TO COMPARE THE ACCURACY OF COMPUTER AIDED GRADING FOR PRESENCE OR ABSENCE OF DIABETIC RETINOPATHY FOR TYPE 2 DIABETES PATIENTS IN A TELE-SCREENING PROGRAM.

THESIS

Submitted to

THE TAMIL NADU Dr.M.G.R. MEDICAL UNIVERSITY

In Partial Fulfillment of the Requirements for the Degree of

DOCTOR OF PHILOSOPHY

By

DR SHEILA JOHN M.B.B.S. , D.O.

DEPARTMENT OF OPHTHALMOLOGY

MEDICAL RESEARCH FOUNDATION

SANKARA NETHRALAYA

CHENNAI- 600006, INDIA

November, 2017

CERTIFICATE AND DECLARATION

I, hereby declare that the thesis entitled, **“ TO COMPARE THE ACCURACY OF COMPUTER AIDED GRADING FOR PRESENCE OR ABSENCE OF DIABETIC RETINOPATHY FOR TYPE 2 DIABETES PATIENTS IN A TELE-SCREENING PROGRAM .”** is an independent work carried out by me in the CU Shah Post Graduate Institute of Ophthalmology, Sankara Nethralaya, Medical Research Foundation, New No. 41, College Road, Chennai, India. PIN: 600006 and it has not been submitted anywhere else for any degree, diploma or title.

Dr SHEILA JOHN **Date:**

CERTIFICATE

This is to certify that the manuscript submitted here is the thesis entitled, **"To compare the accuracy of Computer Aided grading for presence or absence of Diabetic Retinopathy for Type 2 Diabetes patients in a Tele-screening program"** of the candidate **Dr SHEILA JOHN** (Part time), being the result of research work done for the award of Ph.D. in the faculty of Ophthalmology of The Tamilnadu Dr. MGR Medical University under my supervision and guidance in the CU Shah Post Graduate Institute of Ophthalmology, Sankara Nethralaya, Medical Research Foundation, College Road, Chennai, India during the years 2013-2017

Guide and Supervisor **Date:**

Dr. Jyotirmay Biswas, M.S
Director of Uveitis &
Ophthalmic Pathology
Sankara Nethralaya
Chennai 600 006

ACKNOWLEDGEMENT

To start with, I would like to express my deepest and sincere gratitude to my doctoral mentor Dr. Jyotirmay Biswas, M.S, Director of Uvea and Ocular Pathology Department , Sankara Nethralaya for his able guidance and support in moulding this piece of research work. Apart from being a committed scientist, he has rendered immense assistance at all times.

I take this opportunity to thank Dr. S.S Badrinath, Chairman Emeritus, for permitting me to pursue my research in this esteem organisation and also for providing excellent research facilities at the Centre. He has been consistently motivating me to carry out PHD work in Telemedcine .

I take this opportunity to express sincere thanks to my Co-guide Dr. Mohanasankar Sivaprakasam, Head, Healthcare Technology Innovation Centre, Indian Institute of Technology, Madras and his team including Keerthi Ram, Supriti Mulay, Kulasekaran for their technical inputs for developing the image analysis technology and engineering. I would like to specially thank Keerthi Ram for helping me and motivating me to complete my thesis. I would like to thank Dr Vijay Viswanathan my co guide who helped me with my thesis.

My sincere thanks are due to Dr Girish Shiva Rao, Medical Director – Administration, Dr. Ronnie George, Director Research, Dr. S Meenakshi, Director Academics, Sankara Nethralaya for their excellent support, Mr. N. Sivakumar, Academic Officer, Sankara Nethralaya for processing the academic documents. My sincere thanks to Dr Sabyasachi Sengupta, who has been a co-author in my earlier teleophthalmology publications and also for his novel ideas.

I wish to express my deep sense of gratitude and indebtedness to my team members including Ms. M. Premila, Mr. K.P.T. Kannan, Mr. M. Arasakumar, Mr. M. Martin Manoj, Mr. S. Ramesh Babu, Ms. A. Padmavathy, Ms. J. Divya, Mr. A. Muthusaravanan, Mr. A. Murugapandian, Mr. C. Jaikumar, Mr. N. Ravi, Mr. Nagappan and Ms. Hemalatha S for their extensive help throughout my thesis period. A special thanks to Librarians Mr. Shankar Kumar, Ms. Saradha Vasan and Mr. Arivumuthu for helping me with the references for the thesis. My thanks are due Dr. Rajiv Raman, Dr. Dhanashree Ratra and Ms. Sangeetha for their support in my thesis. My heartfelt thanks to Mr. Deenadayalan and Mr. Vijayakumar from multimedia department for helping me in printing and designing work of my thesis. I owe my gratitude to my close friends for their constant motivation during the study period.

I am indebted to my sister and brother in law, niece and nephew for their support during the entire research period. My humble and profound respects to the Almighty for all that He has bestowed upon me.

Dr Sheila John **Date:**

TABLE OF CONTENTS

TITLE

To compare the accuracy of Computer Aided grading for presence or absence of diabetic retinopathy for type 2 diabetic patients in a Tele-screening program.

INTRODUCTION

The prevalence of Diabetes Mellitus in the world is estimated to be 439 million by 2030 (1) out of which 80% reside in Asia (1-3) and more than 60 million are in India and this is expected to increase to more than 100 million (3,4) by 2030.The first national study conducted by the Indian Council of Medical Research - India Diabetes study (5) for people >20 years, determined the prevalence of pre -diabetes (impaired fasting blood glucose and impaired glucose tolerance) and diabetes to be 77.2 million and 62.4 million people respectively. The conversion rate of pre-diabetes to diabetes was 58.9% and for normal persons the conversion rate to dysglycemia was 45% in the 10 year follow up of patients in the Chennai Urban Rural Epidemiology Study (CURES) (6).

Based on the reports of the international federation of diabetes (IFD) (3) there will be 629 million people with diabetes aged (20-79 years) by 2045.12% of global expenditure is spent on diabetes. Three quarters of the people with diabetes live in low and middle income countries(7)

DIABETES AND ITS MANY COMPLICATIONS

Diabetes Mellitus (3) is a chronic disease that occurs either when the pancreas does not produce enough insulin (type 1) or when the body cannot effectively use the insulin it produces (type 2). Insulin is a hormone that regulates blood sugar by enabling the glucose from food to enter the body cells and be used as a source of energy. Hyperglycemia, is a common effect of uncontrolled diabetes and leads to serious damage to many of the body's organs.

Long-term complications of diabetes develop gradually, depending on the duration and glycemiccontrol of blood sugar and are macrovascular and microvascular (8) complications in nature. Microvascular complications include diabetic neuropathy, nephropathy and retinopathy.

1) Macrovacular - Blood vessel (vascular disease) damage: Diabetes dramatically increases the risk of various cardiovascular problems, (9) including hypertension, heart attack, and stroke.

2) Nerve damage (neuropathy) and foot damage: Excess sugar can injure the walls of the tiny blood vessels (capillaries) that nourish the nerves, especially in the legs foot region and this could lead to loss of all sensation in the affected limbs and foot ulcers.

3) Kidney damage (nephropathy): The kidneys have millions of tiny blood vessel clusters (glomeruli) that filter waste from the blood. Hyperglycemia can damage this delicate filtering system and can lead to kidney failure or irreversible end-stage kidney disease, which may require dialysis or a kidney transplant.

4) Eye damage (retinopathy): Diabetes can damage the blood vessels of the retina (diabetic retinopathy), leading to blindness. Hyperglycemia increases the risk of cataracts and glaucoma.

Diabetic Retinopathy (DR) is one of the micro vascular complications of Diabetes where leakage and blockage of capillaries in the retina cause swelling, abnormal blood vessel growth, cell death and retinal detachment leading to visual loss and blindness. The prevalence of DR across the world (10) was higher in Caucasians (45.7%), African-Americans (49.6%), Hispanics (34.6%) as compared to Asians(19.9%). In India the prevalence of DR ranges from 17.6% to 28.2%, based on various population studies, published from various groups across the country such as Namperumalsamy (11) , Dandona(12) , CURES (13,14) , SNDREAMS (15,16) and Thomas RL (17). Gadkari et al (18) have estimated the prevalence of Diabetic retinopathy (DR) in rural India to be between 10%-12% and the prevalence of DR in rural India could rise to 10.97 million by the year 2030 as 70% of Indians live in rural areas.

Diabetic Retinopathy in India

There are an estimated 65 million diabetics in India and they would require an annual dilated eye examination and many studies have suggested that mydriatic fundus photography (19) is equivalent to ophthalmologist examination (20,21) .

Raman et al have (22) reported the prevalence of DR in urban areas is 13-18% and in rural areas is 9-10% in India . They have also reported on literature survey that the risk factors associated with development of DR, were duration of diabetes, age, hyperglycaemia, hypertension, anemia and use of insulin .Diabetic nephropathy patients have six times more risk of DR .The diabetic patients are expected to increase to 79.4 in future and hence DR will increase to 22.4 million and increase in patients with sight threatening retinopathy to 2 million. Awareness about risks of DR was poor among the people in the community. 60-75% of patients have not undergone eye examination for DR in the urban and rural population .45%- 50% patients with sight threatening retinopathy had never undergone an eye examination .

Gadkari et al (18) have reported that the All India Ophthalmological society conducted a nation wide survey for the presence of DR in Nov 2014 . 194 centres across india participated and 5130 diabetics were enrolled in the study The prevalence of DR in patients less than 6 months of duration of diabetes is 9.3% and in persons who have more than 5 years duration of diabetes is 35%.Majority of the patients underwent retinal examination by an ophthalmologist and only 15% underwent fundus photography in this study

Jotheeswaran AT et al (23) have done Systematic review and Meta analysis for estimating the number of diabetics developing DR in india . Diabetes and DR leads to blindness which increases the number of people with disability in India . Prevalence of undiagnosed diabetes is from 4.2% to 10.5% and type 2 diabetic patients having DR at the time of diagnosis of diabetes is 20% .

AIMS AND OBJECTIVES

AIM:

The aim of this study was to compare accuracy of a novel Computer Aided software application for the "Presence or absence of" Diabetic Retinopathy with the existing manual systems of grading done by human graders in a Tele screening program

TYPE OF STUDY

Assessment of a screening tool for Diabetic Retinopathy in a Diabetic clinic in Chennai.

OBJECTIVE:

The main objectives of the study

1) Development of the computer aided Algorithm (CAD) as a screening tool for DR by Healthcare Technology Innovation Center (HTIC) in IIT Madras

2) Utilize the CAD real-time in vitreo retinal outpatient department (OPD), Tele camps and diabetic clinics and to compare the sensitivity, specificity and accuracy of Computer Aided automated grading to a human grader

3) Patients underwent fundus photography and the images were run through the CAD system as well as graded by a human grader. The effectiveness of the CAD to detect diabetic retinopathy lesions was examined in comparison to that by the human grader -ophthalmologist- the 'gold standard'.

Review of Literature

Clinical features of diabetic retinopathy

Diabetic retinopathy is divided into various stages. The early sign and clinical feature of non-proliferative diabetic retinopathy NPDR is micro aneurysm followed by retinal dot and blot retinal haemorrhages venous beading (VB) cotton wool spots (24), intraretinal microvascular abnormalities (IRMA) and arteriolar abnormalities.These features are due to abnormal permeability and non-perfusion of capillaries.Diabetic macular edema is characterized by retinal oedema secondary to leaking microaneurysms or capillary plexus and resultant hard exudates. Diabetic macular edema (DME) develops when fluid leakage is located in the macular area These features have been classified into mild, moderate and severe NPDR by the international classification of diabetic retinopathy based on the distribution of microaneurysms, hemorrhages, venous changes and IRMA.

Proliferative diabetic retinopathy (PDR) develops from occluded capillaries which causes retinal ischemia and formation of new vessels on the surface of the retina near the optic disc or retinal periphery, vitreous/preretinal haemorrhages, fibrosis, and retinal detachments.Neovascularization on the optic disc or elsewhere in the retina is the hallmark feature of proliferative diabetic retinopathy. Vision/Sight threatening retinopathy (VTDR/STDR) has three components i.e. DME, Severe NPDR and PDR.

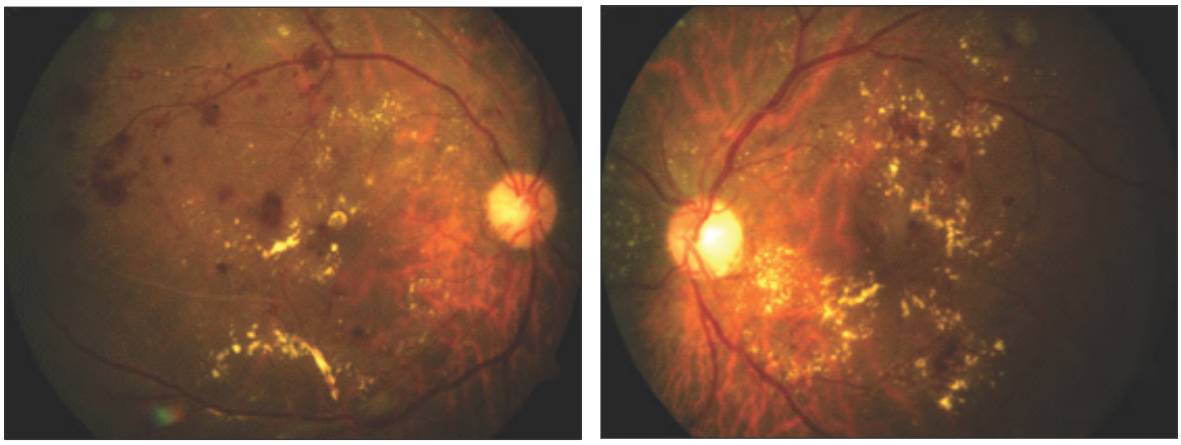

Fig 1 : Severe NPDR with Diabetic Maculopathy

Source: Sankara Nethralaya

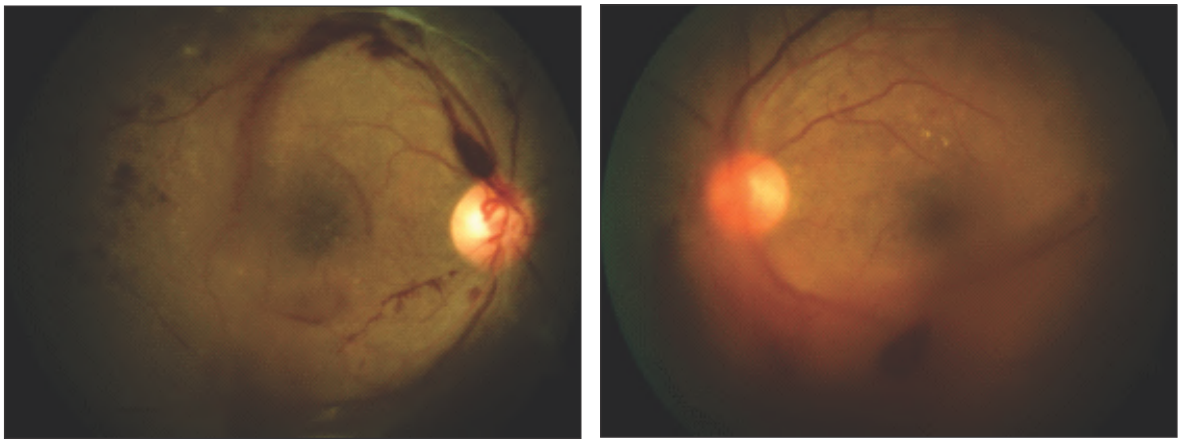

Fig 2 : Proliferative Diabetic Retinopathy

Source: Sankara Nethralaya

International classification of Clinical diabetic retinopathy and diabetic macular edema disease scales .

Early Treatment diabetic Retinopathy Study (ETDRS) grading system is the gold standard for clinical trials but in clinical practice it was difficult to implement. There were too many levels and complicated grading rules which are difficult to remember.

This international DR grading system is based on an evidence-based approach derived from the findings of the Early Treatment of Diabetic Retinopathy Study (ETDRS) (25), the diabetic (retinopathy study) (26) and Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR). These studies have provided the foundation of the understanding of diabetic retinopathy progression, risk factors, and outcomes of treatment .The pathology of the retina which leads to decreased capillary perfusion and ischemia are the main factors which contribute to clinical findings of DR. With an increase in diabetes prevalence, the prevalence and incidence of diabetic retinopathy has increased.

Principles for Development:

The disease severity scales were based on the following principles:

1. This should be based on solid scientific evidence, i.e., the ETDRS data. Science should not be compromised.
2. This would not replace the ETDRS, but provide a common, user-friendly terminology to describe disease severity and risk of progression categories.
3. This should be tied to levels of risk of progression to more severe disease, as described in the ETDRS and other research.
4. The number of levels or stages of disease severity should be appropriate for communication, based on scientific evidence and practical for everyday use.

The recognition of the basic lesions (27) associated with diabetic retinopathy (28) will result in appropriate grading for communicating the status of patients between ophthalmologists and endocrinologists, diabetologists and primary care physicians who take care of diabetic patients. The international clinical retinopathy (29) and Diabetic macular severity scales - ICDR was formulated with the help of international experts to capture the various clinical stages of of DR .

Table 1. International Classification of Diabetic Retinopathy Disease Severity Scale (29)

Proposed Disease Severity Level	Findings Observable on Dilated Ophthalmoscopy
No DR	No abnormality
Mild NPDR	Only Micro aneurysm
Moderate NPDR	More than mild, but less than severe NPDR
Severe NPDR	Any of the following: 20 or more intraretinal haemorrhages in each of 4 quadrants; venous beading in 2 + quadrants; intraretinal microvascular abnormalities in 1 + quadrant ; 4:2:1 rule. No signs of PDR
Proliferative DR (PDR)	one or more of the following: neovascularization or pre-retinal or vitreous haemorrhage.

NPDR – Non proliferative diabetic Retinopathy

Table 2. Diabetic Macular Edema Disease (DME) Severity Scale

Proposed Disease Severity Level	Findings Observable on Dilated Ophthalmoscopy
Diabetic macular edema apparently absent	No apparent retinal thickening or hard exudates in posterior pole
Diabetic macular edema apparently present	Some apparent retinal thickening or hard exudates in posterior pole

Table 3. If diabetic macular edema is present, it can be categorized as follows

Proposed Disease Severity Level	Findings Observable on Dilated Ophthalmoscopy *
Diabetic macular edema present	Mild diabetic macular edema: Some retinal thickening or hard exudates in posterior pole but distant from the center of the macula.
	Moderate diabetic macular edema: Retinal thickening or hard exudates approaching the center of the macula but not involving the center.
	Severe diabetic macular edema: Retinal thickening or hard exudates involving the center of the macula.

