpupillary thermotherapy (TTT) for chronic central serous chorioretinopathy (CSCR)

Principal Investigator : Dr. Dhananjay Shukla, Aravind - Madurai
Co-Investigator : Dr. T.P. Vignesh, Aravind - Madurai
Dr. Anand Rajendran, Aravind - Madurai
Dr. Shashank, Aravind - Madurai

### Objective

To evaluate TTT as a potential treatment for subfoveal and juxtafoveal leaks in chronic CSCR as compared to observation in a prospective non-randomised controlled trial.

## Atypical acute posterior multifocal placoid pigment epitheliopathy associated with serous retinal detachment: Clinical and angiographic features and treatment

Principal Investigator : Dr. Dhananjay Shukla, Aravind - Madurai
Co-Investigator : Dr. Umesh Behera, Aravind - Madurai
Dr. S.R. Rathinam, Aravind - Madurai
Dr. Emmett T. Cunningham, Aravind - Madurai
Dr. Anuradha Dhawan, Aravind - Madurai

### Objective

To report an atypical variant of acute posterior multifocal placoid pigment epitheliopathy with retinal detachment and its response to systemic corticosteroids over a long follow-up.

## Post pan retinal photocoagulation (PRP) serous macular detachment in patient with nephropathy

Principal Clinician : Dr. Dhananjay Shukla, Aravind - Madurai
Team : Dr. Mahesh Chandargi, Aravind - Madurai
Dr. Bharat Ramchandani, Aravind - Madurai
Dr. Anuradha Dhawan, Aravind - Madurai

### Objective

To report serous macular detachment as a cause of severe visual loss following PRP. Authors enlist the recommended management and salient tips to prevent the complication.

## Serous macular detachment as a predictor of resolution of vascular macular edema with intravitreal Triamcinolone injection

Principal Clinician : Dr. Dhananjay Shukla, Aravind - Madurai
Team : Dr. Umesh C Behera, Aravind - Madurai
Dr. Somnath Chakraborty, Aravind - Madurai

### Objective

To analyse and conclude the visual outcome and anatomical changes as on OCT, following treatment with intravitreal triamcinolone acetate in macular edema with serous detachment from retinal vascular diseases.

## Pigment epithelial detachment (PED) in chronic central serous retinopathy (CSCR)

Principal Clinician : Dr. Dhananjay Shukla, Aravind - Madurai
Team : Dr. Jay Kalliath, Aravind - Madurai
Dr. Sangamitra Kanungo, Aravind - Madurai

### Objective

To demonstrate the advantage of OCT over fluorescein angiography in detecting occult PED's in Chronic CSCR.

## Serous macular detachment as a predictor of malignant hypertension

Principal Clinician : Dr. Dhananjay Shukla, Aravind - Madurai
Team : Dr. Bharat Ramchandani, Aravind - Madurai
Dr. T.P. Vignesh, Aravind - Madurai
Dr. Anand Rajendran, Aravind - Madurai
Ms. Nithya Neelakandan, Aravind - Madurai

### Objective

To highlight serous macular detachment as a sign in the diagnosis of accelerated hypertension in hypertensive retinopathy vis-a-vis disc edema.

## Vitrectomy for macular hole associated with rhegmatogenous retinal detachment

Principal Clinician : Dr. Dhananjay Shukla, Aravind - Madurai
Team : Dr. Anand Rajendran, Aravind - Madurai
Dr. Somnath Chakraborty, Aravind - Madurai

### Objective

To evaluate the usefulness of internal limiting membrane peeling for macular hole associated with rhegmatogenous retinal detachment in a prospective case-control study.

## Radial optic neurotomy for ischaemic central retinal vein occlusion: a case-control study

Principal clinician : Dr. Dhananjay Shukla, Aravind - Madurai
Team : Dr. Anand Rajendran, Aravind - Madurai
Dr. Sathya Kakade, Aravind - Madurai

### Objective

To evaluate radial optic neurotomy as a treatment option for ischaemic central retinal vein occlusion against conventional treatment with photocoagulation.

## Brilliant blue dye for internal limiting membrane peeling in macular surgery

Principal Clinician : Dr. Dhananjay Shukla, Aravind - Madurai
Team : Dr. Jay Kalliath, Aravind - Madurai

### Objective

To evaluate brilliant blue dye for internal limiting membrane peeling in macular surgeries like macular hole, epimacular membrane and tractional macular edema.

## Vitrectomy for fovea-threatening tractional retinal detachment in diabetic retinopathy

Principal Clinician : Dr. Jay Kalliath, Aravind - Madurai
Team : Dr. Dhananjay Shukla, Aravind - Madurai

### Objective

To evaluate the results of vitrectomy for fovea-threatening tractional retinal detachment in diabetic retinopathy.

## Laser photocoagulation for diabetic macular edema with serous retinal detachment

Principal Clinician : Dr. Dhananjay Shukla, Aravind - Madurai
Team : Dr. Jay Kalliath, Aravind - Madurai

### Objective

To evaluate the results of focal or grid photocoagulation for diabetic macular edema with serous retinal detachment as documented by optical coherence tomography

## Optical coherence tomography evaluation of subhyaloid haemorrhage of various etiologies

Principal Clinician : Dr. Dhananjay Shukla, Aravind - Madurai
Team : Dr. Jay Kalliath, Aravind - Madurai

### Objective

To determine the plane of cleavage in subhyaloid haemorrhage of various etiologies by optical coherence tomography.

## A study of combined occlusion of central retinal artery and vein

Principal Clinician : Dr. Dhananjay Shukla, Aravind - Madurai
Team : Dr. Sanghamitra Kanungo, Aravind - Madurai
Dr. Anuradha Dhawan, Aravind - Madurai

### Objective

To determine the systemic associations, diagnostic pitfalls and management options in combined occlusion of central retinal artery and vein.

## An invited review on leptospirosis (international ophthalmology clinics)

Ist author : Dr. Dhananjay Shukla, Aravind - Madurai
IInd author : Dr. Emmett T. Cunningham, Aravind - Madurai
Corresponding author : Dr. Rathinam Sivakumar, Aravind - Madurai

### Objective

To review the epidemiology, clinical features and ocular involvement in leptospirosis with focus on the developing world.

## Silicone oil tamponade in 23 gauge sutureless vitrectomy : long term anatomical and functional outcome

Principal Clinician : Dr. Naresh Babu, Aravind - Madurai
Team : Dr. R.Kim, Aravind - Madurai
Dr. Bharat Ramchandani, Aravind - Madurai

### Objective

To describe the feasibility of silicone oil tamponade as an option with sutureless 23 gauge vitrectomy system in varied vitreo-retinal etiologies.

## YAG hyaloidotomy with gas tamponade as a viable option for pre macular haemorrhage in PDR against surgical intervention by pars plana vitrectomy

Principal Clinician : Dr. Naresh Babu, Aravind - Madurai
Team : Dr. Bharat Ramchandani, Aravind - Madurai

### Objective

To put up a viable and equally successful minimal intervention procedure for pre macular haemorrhage in PDR patients

## IVTA Vs macular PHC for diffuse diabetic macular edema – prospective study

Principal Investigator : Dr. Anand Rajendran, Aravind - Madurai
Co-Investigator : Dr. Sumi, Aravind - Madurai
Dr. Priyanka Mohini, Aravind - Madurai

### Objective

To compare IVTA alone Vs macular PHC alone treatment of diffuse diabetic macular edema

## Isolated intravitreal bevacizumab therapy for choroidal neovascular membranes of multiple aetiologies

Principal Clinician : Dr. Anand Rajendran, Aravind - Madurai
Team : Dr. Bharat Ramchandani, Aravind - Madurai
Dr. Jay Kalliath, Aravind - Madurai
Dr. Shashank Rai Gupt, Aravind - Madurai

### Objective

To report an angiographic and tomographic analysis of intravitreal bevacizumab monotherapy on choroidal neovascular membranes of various aetiologies.

## Intravitreal bevacizumab as a preoperative adjuvant for diabetic macular tractional detachments with active new vessels

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| Principal Clinician | : | Dr. Anand Rajendran, Aravind - Madurai |
| Team | : | Dr. R. Kim, Aravind - Madurai |
| | | Dr. Deepak Agarwal, Aravind - Madurai |
| | | Dr. Anuradha Dhawan, Aravind - Madurai |

### Objective

To determine the visual and anatomic outcome of intravitreal bevacizumab as a preoperative adjuvant for diabetic macular tractional detachments with active new vessels.

## Intravitreal bevacizumab therapy for polypoidal choroidal vasculopathy

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| Principal Clinician | : | Dr. Anand Rajendran, Aravind - Madurai |
| Team | : | Dr. Shashank Rai Gupt, Aravind - Madurai |

### Objective

To evaluate Intravitreal bevacizumab therapy for polypoidal choroidal vasculopathy.

## A randomised, double-masked, parallel-group, multicenter, dose-finding comparison of the safety and efficacy of ASI-001A 0.5mg/day and ASI-001B 0.2mg/day flucinolone acetonide intravitreal inserts to sham injection in subjects with diabetic macular edema.

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| Principal Investigator | : | Dr. R. Ramakrishnan, Aravind - Tirunelveli |
| Co-Investigator | : | Dr. Ankit Avasthi, Aravind - Tirunelveli |
| | | Dr. Sachin Bodhale, Aravind - Tirunelveli |
| | | Dr. Divya Lakshmi K.S, Aravind - Tirunelveli |
| Funding Agency | : | Alimera Sciences, United States |
| Duration | : | 2007 - 2010 (3 years) |

### Purpose

To compare safety and efficacy of two different concentrations of intravitreal flucinolone acetonide in patients with diabetic macular edema.

## A randomised, double-masked, parallel group, multicenter, dose- finding comparison of the safety and efficacy of ASI-001A 0.5µg/day and ASI-001B 0.2µg/day fluocinolone acetonide intravitreal inserts to sham injection in subjects with diabetic macular edema

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| Principal Investigator | : | Dr. R.D. Ravindran, Aravind - Pondicherry |
| Co-Investigator | : | Dr. T.A. Aniruddha, Aravind - Pondicherry |
| | | Dr. Pankaja Dhoble, Aravind - Pondicherry |
| Funding Agency | : | Alimera Sciences, United States |
| Duration | : | 2006 - 2011 |

### Major objectives

#### Primary objectives

- The primary objectives are to determine whether either dose level of the injectable insert is superior to the control group with respect to the proportion of subjects who have an increase of 15 or more letters of BCVA (VA responders) at Months 18 and 36 compared to baseline.
- This trial will have two primary efficacy variables which will be split into 3 co primary endpoints across 18 and 36 months. The first primary variable will represent a clinically significant visual acuity improvement and will be tested at months 18 and 36, and the second will represent a clinically significant worsening in the diabetic retinopathy scale and will be tested at month 36

### Secondary objectives

Secondary study objectives are

- To choose the optimum dose level of intravitreal fluocinolone acetonide
- To compare the 2 dose levels versus the control group at other timepoints
- To evaluate the efficacy of ASI-001A and ASI-001 B in DME and diabetic retinopathy using other relevant measures.