*Hard exudates are a sign of current or previous macular edema. Diabetic macular edema is defined as retinal thickening, and this requires a three-dimensional assessment that is best performed by a dilated examination using slit-lamp biomicroscopy and/or stereo fundus photography.

Based on the ICDR Classification DR was divided into 5 stages and Severe NPDR, PDR and macular edema are termed as sight threatening retinopathy.The progression of the disease takes several years from mild DR to sight threatening DR and hence annual screening and timely treatment has the potential to prevent visual loss .

There are features of DR which are not visible to the human eye and these features have to be measured and metrics developed to identify like in the case of macular edema . Healthy retinal images have variations and even the pathological signs of DR may have similarity to each other .Fundus photography has been used for diagnosis and documentation of clinical features of DR .The minimum field of view is 45° horizontal and 40° vertical and image should be centred on the macula and include the optic disc .

Confocal Scanning laser ophthalmoscopy: This imaging modality is based on the basic principles of confocal scanning which uses a specific type of laser to produce extremely high resolution images of the retina with very high special sensitivity. The images are usually presented in pseudo color depending on the wavelength of light used to acquire the image. Adaptive optics have been added to the scanning laser ophthalmoscopy systems to improve their lateral spatial resolution such that photoreceptors can be visualized in vivo using this technique. However, this technique is cost prohibitive and used only in clinical research settings currently. In addition to the high cost, these cameras are table mounted and heavy, making it difficult to carry in remote settings such as camps

Ultra Wide field retinal imaging: The conventional fundus cameras produce images covering the central 45 degrees field of view. Fundus cameras capable of wide field imaging (Heidelberg Retinal Analyzer, Heidelberg, Germany) help in acquiring images that span 100 degrees of the retinal surface in one capture. Ultra wide field imaging captures 200 degrees field of view in a single capture and these fundus cameras are available from Optos Inc, USA. The advantages of using wide field and ultra widefield imaging is that larger areas of the retina can be visualized, greater pathology identified and fluorescein angiography done using these cameras yield extensive information regarding the perfusion status of peripheral retinal areas. These studies have (30) led to insight into the pathogenesis of DR, and have lead to newer classifications of DR, identification of predominantly mid-peripheral DR, correlation between DME and peripheral retinal ischemia and targeted scatter laser photocoagulation for treating DME and localized forms of DR.Ultra wide field imaging has also been employed for screening of DR (31) for camp settings in the USA because it can now be performedeven in the nonmydriatic state. However, the technology is cost prohibitive and has not been widely adopted due to the cost.

Optical Coherence Tomography (OCT) for diagnosing macular edema

The availability of OCT is the single most influential factor that has led to paradigm shifts in the management of DME. The OCT technology has evolved from time domain OCT to spectral domain OCT and the current versions belong to the Swept – source OCT. Each iteration of the OCT technology has brought greater resolution in image quality.

The OCT essentially provides real life in vivo histopathology scans of the retina, spanning from the internal limiting membrane till the retinal pigment epithelium. Newer generation OCT are able to clearly visualize the choroid up to the chorio-scleral junction.

DME is classified as either (32) spongy edema, cystoid macular edema, predominantly greater subretinal fluid, taut posterior hyaloid face and vitreomacular traction. The former three conditions, when involving the center of the fovea, is treated with intravitreal pharmacotherapy using either Vascular endothelial growth factor (Anti_VEGf agents) or steroids. The latter two conditions are treated with vitreous surgery. The treatment and retreatment criteria for DME is predominantly based on the OCT findings as well.

CRITERIA FOR REFERRAL OF DR-to ophthalmologists

Diabetic retinopathy preceded the diagnosis of diabetes in Wisconsin study and hence it is important to do retinal evaluation for patients (33) above 40 years of age .Type 2 Diabetic patients require fundus examination at the time of diagnosis (34) itself as 30% present with DR at the time of diagnosis of Diabetes.

.

Early diagnosis of DR prevents visual loss and protocols established for referral after screening for diabetic retinopathy by Bresnick GH et al (35). Patients with diabetes (36) but without diabetic retinopathy are advised annual or 15 months interval of dilated fundus examination to rule out diabetic retinopathy. But less than one third report for DR screening due to challenges in transportation. Community based screening programs and innovative telemedicine strategies may improve compliance.

The ophthalmologists will do comprehensive examination with dilated fundus examination for all diabetic patients and based on the clinical features and visual disability, they are treated.

Diabetic patients should be advised to consult physician for control of blood sugar and associated systemic complications., In type 2 diabetic patients, macular edema (8) occurs most frequently and is about 7.5 % and is most common cause of moderate visual impairment in the working age adults .American academy of ophthalmology recommendations for treatment of DR is given below .

TABLE 4. MANAGEMENT RECOMMENDATIONS FOR DIABETIC (37) PATIENTS WITH DR

Severity of Retinopathy	Presence of Macular Edema	Follow-up (Months)
Normal or minimal NPDR	No	12
Mild NPDR	No	12
	ME	4-6
	CSME	1*
Moderate NPDR	No	12
	ME	3-6
	CSME	1*
Severe NPDR	No	4
	ME	2-4
	CSME	1*
Non-high-risk PDR	No	4
	ME	2-4
	CSME	1*
High-risk PDR	No	4
	ME	4
	CSME	1*

CSME = clinically significant macular edema; ME = non-clinically significant macular edema; NPDR = nonproliferative diabetic retinopathy; PDR = proliferative diabetic retinopathy.

TABLE 5: Criteria and degree of urgency for referral of a patient (8) with DR to the ophthalmologist.

"Lesions requiring immediate assessment by the ophthalmologist"	Proliferative retinopathy	(i) New vessels on the optic disc or at any location in the retina (ii) Preretinal hemorrhage
	Advanced diabetic	(i) Vitreous hemorrhage (ii) Fibrotic tissue (epiretinal membrane) (iii) Recent retinal detachment (iv) Iris neovascularization
"Lesions that should be referred to the ophthalmologist for assessment as soon as possible"	Preproliferative retinopathy	(i) Venous irregularities (ii) Multiple hemorrhages (iii) Multiple cotton-wool exudates (iv) Intraretinal microvascular abnormalities (IRMA)
	“Nonproliferative retinopathywith macular involvement"	“(i) Decreased visual acuity uncorrected with a pinhole occluder(suggestive of macular edema)" (ii) Microaneurysms, hemorrhages, or exudates within less than one disc diameter of the center of the macula (with or without vision loss)
	"Nonproliferative retinopathywithout macular involvement"	“(I) Hard exudates with a circinate or plaque pattern in the major temporal vascular arcades"

CSME = clinically significant macular edema; ME = non-clinically significant macular edema; NPDR = nonproliferative diabetic retinopathy; PDR = proliferative diabetic retinopathy.

Visual Impairment and blindness due to DR

Thomas et al (38) had conducted a large national community based screening program involving 91,398 diabetics for detection of DR in Wales. The prevalence of DR was 30% .The major risk factor was duration of diabetes .A structured screening program with early detection will reduce the incidence of blindness .

Diabetic retinopathy in its early form is often asymptomatic, but amenable to treatment. The progression from no retinopathy to blindness can occur quickly within a decade or can take up to two decades and this relatively slow rate enables DR to be identified and treated at an early stage. Development and progression of DR is related to duration and control of diabetes as shown by the UK Prospective Diabetes Study (UKPDS). The Early Treatment of Diabetic Retinopathy Study (ETDRS) showed that treatment with laser photocoagulation can more than halve the risk of developing visual loss from proliferative diabetic retinopathy (PDR) and macular edema. Every effort must be made to help patients never to reach this advanced stage DR, as, by then, full sight recovery may no longer be possible and even the best treatment may still leave many severely visually impaired.Broad guidelines estimate that 1 in 3 diabetic patients (39) will develop DR and 1 in 10 diabetic patients will develop vision threatening DR.

Janet L.Leasher et al based (40) on Global burden of disease study 2010 reported that globally 32.4 million were blind and 191million had visual impairment out of which 0.8 million blind and 3.7 had visual impairment due to DR .

Fundus photography

Retinal photography reflects the health status of the human eye and aids in the diagnosis of various eye conditions. Medical imaging (41) has undergone rapid transition and enhancement from non-digital imaging to digital imaging Choices of digital cameras available from photographic cameras to cell phones .Non mydriatic cameras capture images through small pupil and depend on physiologic dilation. They are used in screening programs and physician offices .Mydriatic cameras require pupillary dilation and provide better fundus images and are used in ophthalmology clinics.

An image based system ,the Picture Archiving and communications system(PACS) is used for the acquisition, storage, archiving, display and remote manipulation of retinal images .The universal PACS storage is Digital imaging and communications in Medicine (DICOM) .The fundus images in this study are stored as Joint photographers experts group (JPEG) images

Fundus photography (42) has been the cornerstone of documenting diabetic retinopathy (DR) for the past few decades. Photography criteria were established by international researchers at the Airlie House Symposium in 1968, followed in 1981 by the Diabetic Retinopathy Study's standards for detecting and grading DR severity by using stereoscopic 35-mm slides (film).

The evolving protocol and DR severity classification system were expanded in 1991 by the Early Treatment Diabetic Retinopathy Study (ETDRS). Today, ETDRS 7 field photography is the gold standard for diagnosing DR against which other DR assessment approaches are measured. Expert photographer and pupillary dilation is required for 7 field photography and it is time consuming and hence not effective as a screening tool . Helen k..li et al have (42) compared film versus digital fundus photography and the results that there was substantial agreement in grading DR. in both methods Fundus photographs (43) is a permanent method of documentation for DR. The sensitivity and specificity (44) of fundus photographs for detecting the presence or absence of DR depends on the site (hospital /campsite) camera (nonmydriatric /mydriatric) with or without dilation and trained fundus photographer with qualifications or lay person. Mydriatic fundus photographs taken with the help of trained photographers have good sensitivity and specificity

Helen .k.li and Hubbard et al (45) have assessed and compared monoscopic and stereoscopic digital fundus photography for grading severity of DR .Stero fundus photography has been used in many clinical studies. By taking photographs of the retinal image from two different positions a stereo image is produced. Depth perception helps to differentiate neovascularization above the plane of retina from intraretinal microvascular abnormalities (IRMAs).Steropsis helps in identifying fibrous proliferation ,preretinal Haemorrhage and Macular edema .Stero imaging requires clear media and well dilated pupils more than 6mm for depth perception .Dilation in diabetics is limited by autonomic neuropathy .Optical viewers are required to view stereo fundus photographs. Observers with unequal visual acuity in both eyes have difficulty in viewing stereopsis. 85 patients were enrolled in this study and three readers evaluated all the retinal images .The results from this study showed good agreement between the monoscopic(dilated) and stero digital fundus photographs .For detection of Neovascularization stereopsis is better but in monoscopic images there were other features of retinopathy to identify the stage of PDR

Mydriatic versus Non mydriatic fundus photographs

Vujosevic et al performed a study to evaluate whether Non mydriatic 45 degree single/multiple retinal photographs can replace the mydriatic seven field fundus photographs and (46) found results to support that a single Non mydriatic 45 degree fundus photograph centred on the macula is sufficient to diagnose the presence or absence of DR.

Silva et al (47) have used a fundus camera with low flash light for taking Non mydriatic images(45 degree) and compared it the Standard mydriatic seven field (30 degree) and dilated clinical examination by a retinal specialist. The study was conducted in 67 subjects with 126 eyes .There was good agreement within the three modalities with a significant Kappa value .

High flash exposure is a barrier during nonmydriatic retinal imaging and hence low flash will improve the quality of images .

Single field fundus photography for screening diabetic retinopathy is not a substitute for comprehensive eye examination but can be used as a screening tool to identify DR..The authors George A.williams et al (48) had reviewed 32 articles and confirmed Non nonmydriatic single field fundus photography is convenient and cost effective when interpreted by trained readers when compared to 7 field fundus photographs. The sensitivity and specificity of nonmydriatic single field fundus photographswas 61-90% and 65-90% when compared with standard seven field fundus photography .

Eric K.chin et al (49) evaluated the accuracy of non nonmydriatic single 45 degrees fundus photographs of the disc and macula in remote rural sites and in the urban medical center for diagnosis of DR, using a retrospective study design. These images following transmission were read by the retinal specialist. Diabetic patients who had not adhered to the annual eye examination were chosen as subjects .872 patients from rural sites and 517 subjects from urban sites underwent fundus photography and the images were of good quality in 82%-85% of subjects. DR was diagnosed in 29.6% of urban patients and 12.6% of rural patients. Authors concluded that nonmydriatic single field photography was useful for diagnosing DR .

Gupta et al (50) in this prospective study enrolled 500 diabetic patients(1000 eyes) in the endocrinology clinic .All the patients underwent nonmydriatic three 45 degree retinal fields ,optic disc and macula ,superotemporal and nasal to the disc and then underwent dilated fundus photography for the same fields .Two retinal specialists independently reviewed the retinal images and noted the gradability of the images and the presence of DR .25% of the nonmydriatic images were not gradable out of 1000 eyes .In the gradable images the results showed 83-84% sensitivity .The authors have reported that in Indian eyes due to dark iris and pupillary constriction the number of unreadable images is high and hence the referable rate to the ophthalmologist has also increased. Diabetic (51) Patients older than 60 years had more incidence of ungradable (52) images .

Murgatroyd H.et al (53) had evaluated the effect of mydriasis and 3 field fundus photography on screening for DR .This study had 398 patients and the results showed that mydriasis reduced the number of ungradable images .Mydriasis and 3 field fundus photography did not improve the sensitivity and specificity of diagnosis of DR .

Silva et al (54) compared the diagnosis of DR and the rate of ungradable images between nonmydriatic ultrawide field imaging (n=8109 patients)and nonmydriatic multifield fundus photography (n=17526patients) The severity of DR peripheral lesions could be identified and the number of ungradable images were reduced and accuracy of DR diagnosis improved with nonmydriaticultrawide field imaging In a national teleophthalmology program. Authors also noted that neovascularization elsewhere can be easily diagnosed with ultrawide field fundus photography (55) .

Fundus camera

First commercially available fundus camera was made by Carl Zeiss in 1926 and with the advent of digital revolution the fundus camera have evolved with many changes The traditional fundus (56) cameras are costly, bulky, office based table top and technician dependent .Advanced camera systems have filters for autofluoresence ,fundus Fluorescein angiography ,indocyanine green angiography and automated analysis .The latest versions of table top fundus camera are less costly and provide good quality retinal images .The various fundus camera are given in the tabular form.

Table 6. Technical Specifications of Fundus Cameras

Name	Design Principle	Pupil	Field Of View	Image Sensor/ Display
Miniature table-top design				
iCam	Reflective imaging using white light	Nonmydriatic	45°	12-bit CCD, 5.2 MP, computer interface
3nethra (Classic and Royal)	Reflective imaging using white light	Nonmydriatic	45°	3 MP, computer interface
dRS	Reflective imaging using white light	Nonmydriatic	45°H 40°V	5 MP, 10.4-inch touchscreen color display; WiFi and Ethernet connected
EasyScan	Confocal SLO, with green, NIR	Nonmydriatic	60°H 45°V	Photodetector-based computer interface; network connectivity
Topcon TRC-NW8Fplus	Reflective imaging using white light	Nonmydriatic	45°	8 MP digital SRL camera
Zeiss VISUCAM 200	Reflective imaging using white light	Nonmydriatic	45°and 30°	CCD 5.0 MP, 19-inch TFT
Kowa Nonmyd7	Reflective imaging using white light	Nonmydriatic	45°	12 MP digital camera
Canon CR-2	Reflective imaging using white light	Nonmydriatic	45°	18 MP EOS digital camera
OCULUS Image-Cam 2 digital slit lamp camera	Slit lamp-based	Not specified	Not specified	2 MP resolution
California ultra-widefield Retinalimaging	Reflective imaging using multiple wavelengths	Nonmydriatic	200°	Not specified
Point-and-shoot off-the-shelf digital camera-based	Conventional optics + camera lens	Mydriatic	50°	Camera CMOS sensor

Table 7. Technical Specifications of Fundus Cameras

Name	Design Principle	Pupil	Field Of View	Image Sensor/ Display
Integrated adaptor-detector-based (hand-held)				
iExaminer+ PanOptic ophthalmoscope	iPhone + PanOptic ophthalmoscope	Nonmydriatic	25°	iPhone 4S camera
Volk Pictor	Reflective imaging using white light	Nonmydriatic	40°	5 MP, TFT LCD detector, WiFi/USB connectivity
VersaCam	Reflective imaging using white light	Nonmydriatic	40°	2 MP camera, 3.5-inch color LCD
JedMed Horus Scope	Reflective imaging	Nonmydriatic	Not specified	2 MP HD camera, 3.5-inch color LCD, PC connectivity through USB
Optomed Smartscope	Conventional optics	Nonmydriatic	40°	5 MP CMOS image sensor, 2.4-inch TFT LCD detector, PC connectivity through USB
Kowa Genesis-D	Conventional optics	Mydriatic	Not specified	2 MP digital camera, 2.5-inch TFT LCD display
Riester ri-screen multifunctional digital camera system	Slit lamp-based	Nonmydriatic	25°or 40°	3.5-inch full HD full color TFT-LCD display
Smartphone-based (hand-held)				
Ocular Cellscope	iPhone + conventional optics	Mydriatic	55°	iPhone
PEEK	iPhone + external lens	Mydriatic	20°	iPhone
Harvard Medical School prototype	iPhone + external lens	Nonmydriatic	45°	iPhone

3D - three-dimensional; CCD - charge-coupled device; Cyl- cylindrical; D -diopters; H- horizontal; HD- high-definition; LCD- liquid crystal display; MP- megapixels; NIR-near-infrared; PC- personal computer; PEEK- Portable Eye Examination Kit; SLO- scanning laser ophthalmoscopy; Sph- spherical; V- vertical; TFT- thin-film transistor.

Chole Bedard et al (57) has done systematic review on usage of non mydriatic retinal cameras without pupillary dilation .He also compared non mydriatic fundus photography with the reference standard of seven field 30 degree mydriatic fundus photograph in the community . The sensitivity to detect DR ranged from 68-98% and specificity from 65-98% .The sensitivity increased with use of Optus fundus camera in comparison to traditional fundus cameras like Topcon and cannon .Sensitivity increased with multiple fields than with single field.