## A phase 3 safety and efficacy study of vitreosolve® for ophthalmic intravitreal injection for inducing posterior vitreous detachment in retinopathy subjects

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| Principal Investigator | : | Dr. R.D. Ravindran, Aravind - Pondicherry |
| Co-Investigator | : | Dr. T.A. Aniruddha, Aravind - Pondicherry |
| | | Dr. Prasanna Raj, Aravind - Pondicherry |
| Funding Agency | : | Vitreoretinal Technologies |
| Duration | : | 2008 - 2009 |

### Objective

The objective of this study is to evaluate the safety and efficacy study of vitreosolve® ophthalmic intravitreal injection for inducing a posterior vitreous detachment in non proliferative diabetic retinopathy subjects.

## VEGF trap – eye: investigation of efficacy and safety in Wet AMD - A randomised, double masked, active controlled, phase 3 study of the efficacy, safety, and tolerability of repeated doses of intravitreal VEGF trap-eye in subjects either neovascular age-related macular degeneration (AMD)

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| Principal Investigator | : | Dr. R.D. Ravindran, Aravind - Pondicherry |
| Co-Investigator | : | Dr. T.A. Aniruddha, Aravind - Pondicherry |
| | | Dr. Pankaja Dhoble, Aravind - Pondicherry |
| | | Dr. Venugopal Reddy, Aravind - Pondicherry |
| Funding Agency | : | Bayer Schering Pharma |
| Duration | : | 2008 - 2010 |

### Objectives

#### Primary objective

To assess the efficacy of intravitreally (ITV) administered VEGF Trap-Eye compared to ranibizumab (in a non-inferiority paradigm) in preventing moderate vision loss in subjects with all subtypes of neovascular AMD.

#### Secondary objectives

To assess the safety and tolerability of repeated ITV administration of VEGF trap-eye in subjects with all subtypes of neovascular AMD for up to 2 years. To assess the effect of repeated ITV administration of VEGF trap-eye in vision-related quality of Life (QOL) in subjects with all subtypes of neovascular AMD, as assessed using the NEI VFQ-25.To describe systemic exposure to study drug.

## INDGEN AMD study (An add-on study to the INDEYE Study)

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| Principal Investigator | : | Dr. R.D. Ravindran, Aravind - Pondicherry |
| Co-Investigator | : | Dr. T.A. Aniruddha, Aravind - Pondicherry |
| | | Dr. Pankaja Dhoble, Aravind - Pondicherry |
| Funding Agency | : | Welcome Trust |
| Duration | : | 2008 - 2009 |

### Objectives

- To investigate genetic variants as possible contributors to the high rates of cataract in India.
- To enrich the sample acquired in the INDEYE study of environmental and nutritional factors in cataract and age related macular degeneration in India with cases from the same geographical location in order to achieve adequate power to test for disease associations in genetic studies by
  - Extending the data collection up to 3000 (Aravind Eye Hospital and Rajendra Prasad Centre) among 40 – 59 yrs in the same geographical location.
  - Recruiting an additional 500 cases of AMD patients from hospital clinics

DNA extraction and genetic association studies will be undertaken in the blood samples already banked from the 6000 participants (Aravind Eye Hospital and Rajendra Prasad Centre) of the INDEYE study and in the samples from newly recruited participants.

## Retinochoroidal coloboma - a comparison of laser barrage photocoagulation versus natural history

Principal Clinician : Dr. Anand Rajendran, Aravind - Madurai
Team : Dr. Bharat Ramchandani, Aravind - Madurai

### Objective

To analyse the role of laser barrage of RCC without retinal detachment when compared to observation.

## PVD-301- A Phase 3 safety and efficacy study of vitreosolve® for ophthalmic intravitreal injection for inducing posterior vitreous detachment in retinopathy subjects

Principal Investigator : Dr. V. Narendran, Aravind - Coimbatore
Co – Investigator : Dr. V.R. Saravanan, Aravind - Coimbatore
Dr. Parag K.Shah, Aravind - Coimbatore
Funding Agency : Vitreoretinal Technologies
Duration : 2008 - 2009

### Objective

The objective of the Study is to evaluate the Safety and Efficacy of Vitreosolve® Ophthalmic Intravitreal Injection for Posterior Vitreous Detachment (PVD) in Non-Proliferative Diabetic Retinopathy (NPDR) Subjects.

## A 12-month randomised, pilot study to compare the efficacy and safety of verteporfin (visudyne) photodynamic therapy (standard fluence) plus intravitreal ranibizumab (lucentis) versus verteporfin (visudyne) photodynamic therapy (reduced fluence) plus intravitreal ranibizumab (lucentis) in patients with subfoveal of juxtafoveal choroidal neovascularisation secondary to age-related macular degeneration.

Principal Investigator : Dr. V. Narendran, Aravind - Coimbatore
Co – Investigator : Dr. Rodney J. Morris, Aravind - Coimbatore
Funding Agency : Novartis Pvt Ltd
Duration : 2007 - 2009

### Objective

The aim of this study is to evaluate whether the combination therapy of visudyne PDT (a standard light dose) with Lucentis or visudyne PDT (a reduced light dose) with Lucentis is effective and safe for the treatment of choroidal neovascularisation (CNV) secondary to age related macular degeneration (AMD).

## Intravitreal VEGF trap-eye in subjects with neovascular age-related macular degeneration

Principal Investigator : Dr. V. Narendran, Aravind - Coimbatore
Co-Investigators : Dr. Rodney J. Morris, Aravind - Coimbatore
Dr. V.R. Saravanan, Aravind - Coimbatore
Funding Agency : Bayer Schering Pharma
Duration : 2008 - 2010

### Objectives

#### Primary objective

To assess the efficacy of intravitreally (ITV) administered VEGF trap-eye compared to ranibizumab (in a non-inferiority paradigm) in preventing moderate vision loss in subjects with all subtypes of neovascular AMD.

#### Secondary objectives

To assess the safety and tolerability of repeated ITV administration of VEGF Trap-Eye in subjects with all subtypes of neovascular AMD for up to 2 years. To assess the effect of repeated ITV administration of VEGF trap-eye in vision-related quality of Life (QOL) in subjects with all subtypes of neovascular AMD, as assessed using the NEI VFQ-25.To describe systemic exposure to study drug.

## Randomised controlled trial of Aurolase 532-I-1 with already available green laser (Iridex) in proliferative diabetic retinopathy

Principal Investigator : Dr. K. Naresh Babu, Aravind - Madurai
Setting : Retina Clinic, Aravind Eye Hospital, Madurai

### Objective

Ingeneus, Australia has designed a new frequency-doubled Nd:YVO4 green laser for Aurolab. System specifications, control parameters and safety and security features have been upgraded. Objective of this study is to demonstrate that green laser of Aurolab produces similar treatment effects on the retina when compared with commercially available green laser. 28 Diabetic retinopathy patients needing pan retinal photocoagulation (High risk PDR, Early PDR) for both eyes who are visiting the vitreo-retinal service of Aravind Eye Hospital, Madurai. Exclusion criteria are Advanced PDR, Clinically Significant Macular Edema (CSME), Nephropathy (Creatinine >2.0 mgs%, Urea >55 mgs), uncontrolled hypertension (160/100 mmHg), media opacities and prior laser. Study design is double blinded, two arm, Randomised Controlled Trial (RCT). Primary outcome measures are visual acuity and burn characteristics, the later will be assessed by pigmentation of burn and lateral spread of burn. Secondary endpoint is regression of retinopathy. After getting informed consent, patient will be included in this study. Laser for first eye will be randomly assigned. Next day second eye will be treated with other laser. A full scatter laser photocoagulation is done in each eye using the ETDRS guide lines. Patient is asked to compare the degree of pain with each eye. Pre and post OCT will be taken. After 15 days patient will come for next sittings of laser. After each sitting of laser photocoagulation, fundus photography shall be done to compare the course of the laser reaction. After completion of both the laser sessions, the patients are followed at 2nd month, 4th month and 6th month post laser. At each follow up visit, fundus photographs are taken covering the same areas photographed at the treatment visits. A separate retina specialist masked for the treatment areas will compare the laser reaction in treated areas at each visit, by looking at the fundus photographs. Final analysis will be done comparing the two types of green lasers with regard to subjective pain perceived by the patients, Laser scar progression, laser parameters required to achieve the optimal retinal treatment. As of now 32 eyes have been enrolled into this study and 31 eyes have completed 6th months follow up.

# ORBIT AND OCULOPLASTY

## Randomised, double blind, active controlled study of the efficacy, surgical outcome and complications of Silicone Rod Sling in frontalis sling suspension surgery

Principle Investigator : Dr. Usha Kim, Aravind - Madurai
Co-Investigators : Dr. Akash D Shah, Aravind - Madurai
Dr. Urvasi Solanki, Aravind - Madurai

### Objective

To compare the efficacy, surgical outcome and complication of Aurosling with Ethibond material in frontalis sling suspension surgery

### Methodology

Patients eligible on the basis of inclusion and exclusion criteria will be included in this study after getting informed consent. Frontalis sling suspension surgery using Aurosling or Ethibond will be done. Patients will be followed up for observing the surgical outcome, amount of Ptosis correction and post surgical complication in all cases. The results will be statistically analysed.

### Sample size

Subjects will be randomly assigned in a 1:1 ratio. 20 patients will be allotted to each arm

### Inclusion criteria

- Congenital ptosis
- Severe ptosis (MRD<0)
- Poor levator function (<4mm by Berke's method)
- Myogenic ptosis (Myasthenia gravis)
- Chronic progressive external ophthalmoplegia
- Neurogenic ptosis (Third cranial palsy)
- Blepharospasm
- Ptosis caused by trauma

### Exclusion criteria

- Acquired ptosis
- Horners syndrome
- Blepharochalasis / dermatochalasis
- Mechanical ptosis
- Mild or moderate ptosis (MRD 1>1)
- Good or fair levator function (>4 mm by Berke's method)
- Previous ptosis surgery
- Ptosis associated syndromes / other anomalies including
- Marcus Gunn jaw winking syndrome
- Blepharophimosis syndrome
- Dry eye syndromes
- Corneal anesthesia
- Medical / pediatric / Anesthesia condition contraindicating to surgery or anesthesia
- Nystagmus where adequate measurements could not be done
- Uncorrected vertical squint of any sort

### Budget

- Ethibond material = Rs.7,500
- Surgery cost (ptosis) = Rs.50,000
- Follow-up (including TA) = Rs. 11,250

Total budget is 68,750 Indian Rupees

### Out come measure

- Primary Outcome : Ptosis correction
- Primary Endpoints : MRD 1, Grading of Lagophthalmos
- Funding Agency : Aurolab
- Follow-up : 1st month, 3rd month, 12th month
- Starting Date : January 2009
- Duration : 24 months

## Socket reconstruction using bio-engineered autologous oral mucosal epithelium

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|---|---|---|
| Principal Investigator | : | Dr. Usha Kim, Aravind - Madurai |
| Co-Investigators | : | Dr. Gowri Priya Chidambaranathan, Aravind - Madurai |
| | | Dr. VR. Muthukkaruppan, Aravind - Madurai |
| | | Dr. Swarna Panigrahi, Aravind - Madurai |
| Period | : | January 2007 - May 2009 |

The loss of eye is often followed by scar tissue contracture if not taken care properly. Custom-made conformers can be used to enlarge unfavorably small sockets, improve hygiene, assist the clinician develop the final shape for the definitive prosthesis fitting. In order to retain the conformers in the socket, there is a need for a healthy epithelial support. In cases where the socket contraction is maximal, it is not possible to reconstruct the socket for the epithelial support with alternative tissue sources like dermis, conjunctival tissue etc., Therefore, it is essential to identify another alternative source in such cases. The objective of the present proposal is to use the patients own nonkeratinised buccal mucosal tissue for *ex vivo* expansion of buccal epithelium for socket reconstruction.