Smartphones used as fundus camera

Smartphone (58) are portable, affordable, have advanced image viewing capacity and have connectivity for transmission of images and hence smart phone ophthalmoscopy is suitable for community screening programs . Smart phones (59) are android and apple phones (iphones) (60) and are widely used in many clinical applications(EMR,clinical support system ,pupillary evaluation, amsler chart,near vision charts ,fundus photographs and others) (61) in ophthalmology.Most doctors own a smart phone and are familiar with it. Patient information must be kept confidential when phones are used for patient data.

Sajeesh Kumar et al (61) have compared the diagnostic accuracy of DR fundus images for iphone and office computer workstation.Fundus images were taken using Topcon fundus camera NW 300 (non mydriatic camera)stored as DICOM images and viewed remotely (teleophthalmology) by two ophthalmologists either in the smartphone or computer workstation and graded the DR independently. The quality of fundus images viewed by smartphone and computer workstation matched well with each other .

Previous work has been done at Sankara nethralaya to determine if , smartphones (62) are comparable to laptop computers for image diagnosis in Teleophthalmology. 114 patients (228 eyes) underwent fundus photography with Topcon fundus camera NW 200 and were transferred to the smart phone and laptop .The smart phones in this study are HTC sensation and LG optimus G2X . and 92.5 % cases were correctly diagnosed by the smart phone and laptop.Smartphone analysis revealed 98% sensitivity,57% specificity 26.5% of patients had DR ..Smart phones are effective in diagnosing various retinal conditions .

Andrea Russo et al (63) have compared smart phone ophthalmoscopy with slit lamp biomicrposcopy for grading DR and detection of diabetic macular edema . The D-eye adapter was attached to the apple phone 5 and by a retinal specialist dilated fundus examination was done on 120 patients (240 eyes) .

By an another retinal specialist , slit lamp biomicroscopy was done for all the patients. Good agreement of 85% between both methods was reported by the authors.

Ryan ME and Rajalakshmi et al (64) compared smart phone fundus photography ,non mydriatic fundus photography and dilated 7 field mydriatic fundus photography for detection and grading of DR .300 patients underwent fundus photography by all 3 modalities and gold standard was 7 field fundus photography ,Smartphone and non mydriatic fundus photography were able to diagnose DR but mydriatic fundus photography is more sensitive to diagnose of DR .Smart phone is cheaper ,portable and has transmission capabilities .

Nigel M. et al (65) have reported that welch Allyn the ophthalmocope has manufactured iExamineris attached to iphone4 which can capture retinal images .Adapters which allow retinal photographs to be taken through direct ophthalmoscopy is PEEK (66) Fundus photographs taken by non health workers was compared with fundus photographs taken by trained technician using table top fundus camera.The photographs were analzed (67) by Moorfield eye Hospital reading centre London UK The authors repoeted good agreement and a Kappa value of 0.71.for optic nerve head imaging. PEEK is being compared with retinal cameras. Topcon NRW6, in 18 sites of DR screening programs in Tanzia and initial results are good for dilated fundus images and complete results have not be published yet .Standard policies and (68) framework is needed for M Heath and there has to be understanding between clinicians and technical persons .

A mobile phone-based retinal camera (69) for portable wide field imaging. Robi N Maamari et al have mentioned a mobile phone based retinal camera ocular cellscope attachment to the iphone 4s which has the capacity to take fundus photographs with 55^0 field of view .The fundus photograph has about 46 pixel per retinal degree and the minimal requirement is only 30 pixel per degree as given by UK Nation Health Service (70) for diabetic retinopathy screening .

Diabetic Retinopathy screening in the global scernio

Worldwide there will 439 million diabetic patients by 2030 and they will require an annual retinal evaluation as advised by WHO , American Academy of ophthalmology and American diabetic (71) Association. In the diabetic population Hazin R et al (72) have observed that less than 65% undergo the annual retinal examination (73) and in the rural population it is only 10-20%.

Sheppler CR et al (74) have indicated Clinicians should explain the importance of annual eye examination to all diabetic patients and also discuss the perceived misconceptions and barriers. The common barriers are transportation ,lack of awareness ,cost and others .

Different models have been developed (75) for DR screening and they are implemented to varying degrees across the world which are Ophthalmologist led model, Telemedicine /Teleophthalmology and Opportunistic screening.

1) Ophthalmologist led model: Outreach screening camps in the community conducted by ophthalmologists (12) , screen people for diabetes (76) and its complications, and patients with sight threatening DR are referred to the hospital for treatment. the sensitivity of the indirect ophthalmoscopy to detect DR was 85% and 95% and sight threatening DR was 72 % and 100%.

MANPOWER

Concentration of ophthalmologists and paramedics in urban settings, lack of infrastructure as well as adequately trained manpower are a few significant reasons for the high magnitude of avoidable blindness in remote and (77) underserved areas. In order to prevail over the barriers to utilization of eye care services, there is an imperative need to design comprehensive yet sustainable eye care programs to facilitate easily accessibility to the remote areas.. Comprehensive eye examination at such camps must ensure quality and identify the various vision threatening ocular diseases and refer to the hospital.

Ophthalmologist to patient ratio is 0.9:100000 for the Indian population (78). There is an acute shortage of skilled manpower to screen DR in rural India where only 0.3 ophthalmologists per 100000 population is available. The two methods of DR screening are either ophthalmologist led or optometrist led. The limited number of ophthalmologist available has led to use of teleophthalmology as a screening tool. In the optimal screening model, paramedical staff visit the venue and acquire the images and transfer the images to the ophthalmologist at the base hospital. We have introduced mobile units for comprehensive eye care delivery and have successfully conducted eye camps since 2003 .

Majority of the ophthalmologists (79) are trained in cataract surgery and only 7-8% are trained in the management of DR .There is lack of resources for implementation of large scale diabetic retinopathy screening and to bridge this gap and to overcome geographic and economic constraints automated DR screening is being considered .

The eye care facilities to tackle the treatment of diabetic retinopathy across India was evaluated by the authors Gilbert c et al (80). A total of 86 centers was enrolled in this study and results showed that gap existed and the need for more resources.

2) Telemedicine / Teleophthalmology

Telemedicine (81) helps in remote imaging of fundus photographs for vision threatening retinopathy (82) which may be asymptomatic. A significant application of Tele medicine, integrating electronic communication and medical technology (83) is emerging as an important tool connecting specialized care of health care providers and people living in far and remote underserved areas using live video conferencing, or real-time medical image sharing/communication portals.

This combination of telemedicine technology paired with specialty medical devices enables a remote physician to "see" the patient as if they were actually in the exam room with the patient.Teleopthalmology (84) also address issues such as transportation, costs, concern over pupillary dilation and adherence to recommended annual examination.

Standard guidelines for Telemedicine based DR Assessment programs (84)

1)Goals and end results of the program have to be defined

2) Efficient comprehensive eye examination to detect the presence of DR .

3) Cost effectiveness and reimbursement from insurance companies

4) Program meets the legal and regulatory requirements

5) Efficient Technology platform with support from information and technology experts .

6) Repeated evaluation of the program based on evidence based medicine

Severe visual loss is prevented in 90% of DR patients by timely diagnosis and (85, 86) treatment Accuracy of DR diagnosis in various Telemedicine programs have been published.

Lili Shi et al (87)had evaluated 20 or more publications on DR Telemedicine programs and evaluated the accuracy of detection of various stages of DR especially sight threatening DR .The study involved 1960 participants and the sensitivity varied from 53% -80% for various stages of DR and specificity was 89 %- 91%.Telemedcine programs combining mydriasis with wide angle(100 -200 degree) digital fundus photographs were more efficient in diagnosing DR than non mydriatic combined with narrow angle (45-60 degree) fundus photographs .

Irena Tsui et al (88) evaluated the tele retinal program at the West Los Angels Veterans Affairs Medical centre in USA.516 patients referred from primary care physicians office underwent nonmydriatic photography by TRC -NW8 Topcon camera and 120 patients were taken up for Analysis .15% had DR and 50% of total patients were referred due to other ocular diseases .

The various ocular diseases(89)in patients with diabetes were also diagnosed in the teleretinal screening programs (90) for DR using non mydriatic camera .Age related macular degeneration, glaucoma and other ocular disease were diagnosed.

Various studies indicate that telemedicine (91) increased the percentage of diabetic patients who underwent annual eye examination compared with traditional eye examination .Poor quality of images obtained from nonmydriatic cameras are the common causes for referral to the ophthalmologists .

Teleophthalmology was implemented in all the optometry centres (92) in Spain and all patients underwent fundus photography using nonmydriatric camera .50384 patients were part of the study and 75 % of the patients were normal and 1% had diabetic retinopathy .Telemedicine was a useful screening tool for ocular diseases.

Sajeesh Kumar et al (93) have confirmed that teleophthalmology services are much cost effective in remote and rural areas in comparison to consultation with an ophthalmologist. The cost of setting up a telemedicine unit is also considered .

Nita .G .Vaikodath et al (94) had enrolled about 97 diabetic patients to study patient attitude to telemedicine.97% of patients had not heard about telemedicine and 32% of the population were unsure about participating in the program.48% participants insisted on the interaction with the ophthalmologist and 69% were willing to participate in the telemedicine program compared to in person eye examination .Diabetic patients with longer duration of diabetes with systemic comorbidities were the persons who were unwilling to use telemedicine .

Mobile Teleophthalmology vans conduct camp in the rural villages where patients with diabetes have nonmydriatic digital retinal images taken by paramedical staff at an outreach location, and transmitted via satellite or internet connectivity to the central telemedicine HUB and fundus images are analyzed remotely by an ophthalmologist from the hospital. Telemedicine has been shown to be effective as a screening tool (95)in the diagnosis of Diabetic retinopathy and the SN-DREAMS study from Sankara Nethralaya has published several papers showing thisit is a cost effective screening tool.

Opportunistic screening- diabetics can be screened when they visit a physician (96) or diabetes specialist. A trained technician takes the fundus photos of these diabetic patients using nonmydriatic fundus cameras, and sends them for diagnosis and grading by an ophthalmologist remotely. The images are read and a report is generated and sent back to the diabetic center on the same day. The patient is advised based on the report received. The physicians (97) themselves examined the patients for diagnosis of DR with direct and indirect ophthalmoscopy and fundus photographs and referred the patients to ophthalmologist. Good control of diabetes with lower values of Glycosylated hemoglobin (98) lowers the risk of diabetic retinopathy .Moreover discussion of DR findings after nonmydriatic imaging during an endocrinologist visit (99)improved the glycemic control .

Pia Roser et al (100) have reported that using a non mydriatic fundus camera in a diabetes clinic improves the early detection of diabetic retinopathy and the study included 502 patients.

A.chabouis et al (101) evaluated a telemedical program (OPHDIAT) in France and they evaluated 500 case reports of patients from five reference hospitals who had attended the OPHDIAT program and the results showed that diagnosis of DR improved in the diabetology departments.

Pharmacy Based Screening

Diabetic patients (102) will have to visit pharamacy (103) for antidiabetic medicines and hence teleophthalmology program using non mydriatic camera is implemented here and was found to be effective .

Telescreening for DR in India

Screening programs for DR are very varied and suffer from a lack of information about the best screening protocol , in terms of how frequently people should be screened and who should be targeted and hence new models have to be developed. Another limitation is the lack of engagement with physicians and endocrinologists in screening, as most activities did not entail joint planning, implementation or monitoring of screening . There is no national screening program for DR in India .

Since 1990, India has made rapid strides in the fields of communication and information technology. For decades, research has revealed that communities most likely to benefit from tele-ophthalmology are those least likely to afford it, or to have the requisite telecommunication infrastructure. However, this may no longer be accurate. In contrast to the challenge of providing quality care to patients in rural villages, Internet connections and computer literacy are becoming more affordable and widespread thus enabling increased interest shown by health care providers and patients alike .

Tele Ophthalmology, being one such area of great potential aims to provide diagnostic and medical care to the large, rural regions of India. Telemedicine is most effective in India(78) as it has a vast land area coupled with varied topography. With the majority of the population living in rural areas, and specialist doctors living in urban area, telemedicine gives benefits, such as improved and convenient access, reduced health care cost, extended access to specialist's consultation, increased patient care and improved quality (1) of health care.22.4 million persons are expected to have DR by 2030.

Teleophthalmology has enabled screening of common ophthalmic diseases especially diabetic retinopathy (DR) age related macular degeneration ,retinopathy of prematurity, glaucoma and orbital disorders. Digitized Imaging modalities transmitted via tele link using store and retrieval system has aided diagnosis of clinical diseases and ophthalmology lends itself easily to tele ophthalmology.

Remote imaging of fundus photographs of diabetic patients who may be asymptomatic to rule out vision threatening DR will result in early detection and treatment and hence reduce the cost .Implementation of Telemedcine programs in rural India requires financial viability for use at national level .

Sankara Nethralaya (104) is the pioneer in mobile tele ophthalmology practice in rural India. The project was inaugurated by Former President of India – Dr. A. P. J. Abdul Kalam on 10th October 2003. With the help of the Indian Space Research (105) Organization(ISRO) and VSAT, satellite connectivity was implemented for establishing communication to the base hospital from Eye

camps that were conducted at remote villages.Similiar programs (106) were also in other hospitals .

Concept of Vision Centre

The model of vision centre (107) is envisaged by the Vision 2020 – The Right to Sight, a global initiative of International Agency of Prevention of Blindness (IAPB – a global machinery working across the world for the prevention of avoidable blindness). IAPB has unveiled four tier pyramid model to provide eye care for the needy population where vision centres (108) are at the primary level. Aligning with this initiative, Government of India is planning to set up many vision centres across the country.for providing basic eye care services on a permanent basis in villages. Each vision centre will cover a population of about 45,000 - 50,000.

All the patients examined at the vision centre are consulted with the ophthalmologist at base eye Hospital who will interact with patients. Patients who require procedural intervention are asked to come to the hospital. These vision centres work closely with the community through community workers who create awareness about the eye problems in the community. This model is implemented in Arvind eye care ,Madurai and LV Prasad ,Hyderabad.

Previous Work Done at Sankara Nethralaya on Telescreening for DR:

Tamil Nadu:

Raman R et al estimated the prevalence of DR to be 18% in an urban south Indian population of 5999 (109)diabetic subjects older than 40 years of age. Duration of diabetes was the most common causeof DR .The methodology is given in detail (110) .

Raman et al in another study (111) found that prevalence of diabetic retinopathy was related to age of onset of diabetes .Diabetic patients younger than 40 years of age (30-39 years) had a prevalence of 33% of DR and 5.8% of sight threatening retinopathy in an urban south indian population of 1414 diabetic patients. Agarwal and Raman et al (111) have reported the occurrence of DR in the targeted diabetic group (6.7%) as well the occurrence of DR in the new diagnosed diabetics (11.7%) in the general population as well in the diabetic clinics in rural and urban south India .No significant difference was noted in the occurrence of sight threatening DRin the urban versus rural population. DR occurs much earlier before the patients are symptomatic and hence it is important to diagnose DR before visual loss

Raman et al (112) have also reported that increase in glycosylated HbA1C increases the incidence of sight threatening retinopathy from 5-8% to 11-20% .All patients underwent dilated four field fundus photography for diagnosis of sight threatening diabetic retinopathy .

Sankara Nethralaya (113) compared the prevalence of diabetic retinopathy in the ophthalmologist based model versus the ophthalmologist led model (114) . In the latter, the optometrist (115)examines the patient at the remote site and transmits the patient's data and

images using tele connectivity to the base hospital. From 2004 to 2005 in rural South India, 3,522 diabetics underwent the ophthalmologist - based diabetic retinopathy screening, and 4,456 diabetics underwent the ophthalmologist-led model. 519 (14.7%) were diagnosed with diabetic retinopathy in the ophthalmologist- based model and 853 (19.1%) in the Ophthalmologist– led model and had more prevalence of sight –threatening retinopathy than the ophthalmologist – based model (6.3% vs. 5%).

Raman et al evaluated the efficiency of Telehealth program (116) for diabetic retinopathy in 511 diabetics in rural south India by conducting screening camps. All patients underwent dilated single field 45° macula centered fundus photographs and indirect ophthalmoscopy by retinal specialist and there was good agreement between both methods of examination for diagnosis of DR .19% of patients had DR in this study.Telemedcine programs are effective as a screening tool for DR .It has was proven in this study(117) that single field 45 degree fundus photograph is sufficient for diagnosis of DR .

Study conducted by Kumari Rani (118) et al evaluated whether patient were satisfied from using telemedicine services. 97 % patients were willing to undergo eye examination using teleophthalmology camps .74% patients felt that doctors instructions were clear on videoconferencing .

To prevent visual loss from sight threatening retinopathy the authors PK Rani and Raman et al suggest (119) the need for comprehensive education of diabetic patients. This was implemented in five districts of Tamilnadu.

Karnataka:

Currently nearly 60,000 diabetics have been screened for DR and approximately 5,000 sight – threatening diseases have been identified and treated.

Telescreening program for diagnosis of DR in five districts of Karnataka was found to be cost effective by Sudhir et al (120). Teleophhalmology was implemented using satellite connectivity provided by the Indian space and research organization (ISRO).The fundus images are beamed to the base hospital and a retinal specialist or general ophthalmologist diagnoses the fundus images and interacts and advises the patient .The ophthalmologists / population ratio is 1:107,000 ratio and hence in rural India teleophthalmology is effective for screening DR .Cost Sudhir et al have compared the cost of DR screening in camps and hospital based consultations in rural south India. They concluded that two yearly screening (121) was cost effective but annual screening is not cost effective in the rural Indian villages .

DR Screening guidelines by American Telemedcine Association

The American telemedicine association has established evidence based (122) standards for robust platform and effective workflows .The Classification of diabetic retinopathy by the

American Telemedicine Association for Tele-screening is given below:- **Category 1**

Category 1 validation indicates a system can separate patients into two categories: (a) those who have no or very mild non-proliferative DR (ETDRS level 20 or below), and (b) those with levels of DR more severe than ETDRS level 20. Functionally, Category 1 validation allows identification of patients who have no or minimal DR and those who have more than minimal DR.

Category 2

Category 2 validation indicates a system can accurately determine if sight-threatening DR is present or not present as evidenced by any level of DME, severe or worse levels of no proliferative DR (ETDRS level 53 or worse), or proliferative DR (ETDRS level 61 or worse).25 Category 2 validation allows identification of patients who do not have sight threatening DR and those who have potentially sight-threatening DR. Patients with sight threatening DR(STDR) generally requires prompt referral for management.

Category 3

Category 3 validation indicates a system can identify ETDRS defined levels of non-proliferative DR (mild, moderate, or severe), proliferative DR (early, high-risk), and DME with accuracy sufficient to determine appropriate follow-up and treatment strategies. Category 3 validation allows patient management to match clinical recommendations based on clinical retinal examination through dilated pupils.

Category 4

Category 4 validation indicates a system matches or exceeds the ability of ETDRS photos to identify lesions of DR to determine levels of DR and DME. Functionally, Category 4 validation indicates a program can replace ETDRS photos in any clinical or research program

Development of DR Algorithm

Software applications are being developed for automated detection of DR, as recent advances in the imaging of the retina have led to high quality digital fundus images .The development of the Automatic retinal assessment software lays emphasis on identifying and quantification of pathological features of diabetic retinopathy. The diabetic retinopathy Algorithm should perform like a human pathologist in identifying the features of DR.Examination of prior art and existing DR systems indicates that two approaches are possible for the design of DR analyser software:

Bottom-up approach: closely simulates the image reading process performed by human experts -- first detects visible lesions related to DR, such as red and bright lesions. Based on the detection, the module estimates the probability that the image depicts a referable case. Majority of the published DR screening research uses bottom-up approach.

Black-box approach: directly arrives at outcome of whether the image is normal or pathological, based on implicitly determined image descriptors. The set of descriptor values observed in normal and pathological images provides a statistical basis for the final decision.

The notable groups working in development of DR screening module outside India are

- US (University of Iowa)
- UK (Scotland)
- Europe: Finland, Portugal, Netherlands
- Australia, New Zealand.

The retinal images are identified for normal anatomical features as optic disc, macula and blood vessels and then features of DR like micro aneurysms, retinal hemorrhages, exudates, new vessels and others can be quantified in terms of location and pathology. There are two basic ways in which automated image analysis software are designed.

- Image processing (Image/ Signal de-noising, Spatial/ frequency domain filtering, Image enhancement, Histogram equalization, Contrast stretching, Low pass filtering (to obtain the overall information), High pass filtering to obtain only the edge information) .
- Deep machine learning including training neural networks and artificial intelligence protocols.

Review of literature of different modalities of development of the Algorithm are given below.

(M.R.K.Mookiah, et al., 2013)Proposed a system for (123) automated classification of normal, NPDR and PDR images by detecting blood vessels area, bifurcation (node) points, exudates area, and other texture information from processed retinal images. The authors report a comparison among different machine learning techniques for predicting the DR grade of a given image.

(Antal, et al., 2012) proposed a (124) method to reduce the computational burden of automatic screening system with a two-phase decision support framework. The first step is a pre-screening algorithm to classify input images based on severity of abnormalities, and a second step identifies regions of interest in the fundus. The regions are used as input to specific lesion detectors for detailed analysis.

(D.Saleh & C.Eswaran, 2012) have designed (125) an automated diagnosis system for NPDR based on detection and analysis of micro aneurysms (MA) and hemorrhages. Their system quantifies severity level of DR based on the number and location of MA and hemorrhages.

(Roychowdhury, Koozekanani, & Parhi, 2012) presents a system (126) which suppresses optic disc, and detects bright lesions and red lesions at very low false-positives per image.

(Quellec, et al., 2012) present a multiple-instance (127) learning framework for automated image classification based on set of reference images marked by clinicians. The system detects patterns occurring only in the referable images, and after training, similar patterns are sought in new images in order to classify them as referable.

(Pires, et al., 2013) introduce an (128) algorithm to make referral decision based on the fusion of results of lesion detectors and creating a high-level representation for retinal images.

(Roychowdhury, Koozekanani, & Parhi, 2013) analyze fundus (129) images with varying illumination and fields of view, and generates a severity grade for DR using machine learning.

(Venkatesan, Chandakkar, Li, & Li, 2012) present an automatic (130) method for classifying fundus images into 3 classes: normal, image with micro aneurysms, image with neovascularization. They propose a multi-class multiple instance learning framework for classification.

Meindert Niemeijer et al have (131) evaluated a computer Algorithm for detection of Bright lesions in DR like soft and hard exudates and differentiate it from drusen which occurs in age related macular degeneration .About 300 patients from a teleophthalmology program in Netherlands (eye check project).100 patients with bright lesions, 200 normal patients without lesions and 130 patients with bright lesions were used to train the algorithm .All fundus photographs were non mydriatic obtained from 3 different table top fundus cameras.Two images per eye ,disc centred and macula centred . 3 masked retinal specialist annotated the retinal images indepentedly in a masked manner. The result showed the Algorithm was able to identify the soft exudates,hard exudates and drusen as bright lesion and the sensitivity and specificity matched the human grader.But in differentiating the three lesions the algorithm faced difficulty and future studies are required .Flash artifacts can mimic bright lesions .

Computer aided solutions are capable of producing low cost diagnostic tools for diabetic retinopathy. The main objective of Computer Aided solution is to detect the presence (referral to the hospital) or absence of diabetic retinopathy (No referral). Computer Aided image analysis, as a screening tool for diabetic retinopathy in India is still to be established.

Automated DR international programs

Many automated programshave (132) been developed over the years to interpret retinal images, however, they have generally been tested against standard reference retinalimage databases, such as MESSIDOR (133) , DRIVE (134) and ARIA (135) which provide ground truth in hundreds of retinal images for testing. However, these programs may perform inadequately when deployed in actual clinical practice where image quality, pupil size, fundus pigmentation, illumination conditions, and retinal cameras are quite variable. Many countries in the world have implemented national screening programs using Automated DR Algorthim but in India there is no national program .

(Abràmoff, et al, 2013) studied (136) the sensitivity and specificity of the Iowa Detection Program IDP to detect referable diabetic retinopathy, in a total of 874 participants with diabetes. The study concluded that computer analysis of retinal photographs for DR and automated detection of referable DR can be implemented safely into the DR screening pipeline.

(Alan D. Fleming, 2010)assessed (137) whether introduction of automated grading software into Scotland's National Diabetic Retinopathy Screening Collaborative program would be safe, robust and effective. The study was carried out on 78601 images from 33535 consecutive patients, manually graded. The software showed 100% results for detection for Proliferative diabetic retinopathy and referable background DR .The study concluded that automated grading software confirmed to previously published results when applied to a large, unselected population attending two regional screening programs. The manual grading workload reduction was estimated to be 36.3%.

Gs Scotland et al had done (138) comparison of improved Algorithm with previous algorithm and manual grading from 3 screening centers in Scotland and 180,000 participated in this study and the results showed that Software assisted automatic grading was cost effective to manual grading

Michael Abromoff had evaluated (139) the eyecheck algorithim on 17,670 people with diabetes,two fundus images per eye and the gold standard was the ophthalmologist reading .The Eyecheck showed 97% sensitivity and 47 % Specificity.

Several groups world wide have proposed (140) the use of automated computer systems for determining what screened patients should be seen by an ophthalmologist and what patients can safely return for screening 1 year later. These types of automated systems maintain a high sensitivity and have the potential to reduce the workload (141) for ophthalmologists .

International research group on Automatic retinal image analysis –ARIA

The commercial available (142) Algorithm are given below

Table 8. Summary of Current Automated Diabetic Retinopathy (DR) Lesion Detection Systems

System	Company	Location	Grading details	Algorithm
DR-RACS™	Vision Quest Biomedical LLC	Vision Quest Biomedical LLC, Albuquerque, NM	Low risk/high risk for DR	Amplitude modulation-frequency modulation (AM-FM), k-means clustering, and a partial least square classifier
EyeArt	Eyenuk Inc	Woodland Hills, CA	Refer/no refer recommendation; microaneurysm turnover	Machine learning; morphologyinspired filter bank descriptors
IDx-DR	IDx, LLC	University of Iowa, USA	Diabetic retinopathy index; referable/nonreferable disease	Fusion algorithm produces a DR index
iGradingM	Medalytix LLC; Digital	University of Aberdeen, Scotland, UK	Presence/absence of DR	Local contrast, normalization and local vessel detection
RetinaLyze A/S	RetinaLyze A/S	Denmark	Presence/absence of DR based on microaneurysm and hemorrhage detection	Automated red lesion detection, including microaneurysm and hemorrhage using vector based Algorithm.
Retmarker DR	Retmarker Ltd	Coimbra University, Portugal	Presence/absence of DR; microaneurysm turnover	Longitudinal analysis by comparing with baseline image
Singapore Eye Lesion Analyzer (SELENA)	-	Singapore Eye Research Institute and National University of Singapore, Singapore	Grade of DR and referable/ nonreferable	Deep learning technology using convolutional neural network and region extraction algorithms
RetinaVue (formerly The TRIAD Network)	Welch Allyn, Inc (Hubble Telemedicine Inc)	University of Tennessee Health Science Center and the Oak Ridge National Laboratory, USA	Presence/absence of DR; grade of DR	Content-based image retrieval techniques for automated diagnosis

The current methods for (143) validating DR algorithms are neither uniform nor widely agreed upon. Issues include how to deal with the variable expert annotations; definition of gold standards and the availability of public, "real-life" datasets for testing .

In a large study from UK (144) involving retinal images from 20,258 consecutive patients, images were manually graded following a standard national protocol for DR screening and were processed by 3 ARIAS: iGradingM, Retmarker, and EyeArt. Authors concluded that Retmarker and EyeArt systems achieved acceptable sensitivity for referable retinopathy when compared with that of human graders and had sufficient specificity to make them cost-effective alternatives to manual grading alone. ARIAS have the potential to reduce costs in developed-world health care economies and to aid delivery of DR screening in developing or remote health care settings. All the software tested in this study used image analysis techniques to yield reports.

In another recent landmark study, using deep machine (145) learning EyePACS1 from Google in validation sets of 9963 images and 1748 images, at the operating point selected for high specificity, the EyePACS1 algorithm had 90.3%and 87.0% sensitivity and 98.1% and 98.5% specificity for detecting referable diabetic retinopathy, defined as moderate or worse diabetic retinopathy or referable macular edema by the majority decision of a panel of at least 7 US board-certified ophthalmologists. Authors concluded that Deep learning algorithms had high sensitivity and specificity for detecting diabetic retinopathy and macular edema in retinal fundus photographs.

Clara I. Sa´nchez et al have (146) indicated that Automated systems ref should have good sensitivity and be able to detect DR comparable to that of a human grader. Evaluation of systems should be performed on independent and, preferably, publicly available data so that different groups can compare the performance of their automated systems on the same set of data. Of additional importance, the performance record of several expert observers on this same dataset should also be available to facilitate the comparison between automated systems and humans.

A fully-automated computerized screening system used for diabetic patients will reduce the workload of human graders (ophthalmologists and trained graders) in telemedicine screening programs and the process is also cost-effective in rural areas and in less developed countries.

Research Gap

The prevalence of DM and DR is on the rise in India. The sheer number of patients who require repeated screening means that millions of images are generated every month. If DR screening improves, it will mean that there may be billions of images that will be required to be analyzed to detect those with DR and sight threatening DR so that they can be referred for timely ophthalmic information. Given the lack of a government approved reading center to analyze these images and the extreme lack of retina specialists to handle the load of analyzing images, it appears prudent that machines be trained to perform the baseline analysis of images automatically and provide reports with reasonable accuracy to facilitate timely referral. Hence, it is imperative that we adopt automated image analysis software in the near future.

Though there are commercially available software available for automated DR screening, as noted above, each has its limitations and have been tested only in controlled environments thus far. Besides, none of them have been tested on images from large Indian datasets.

Thus we performed a study to design and validate a new proprietary automated analysis software and see its accuracy in detection of DR in various clinical settings including the ophthalmologists' clinic, outreach teleophthalmology camps as well as diabetologists' clinics.

Scope and Plan of Work

Healthcare Technology Innovation Center (HTIC) at IIT Madras will develop a software application- DR Algorithm . In this study, we aim to validate the accuracy of this new automated image analysis software to detect presence or absence of DR in terms of sensitivity and specificity in various settings such as a busy tertiary referral ophthalmic center, outreach camps using tele ophthalmology and diabetic clinics. Additionally, we also report the effectiveness of the software on images acquired by various different imaging devices including non -mydriatic imaging and smart phone based imaging.

Various DR Algorithm are commercial available and they have been reported in various parts of the world .The incidence of diabetes is increasing year by year in India and world over and almost 440 million people worldwide will have diabetes by 2030 we will require national screening programs to be implemented but due to lack of human graders , we need alternative methods like automated retinal analysis of fundus photographs at physicians clinic .Our aim was to develop algorithm based on the presentation of DR in Indian eyes and validate it on diabetic patients in various settings .This will help us to evaluate the algorithm as a screening tool

Patients and Methods

Ethics Approval

The study was initiated after the approval of the Institutional Ethics Committee of Vision Research Foundation, Sankara Nethralaya, Chennai, India. Informed consent was obtained from each patient and the study was conducted with the Health Insurance Portability and Accountability Act and followed the tenets of Declaration of Helsinki .The study was conducted in the outpatients department of the Vitreoretinal services at Sankara Nethralaya, in outreach Teleophthalmology camps organized by Sankara Nethralaya and in different clinics offering comprehensive diabetic care in Chennai .

Memorandum of understanding

Healthcare Technology Innovation Centre (HTIC), a multi-disciplinary Research & Development Centre, is a joint initiative of Indian Institute of Technology Madras (IITM) and Department of Biotechnology (DBT), Government of India that brings together technologists, engineers, doctors and healthcare professionals, industry and government to develop healthcare technologies for the country. The vision of HTIC is to develop technologies that create impact and drive innovation in healthcare and be a leader known for technical excellence and collaborative spirit.

HTIC collaborates with leading medical institutions and wide range of industry players in various areas such as ophthalmology, ultrasonography, orthopedics, neonatal care, patient monitoring, to develop and deploy healthcare technologies.In addition to technology research and development, HTIC works closely with industry in developing R&D solutions, joint development of technology products, technology assessment and evaluation.

The Centre is located in IITM Research Park Chennai which has a vibrant technology ecosystem. Memorandum of understanding signed with Healthcare Technology Innovation Center (HTIC) in IIT Madras for development of DR Algorithm.

Sample Size Estimation, Sampling Method and Study Area

Sample Size Estimation: According to the previous study (15, 16), we found that prevalence of DR was 18% in Diabetic patients. The sample size at the required absolute precision level for sensitivity and specificity was calculated by Buderer's formula:[1]

Sample size (n) based on sensitivity

$$n = \frac{Z^2_{1-\frac{\alpha}{2}} \times S_N \times (1 - S_N)}{L^2 \times Prevalence}$$

Sample size (n) based on specificity

$$n = \frac{Z^2_{1-\frac{\alpha}{2}} \times S_P \times (1 - S_P)}{L^2 \times (1 - Prevalence)}$$

where n = required sample size, Prevalence -18%

S_N = anticipated sensitivity, S_P = anticipated specificity,

α = size of the critical region ($1-\alpha$ is the confidence level),

$Z_{1-\alpha/2}$ = standard normal deviate corresponding to the specified size of the critical region (α), and

L = absolute precision desired on either side (half-width of the confidence interval) of sensitivity or specificity.

Assumptions

Sensitivity	$S_N = 95\%$	,	Specificity	$S_P = 80\%$
Precision	L= 2%		,$Z_{1-\alpha/2} = 1.96$	

The required sample size was 2539.

Sample Size Calculation

The sample size using sensitivity and specificity is calculated by using the formula given below:

$$n = (a+b) = \frac{Z^2_{\alpha/2} * P * (1-P)}{\Delta^2}$$

$Z^2_{\alpha/2}$ ÔZ table value (the table value of z at 5% level of significance is 1.96)

Δ ÔPrecision Value (Assumed to be 0.02)

P ÔSensitivity Value = 0.95 ,Prevalence = 0.18

The calculation of sample size is given below:

$$n = \frac{Z^2_{\alpha/2} * P * (1-P)}{\Delta^2} = \frac{(1.96)^2 * 0.95 * (1-0.95)}{0.02^2} = 456.1732 \lceil 457$$

The total sample size N is calculated by using the formula given below:

$$N = \frac{a+b}{\Pr evalence} = \frac{457}{0.18} = 2538.89 \lceil 2539$$

Therefore, the required sample size for our study is 2539 .

Total of 2539 type 2 diabetic patients were required to be examined in the second and third years to estimate the accuracy of the computer aided solution.

Inclusion criteria

Diabetic patients (type 2 only) aged 35 years and above or those turning 35 years in the current calendar year were included in this study.

Known diabetics/self-reported- Diagnosis of diabetes made by a medical practitioner or diabetologist and newly diagnosed diabetics.

Exclusion criteria

The patients during ophthalmic examination, found to have small or mitotic pupil, nystagmus, patients who have undergone treatment for diabetic retinopathy were excluded from the study, except panretinal photocoagulation treatment.

Other than cataract surgery, have no history of intraocular surgery, ocular injections and surgery for diabetic macular edema or proliferative DR.

Training program

The fundus photographer / optometrist / paramedical staff were trained in fundus photography for the non-mydriatic and Mydriatic fundus photographs. In the Fundus photography Department experienced fundus photographer was responsible for the training of the staff members. The paramedical staff ensured that the patients were not fatigued while fundus photographs are taken.

The screening tool -Fundus photography

Fundus Photography - To document and diagnose diabetic retinopathy, all participants underwent fundus photographs. Images were stored as jpeg (Joint Photographic Experts Group format) files, copied to DVDs and sent for grading. Independent photo grading of digital fundus photographs by optometrists and ophthalmologists was done in a masked manner. It is important to take note of the image file formats as storage should not result in the loss of any clinically significant information in the retinal photograph .The original image from the camera should be 20 pixels per degree of retinal image both horizontal and vertical directions. The field of view of the fundus photograph should be 45^0 horizontally and 40^0 vertically. The fundus images must confirm to the Digital imaging and communications in medicine (DICOM) standards.

Evaluation of image quality and gradablity of fundus photographs : The photographic grading and quality42 were assessed using the image quality parameters given by HTIC Chennai. .Photographs of each eye were reviewed and given grades for overall quality. Field definition and image clarity were graded as

1) Inadequate for reading or grading if unable to visualize disc, macula and retinal vessels

2) Adequate for reading or grading if sufficient visualization of disc, macula, and retinal vessels .
In addition to noting presence and absence of DR, graders also noted the stage of DR as per the International classification of diabetic retinopathy.