## Corneal surface reconstruction using bio-engineered autologous oral (Buccal) mucosal epithelium

| | | |
|---|---|---|
| Investigators | : | Dr. VR. Muthukkaruppan, Aravind - Madurai |
| | | Dr. N. Venkatesh Prajna, Aravind - Madurai |
| | | Dr. Usha Kim, Aravind - Madurai |
| | | Dr. M. Srinivasan, Aravind - Madurai |
| Funded by | : | Defence Research and Development Organisation – Life Science Research Board (DRDO – LSRB) |
| Duration | : | 2006 - 2009 |

When the limbel stem cells are completely depleted in both eyes, one possible therapy is to transplant the limbal tissue along with stem cells, either from a living donor or from cadaver eyes. In both instanses, there is a constant risk of immune rejection even with long-term immunosuppression. Therefore, the objective of the present proposal is to make use of an alternative source of nonkeratinised oral (Buccal) mucosal epithelium from the same patient. Autologous buccal mucosal epithelium, after separating from the underlying stroma will be cultured under appropriate conditions to generate epithelial sheet of 2.5cm diameter, which will be transplanted on to the defective corneal surface. The patients will be followed at least for a year to evaluate the restoration of ocular surface and vision. It is expected that the corneal transparency will be restored with good visual acuity in about 3-4 weeks of transplantation. The cellular profile of this alternative source of the corneal epithelium

will be characterised. Further, the presence of stem cells in Bio-engineered buccal mucosal epithelium will be determined. This new method of using autologous non-ocular source of stem cells would form a major advancement in the field of corneal surface reconstruction. The study will also elucidate the importance of adult stem cells in second generation therapeutic transplantation.

## Factors responsible for the generation of epithelial sheet rich in stem cells under *ex-vivo* conditions from the limbal and buccal biopsy

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| Principal Investigator | : | Dr. Gowri Priya Chidambaranathan, Aravind - Madurai |
| Co-Investigators | : | Dr. NV. Prajna, Aravind - Madurai |
| | | Dr. Usha Kim, Aravind - Madurai |
| Funding Source | : | Champalimaud - Aravind Research Grant |
| Period | : | June 2008 to May 2009 |

In order to expand the limbal stem cell population in culture, identification of proper niche/culture condition is essential. Since stem cells reside in the basal layer of the limbus and not in cornea, we hypothesise that certain factors in the limbal stroma are responsible for the maintenance of the stem cells. Further, it is of major concern to develop xenobiotic-free culture system for *ex vivo* expansion of stem cells. Hence the current study aims in developing a better culture condition for expanding the stem cells which can be used for transplantation in patients with limbal stem cell deficiency.
In order to validate the culture conditions for ex-vivo expansion of SCs, it is essential to have a specific SC marker. Recently, we have established a new method for identification of LESC by two parameter analysis – a greater N/C ratio and high expression of transcription factor p63 (Arpitha et al., 2005). In continuation to this, this study also aims to analyze the expression profile of the various isoforms of p63 and comparison with other putative stem cell markers like ABCG2.

### CV of the principal investigator

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| Name | : | Gowri Priya Chidambaranathan |
| Designation | : | Junior Scientist |
| Department/Institute | : | Department of Immunology, Dr. G. Venkataswamy Eye Research Institute |
| | | Aravind Medical Research Foundation |

## Developing xenobiotic-free culture conditions to generate stem-cell rich epithelium for corneal surface reconstruction

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|---|---|---|
| Principal Investigator | : | Dr. Gowri Priya Chidambaranathan, Aravind - Madurai |
| Co-Investigators | : | Dr. VR. Muthukkaruppan, Aravind - Madurai |
| | | Dr. NV. Prajna, Aravind - Madurai |
| | | Dr. Usha Kim, Aravind - Madurai |
| Funding Agency | : | Alcon Anterior Segment Research Grant |
| Period | : | October 2008 - September 2011 |

In patients with bilateral limbal stem cell deficiency, autologous buccal mucosal epithelial cells (BMECs) are used for in vitro expansion and corneal surface reconstruction. The most commonly used method for therapeutic in vitro expansion of SCs involves the use of a growth-arrested murine fibroblast feeder layer and serum supplemented culture medium. With growing concerns regarding the potential transmission of adventitious agents such as prions and animal viruses, it would be preferable to culture cells for human transplantation under xenobiotic-free conditions that can maintain stem cells. Hence, the objectives of the proposed study are to determine the role of serum-free culture condition in the generation of stem cell rich epithelial sheet and to identify culture conditions that provide a suitable niche to maintain SCs and corneal phenotype.

## A clinical study on microbiological analysis, culture and sensitivity of chronic dacryocystitis and results following surgical treatment

Investigators : Dr.V.Maneksha, Aravind - Tirunelveli
Dr.V.Anitha, Aravind - Tirunelveli

### Aim

To identify the common causative microorganisms in chronic Dacryocystitis, to determine antibiotic sensitivity and also to study the success rate following surgical treatment.

### Material and methods

A prospective randomised study. A total of 135 eyes of 123 patients fulfilled the inclusion criteria for the study were subjected for clinical evaluation. Microbiological analysis and culture and sensitivity of discharge were done. Surgery (DCT/DCR) was done for all patients. Detailed examination was done during following visits.

### Results

Of the total 135 eyes sent for culture and sensitivity 104 (77%) eyes had positive culture, 31 eyes (23%) had no growth of organisms. 82 eyes (60.8%) had gram positive organisms in which staphylococcus aureus was the most common microorganism (44.5%). 21 eyes (15.5%) had gram negative organisms, 1 eye had rhinospordiais (0.7%). Gatifloxcin showed highest sensitivity (96.3%) for gram positive organisms; Cefazolin (90.4%) for gram negative organisms. Dacryocystectomy was done in 113 eyes and showed 77.8% (105 eyes) success rate. Dacryocystorhinostomy was done in 22 eyes and showed 100% success rate.

### Conclusion

Staphylococus aureus was the most common micro organism isolated in cases of chronic dacryocystitis. Gatifloxcin was the most sensitive antibiotic for gram Positive organisms and Cefazolin for gram negative organism. Dacryocystectomy showed 77.8% success rate and DCR showed 100% success rate.

## To study the functional results and complications of frontalis sling surgery by using silicon rod (auro sling)

Investigators : Dr. V. Maneksha, Aravind - Tirunelveli

### Objective

Frontalis sling surgery is the surgery of choice for poor levator function ptosis. Various materials can be used for sling surgery. In this study we are using silicon rod (Auro sling) for correction of ptosis. Our purpose is to evaluate the functional results and complications of silicon rod in long term follow up.

# CORNEA CLINIC

## Outcome and safety of supratarsal injecton of triamcinolone acetonide in improving the quality of life in patients with refractory vernal keratoconjunctivitis.

Investigators : Dr. Uma Agshikar, Aravind - Madurai
Dr. Jeena Mascarenhas, Aravind - Madurai
Dr. N.V. Prajna, Aravind - Madurai
Dr. M. Srinivasan, Aravind - Madurai
Sponsor : Champalimaud Fund
Setting : Cornea and External Diseases Clinic, Aravind Eye Hospital, Madurai.

### Objective

To analyse the safety and outcome of supratarsal injection of Triamcinolone acetonide in patients with severe VKC who are refractory to all other standard topical treatment and to assess the changes in the quality of life in these patients after this therapy.

**Study design:** - Prospective, interventional, comparative study.

The study started on 1st May 2008. To date, we have enrolled 11 patients with VKC upsetting their normal daily activities like driving and studying, and those who having been on topical treatment for VKC and have not experienced any long term relief. 8 received 20mg Triamcinolone Acetonide (TA) and 3 received 10mg TA as a supratarsal injection under topical anaesthesia.

Patients are followed up at 2 weeks, 6 weeks, 3 months and 6 months. 8 patients have completed a follow up period of more than 5 months. 3 have completed more than 3 months follow-up.

All the patients are extremely comfortable in the eye that has received the injection and often present with complaints in the fellow eye requesting for the injection in the fellow eye. A single injection of TA improves their quality of life and improves their social interaction. Boys can resume outdoor sports and activities of daily living without having to worry about visual blurriness, red-watery eyes, and itching. Statisticed analysis is awaited.

One patient developed ocular hypertension after 10mg TA. The IOP has been within 20mm Hg on 0.5% Timolol maleate eyedrops BID. The best corrected visual acuities improve to 6/6 on Snellen's chart within 2 weeks of the injection. 2 patients developed severe recurrent VKC after 8months of being symptom free after the injection. We have not seen steroid induced cataract, ptosis, or conjunctival necrosis.

**Present status** - The follow up and recruitment of patients is on.

## Steroids for Corneal Ulcers Trial (SCUT)

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| Principal Investigator | : | Dr. M. Srinivasan, Aravind - Madurai |
| Project | : | Dr. Thomas Lietman, Aravind - Madurai |
| Sponsor | : | NEI |
| Centres | : | Aravind-Madurai, Tirunelveli and Coimbatore<br>Francis I. Proctor Foundation UCSF Dartmouth Medical School |

### Study objectives

This study was initiated at 4 centers in September 2006 and at Aravind - Coimbatore from March 2007. The specific objectives of the study are to determine whether adding topical steroids to the treatment regimen of culture proven bacterial corneal ulcers improves the outcome. The primary outcome of this trial will be the best spectacle corrected log MAR three months after enrolment. This is a randomised, double masked placebo controlled trial. Five hundred ulcers are randomised to receive antibiotics and steroids or antibiotics and placebo. The patients are closely followed until re-epithelisation and rechecked at three weeks, three months and one year.

### Present status

The study is on at three of the Aravind Eye Hospitals - Madurai, Tirunelveli and Coimbatore. 380 patients have been enrolled. Recruitment of patients will continue until the target (500 patients) is achieved as advised by the DSMC (data and safety monitoring committee). Regular monitoring and reporting is on. The results will be analysed once the study is complete.

## Mycotic Ulcer Treatment Trial (MUTT)

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| Principal Investigator | : | Dr. N. Venkatesh Prajna, Aravind - Madurai |
| Project | : | Dr. Thomas Lietman, Aravind - Madurai |
| Sponsor | : | NEI |
| Study Centre | : | Aravind Eye Hospital (Madurai - Puducherry) |

### Study Objectives

The objective of the MUTT study is to determine which topical antifungal treatment, voriconazole or natamycin, results in a better visual acuity and in better clinical outcome for a subgroup of organisms. The study also aims to determine whether there is a co-relation between antifungal susceptibility and

clinical outcome in fungal keratitis. The primary outcome is best spectacle corrected visual acuity three months after enrolment. This is a fixed block, randomized double masked controlled trial.

They will be followed closely until re-epithilisation and then rechecked at 3 weeks, 3 months of 1 year (only main study) after enrollment.

### Status

The Pilot study started in November 2007 and was completed in April 2008. A total of 120 patients were enrolled (72 Madurai and 48 at Puducherry). The results are being analysed but preliminary results show that there is no statistically significant difference in outcomes in patients prescribed with either voicongol or metamycin lepicells.

## CATARACT & IOL SERVICES

### Comparison of accuracy of IOL master and conventional A-scan biometry in IOL power calculation in high myopes

Investigators : Dr. Neelam Pawar, Aravind - Madurai
Dr. Shivakumar C, Aravind - Madurai

### Aim

To study the accuracy of the IOL Master and conventional A-Scan Biometry in prediction of IOL power in High Myopes (Axial length > 26mm).

### Method

Patients with axial length > 26mm calculated by the IOL Master, are taken for the study and the IOL power is calculated with the help of both the IOL master and the A-scan, and the same formula ( SRK-T) is employed for the calculation . The IOL power placed is according to the calculations of the IOL Master. The spherical equivalent of the correction at the one month follow-up is taken into consideration for considering the accuracy.

### Status

Twenty five patients have so far been included in the study, and the data has been submitted to the statistician.

### Comparison of accuracy of IOL master and conventional A-scan in IOL power calculations

Investigators : Dr. Ashish Gangwar, Aravind - Madurai
Dr. Shivakumar. C, Aravind - Madurai

### Aim

To study the accuracy of the IOL power calculations with IOL Master and A-Scan Biometry (axial length range 21 to 26mm).

### Method

IOL power calculation is done in patients about to undergo cataract surgery by either of the methods (first by the IOL Master, and if not possible by A-scan) and the IOL implanted accordingly. The spherical equivalent of the correction at the end of one month is calculated and accuracy determined by its variation from emmetropia, and the predicted refractive error.

**Status:** Patients are being recruited for the study

## Study of visual outcome and complications following posterior capsular rupture during IOL surgery

Investigators : Dr. Rahul Dubewar, Aravind - Madurai
Dr. Shivakumar C, Aravind - Madurai

### Aim

To study the visual outcome and associated complications following Posterior Capsular Rupture in cases undergoing IOL surgery.

### Methods

Patients who have Posterior Capsular Rupture during cataract surgery ( Phacoemulsification or MSISCS) , without coexisting morbidity contributing to poor visual outcome are included in the study (October 2007 to April 2008) The type of surgery, preoperative and intraoperative condition of the eye, and the stage at which PCR occurred are noted. The patients are being followed up at day 1, 7, 30, 3 months, 6 months and one year, and the visual outcome, any associated complication, posterior segment findings, any change in the best corrected acuity are noted.

**Status:** 100 patients have been recruited, of which 36 patients have completed one year follow up

## Capsule wash for pediatric eyes

Investigators : Dr. Aravind Haripriya, Aravind - Madurai
Dr. Perumalsamy Vijayalakshmi, Aravind - Madurai
Dr. Kavitha Vadi, Aravind - Madurai
Dr. Rupal H. Trivedi, Edward Wilson
Storm Eye Institute, Medical University of South Carolina, USA

### Objective

To determine if the capsule wash decreases posterior capsular opacification (PCO) in paediatric eyes.

### Method

Prospective, double-masked, controlled, randomised study

### Inclusion criteria

Bilateral, visually significant cataract (ages 5-15 years), 20 subjects (40 eyes).

### Surgical technique

Lens substance aspiration will be performed in both the groups. Until thorough lens substance aspiration is complete, the operating surgeon will be masked to random assignment of the treatment. If the eye receives a randomisation code to use the capsule wash, it will be performed. Follow up will be at day1, day 30, day90, day 180, day 365 and day 540.

### Outcome analysis

PCO will be graded clinically and using the EPCO software.

## Role of CTR on anterior capsular contraction in patients with retinitis pigmentosa (to start in April 2008)

Investigators : Dr. Rathini David, Aravind - Madurai
Dr. Haripriya Aravind, Aravind - Madurai

### Objective

To analyse the effect of CTR on Anterior Capsular Opening (ACO) in eyes with Retinitis Pigmentosa.

**Design:** This is a prospective, double blinded, Randomised Controlled Trial.

**Sample size:** 40 eyes with Retinitis Pigmentosa

**Follow up:** 1st day, 1st month, 3rd month, 6th month and 9th months

### Randomisation

Population will be divided into two arms. Following Phacoemulsification and cortex wash, one arm will receive CTR and other will not. All eyes will receive a foldable IOL.

### Analysis

Extent of anterior capsule contraction will be calculated using the following formula

$$\text{Extent of Anterior Capsule Contraction} = \frac{\text{Reduction of ACO (\%)}}{\text{Baseline ACO (\%) (1day Post operative)}} \times 100$$

The extent of Anterior Capsule Contraction shall be compared between CTR arm and non CTR arm to find significant difference.

## Contra lateral eye study to compare the incidence of PCO between square edge PMMA IOL and round edge PMMA IOL and between square edge PMMA IOL and acrys of IOL

Investigators : Dr. Haripriya Aravind, Aravind - Madurai
Dr. Aravind Srinivasan, Aravind - Madurai
Dr. Anand Dev, Aravind - Madurai

### Objective

To evaluate the efficacy of different intraocular lens materials and optic edge designs in preventing PCO.

**Design:** Double blind prospective randomised control study.

**Sample size:** Hundred patients in the age group between 40 to 65 years with bilateral cataracts

**Follow up:** Postoperative follow up examination was done at day 1, 6 months, and 12 months.

### Randomisation

The patients were randomly divided into 2 groups, group A and group B. Another randomisation was done in each group for selection of IOL design and material. In group 'A', comparison was done between square edge single piece PMMA IOL (A1) and round edge single piece PMMA IOL (A2). In group 'B', comparison was made between square edge single piece PMMA IOL (B1) and square edge single piece hydrophobic acrylic IOL (B2).

### Analysis

Six months and one year data consisted of BCVA, PCO grades and PCO score. The results were statistically analysed using Mann - Whitney u test and wilcoxon-w test.

## To compare safety and efficacy between SICS and phacoemulsification using ozil infinity system in immature cataracts with pseudoexfoliation

Investigators : Dr. Aravind Srinivasan, Aravind - Madurai
Dr. Haripriya Aravind, Aravind - Madurai
Dr. Praveen Subudhi, Aravind - Madurai

### Objective

To compare

### Safety

i. Intra operative complications
ii. Post operative complications especially first post op day

### Efficacy

i. Best corrected visual acuity on first post op day
ii. Best post op visual acuity at the end of first month
iii. Central corneal thickness on first post op day and first month

Between small incision cataract surgery and phacoemulsification in eyes with pseudoexfoliation and immature cataracts.

**Design:** Comprehensive randomised cohort study

### Sample size

Study of 52 eyes of 52 patients with immature cataracts associated with pseudoexfoliation, presented to our institution over a period of six months.

### Surgical technique

Group A: - (30 Patients) - Small incision cataract surgery

Group B: - (22 Patients) - Co-axial phaco torsional ultrasound

### Follow up

Patients were reviewed on their 1st postoperative day and 1st postoperative month for following:

A. Vision (unaided and aided)
B. Slit lamp examination
C. Pachymetry by pacscan

### Analysis

Statistical analysis was done using Mann Whitney U test to determine significant difference between Phaco and SICS. Pearson correlation was also used to determine the correlation between CCT and effective Phaco time.

## Comparison of intraocular lens power calculation in eyes with long axial length using two formulae

Investigators : Dr. Santosh Gouda, Aravind - Coimbatore
Dr. Renny Zachariah, Aravind - Coimbatore
Dr. Kalpana Narendran, Aravind - Coimbatore
Dr. Kavitha Yuvarajan, Aravind - Coimbatore
Dr. Jay Mathew Perumal, Aravind - Coimbatore

### Aim

To evaluate the predictability of intraocular lens (IOL) power calculations using the IOL Master and different IOL power calculation formulae in eyes with a long axial length (AL).

### Introduction

- The accurate calculation of intraocular lens (IOL) power is essential for attaining the desired refractive outcome after cataract surgery. Precise preoperative measurement of AL is the most critical step to improve IOL power prediction .Traditionally, the AL is measured by applanation A-scan ultrasound.
- Because of the indentation of the globe and off-axis measurement of the AL by the transducer, erroneous AL detection and an undesired postoperative refractive outcome can occur. The error in measurement is theoretically more obvious in highly myopic eyes, which have a long AL and low scleral rigidity.
- The AL measurement will be inaccurately shorter with corneal indentation in highly myopic eyes. Recently, the IOLMaster (Carl Zeiss) became commercially available for IOL power calculations.

This quick, easy-to-use, noncontact technique measures AL along the visual axis with maintenance of ocular fixation on targets in space. No anesthesia is needed, there is no risk for corneal trauma or infection. Pupil dilation is not required.

- The IOL Master is less operator dependent than applanation ultrasound devices.

### Inclusion criteria

Eyes with an axial length 25.0 mm and longer.

### Exclusion criteria

Patients with severe opacities (eg dense cataract, vitreous hemorrhage) will be excluded as the axial length cannot be measured by the IOL Master because the laser beam cannot penetrate the opacity. Patients with poor ocular fixation, nystagmus, mental retardation or patients younger than 6 years will be excluded from the study.

### Patients and methods

- This study includes 60 eyes with an axial length 25.0mm and longer undergoing manual small incision cataract surgery with PMMA IOL implantation at Aravind Eye Hospital Coimbatore.
- Preoperative axial length would be measured by IOL Master and applanation ultrasound for patients with axial length 25.0 – 28.0 mm.
- Patients having axial length greater than 28.00mm, and B scan also would need in addition to the above methods. Keratometry would be determined by IOL master.
- IOL power would be calculated by SRK2 and SRK –T formula. First 30 patients in this study would be getting SRK2 and next 30 patients SRK T formula. PMMA lens would be used for the surgery and all the surgeries would be done by a single surgeon.