COMPUTERS

Image grading was done using Dell work station computer and standardized computer screens (Monitor: 23" or more flat screen with CPU capabilities Intel core i7 processor, Hard Drive: 1 TB and above, RAM: 8 GB and above, Four standard USB2 inputs, Video card 2 GB ; Supports 1600 x 900 resolution were used throughout the study.
For implementing and testing the algorithm we used a Dell workstation computer with 8 GB RAM and Intel core i7 processor, with 2GB dedicated video card, and 23" flat screen display.

Development of Diabetic retinopathy Algorithm by Healthcare Technology Innovation Center (HTIC) - IIT Madras

Description of publicly available image datasets for diabetic retinopathy

Below is a description of datasets available in public domain, provided by researchers along with ground truth.The ground truth may be in the form of lesion annotations (indicating regions affected – e.g. hemorrhages, cotton wool spots). This publicly available data sets are available to researchers worldwide to develop the Algorithm and to have uniformity in development of optic disc localization ,vessel segmentation and other features of DR Algorithm
The prominent ground truth lesions marked in public datasets are:

- Small red dots (including microaneurysms and dot hemorrhages) – 4 datasets (DiaretDB, eOphtha-MA, Messidor, ROC09)
- Hemorrhages – 1 dataset (DiaretDB)
- Hard exudates – 3 datasets (DiaretDB, eOphtha, Hei-Med)
- Soft exudates – 1 dataset (DiaretDB)

Ground truth for normal anatomy is also available in various datasets:

- Blood vessels – 5 datasets (DRIVE, ARIA, STARE, HRF, ChaseDb1)
- Optic disc– 5 datasets (ARIA, ReviewDB, STARE, HRF, Drions-db)
- Macula – 2 datasets (ARIA, Messidor)

There are publicly available datasets which have image level DR screening and grading information.

1. MESSIDOR

Below is a description of some of the main DR related datasets in public domain.Datasets with Lesion ground truth

1. DiaretDB 89 (MA, hemorrhages, Exudates, Cotton wool spots)

Web URL: http://www.it.lut.fi/project/imageret/

The ImageRet database was made publicly available in 2008 and is subdivided into two sub-databases, DIARETDB0 and DIARETDB1. DIARETDB0 contains 130 retinal images of which 20 are normal and 110 contain various signs of diabetic retinopathy. It has been superseded by DIARETDB1 dataset, which contains 89 images out of which 5 images represent healthy retinas while the other 84 have some diabetic retinopathy signs. The images were acquired with a 50 degree FOV using a fundus camera at a size of 1500×1152 pixels in PNG format. The images were annotated by four experts for the presence of microaneurysms, hemorrhages, and hard and soft exudates. Annotated images from four experts were combined to produce a single ground truth image. There are no manually segmented vessel images in this database.

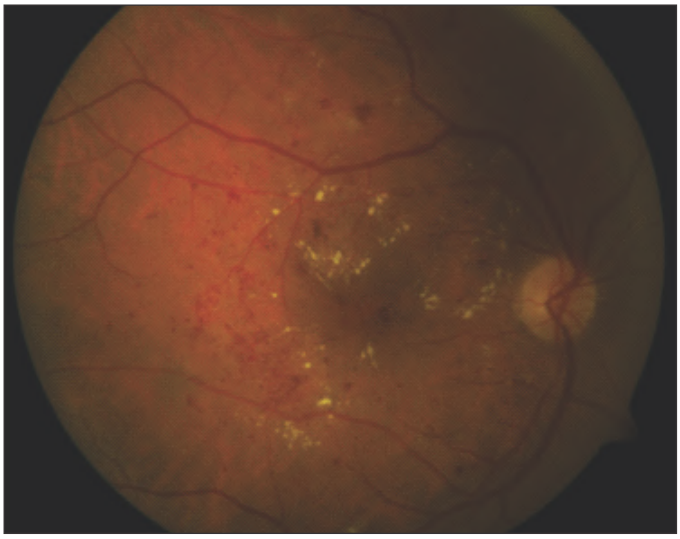

Fig 3 : DiaretDB 89

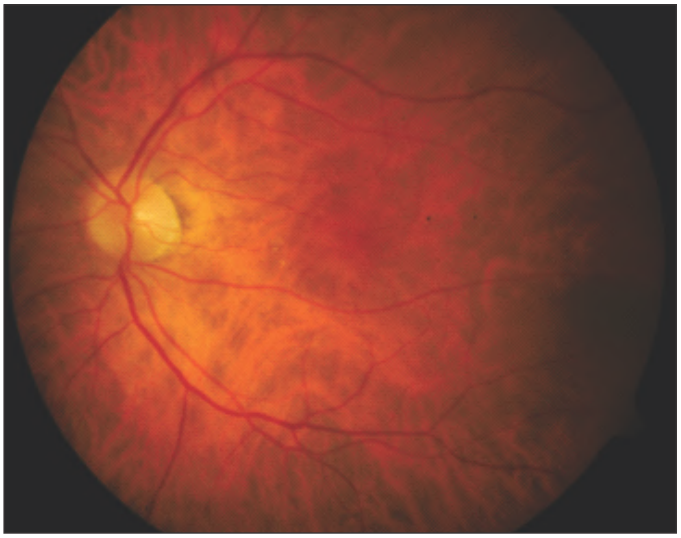

Fig 4 : DiaretDB 89

1. Hei-Med 169 (DME)

Web URL: http://vibot.u-bourgogne.fr/luca/heimed.php

The Hamilton Eye Institute Macular Edema Dataset (HEIMED) (formerly DMED) is a collection of 169 fundus images to train and test image processing algorithms for the detection of exudates and diabetic macular edema. The dataset is composed of 169 JPEG images compressed at highest quality. Each image of the dataset was manually segmented by Dr. Edward Chaum (an expert ophthalmologist from HEI). He identified all the exudation areas and other bright lesions such as cotton wool spots, drusens or clearly visible fluid occurring on the fundus.

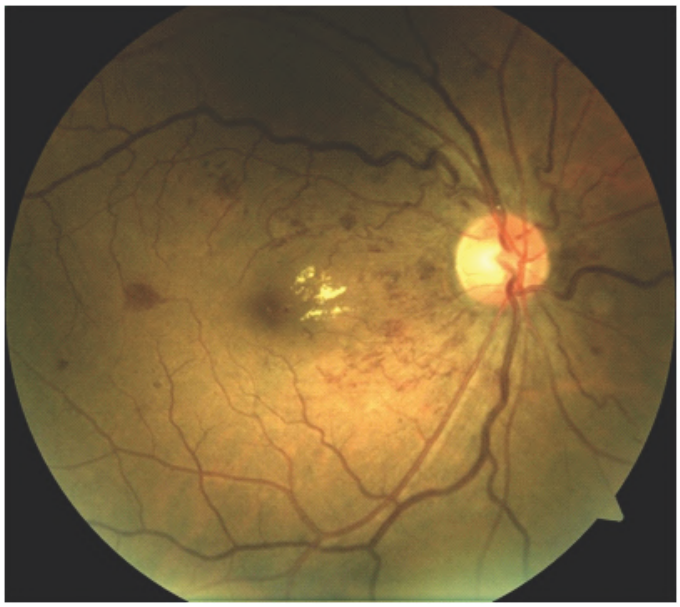

Fig 5 : Hei-Med 169 (DME)

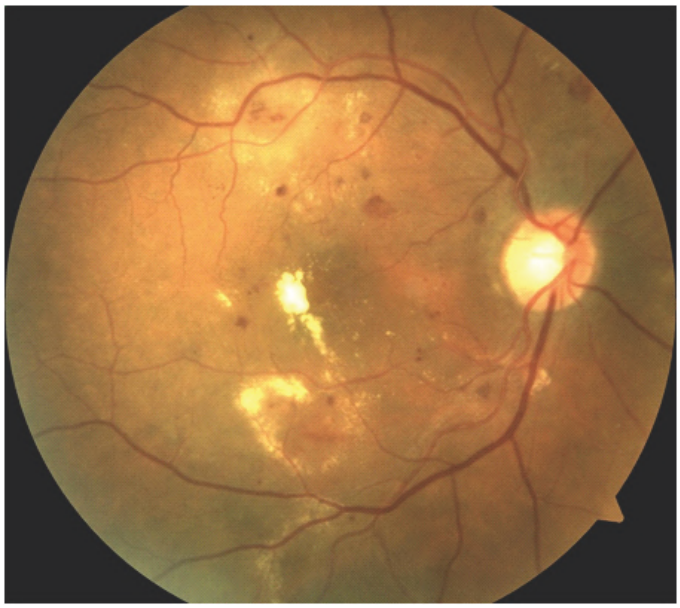

Fig 6 : Hei-Med 169 (DME)

1. e-ophtha (MA, Exudates)

Web URL: http://www.adcis.net/en/DownloadThirdParty/EOphtha.html

E-ophtha is a database of color eye fundus images for scientific research on Diabetic Retinopathy (DR). It has been extracted from the OPHDIAT (c) telemedical network for DR screening, in the framework of the ANR-TECSAN-TELEOPHTA project.

e-ophta-ma is the subset designed for microaneurysms (MA) detection. It contains 148 images with MA or other small red lesions, and 233 MA-free images. The specialists' annotations on the 148 images are given in the form of a binary mask. They correspond to the position of each MA (marked by a dot or a small region).

e-ophtha-ex is the subset designed for exudates detection. It contains 47 images with exudates and 35 exudate-free images. The specialists' annotations on the 47 images are given in the form of a binary mask. The annotations correspond to the position and the contours of each exudate.

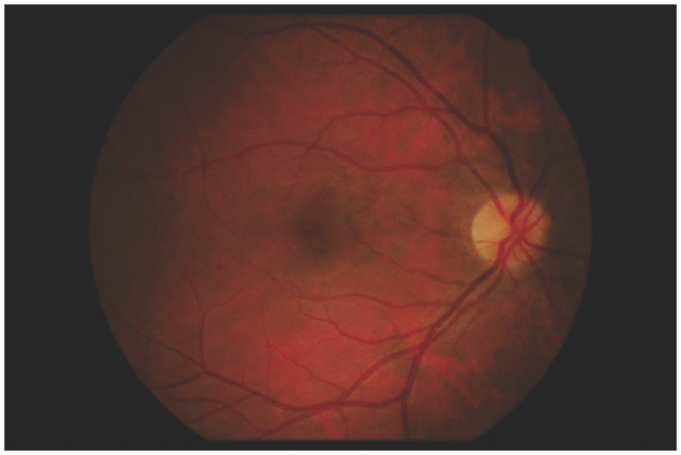

Fig 7: e-ophtha (MA, Exudates)

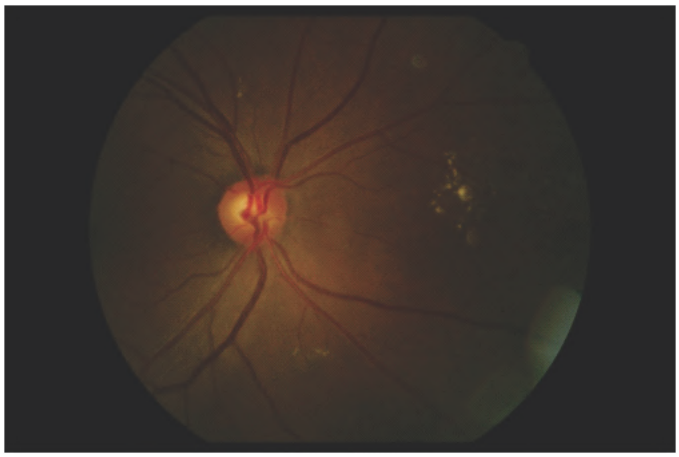

Fig 8: e-ophtha (MA, Exudates)

1. ROC dataset 100 (MA)

Web URL: http://webeye.ophth.uiowa.edu/ROC/var.1/www/

The Retinopathy Online Challenge microaneurysm dataset is part of a multi-year online competition of microaneurysm detection that was arranged by the University of Iowa in 2009. The set of data used for the competition consisted of 50 training images with available reference standard and 50 test images where the reference standard was withheld by the organizers. The images were captured using a Topcon NW100, a Topcon NW200 or a Canon CR5-45NM nonmydriatic camera at 45° FOV and were JPEG compressed in the camera. There are three different image sizes present in the database; 768×576, 1058×1061 and 1389×1383 pixels.

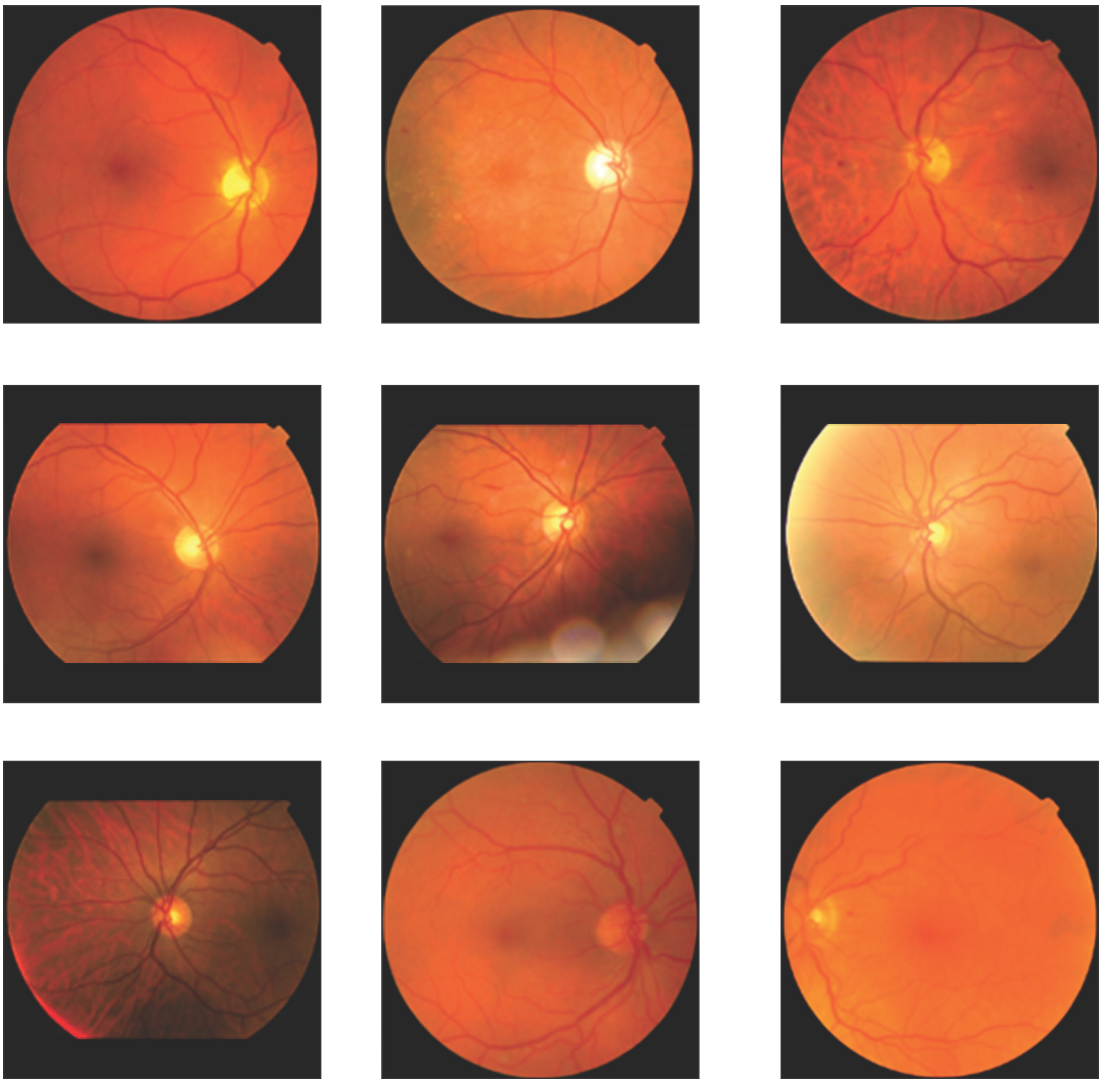

Fig : 9 Retinopathy Online Challenge - microaneurysm

Datasets with ground truth for DR screening/grading

1. Messidor 1200

Web URL: http://messidor.crihan.fr/index-en.php

The Messidor-project database, with 1200 retinal images, is the largest database currently available on the internet and is provided by the Messidor program partners. The images were acquired by 3 ophthalmologic departments using a color video 3CCD camera on a Topcon TRC NW6 non-mydriatic camera with a 45o FOV. The images were captured using 8 bits per color plane at 1440×960, 2240×1488, or 2304×1536 pixels. 800 images were acquired with pupil dilation (one drop of Tropicamide at 0.5%) and 400 without dilation. The reference standard provided contains the grading for diabetic retinopathy and the risk of macular edema in each image. This database does not contain any other annotations and is used to facilitate studies on computer-assisted diagnoses of diabetic retinopathy.

Datasets with normal anatomy (Blood vessels, optic disc, macula) ground truth

1. DRIVE dataset

Web URL: http://www.isi.uu.nl/Research/Databases/DRIVE/

The DRIVE (Digital Retinal Images for Vessel Extraction) is a publicly available database, consisting of a total of 40 color fundus photographs. The photographs were obtained from a diabetic retinopathy screening program in the Netherlands. The screening population consisted of 400 subjects between 25 and 90 years of age. Each image has been JPEG compressed, which is common practice in screening programs. Of the 40 images in the database, 7 contain pathology, namely exudates, hemorrhages and pigment epithelium changes. The images were acquired using a Canon CR5 non-mydriatic 3-CCD camera with a 45o field of view (FOV). Each image was captured using 8 bits per color plane at 768×584 pixels. The FOV of each image was circular with a diameter of approximately 540 pixels. The set of 40 images was divided into a test and training set both containing 20 images. Three observers, the first and second author and a computer science student manually segmented a number of images. All observers were trained by an experienced ophthalmologist (the last author). The first observer segmented 14 images of the training set while the second observer segmented the other 6 images. The test set was segmented twice resulting in a set X and Y. Set X was segmented by both the first and second observer (13 and 7 images, respectively) while set Y was completely segmented by the third observer. The performance of the vessel segmentation algorithms was measured on the test set. In set X the observers marked 577,649 pixels as vessel and 3,960,494 as background (12.7% vessel). In set Y 556,532 pixels we marked as vessel and 3,981,611 as background (12.3% vessel).This database does not contain annotated pathologies and other fundus structures like optic disc and macula.