## Comparison of astigmatism in manual SICS based on incision site

Investigators : Dr. Sobha K, Aravind - Coimbatore
Dr. Sudhira, Aravind - Coimbatore
Dr. Kalpana Narendran, Aravind - Coimbatore
Dr. Kavitha Yuvarajan, Aravind - Coimbatore
Dr. Jay Mathew Perumal, Aravind - Coimbatore

### Aim

To compare the astigmatism induced by superior, super temporal and temporal incision in manual SICS

### Introduction

PHACO - Routine procedure of cataract extraction. No costeffective in developing world. MANUAL SICS – Best option to obtain advantages of self sealing sutureless incision at LOW COST, High Astigmatism is an important cause of poor uncorrected VA after SICS

### Materials and methods

#### Sample size

- 90 eyes divided into 3 groups and allotted. A – Superior incision site
- B – Temporal
- C - Superotemporal

### Inclusion criteria

Patients with keratometric astigmatism of 1.5 D / less, Good fixation, Cataract upto NS-3

### Exclusion criteria

Pt's with K- astigmatism > 1.5 D, Pt's with pterygium, Pt's with ocular pathology which may cause poor post –op visual outcome, Pt's with previous ocular surgeries, Pt's with higher grades of nuclear sclerosis(To keep uniformity in size and architecture of incision)

### Pre-op evaluation

Keratometry, A- scan biometry, thorough ophthalmic evaluation

### Surgical steps

6mm scleral frown incision 2 mm from limbus in the centre, Funnel shaped sclerocorneal pockets created,AC entered 1 mm into clear cornea and internal incision enlarged sideways to 8mm,CCC done in all cases, Single piece PMMA IOL of 6mm optic size and 12.5 mm total size implanted into bag

### Post – OP

Pt examined on 1st, 30th and 90th day, Post op steroid antibiotic eye drops in tapering dosage for 2 months, Refraction and keratometry done at each follow-up visit

## Intra-operative floppy iris syndrome – an Indian perspective

Investigators : Dr. Ajoy Mohan, Aravind - Coimbatore
Dr. Aparna, Aravind - Coimbatore
Dr. Kalpana Narendran, Aravind - Coimbatore
Dr. Kavitha Yuvarajan, Aravind - Coimbatore
Dr. Jay Mathew Perumal, Aravind - Coimbatore

### Aim

### Primary

To evaluate the association between alpha-1 blockers (specifically tamsulosin) and floppy iris syndrome in Indian population

### Secondary

To compare the iris morphology in patients with IFIS utilising UBM to those without patients not having IFIS

### Materials and methods

### Target population

Patients presenting to Aravind Eye Hospital, Coimbatore for undergoing cataract surgery by Phaco-emulsification on treatment with Tamsulosin are included in study. Estimate study population size: 30-50. Study period: 1 year

### Inclusion criteria

Patients presenting to AEH, CBE for phaco-emulsification surgery on treatment with tamsulosin or any other alpha-1 blocker will be included in the study.

### Exclusion criteria

- Previous intraocular surgical procedures like trabeculectomy, Yag PI
- Chronic inflammatory diseases of the eye. All patients undergo a detailed evaluation both medical and ocular, including previous medications. Detailed SLE with assessment of pre-operative pupil diameter under maximum dilatation using external calipers, iris color and morphological patterns will be done. Pre-operative iris morphology and thickness will be documented using UBM to be compared to age matched controls. All patients will undergo a standard pre-op dilating regimen using topical tropicamide and phenylepherine drops
- Tamsulosin will not be stopped before surgery. All patients will undergo standard phaco-emulsification cataract extraction procedure by the same surgeon

### Presence of IFIS will be assessed by the 3 diagnostic criteria

Billowing and undulation of iris in response to ordinary intraocular flow currents. Propensity of iris to Prolapse toward side port and main wound in spite of proper wound construction. Progressive Intraoperative Miosis

### End points of study

Incidence and severity of IFIS in South Indian population. Postulating theory regarding lesser incidence of IFIS in our population.

## Genetic Component of the INDEYE study of Cataract & Age -Related Macular Degeneration in India

Investigators : Dr. R.D. Ravindran, Aravind - Coimbatore
Dr. P. Sundrasen, Aravind - Coimbatore
Dr. Tiruvengatakrishnan, Aravind - Coimbatore
Dr. Badrinath Talwar Aravind - Pondicherry
Prof. Astrid Fletcher (London School of Hygiene and Tropical Medicine)
Dr. Giovanni Maraini, Dr Monica Camparini (University of Parma, Italy)
Dr. Usha Chakravarthy (Queen's University, Belfast)

### Aim

To identify genetic factors associated with two age-related eye diseases age-related macular degeneration (AMD) and cataract.

### Methods

The genetic study is an add-on study to the INDEYE study.

[INDEYE is a recently concluded two centre study to assess the prevalence and identify the risk factors for AMD and cataract in a population sample of persons aged 60 years and above. This study has been done in Cuddalore and Pondicherry (and in Gurgaon district in north India by RP centre, AIIMS). An add-on study is being done by us to enrich the original dataset because there were too few cataract free individuals (controls are too few compared to cases) in the original 60 plus population, and too few late AMD patients (cases are too few compared to controls)].

INDGEN aims to collect clinical data and blood samples from (i) 1500 persons from a younger age group (40-60 yrs) population (ii) 300 cases of AMD from retina clinics. The data collected include blood pressure and anthropometry measurement, visual acuity and refraction, detailed ocular examination, digital lens photography and LOCS III cataract grading, Fundus photography and grading of drusen and AMD, blood collection for blood glucose, Hb A1c and genetic analysis. The lens photographers are certified by Dr Maraini of University of Parma and periodic re-certification/ quality checks are done. The data is collected in specially designed data-collection forms and recorded into a database by means of data-entry software designed at our hospital.

A key aim of the INDEYE and INDGEN studies is to identify putative genes which may be risk factors for cataract and AMD by comparing cases and controls.

### Status

So far we have recruited 1089 participants aged 40-60 yrs from the sample population for the lens component of the study, and 80 patients form the Retina Clinic for the AMD component.

## Evaluation of homoeopathic therapy in treatment of cataract

Investigators : Dr. Arati Sharma
Dr. U. R. Pachegaonkar
Sri Aurobindo International Institute for Integral Health and Research Collaborating Centre
Dr. R.D. Ravindran, Aravind - Pondicherry
Dr. Badrinath Talwar, Aravind - Pondicherry

### Aim

Comparison of progression of cataract in persons under constitutional homoeopathic treatment versus a control group.

### Method

- Evaluation of homoeopathic therapy in treatment of cataract is a randomised control study in which the patients with the age group 40 and above with early stage cataract will be included. The comparison is between an intervention ("Holistic/constitutional homoeopathic treatment") Vs. no-intervention.
- Recruitment and collection of baseline data including lens photography, and 6 monthly follow-up is at Aravind Eye Hospital, Pondicherry. Lens photographs are collected and graded at 3 time points.
- Random allocation of participants is done by Sequentially Numbered Opaque Sealed Envelope method (SNOSE) at Aravind eye hospital. Those allocated to the homoeopathy group undergo monthly evaluation and treatment at SAIIIHR for 2 years.
- Main outcome evaluated is cataract stage (LOCS III grade). Any participant needing surgery will be advised accordingly, and will be included in final statistical analysis.
- The sample size is calculated as: 109 subjects x 2 with 20% dropout rate = 270.
- The study duration includes 3 year recruitment period and 2 year follow up duration.

**Status:** Study in progress. Seven participants have been randomised till now.

## Posterior capsular opacification after implantation of square edge PMMA, round edge PMMA and acrys of intraocular lenses: A prospective, randomised comparative trial

Principal Investigator : Dr. Haripriya Aravind, Aravind - Madurai
Setting : IOL Clinic, Aravind Eye Hospital, Madurai

### Objective

To compare posterior capsule opacification (PCO) with square edge PMMA, round edge PMMA and Acrysof intraocular lenses after in-the-bag implantation. Study design is prospective, double blinded, Randomised Controlled Trial (RCT). This study is registered at www.clinicaltrials.gov 50 patients would receive square edge PMMA (A1) in one eye and round edge PMMA (A2) in fellow eye. Another group of 50 patients would receive square edge PMMA (B1) in one eye and Acrysof (B2) in fellow eye. Patients are followed up 6th month, 1st year, 2nd year, 3rd year, 4th year and 5th year post operatively. Outcome measures are visual acuity and PCO. PCO is assessed during each follow up. PCO is analysed using EPCO software. 94 enrolled patients underwent both eye surgeries.88 patients came for 2nd year follow up. Wilicoxn signed rank test was used to compare the means. Mean EPCO score of A1 is 0.0529 (SD 0.1986), A2 is 0.1789 (SD 0.2440) with a statistically significant difference (P=0.0001). Mean EPCO score of B1 is 0.0332 (SD 0.0668) and B2 is 0.0934 (SD 0.1835) with a statistically significant difference (P=0.03). It is concluded that square edge lens manufactured by Aurolab is having statistically significant lesser PCO than round edge PMMA and Acrysof IOL.

## Clinical evaluation of hydrophobic foldable IOLs

Principal Investigator : Dr. Haripriya Aravind, Aravind - Madurai
Setting : IOL Clinic, Aravind Eye Hospital, Madurai

### Objective

To evaluate the safety and efficacy of hydrophobic foldable intraocular lenses in cataract surgery. Study design is unilateral, prospective, open label clinical trial. This IRB approved study is being carried out in compliance with ISO, GCP and FDA standards and is registered at www.clinicaltrials.gov Pilot study was completed with the sample size of 20. Aurovue lens was implanted by phacoemulsification. Patients are followed up 1st day, 2nd day, 3rd day, 7th day, 15th day, 1st month, 2nd month, 3rd month, 6th month and 1st year post operatively. Main study is

going on and the sample size is 120 subjects. Enrollment was started on 29th March, 2007 and completed on 23rd July, 2007. The accrual enrollment period was 18 months. Patients are followed up 1st day, 10th day, 40th day, 120th days and 1st year post operatively. 118 patients completed 120th days follow up. All the patients have visual acuity 6/12 or better. Minimum number of cases allowed before less than SPE rate is 94 out of 100 patients for posterior chamber IOL. Post operative BCVA is better in all cases. One patient required secondary IOL intervention because of haptic damage. Re surgery was done on the next day with section extension and IOL exchange was done. For this patient Visual Acuity remains 6/6 during all postoperative visits. Maximum number of cases allowed before SPE rate exceeded is 2 for secondary surgical intervention. Hence this adverse event is not significant when compared with historical controls. One patient had iritis with mild severity over 97 days post operatively. Patient visited 4 times with complaints of pain and watering. Antibiotic with tapering steroid and NSAID eye drops were given to the patient. Cycloplegic was also given to the patient. The patient completely recovered from this adverse event. Investigator believed that this adverse event is not related to the interventional medical device. It is concluded that Aurovue made by Aurolab is safe and effective for the treatment of cataract with better visual outcomes.

### Clinical evaluation of aspheric intraocular lenses

Principal Investigator : Dr. Haripriya Aravind, Aravind - Madurai
Setting : IOL Clinic, Aravind Eye Hospital, Madurai

#### Objective

Aspheric IOL is optically designed to partially compensate average corneal positive spherical aberration (SA) of eye, introduces negative SA of -0.15µ to implanted eyes. It enhances functional vision and improves contrast sensitivity under scotopic and mesopic conditions, pupil size between 3.0mm to 4.5mm. This is made up of biocompatible hydrophilic material and designed to induce less effect on retinal image quality to decentration and tilt of IOL. The objective of this study is to evaluate safety and efficacy of aspheric IOL in cataract surgery. Study design is unilateral, prospective, open label clinical trial. This IRB approved study is being carried out in compliance with ISO and GCP. Sample for this pilot study is 20. Aspheric lens was implanted by phacoemulsification. Patients are followed up 1st day, 1st month and 3rd month post operatively. As of now, 20 subjects have been enrolled into this study.

## UVEA SERVICES

### Posurdex – intermediate and posterior uveitis study

Principal Investigator : Dr. Rathinam Sivakumar, Aravind - Madurai
Co-Investigator : Dr. Venu Nadella, Aravind - Madurai
Treating Investigator : Dr. R. Kim, Aravind - Madurai
Funding Agency : Allergan and Charles River Laboratories
Duration : Intermediate or posterior uveitis – 26 weeks (an 8 week multicenter, masked, randomised trial with an 18 - week masked extension)

#### Objectives

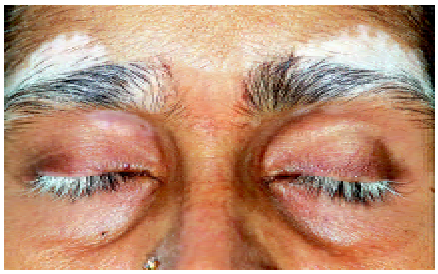
To evaluate the safety and efficacy of the 700 micrograms and 350 micrograms DEX PS DDS (Dexamethasone posterior segment drug delivery system) applicator system compared with Sham (needleless) DEX PS DDS applicator system in the treatment of non-infectious ocular inflammation in intermediate and posterior uveitis.

## HLA-DR determination of Vogt-Koyanagi-Harada syndrome and sympathetic ophthalmia in South Indian patients

| | | |
|---|---|---|
| Principal Investigator | : | Dr. SR. Rathinam, Aravind - Madurai |
| | : | Dr. Edoardo Baglivo, Geneva |
| | : | Dr. J. M.Tiercy, Geneva University Hospital |
| Funding Agency | : | Immunology unit, LNRH/ Unite d'immunologie, De transplantation, HUG Geneva University Hospital |
| Duration | : | One year |

### Objectives

To study the distribution of human leukocyte antigen HLA-B antigens and HLA-DR Alleles and to investigate the immuno-genetic background of Vogt-Koyanagi-Harada (VKH) syndrome and sympathetic ophthalmia in South Indian patients and to analyse possible impact on susceptibility / resistance and prognosis.



## A double - masked, placebo-controlled, multicentric, parallel group, dose ranging study to assess the efficacy and safety of LX211 as therapy in subjects with non - infectious intermediate, anterior and intermediate, posterior or pan-uveitis

| | | |
|---|---|---|
| Principal Investigator | : | Dr. S.R. Rathinam, Aravind - Madurai |
| | | Dr. B. Manohar Babu, Aravind - Coimbatore |
| Co-Investigator | : | Dr. Venu Nadella, Aravind - Madurai |
| Funding Agency | : | Lux Biosciences Inc, Jersey city, NJ 07302 |
| Duration | : | 18 months - 12 months recruitment, 6 months follow-up |

### Objective

LX 211 is likely to have an improved safety profile compared to cyctosporine. A lower therapeutic dose can be used and the correlation of dose with blood concentrations has been improved. The objective was to study the safety and efficacy of LX211 as treatment and as maintenance in subjects with uveitis.

| | | |
|---|---|---|
| LX 211-01 | : | Treatment of active sight threatening non infectious intermediate, anterior and intermediate, posterior or pan-uveitis |
| LX211-02 | : | Treatment of clinically quiescent sight threatening, non-infectious intermediate, anterior and intermediate, posterior or pan uveitis |
| LX211-03 | : | Treatment of active sight threatening non infectious anterior uveitis |

# PAEDIATRIC OPHTHALMOLOGY SERVICES

## How valid (sensitive and specific) is teacher's screening for refractive errors as compared to that done by trained refractionists?

| | | |
|---|---|---|
| Principal Investigator | : | Dr. P. Vijayalakshmi, Aravind - Madurai |
| Field co-ordination, training, data collection | : | Dr. Muralidhar, Aravind - Madurai |

### Objectives

- To determine the agreement, sensitivity and specificity of screening for refractive errors by teachers, using that done by refractionists as the gold standard.

- To compare agreement, specificity and sensitivity of screening using ETDRS 6/9.5 versus snellens 6/9 tumbling eoptotypes.
- Determine the sensitivity and specificity of the screening test versus objective cycloplegic refraction in identifying children with refractive errors.

### Sample (selection and recruitment)

All children at the school between 5-10 years of age are included; the children who require atropinisation for cycloplegia, those unwilling or uncooperative for the complete examination, and those absent from the school on the day of screening are excluded. To detect a 5% difference between the proportion of children deemed 'passed' among each pair of the 3 arms, with 95% confidence and 80% power, we need to study 1000 children. The 'Phase 2', where we intend validating screening for refractive errors against objective cycloplegic refraction require 655 children to be examined to detect a 5% difference in 'passes' with 95% confidence and 80% power.

### Dissemination plan

- Feedback on the usefulness of snellen's tumbling E for screening will be provided to all teachers who participated.
- Results of the study will be provided to all refractionists, doctors, school authorities and teachers involved in school screening through Aravind Eye Care System.

**Status:** Data collection over and analysis pending.

## Clinical profile with ocular and oculocutaneous albinism at a tertiary care centre

| | | |
|---|---|---|
| Investigators | : | Dr. Jothi Prakash, Aravind - Madurai<br>Dr. Muralidhar, Aravind - Madurai<br>Dr. P. Vijayalakshmi, Aravind - Madurai |
| Duration | : | March 2007 - August 2008 |

### Purpose

To document the various clinical features in patients with ocular and oculocutaneous albinism presenting in our outpatient department from March 2007 to August 2008, in a tertiary care hospital.

### Methods

A prospective observational study carried out in a group of 40 patients of ocular and oculocutaneous albinism taking into account the visual acuity, family history, anterior and posterior segment examination, ocular movements, presence or absence of foveal hypoplasia confirmed by 3D OCT, cutaneous involvement (if present) and treatment taken in the form of surgery or spectacle correction.

### Results

The results of the study would be interpreted on the basis of the following parameters like gender predisposition, presence or absence of family history, age group affected, cut off visual acuity, anterior segment findings, normal or abnormal ocular motility, fundus showing presence or absence of albinoid fundus with or without foveal hypoplasia, presence or absence of cutaneous involvement.

**Status:** Thesis submitted and paper pending.

# A. SUBMITTED FOR PUBLICATION (UNDER REVIEW)

## Surgical outcome of membranectomy via limbal route

| | | |
|---|---|---|
| Principal Clinician | : | Dr. Anupam, Aravind - Madurai<br>Dr. Muralidhar, Aravind - Madurai |
| Team | : | Dr. Vijayalakshmi, Aravind - Madurai<br>Dr. Shetty, Aravind - Madurai |

### Objective

To determine anatomic and functional success of limbal route membranectomy for visual axis opacification following paediatric cataract surgery

**Status :** Submitted to JCRS

## Wildervanck syndrome

Principal Clinician : Dr. Anand, Aravind - Madurai
Dr. Shetty, Aravind - Madurai
Team : Dr. P.Vijayalakshmi, Aravind - Madurai

### Objective

Features of wildervanck syndrome.

**Status :** Submitted to IJO – Editorial review.

## Clinical features of joubert syndrome

Principal Clinician : Dr. Anand, Aravind - Madurai
Dr. Shetty, Aravind - Madurai
Team : Dr. P.Vijayalakshmi, Aravind - Madurai

### Objective

Features of Joubert syndrome.

**Status :** Submitted to IJO – Peer review

## Clinical course and outcome of bilateral PFV (persistent fetal vasculature)

Principal Clinician : Dr. Anand, Aravind - Madurai
Dr. Shetty, Aravind - Madurai
Team : Dr. P.Vijayalakshmi, Aravind - Madurai
Dr. Jithendra, Aravind - Madurai
Dr. Muralidhar, Aravind - Madurai

### Objective

Clinical course and outcome of bilateral PFV (Persistent fetal vasculature)

**Status :** Submitted to IJO – Peer review.

## Jensen procedure for sixth nerve palsy – retrospective study

Principal clinician : Dr. Shetty, Aravind - Madurai
Dr. Anurag, Aravind - Madurai
Team : Dr. Fredrik, Aravind - Madurai
Dr. Muralidhar, Aravind - Madurai
Dr. P. Vijayalakshmi, Aravind - Madurai

### Objective

To determine the outcome of the surgery and long term follow up

**Status :** Editorial review.

## B. PREPARATION OF MANUSCRIPT PENDING

### Surgical outcome of traumatic cataracts in children

Principal Clinician : Dr. Pratheek, Aravind - Madurai
Dr. Muralidhar, Aravind - Madurai
Team : Dr. P.Vijayalakshmi, Aravind - Madurai
Dr. Shetty, Aravind - Madurai

#### Objective

To determine the visual outcome, resurgery rates, complications and visual axis opacification for paediatric patients undergoing surgery for traumatic cataracts

**Status :** Data collection over.

### Surgical outcome of microspheroaphakia

Principal Clinician : Dr. Ankush, Aravind - Madurai
Dr. Mona, Aravind - Madurai
Team : Dr. Muralidhar, Aravind - Madurai
Dr. P.Vijayalakshmi, Aravind - Madurai
Dr. Shetty, Aravind - Madurai

#### Objective

To determine visual outcome and incidence of glaucoma for patients with microspherophakia managed by surgery/YAG PI

**Status :** Data collection over.

### Optic atrophy in children

Principal Clinician : Dr. Shetty, Aravind - Madurai
Dr. Rajendra, Aravind - Madurai
Team : Dr. Pradeep, Aravind - Madurai
Dr. P.Vijayalakshmi, Aravind - Madurai
Dr. Muralidhar, Aravind - Madurai

#### Objective

To evaluate the causes of optic atrophy in children presenting to our institute

**Status :** Final phase.

### Surgical outcome in duane retraction syndrome

Principal Clinician : Dr. Anand, Aravind - Madurai
Dr. Shetty, Aravind - Madurai
Team : Dr. Fredrik, Aravind - Madurai
Dr. Muralidhar, Aravind - Madurai
Dr. P.Vijayalakshmi, Aravind - Madurai

#### Objective

To determine outcome following surgery for duane syndrome

**Status :** Preparation of manuscript.

## C. ANALYSIS OF COLLECTED DATA PENDING

### Validating teachers screening for refractive error

Principal Clinician : Dr. Muralidhar, Aravind - Madurai
Team : Dr. Noela, Aravind - Madurai
Dr. P. Vijayalakshmi, Aravind - Madurai

#### Objective

- To determine the agreement, sensitivity and specificity of screening for refractive errors by teachers, using a comprehensive ophthalmic examination as the gold standard.
- To compare agreement, specificity and sensitivity of screening using ETDRS 6/9.5 versus Snellens 6/9 tumbling E optotypes.
- Determine the sensitivity and specificity of the screening test versus objective cycloplegic refraction in identifying children with refractive errors.

**Status :** Data collection over, analysis pending

### Surgical outcome of combined squint with IOL surgery

Principal Clinician : Dr. Muralidhar, Aravind - Madurai
Team : Dr. Aparajitha, Aravind - Madurai
Dr. Shetty, Aravind - Madurai
Dr. Anupam, Aravind - Madurai

#### Objective

To determine success rates and complications for combined squint and cataract surgery with IOL implantation.