1. ARIA

Web URL: http://www.eyecharity.com/aria_online.html

This database was created in 2006, in a research collaboration between St. Paul's Eye Unit, Royal Liverpool University Hospital Trust, Liverpool, UK and the Department of Ophthalmology, Clinical Sciences, University of Liverpool, Liverpool, UK. The database consists of three groups; the first group has 92 images with age-related macular degeneration, the second group has 59 images with diabetes and the control group consists of 61 images. The trace of blood vessels, the optic disc and fovea location was marked by two image analysis experts as the reference standard. The images were captured at a resolution of 768×576 pixels in RGB color with 8-bits per color plane with a Zeiss FF450+ fundus camera at a 50o FOV and stored as uncompressed TIFF files.

3.STARE

Web URL: http://www.parl.clemson.edu/~ahoover/stare/index.html

The STARE (Structured Analysis of the Retina) Project was conceived and initiated in 1975 by Michael Goldbaum, M.D., at the University of California, San Diego. It was funded by the U.S. National Institutes of Health . During its history, over thirty people contributed to the project, with backgrounds ranging from medicine to science to engineering. Images and clinical data were provided by the Shiley Eye Center at the University of California, San Diego, and by the Veterans Administration Medical Center in San Diego .

The STARE database contains 20 images for blood vessel segmentation; ten of these contain pathology. The slides were captured by a Topcon TRV-50 fundus camera at 35 field of view. Each slide was digitized to produce a 605×700 pixel image, 24 bits per pixel (standard RGB). Two observers manually segmented all the images. On average, the first person labeled 32,200 pixels in each image as vessel, while the second person labeled 46,100 pixels in each image as vessel. A subsequent review indicated that the first person took a more conservative view of the boundaries of vessels and in the identification of small vessels than the second person. Performance was computed with the segmentation of the first observer as the ground truth.

Annotation tool for diabetic retinopathy (DR) lesion level and image level annotation

The annotation tool (147) developed for this study by HTIC presents images one by one to the ophthalmologist, and can be used to mark different clinical signs of DR, as well as provide a grade for the image. It also collects image quality, which contains 3 parameters:

1. Whether the image is well centered
2. Whether the image is well captured (good illumination, structures are comprehendible)
3. Whether the image is gradable (Yes/No).

The tool has an import folder option, by which the expert can load their images into the tool. The tool takes care of patient anonymization according to the Declaration of Helsinki, and also can randomize the images that are presented to the expert. An ophthalmologist performed annotation of DR lesions in the selected set of images using a specially developed tool, based on marking of hand-drawn polygons and small regions of interest for lesions. The tool saves the marking and grading's.

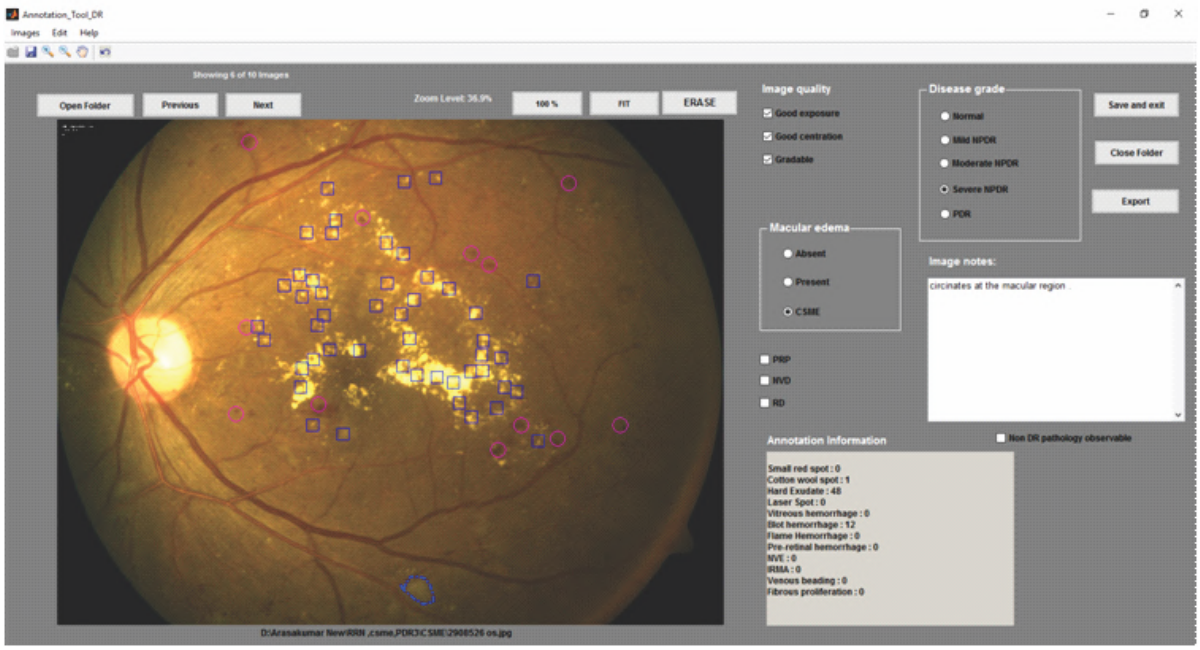

Figure 10 : Annotation tool with annotations given by the ophthalmologist

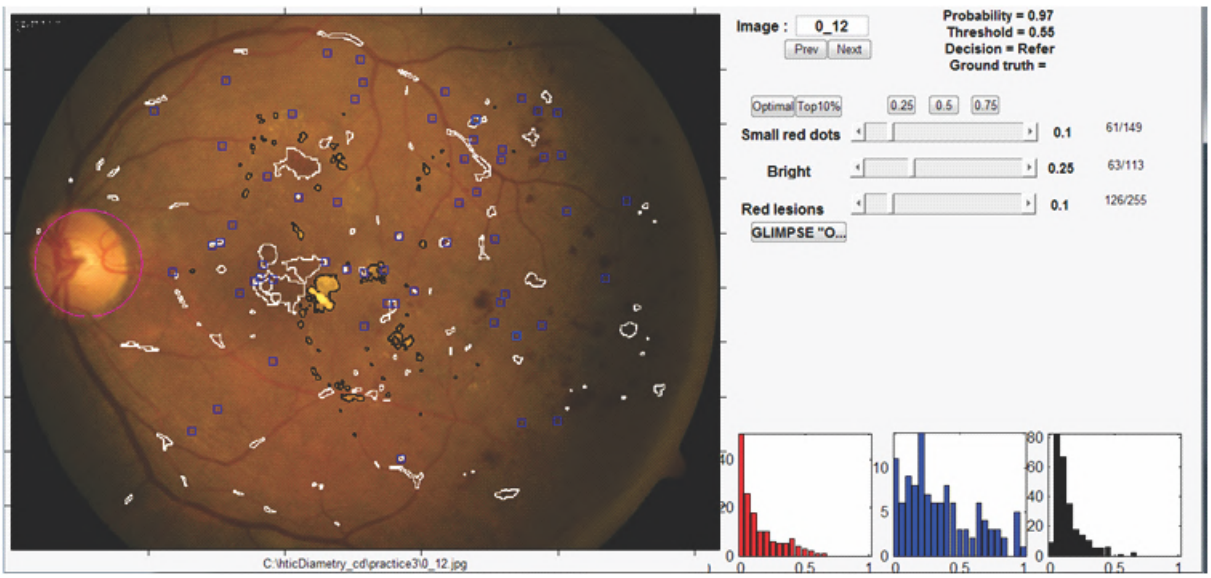

Figure 11: Annotations given by algorithm

The image grades provided by the ophthalmologists follow the ICDR scheme for DR which includes:

1. No DR
2. Mild DR
3. Moderate DR
4. Severe DR
5. Proliferative (PDR)

The tool also captures macular edema grades which are:

1 Macular edema absent

2 Clinically significant macular edema (CSME) Present .

Machine learning algorithms require expert supervision to instruct which are the clinical signs that are identified by the expert. The algorithm uses the supervision to train its recognition patterns.

The supervision that experts provide with the help of annotation tool is used in two forms:

1. Gold standard ground truth for learning of Algorithm
2. For comparison of algorithm performance against expert.

Development of DR Algorithim .

Given a retinal image that was acquired from a retinal camera, DR analyzer software aims to identify if the retinal image has the presence of DR and is referable to the ophthalmologists based on clinical signs observable in the image or absence of DR and not referred to the ophthalmologist.

DR analyzer software is made up of modules, each of which adhere to the design paradigm of HTIC's proprietary Eye-PAC platform.

The system consists of image computing modules for the following tasks:

- Localization of normal anatomy
- Detection of clinical signs

Numerous pixel-level parameters are computed from the detected signs. The information of location, extent, distribution, and appearance of the recognized pathology is used to arrive at an image level decision of referral.

A categorized review of techniques used in digital colour fundus image processing in Diabetic Retinopathy is presented by R.J .winder et al (148) under 5 categories: 1) Image enhancement, 2) Localization and segmentation of optic disc, 3) segmentation of retinal vasculature, 4) localization of fovea and macula, 5) Localization and segmentation of retinopathy.

Publicly available datasets for DR system development and evaluation

A computer-assisted DR screening system was built (149) for the purpose of this study, adhering to the botom up data-driven approach, comprising of modules for determining gradability, normal anatomy detection, pathological signs detection, and analysis for computing the screening decision. The block diagram of the system is shown below: Fig – 12.

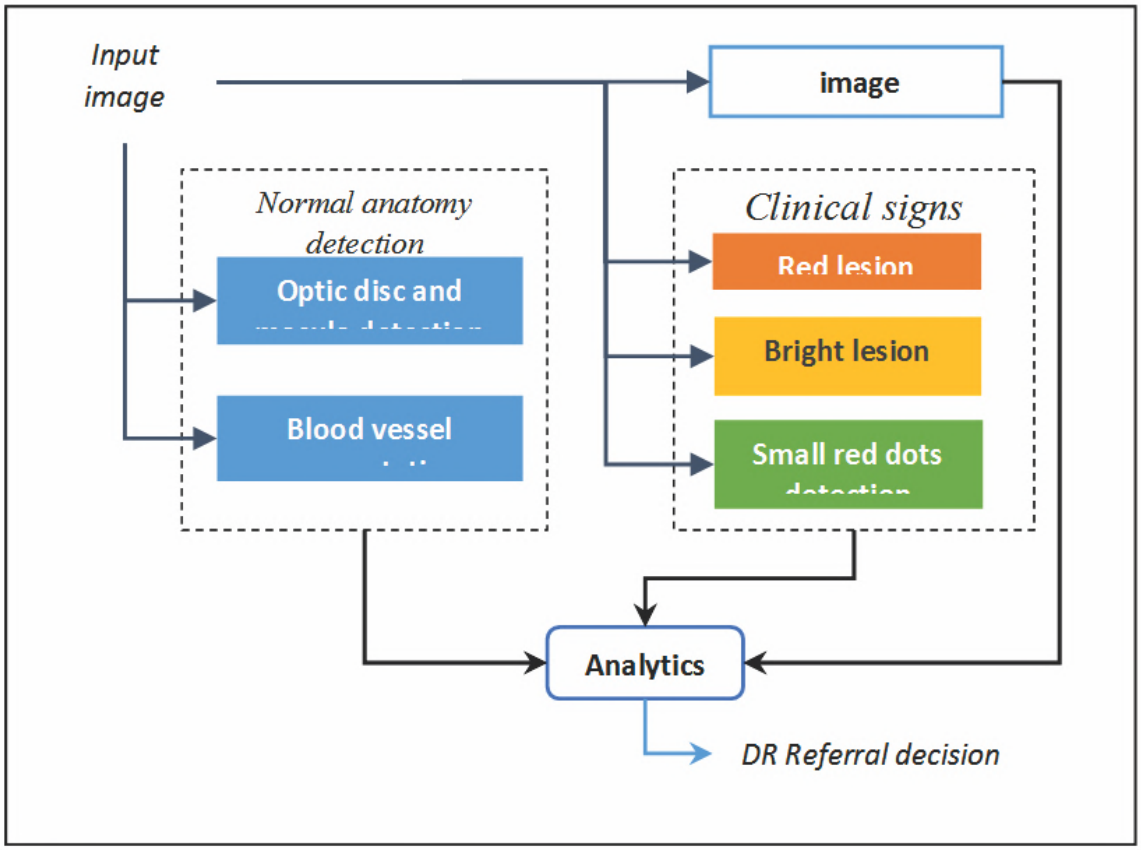

Figure 12: Block diagram of Algorithim for diabetic retinopathy screening from fundus images

The types of lesions annotated are:

- Red structures: small red spots, blot, flame, vitreous hemorrhage, neovascularization
- Blood vessels: upto 3rd order branching – this was done on normal images
- Bright structures: optic disc, cup, small hard exudates, confluent plaque, soft exudates,
- Indication of presence of fibrous proliferation and Traction retinal detachment

Each of the detectors finds lesions and assigns a confidence score for the detected lesion at every detected position.

In order to develop these modules and verify the functionality of the DR modules, publicly available retinal fundus image datasets were used. Table given below, the names and details of the public image databases used for developing the corresponding modules. The two classes of information available in the public datasets are lesion-level manual annotations of various individual signs (such as DiaretDB) and image level readings which provide the screening and grading ground truth for each retinal image ,such as Messidor. Given the output of the lesion detection modules and the anatomy detection modules the screening decision is learnt by training against several manually graded images .

Sánchez CI Niemeijer M et al (146) had applied DR algorithm to public available Messidor data set which consisted of 1200 eyes with fundus photographs .The performance of the Algorithm was good and could be compared to human graders

Table 9.Public datasets used for developing and verifying the modules of the DR system. The references are given in numbers and indicate the source of the data.

Module	Databases	Number of Images	Description of dataset
Image gradability	HRF[6]	36	Folder of good and bad quality images
Optic disc and macula detection	Stare[7]	81	Location of optic disc
	ReviewDB[8]	99	
Blood vessel segmentation	Drive[9]	40	Manual segmentationof blood vessels
	Stare[7]	20	
	Aria[10]	143	
Red lesion detection	DiaretDB[11]	89	Location of lesions
Bright lesion detection	Hei-Med[12]	169	Location of lesions, regions of exudates
	DiaretDDB[11]	89	
Small red dots detection	ROC[13]	100	Location of lesions
	DiaretDB[11]	89	
DR referral decision	Messidor[2]	1200	4 grades of DR severity

It is known that publicly available datasets have been acquired in clinical settings and therefore might not capture population level statistical distribution of DR prevalence. Therefore the study included a first pass observation of performance of the developed system on a selected set of images sampled from an epidemiological study followed by refinement of the algorithms to adapt to observations in Indian images, and a pilot study to evaluate the system on limited scale field data from Indian settings .

Report of performance of Indian Institute of Technology Madras Diabetic Retinopathy screening software against Sankara Nethralaya –Diabetic Retinopathy Epidemiology and Molecular Genetic Study (SN-DREAMS) data and London School data

Indian Institute of Technology Madras (IITM) Diabetic Retinopathy screening software was trained on 100 cases (first data set) from Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular genetic Study (SN-DREAMS) project data, and the detection performance (sensitivity and specificity) of the software for screening (refer vs don't refer) was evaluated on another set of data (100 images –second set of data) of London school data which was also a part of Sankara Nethralaya-Diabetic Retinopathy Epidemiology and Molecular genetic Study (SN-DREAMS). The performance observed on the test set was 80% sensitivity at >90% specificity on 100 cases.

Training Dataset selection:

A subset of 100 cases was selected randomly from retrospective SN DREAMS data: 2 images per eye,macula centred view and disc-centred view:

Grading was done against 5 criteria:

1. Image quality
2. Image grading (gradable or not gradable)
3. Diabetic Retinopathy (DR) grades (normal, mild, moderate, severe, proliferative)
4. Clinically Significant Macular edema present
5. Absence of Macular edema

Among the 100 cases randomly selected, 17 cases were not graded due to poor quality of images and 83 cases were graded. For the purpose of this study, the Diabetic Retinopathy (DR) grade against each eye was used, and the gold standard was ophthalmologist grading of DR,mild, moderate, severe and proliferative DR. Presence of DR is considered as referable. Normal and absence of DR was considered as non-referable.

Figure 13 shows the distribution of age among the 100 cases selected from SN DREAMS. Figure 14 shows the distribution of Diabetic Retinopathy grades among of 83 cases.

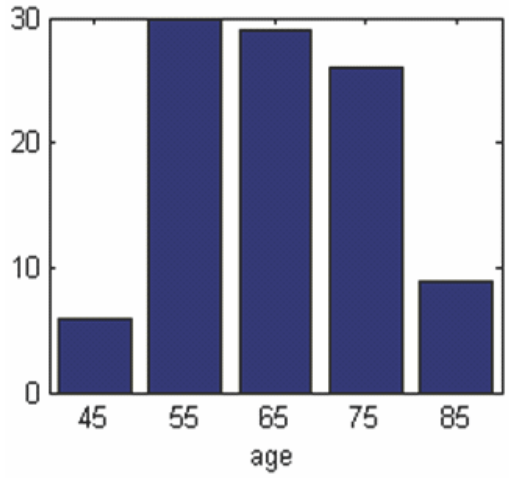

Figure 13: Distribution of age among the sample 100 cases selected from SN - DREAMS - data

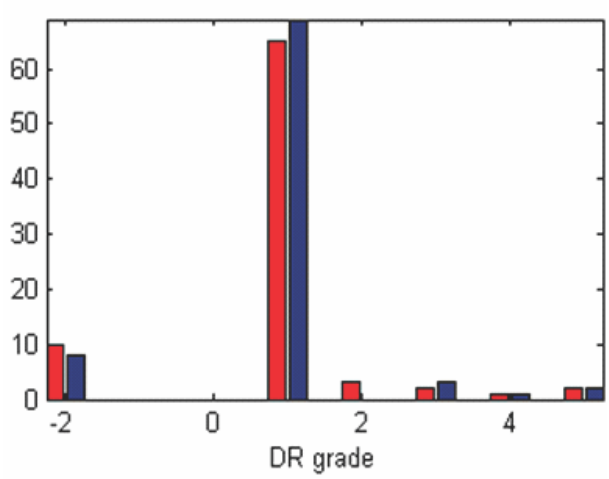

Figure 14: Distribution of Diabetic Retinopathy grades among the 100 cases (first data set)Percentage of normal cases is 69%. Graph shows distribution for OD (blue) and OS (red). Grade of -2 corresponds to 'not gradable'

In the SN-DREAMS data, all images were mydriatic, 30 degree images.seven field taken Carl Zeis FF450plus fundus camera .

DR Software functioning:

The screening software analyzes the image and produces a confidence score in the range 0 to 1 for each image. Higher confidence indicates greater reference to the ophthalmologist. This score has to have thresholds for obtaining the referral decision (images having confidence greater than threshold are referable)

The performance of the decision can be evaluated by setting different thresholds for the decision and observing the correctness of the decision against screening outcome based on manual grading in a test dataset (that has images not used in training).

Training specification:

Among the 400 images (2 images per eye x 100 patients), 332 images (83 cases) were gradable, 68 images (17 cases) were not gradable. Two-fold cross validation has been used for first level of evaluation. The gradable 332 images were used for training the DR screening software, and evaluated using cross-validation technique with 2 folds. In each fold, 50% of the data is used for training, and the other 50% undergo prediction. Using this method the performance curve of the screening decision for SN-DREAMS data is shown in figure 15. Each point on the performance curve is obtained by setting the threshold at a certain level. The top-right point corresponds to the lowest threshold (0) and every subsequent point represents the sensitivity, specificity of the algorithm at the selected threshold.

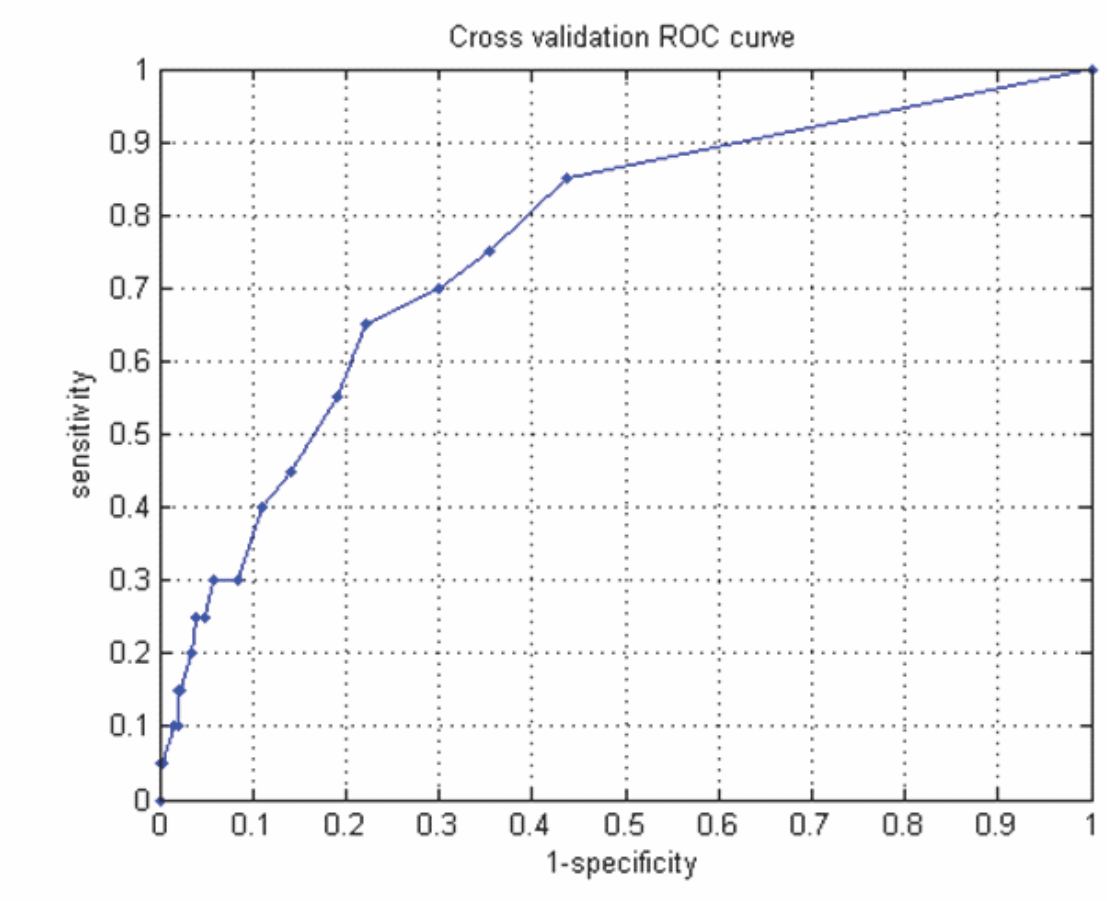

Fig 15: SN DREAMS 100 CASES

From the cross-validation curve it can be seen that at 70% sensitivity, the specificity achieved is 70%, corresponding to threshold of 0.15. The low threshold indicates that the system is biased towards providing lower confidence scores as learnt from the training, which presented about 83% normal cases.

State of the art performance for Diabetic Retinopathy screening decision is 97% sensitivity at 47% specificity (Michael D.Abramoff, 2010). At the same level of specificity, the IITM software indicates 85% sensitivity (based on cross-validation).The slightly lower performance can be attributed to non-usage of image quality check in the Diabetic Retinopathy screening module.

Testing specification:

The test data used was retrospective London school data from 100 patients, with 2 images per eye, total of 400 images, taken with Orion fundus camera from NIDEK.The grading provided had 4 grades of severity: normal, mild, moderate (moderate and severe) and proliferative. In this study we have considered grades moderate, severe and proliferative as 'referable'.

Shown below in figure 16 is the distribution of age among the 100 cases. The distribution of DR grades in the 100 cases is shown in figure 17. The number of cases in 'moderate' (3) grade is high compared with the SN-DREAMS data.

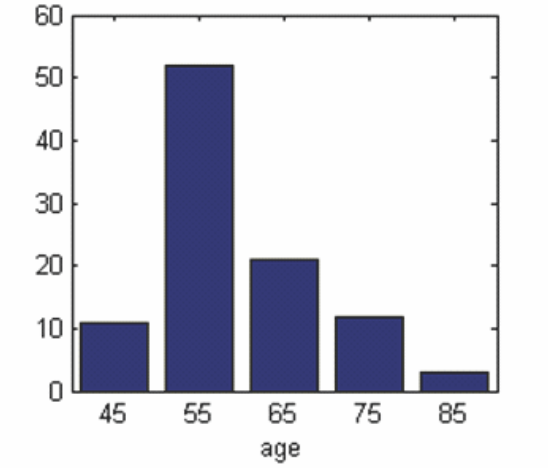

Figure 16: Distribution of age among London school data

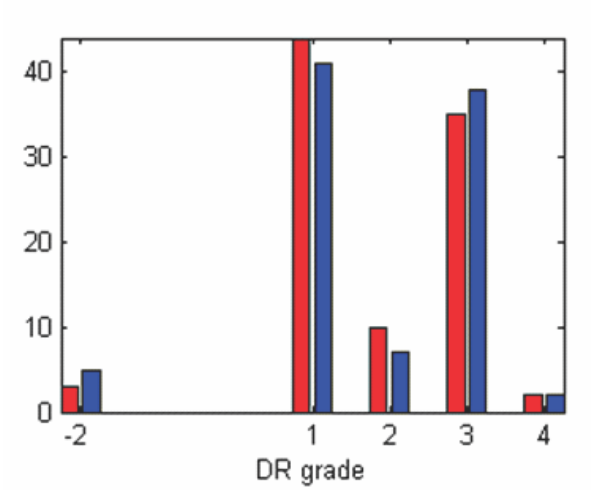

Figure 17: Distribution of grade in London school data: OD (blue) and OS (red). Grade of -2 corresponds to 'ungradable'

The images are mydriatic 300 degree seven field images. The trained system was used to predict the DR referral decision on the test dataset. For each test image, the system predicts the confidence score, and the performance curve obtained is shown in 9

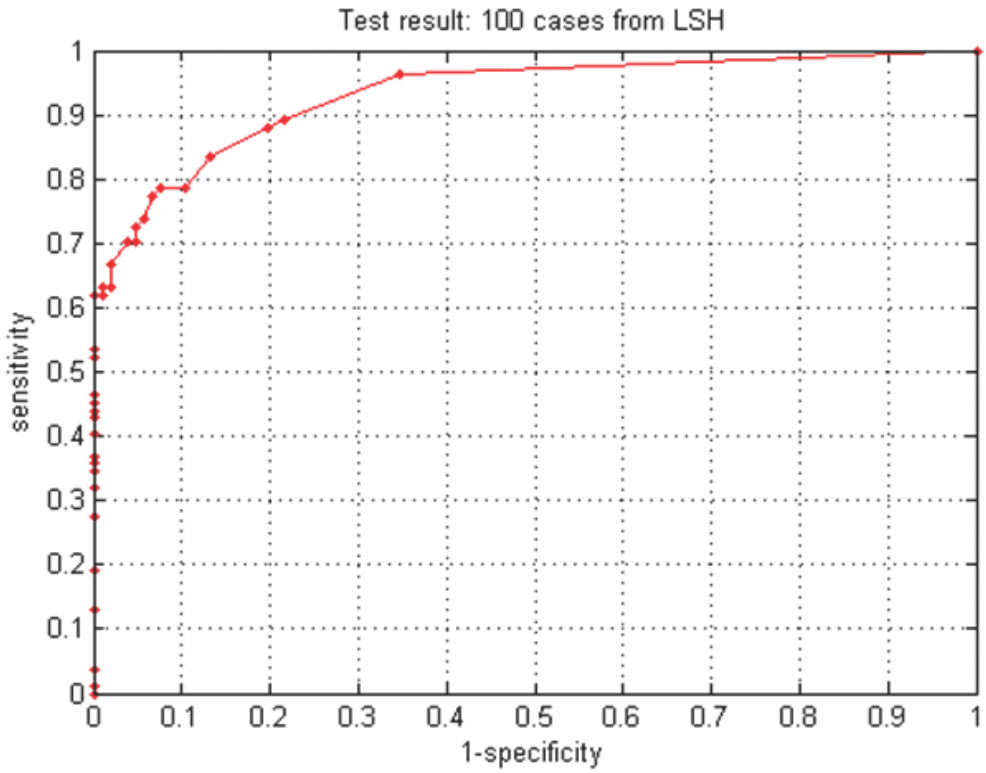

Fig 18 : London school of Hygiene 100 cases

Results :

The performance observed is comparable with state-of art systems (exceeds 83% sensitivity at >85% specificity) for a confidence threshold of 0.2. The curve shows that high specificity of >90% is achieved for sensitivity of up to 80%. Inspection of the confidence scores indicated that among the images graded as moderate DR and PDR, the confidence score assigned was 0.8 (on a scale of 0 to 1), indicating that advanced stages are well-detected.

System redesign and Enhancements to a computer-assisted screening technology for diabetic retinopathy:

Our DR image screening system was developed based on images from publicly available retinal image datasets (about 2000 images) from around the world. The pilot study included 200 cases sampled uniformly from an epidemiological study to represent various levels of pathology. The data and the system outputs showed the need for strong modules examining image quality, specific analysis for clinically significant macular edema and analytics for fail-safe recognition and flagging of proliferative (late-stage) DR. All the 3 modules were evaluated on fundus photographs mydriatric 50° single field from Carl Zeis FF 450plus fundus camera .

1) Module for macular edema detection .

Hard exudate appear as bright yellow regions which can be localized, whereas soft exudates (cotton wool spots) are faint and fuzzy. Detection of exudates on the retinal images is the first step in quantifying and grading DME.

Computer-based assessment of DME severity has been done building upon detection of individual exudate lesions near the macula. In our method, we use a multi-scale histogram based thresholding technique for exudate detection, which detects Hard exudates of various sizes and intensities. Since exudates occur as clusters, we group the exudates based on their spatial distribution to improve the reliability of exudate detection for DME grading.

An essential component of our macular edema detection module is reliable identification of macula in the presence of pathology. We have developed a method for high accuracy joint localization of optic disc and macula in retinal images which uses a combination of anatomical, local image intensity and geometric characteristics, and is robust to variations in imaging conditions, pathology, camera magnification and field of view.

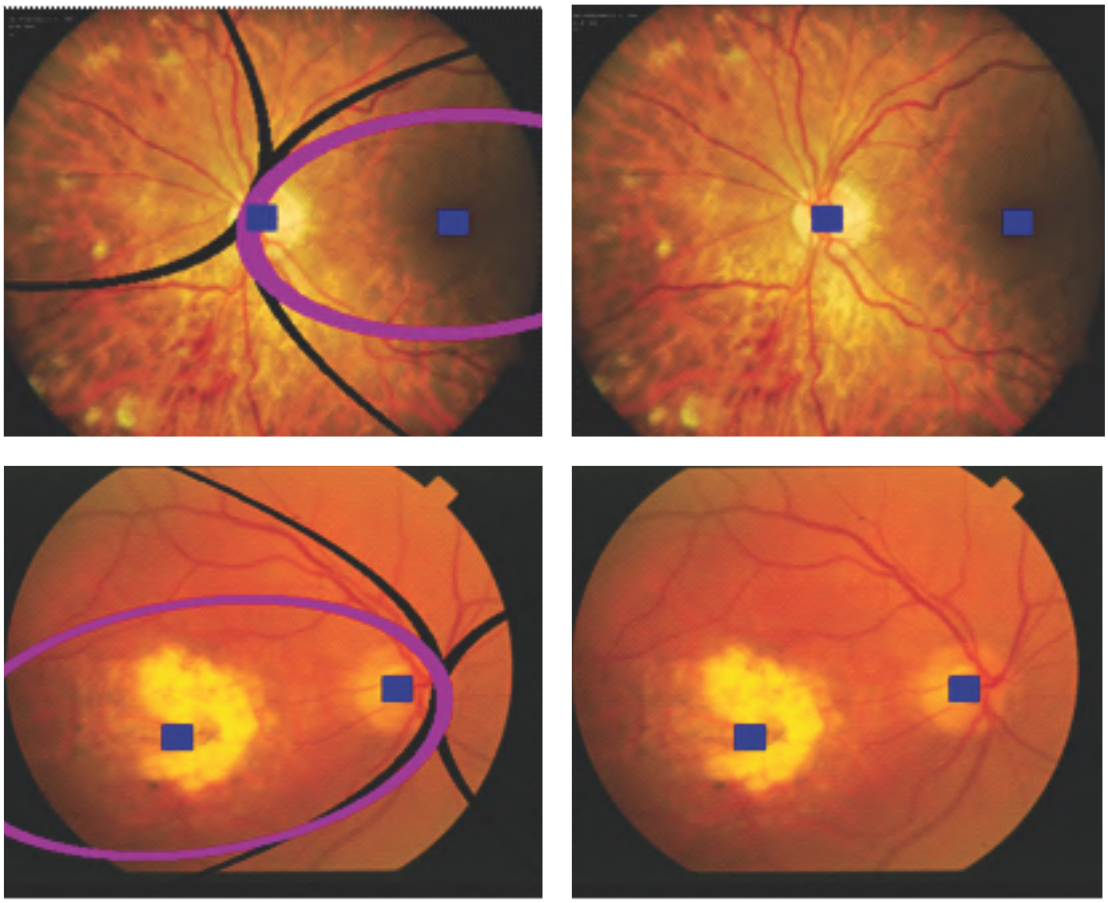

Fig:19 Macular edema detection

Once the optic disc and fovea are localized, we perform automated macular edema grading by considering radially increasing annular rings at 2.5 disc diameters (2.5DD), and 1 DD steps. We use a parametric model for identifying circinate patterns in hard exudates within 2.5 DD from the macula

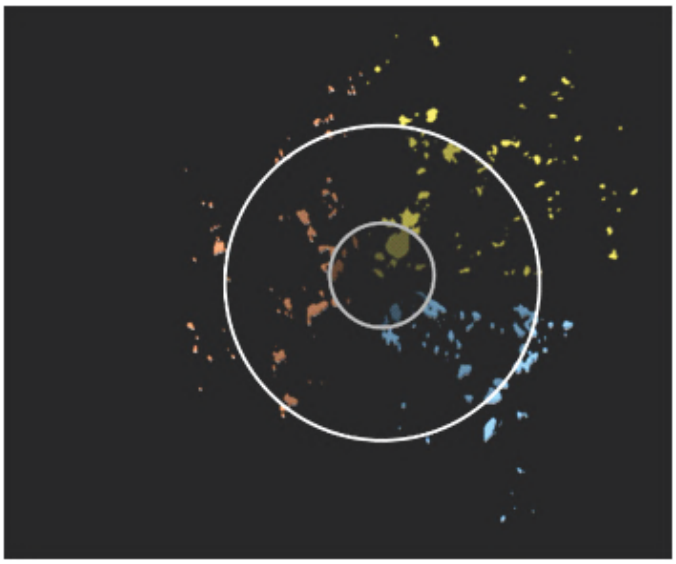

Fig :20 Gaussian mixture model

The centroid coordinates of the detected hard exudates are taken and their spatial distribution is found by coarse resampling of the image space. Using this outcome, the modes of the spatial distribution are used to initialize centres of a Gaussian mixture model. This gives cluster patterns in the macular region and help to identify whether circinate pattern is observed. Depending on the density of the spatial distribution the severity factor of macular edema is computed on a dataset of 587 images.

Module for image quality assessment

This is a module which identifies the quality of the image. This module estimates a quantitative measure of image quality, depicting the suitability of the image for extracting information from it. The module functions by extracting various parameters from the image which represent its quality: such as colour distribution, structure distribution, contrast, homogeneity, illumination, signal-to-noise ratio (SNR), moments of intensity distribution, and compares with a set of reference images identified as being of good (and bad or poor) quality. The final score is arrived at by a supervised learning algorithm which predicts the similarity of the given image to the reference images. Evaluated on 121 retinal photographa .