**Status :** Data collection over, Analysis pending.

## D. DATA COLLECTION GOING ON

### Surgical outcome of intermittent exotropia

Principal Clinician : Dr. Aloka, Aravind - Madurai
Team : Dr. Muralidhar, Aravind - Madurai
Dr. P. Vijayalakshmi, Aravind - Madurai

#### Objective

To determine the anatomical and functional success of strabismus surgery in treating intermittent exotropia

**Status :** Ongoing.

### Strabismus surgery under topical anaesthesia

Principal Clinician : Dr. Muralidhar, Aravind - Madurai
Team : Dr. Aparajitha, Aravind - Madurai
Dr. P. Vijayalakshmi, Aravind - Madurai
Dr. Shetty, Aravind - Madurai

#### Objective

- To determine patient pain scores for strabismus surgery under topical anaesthesia
- To characterise surgeon comfort scores

**Status :** Ongoing.

## Surgical outcome of exotropic duane's retraction syndrome

Principal Clinician : Dr. Fredrick, Aravind - Madurai
Dr. Muralidhar, Aravind - Madurai
Team : Dr. Shetty, Aravind - Madurai
Dr. P. Vijayalakshmi, Aravind - Madurai

### Objective

To determine the outcome of patients with Exo DRS undergoing normal eye lateral rectus recession

**Status :** Ongoing.

## Surgical outcome of posterior lenticonus in children

Principal Clinician : Dr. Ranjith, Aravind - Madurai
Dr. Muralidhar, Aravind - Madurai
Team : Dr. Shetty, Aravind - Madurai
Dr. P. Vijayalakshmi, Aravind - Madurai
Dr. Megha, Aravind - Madurai

### Objective

To determine visual outcome of patients with posterior lenticonus managed surgically.

**Status :** Data collection over.

## Completion of anterior and posterior capsulorhexis using Hydroxy methy cellulose in paediatric cataract surgery

Principal Clinician : Dr. Swamy, Aravind - Madurai
Team : Dr. Muralidhar, Aravind - Madurai
Dr. P. Vijayalakshmi, Aravind - Madurai

### Objective

To determine the completion rates of capsulorhexis done under 2% HPMC in patients <8 years during cataract surgery

**Status :** Data collection.

## Efficacy of nystagmus surgery

Principal Clinician : Dr. Anand, Aravind - Madurai
Dr. S. Shetty, Aravind - Madurai
Dr. Vrushali, Aravind - Madurai
Team : Dr. Muralidhar, Aravind - Madurai
Dr. P. Vijayalakshmi, Aravind - Madurai
Dr. Swamy, Aravind - Madurai

### Objective

To determine the improvement in visual acuity and head posture after nystagmus surgery.

**Status :** IRB approval obtained

## Evaluation post operative predictive errors in paediatric cataract surgery using currently available IOL formulae

Principal Clinician : Dr. Swamy, Aravind - Madurai
Team : Dr. Muralidhar, Aravind - Madurai
Dr. P. Vijayalakshmi, Aravind - Madurai

### Objective

To determine the accuracy of IOL formulae in predicting the postoperative refractive errors in paediatric patients undergoing cataract surgery with IOL implantation, using commonly used IOL formulae.

**Status :** Data collection is going on

## Prospective study on optic neuritis in children

Principal Clinician : Dr. Sreedevi Gunda, Aravind - Madurai
Dr. Shetty, Aravind - Madurai
Team : Dr. Mahesh Kumar, Aravind - Madurai

### Objective

To evaluate the epidemiological features and improvement of visual acuity following the treatment of optic neuritis in children.

**Status :** Data collection going on.

## Third nerve palsy surgical outcome

Principal Clinician : Dr. Bharat, Aravind - Madurai
Dr. Shetty, Aravind - Madurai
Team : Dr. P. Vijayalakshmi, Aravind - Madurai
Dr. Gunda, Aravind - Madurai

### Objective

To evaluate surgical outcome in patients with third nerve palsy

**Status :** Data collection going on.

## Torsion evaluation after muscle displacement procedure

Principal Clinician : Sr. Reena – Orthoptist, Aravind - Madurai
Team : Dr. Shetty, Aravind - Madurai
Dr. P. Vijayalakshmi, Aravind - Madurai

### Objective

To evaluate pre operative and post operative torsion following muscle displacement surgery.

**Status :** Data collection going on

## Outcome of single muscle MR recession in esotropia retrospective study

Principal Clinician : Dr. Swamy, Aravind - Madurai
Team : Dr. Muralidhar, Aravind - Madurai
Dr. P. Vijayalakshmi, Aravind - Madurai

### Objective

To determine the change in angle of deviation following recession of one eye medial rectus in patients with small angle esotropia.

**Status :** Data collection.

## Binocularity following late strabismus surgery for childhood onset strabismus

Investigators : Dr. Sathya.T.Ravilla, Aravind - Madurai
Dr. R. Muralidhar, Aravind - Madurai
Dr. Shashikanth Shetty, Aravind - Madurai
Dr. P.Vijayalakshmi, Aravind - Madurai

### Aim

To evaluate the attainment of binocularity following late strabismus surgery for childhood onset strabismus.

### Objectives

To analyse the factors affecting the final outcome including

- Age of onset of squint, age of surgery
- Duration of misalignment
- Pre operative angle of deviation
- Post operative angle of deviation

## Effect of square edge PMMA IOL in preventing lens epithelial cell migration in paediatric cataract surgery: A randomised controlled trial

Principal investigator : Dr. P. Vijayalakshmi, Aravind - Madurai
Setting : Paediatric Clinic, Aravind Eye Hospital, Madurai

### Objective

To compare posterior capsule opacification (PCO) with Square edge PMMA and Acrysof intraocular lenses in paediatric cataract surgery. Primary posterior capsulotomy with or without anterior vitrectomy has become the standard treatment in very young children. However, in older children, the best surgical alternative needs better definition. Improved IOL material and design have significantly reduced the incidence of PCO in adult cataract. Aurolab extrapolated these observations in paediatric IOLs. It has developed square edge PMMA intraocular lenses for paediatric population. Study design is double blinded, randomised controlled Trial. Paediatric patients with bilateral cataract of 5 to 10 years of age willing to participate in the study are enrolled into this study. Sample size is 30 paediatric patients. Enrolment was started on August, 2006. As of now 19 patients are enrolled. Follow up period is 30th day, 180th day, and 360th day post operatively. PCO will be evaluated using EPCO software.

# PUBLICATIONS

Selected peer-reviewed publications (Ten best publications in chronological order)

### CLIN VACCINE IMMUNOL.

**2008 Apr 9; [Epub ahead of print]**

- VERMA A, RATHINAM SR, PRIYA CG, MUTHUKKARUPPAN VR, STEVENSON B, TIMONEY JF. LRUA AND LRUB
- *Antibodies in sera of human cases of leptospiral uveitis.*

### J POSTGRAD MED.

**2007 Oct-Dec;53(4):236-40.**

PRIYA CG, HOOGENDIJK KT, BERG M, RATHINAM SR, AHMED A, MUTHUKKARUPPAN VR, HARTSKEERL RA.

- *Field rats form a major infection source of leptospirosis in and around Madurai, India.*

### J MED MICROBIOL.

**2003 Aug; 52(Pt 8):667-73.**

PRIYA CG, BHAVANI K, RATHINAM SR, MUTHUKKARUPPAN VR.

- *Identification and evaluation of LPS antigen for serodiagnosis of uveitis associated with leptospirosis.*

### JOURNAL OF TAMIL NADU OPHTHALMIC ASSOCIATION

**September 1999; 40(3): 27-33.**

PRIYA CG, LALITHA S, PRAJNA N.

- *Polymerase Chain Reaction in Ophthalmology*

**June 1999; 40(2): 49-52.**

PRIYA CG, RATHINAM SR, DHARMALINGAM K.

- *Anterior chamber granuloma in adult male. A case report.*

Presented in the Eighteenth Annual Conference (1995) conducted by the Association of Anatomist and Published in Anatomical Adjuncts

**1996;1 2(2): 99-103**

PRIYA CG, BANUMATHY SP, DHARMALINGAM K.

- *DNA fingerprinting – A method for biological individualization*

# OPERATIONS RESEARCH

## Investigating gender equity in the utilisation of cataract surgical services in Aravind Eye Hospitals, Madurai - SEVA Canada

Principal Investigator : Mr. Sanil Joseph
Co-investigator : Mr. R.D. Thulasiraj

### Objectives

The main objectives of the research are

- To assess the existence of gender equity in the utilisation of cataract surgeries in each of the 3 arms (paying walk-in subsidised and camp sections) of Aravind Eye Hospital, Madurai
- To find out factors influencing the utilisation pattern and
- To use the results to bring about desirable changes in the uptake pattern.

### Methodology

This is a prospective study of patients undergoing cataract surgery at Aravind Eye Hospital, Madurai through any one of the three admissions (paying walk-in subsidised and camp sections). The sample size is 6,600 patients recruited from all the three sections together (2200 per arm) so as to be able to detect a difference as small as 6% between the proportion of men and women undergoing cataract surgery in each of the three sections allowing 5% alpha error with 80% power.

### Broad findings and current status

The data collection is completed and the preliminary analysis is done. Among the patients interviewed overall proportions of males and females are found to be 47.2% and 52.8% respectively. But in the paying section proportion of males (53%) found to be higher than the females (475) in the Walk-in free (males: 44% and female: 56%) and the camp section (males: 45% and females: 55%) proportions of the females is found to be higher. The data is being analysed further to find out more findings.

## Uptake of spectacles for refractive errors across different delivery systems

Principal Investigator : Sanil Joseph
Co-investigators : Mr. R.D. Thulasiraj
Mr. V. Vijayakumar
Ms. Nithya Neelakandan

### Objectives

The primary objective of this study is to compare the uptake of spectacles (as a means of refractive error correction) across four different dispensing methods.The four different strategies mentioned, are:

- Giving a prescription for the required correction at a campsite
- Giving a prescription for the required correction at a campsite, and booking an order to be delivered at a later date
- Giving a prescription for the required correction at a campsite and on the spot delivery of spectacles ordered
- Prescription given at an eye-hospital having spectacle shop

The secondary objectives of this research include:

- To measure the impact of wearing spectacles on the quality of life of the wearer
- To compare the costs to the subject, in acquiring a pair of glasses, in each dispensing mode.
- To study the potential barriers and motivators for uptake of spectacles
- To assess the compliance and usage of spectacles prescribed
- To assess the level of overall satisfaction

### Methodology

Based on the existing data on the uptake of refractive correction on the prescription and onsite delivery, the sample size is calculated by fixing the alpha error at 5%, the estimated difference detected between the groups at 20% and with 80% power. Hence the required number of patients in each arm is 100. The sample size after adjusting for non response rate at 20% would be 120 per arm.

This study will be conducted within Theni district of Tamilnadu where Aravind Eye Hospital, Theni will be conducting screening eye camps. The patients receiving prescriptions for refractive error correction at these camps will be subjects of this study. In each of these camps, one of the following interventions will be used:

- Issue of Prescription: The patient is checked for refractive error and prescription for spectacles is issued by a medical officer. No spectacle dispensing is provided
- Booking order for spectacles: The patient receives the prescription and can place order for spectacles by choosing from a range of frames at the campsite. Delivery is done later by mail
- On-the-spot Delivery: Patient receives the prescription and can place an order for spectacles by choosing from a range of frames at the campsite. The lenses are fitted and delivered on the spot

The findings from the camps will then be compared with the similar data collected from a hospital based optical shop

### Current status

The pilot study was over in March 2009. Based on the findings the study design and the tools for data collection will be modified. The actual study will carried out from the second half of April 2009.

## Assess the prevalence and socioeconomic burden of near visual impairment caused by uncorrected presbyopia

Principle Investigator : Mr. R.D. Thulasiraj
Supported by : National Eye Institute and World Health Organization

The overall aim of this epidemiological research is to "Assess the prevalence and socioeconomic burden of near visual impairment caused by uncorrected presbyopia".

This is a multi-country study being carried out by WHO with NEI funding in 7 countries to document the prevalence and socio-economic impact of presbyopia. India is the one of the 7 sites where the field survey is completed with an expected response rate of 90%. The field work was started in 19th July 2008 and data collection was completed on 10th November 2008.

The assessment effort entails four specific aims:

- Aim 1: Estimation of the prevalence of near vision impairment in adults = 35 years of age.
- Aim 2: Assessment of participant-reported near visual functioning.
- Aim 3: Assessment of spectacle usage and work impact associated with near vision impairment.
- Aim 4: Assessment of disability weights associated with near vision impairment.

### Materials and methods

A cross sectional sample of subjects aged = 35 years and older was selected using a cluster sampling technique from Thirumangalam and Alanganallur Blocks in Madurai district of Tamil nadu state, India. Eligible subjects were identified through a door to door survey. 12 item Visual Functioning Questionnaire (VFQ) and Spectacle and Work Productivity Questionnaire (SWP) were administered in a subset of the eligible subjects at home. All the study participants were tested for distance and near visual acuity measurements and basic eye examination at a community site within each cluster. Finally all examined participants who also responded to the VFQ (subset of the eligible subjects) were asked to grade the overall degree of difficulty/problem associated with their eyesight. The disability weight valuation for the participant's vision state, along with that of additional vision states described in vignettes were assessed using an analog rating scale.

### Data analysis

Data entry software, developed in EpiInfo (2002), displays the data form on the computer screen, with built-in logical branching, as appropriate. Comprehensive statistical analysis programs have been developed using stata statistical software (version 11). Appropriate statistical analysis was done using this.

### Results

The total study individuals were 2,922. Eye examination was done in 2631 (90.0%) individuals. Of which 203 (7.7%) individuals were wearing glasses and the rest 2428 (92.3%) individuals were not wearing glasses.

## HR practices which influences employee satisfaction and patient satisfaction

| | | |
|---|---|---|
| Internal Guide | : | Mr. R.D. Thulasiraj |
| External Guide | : | Dr. V.R. Muraleedharan, Professor and Head of Department, Humanities and Social Sciences, IIT Madras<br>Dr. T.J. Kamlanabhan, Professor, Department of Management Studies, IIT Madras |
| Research Scholar | : | Ms. Preethi Pradhan |

### Introduction

This study aims to understand the human resource practices which attempt to understand the patient satisfaction as well as employee satisfaction. This will provide direction to human resource practices which can ensure high levels of patient satisfaction, both internal and external. A comparative exploration of these factors within the cataract departments of stand alone eye hospitals; a public sector eye hospital, and an NGO hospital - in Tamilnadu.

### Objectives of the study

- To develop an instrument for measuring patient satisfaction
- To validate an instrument for measuring employee satisfaction in the hospital context
- To use the instruments developed to measure patient and employee satisfaction in the organisation planned
- To map the overlap of domains and thereby, to enumerate HR policies that could maximize customer delight

### Current status

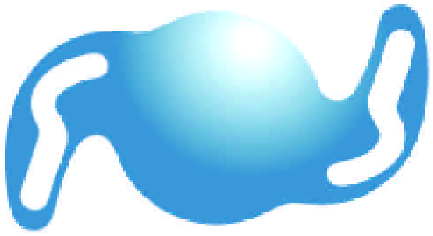
Currently the study is in the final stage with thesis write up going on.

# PRODUCT DEVELOPMENT

## Auroflex – EV

February 2009

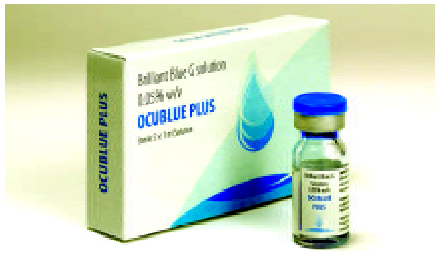
Aurolab's IOL division launched its Aspheric IOL "**Auroflex – EV**". This lens aids in increased contrast sensitivity and better visibility in low light conditions. The Auroflex – EV which is a negative aspheric IOL is the first of its kind manufactured in India. The unique prolate design ensures that all the light rays passing through the lens converge at a single point, thereby ensuring better contrast and sharpness of vision.



## Ocublue Plus

June 2008

Aurolab's Pharmaceutical division launched the Brilliant Blue G Solution "**Ocublue Plus**", an Ophthalmic staining dye. This dye has superior staining of ILM, even at lower concentrations as compared to the more expensive and toxic alternatives like ICG. It makes the delicate manoeuvre of ILM peeling much safer and efficient, with superior functional outcomes for patients.




## Aurosling

July 2008

Aurolab's suture division launched the Frontalis Suspension set "**Aurosling"**. This product is useful in patients with significant Ptosis and poor levator function. Its silicone tubing sleeve provides a method for securing rods and allows postoperative adjustment of the sling. The product is gaining great acceptance in the ophthalmic society due to its affordable pricing and high quality.


## Absorbable suture

February 2009

Aurolab's suture needle division also launched the much awaited absorbable sutures in various sizes namely 6-0, 7-0, 8-0 and 10-0. The PolyGycolic Acid (PGA) absorbable suture comes in braided and monofilament form (only 10-0). These sutures are coated with polycaprolactone and calcium stearates, which render the thread extremely smooth, soft and knot safe.

## Green Laser Photocoagulator

February 2009

Aurolab launched Green Laser Photocoagulator "aurolase 532". With significant increase of diabetes patients in India, a proportional increase in the incidence of diabetic retinopathy is found. The Green laser is used for photocoagulation of the tiny blood –vessels that proliferate on the Retina, particularly with the onset of Diabetic Retinopathy.

# ORGANISATION

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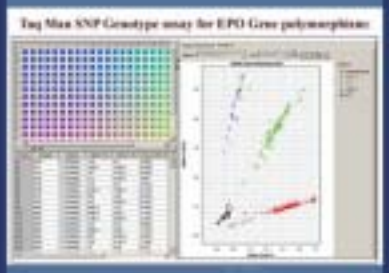
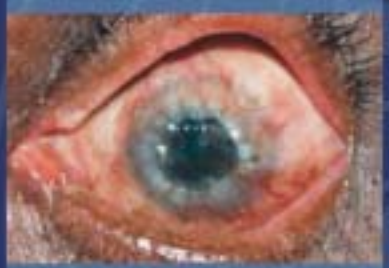
# RESEARCH SCHOLARS

| Name | Guide | Project |
|---|---|---|
| T. Amala Rajasundari<br>Pre doctoral fellow | Dr.P.Sundaresan | Serological and Molecular characterization of Rubella virus in children with ocular defects of Congenital Rubella Syndrome |
| B. Suganthalakshmi<br>SRF - CSIR | Dr.P.Sundaresan | Molecular Genetics of Diabetic Retinopathy |
| P. Murugeswari<br>JRF-DST | Dr.VR.Muthukkaruppan | Studies on Molecular Mechanism of Diabetic Retinopathy |
| S. Ananthi<br>JRF-DBT | Dr.N.V.Prajna<br>Dr.K.Dharmalingam | Pathogen host interaction in human mycotic keratitis |
| B. Hemadevi<br>JRF-DST | Dr.P.Sundaresan | Genetic and Functional analysis of Fuch's Endothelial Corneal Dystrophy (FECD) and Congenital Hereditary Endothelial Dystrophy (CHED) in Indian patients |
| S. Jeyalakshmi, JRF-NEI | Dr.VR.Muthukkaruppan | Will Cytoskeletal drugs prevent PCO? |
| K.Renugadevi<br>JRF-DBT | Dr.P.Sundaresan | Identification of Genetics Defects occurring in Indian Oculocutaneous (OCA) and Ocular Albinism (OA) families |
| Ashwini Shanker<br>Senior Technician-INDEYE | Dr.P.Sundaresan | A Genetic component to the INDEYE study of cataract and age related macular degeneration in India |
| S.Vaishali<br>JRF - DRDO | Dr.VR.Muthukkaruppan | Corneal Surface Reconstruction using Bio-engineered autologous oral mucosal epithelium |
| P.Prabhu<br>Research Assistant - NAB | Dr.VR.Muthukkaruppan | Ex vivo expansion of limbal epithelial cells for Transplantation |
| M.Lalan Kumar Arya<br>JRF- ICMR | Dr.Lalitha Prajna | Standardisation and application of Multiplex PCR in the detection of infectious agents in the intraocular fluid of patients with retinochoroiditis |
| Anshuman Verma<br>JRF- UGC | Dr.P.Sundaresan | Molecular genetics of Leber Congenital Amaurosis in South Indian population |
| Sushil Kumar Dubey<br>JRF -ALCON | Dr.P.Sundaresan | Screening of LOXL1 gene mutations in exfoliation glaucoma patients |
| R.Siva Ganesha Karthikeyan<br>JRF- ALCON | Dr.Lalitha Prajna | Elucidating the virulence genes involved in the patheogenesis of corneal ulcers by Aspergillus sps and the study of host response via the expression of Toll-like receptors |

| Name | Guide | Project |
|---|---|---|
| S.Sudhapriya JRF -ALCON | Dr.VR.Muthukkaruppan | Retinal Stem Cells |
| M.Valar Nila<br>Senior Technician-AMRF | Dr.VR.Muthukkaruppan | Serum Haptoglobin in Diabetic Retinopathy |
| P.Narmathadevi JRF- DBT | Dr.N.V.Prajna<br>Dr.K.Dharmalingam | Pathogen host interaction in human mycotic keratitis |
| C.Jeyashree, JRF - ICMR | Dr.P.Sundaresan | Genetic and functional dissection of FOXL2 gene involved in the pathogenesis of the Blepharomosis syndrome (BPES) |
| P.Mohanapriya<br>Junior Technician - ICMR | Dr. P. Sundaresan | Genetic and functional dissection of FOXL2 gene involved in the pathogenesis of the Blepharomosis, syndrome (BPES) |
| D.Dhivya<br>Senior Technician, AMRF | | RT-PCR & DNA Sequencer |
| V.Saravanan<br>Junior Technician-INDEYE | Dr.P.Sundaresan | A Genetic component to the INDEYE study of cataract and age related macular degeneration in India |
| J.Radha<br>Junior Technician-INDEYE | Dr.P.Sundaresan | A Genetic component to the INDEYE study of cataract and age related macular degeneration in India |
| G.Hema Meenakshi<br>Junior Technician-INDEYE | Dr.P.Sundaresan | A Genetic component to the INDEYE study of cataract and age related macular degeneration in India |
| K.Nithya, JRF-DBT | Dr.Lalitha Prajna | Molecular insights into the etiology of infectious uveitis |
| N.Prasanthi, JRF- DBT | Dr.P.Sundaresan<br>Dr.S.Krishnaswamy | Understanding protein aggregation in relation to Primary Open Angle Glaucoma: Evaluating models, Screening Polymorphisms and database development |

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ARAVIND EYE CARE SYSTEM

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Collaborating Centre
for Prevention of Blindness