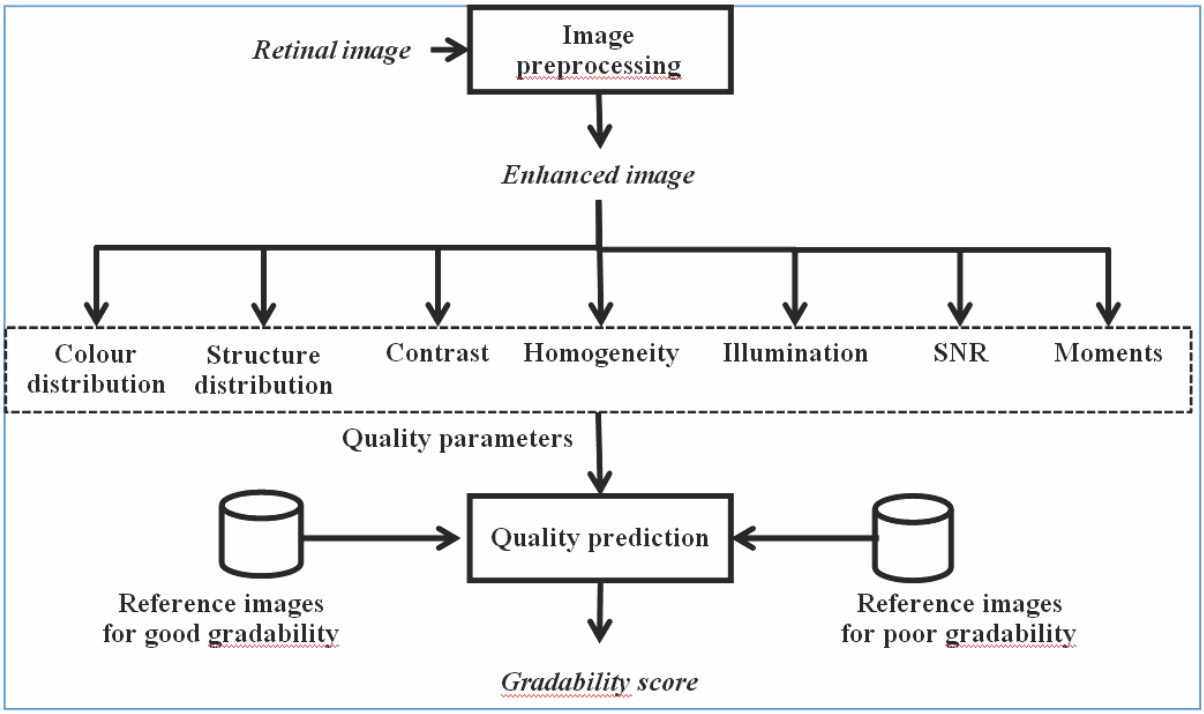

Fig: 21 Modulefor image quality assessment

Module for PDR signs detection

Proliferative diabetic retinopathy PDR (150) and 50 signs such as neovascularization on the disc (NVD) and neovascularization (151) elsewhere (NVE) are computationally challenging to detect individually. PDR was evaluated on 1052 retinal photographs mydriatric 50° single field from carl Zeis FF450 plus fundus camera .

We have devised a method for identifying PDR (152) that divides the image into non-overlapping patches, and within each patch provides the likelihood that PDR signs are found in that patch. The likelihood is found by texture analysis, using training annotations for PDR signs provided by ophthalmologist. We consider 3 kinds of patches: normal patches, patches containing NPDR signs, and patches containing PDR signs. The texture analysis extracts information from the patches and is used by a classifier to determine the PDR status for a given patch. For this method to work effectively, we have created a thin-vessel segmentation algorithm, which is tuned to have high sensitivity for detecting thin vessels especially in peripheral views. Lee J et have obtained good results for image analysis of clinical signs in PDR.

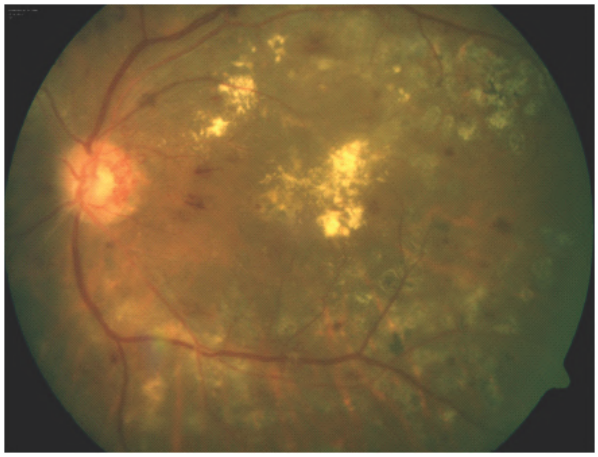

Fig – 22 New vessels on the disc PDR

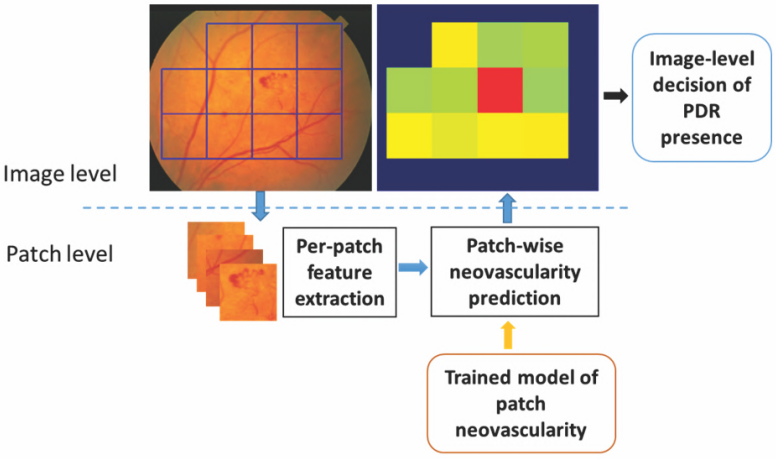

FIG: 23 -Overall workflow for PDR detection by performing patch level and image level analysis

The patch-wise neovascularity prediction produces a heat-map output where red areas indicate high likelihood of neovascularization in the area, and green areas indicate normal. Blue areas are outside the analysis region. This heat-map output can be used to visually identify regions containing neovascularization. This also used to arrive at a image level decision of presence or absence of PDR.

Performance on 981 patients of SN Dreams :

The SN-DREAMS retrospective dataset had 981 cases, each imaged with 7 field mydriatic 30 degree imaging in both eyes from Carl Zeis FF450 plus digital camera and VISUPAC imaging system . The total set has 20177 images, of which 18597 images are marked as gradable.
The performance of the developed algorithm was evaluated with 10 fold cross validation, using 90% of the images for training and the remaining for evaluation. This method is randomized with replacement for the folds, so every image is predicted at least once.

Validation of Computer-Aided Diagnosis (CAD) Algorithim of diabetic retinopathy from retinal photographs in comparison to a human grader

The performance of the CAD will be examined in a real-world situation in type 2 diabetic patients .Three Settings for the acquisition of patient data for the study are given below . A written informed consent was obtained from all the participants and the study was conducted over a period of two year and 6 months (Jan 2015 to May 2017)

1. Validation of Computer-Aided Diagnosis (CAD) Algorithim of diabetic retinopathy in vitreoretinal outpatient department (OPD) of the Sankara nethralaya eye hospital

Methods

The study was a prospective study conducted at the department of vitreoretinal services, Sankara Nethralaya, Chennai, India. Patients with known diagnosis of diabetes and with DR were identified from the medical records on an everyday basis who reported to the department for a routine eye exam. Patients provided written informed consent. Patients were then informed to have their undilated (nonmydriatric) fundus photography. 460 patients underwent single posterior pole 45-degree macula centered fundus photography (Forus 3nethra Classic Non Mydriatic Fundus Camera) in both eyes after dark adaption.
The photo graders received a CD-ROM with all the digital images. Information on the Patients age, sex and duration of diabetes was shared with the reader and rest of the demographic characteristics and medical records of the patients were withheld from the reader. The reader was asked to read the images in order. There was a time limit for the reading.

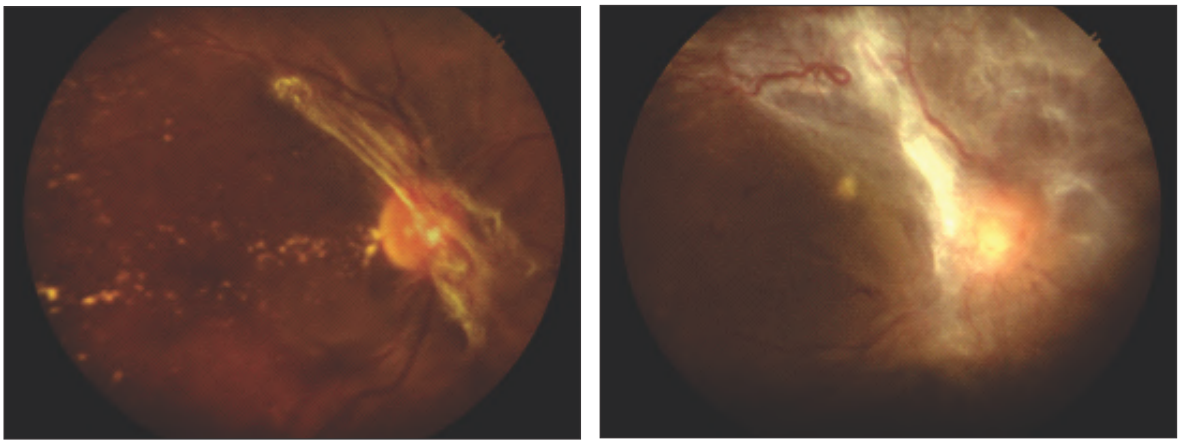

Fig: 24 SN VR OPD - PDR with fibro glial tissue at the disc

The reader was not allowed to contact others concerning his or her reading. The readers used the same computer and monitor for the grading, and they were allowed to magnify and move the images, but not modify brightness or contrast. Readers were allowed to label images as ungradable based on their judgment. A random sample of 10% of the photos was graded by two separate graders, for quality control.

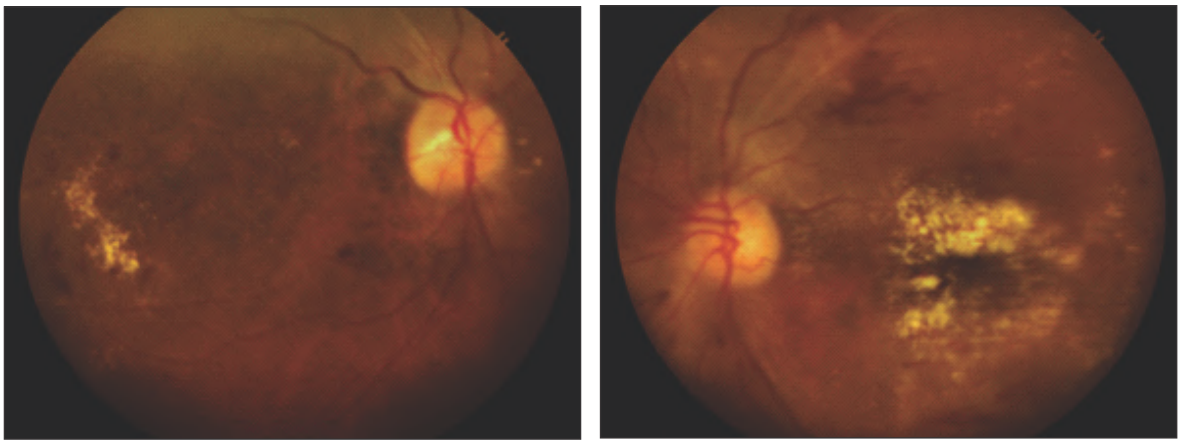

Fig : 25 SN VR OPD - NPDR with DME

The images were run through the automated system and were also graded by a human graders (optometrist) and by an experienced vitreoretinal surgeon. The patient was also examined by various ophthalmologists with the indirect ophthalmoscope who provided further advice and disposal of the patient. The effectiveness of the software in identifying the presence or absence of diabetic retinopathy lesions was examined in comparison to that by the human grader (optometrist) and with that of a vitreoretinal surgeon (the 'gold standard').

2. Telescreening of DR at camp site –Teleophthalmology camps

Sankara Nethralaya's Tele-ophthalmology department as a part of its telemedicine initiative takes high quality eye care to the remote villages of Tamilnadu (Thiruvallur and Kanchipuram). A team of well trained and experienced optometrists and paramedical staff traveled in the outdoor Tele-ophthalmology units comprising of a customized and fully equipped tele-ophthalmology bus.

WHAT DO WE DO USING TELEOPHTHALMOLOGY CAMPS?

- Comprehensive eye examination in the rural areas at patient's door step and dispense spectacles at nominal cost.
- Diabetic Retinopathy Screening Camps are a boon to the villages where diabetic patients undergo screening. Further investigation and treatment - laser photocoagulation or surgery is completely free of cost for the patient referred to the base hospital.
- For those detected with cataract at camp and referred to base hospital for surgical intervention, cost free surgery, post-operative care, boarding and spectacles are provided.

The Tele ophthalmology camp Process

The Tele ophthalmology camp involves the following activities:

(1) Planning
(2) Conducting eye camps
(3) Tele consultation
(4) Providing low cost spectacles to the rural population.
(5) Referral of patients to the base hospital
(6) Conducting awareness programs
(7) Effective follow up of the program

Planning the eye camp

(1) Identification of villages / camp location: The identification of villages/ project location is a process that will involve the directives of the Head of department of Tele ophthalmology. To understand statistics of blindness prevalence, report on study of district-wise blindness as tabulated by the District Blindness Control Society (DBCS) of India was taken into account. The DBCS, a nodal government organization with the objective of monitoring all activities relating to blindness control is engaged with the purpose of planning and implementing blindness control and blindness prevention activities under overall guidance of the state/central organization.

Villages in two districts of Tamilnadu (Kanchipuram and Thiruvallur) in India were chosen to conduct comprehensive eye examination camps and permission was obtained from the head of DBCS to undertake the program.

Once the villages are identified detailed census information about the districts / villages / and amenities of the villages to be covered must be used in planning the camp schedule. The route map to reach the camp site is an important start up for planning the camp.

After having identified the place for conduct of camp along with necessary permission, the social worker – planning will make visits to the villages one month prior to the camp and establish contacts of the Panchayat – Heads of villages and camp organizers and have a preliminary meeting with them either in their village or by bringing them to the base hospital to detail about the purpose of the Teleophthalmology camp, the number of patients that will be seen, explain the purpose and benefits of teleconsultation and gain their support.

While the Social Worker – Planning visits the villages, he would identify the locations for holding camps. Preferred locations for organizing camps would be High Schools with large open grounds or Community halls with necessary basic amenities.

Working in collaboration with Non-Governmental organizations, with the consent of HOD - Teleophthalmology would be a beneficial practice to Sankara Nethralaya. The key person of these NGO's works together with the HOD to understand the program objectives and their roles.

Once the heads of the villages and the organizing NGO's are in agreement of the camp, a "letter of interest" duly Signed by the camp organizer is sent to the Tele ophthalmology HOD. A copy of the same is filed at the department along with camp schedule.

Tentative camp schedules may then be drawn up based on the "Camp Schedule Format" and then the schedule is to be handed over to the Project Officer of Teleophthalmology. He or She will make and keep copies of the schedule in the department, one for the HOD, one for the Administrator of Community Ophthalmology Hospital Wing (to facilitate and obtain necessary permission from the District Collectors' office for conduct of camp). Additionally, Camp schedules are also shared with Transport Department at the beginning of each month to organize logistics and support.

Publicizing the camp schedule in the villages

(1) Handbills/ Banners to be distributed 2 weeks before the camp to be displayed at strategic locations

(2) Public announcements by Auto Rickshaws fitted with loud speakers, one or two days prior to the camp

(3) Pamphlets for those registered at the camp highlighting the features of the camp in vernacular language so that they clearly understand the features of the camp.

A checklist of camp publicity (Camp Publicity Checklist Format) is to be filled along with the camp schedule after reviewing by the respective Project Officer and planning social worker one week before the camp and one day before the camp. If publicity has not been done for any reason, the social worker planning and field social worker needs to ensure to repeat the auto announcements in order to spread awareness about conduct of the camp.

Camp Travel Cycle

The Tele Ophthalmology department's mobile unit shall be scheduled for holding 15 to 20 camps in a month. Two Sundays of the month shall be holidays. On days of Camp off, the team members shall report to the Department to complete their allocated responsibilities and prepare camp reports.

CONDUCTING THE TELEOPHTHALMOLOGY CAMP

The mobile unit comprised of ophthalmic equipment's, Laptops, data card, 2KVA uninterrupted power supply, pamphlets, stools and others accessories.

With the advancement of technology, practice and maintenance of Electronic medical records (EMR) provide a new dimension to outreach eye camps. Ease of usage, integration of different parameters and instant reproduction are the prime advantages of EMR. However, technical challenges with cost of application dependability on an enduring power source, limit its widespread use.

Fig : 26 EMR at campsite

Fig : 27 Teleophthalmology bus

At the camp site, patient's demographic details were registered by social workers with the support of local volunteers in the EMR. However, at places that lacked continuous electric power supply, there were constraints to the use of EMR. Patients registered on the EMR were then given printed identity cards. If EMR was not possible, paper based registration cards were issued, and the patient information was updated in the database at the SN server soon after returning from the camp site.

At Sankara Nethralaya, the Electronic Medical records have been implemented for rural camps since 2011. It has provided valuable information on

1. Study of progression of the disease of the patient on subsequent visits.
2. Patient data readily available on screen thus enhancing the examiner to offer better services to the rural populace.
3. Demographic disease prevalence can be studied.
4. Clinical support system can be incorporated in the EMR.
5. Tracking of camp /rural patients data through EMR facilitated further services, when patients were admitted in the Main hospital.

Table 10 - Brief Work flow at the camp site

S.No	Activity	Time
1	Setting up the equipment at the campsite after travel to the village from the base hospital	8:30 am - 9:30 am
2	Registration And Awareness Program	9:30 am - 1:00 pm
3	Clinical Examination of Patients and tele consultations	9:45 am - 1:00 pm 2:00 pm - 4:00 pm
4	Counseling	9:30 am - 4:00 pm
5	Winding up the equipment, taking stock and Daily Audit of Equipment	4:00 pm - 5: 00 pm

* Every patient must have Electronic medical record with a unique MRD number. Patients must not be seen without a record.

Ideally maintaining good medical records in such camps is a constraint owing to the high turnover of patients, quantitative and voluminous paper work and additional storage space required at the base hospital. This leads to loss of very important data from the rural sector. Another difficulty is that transportation of paper based records is not feasible on most occasions and thus, they are not reproducible across different camp sites at different times. Application of EMR at the camp site has the potential to alleviate these difficulties and help maintain accurate records that are reproducible. All patient records were stored on the EMR server at the camp site and after returning to the base hospital, these records were integrated with the main EMR server of the base hospital. The same server was used for data entry at all the camps over the study period. All the diagnosis was recorded as per the international classification of diseases (ICD – 9).

Fig : 28 Slit lamp examination

Fig : 29 Fundus examination

Registration of patients at camp site was followed by refraction using an Topcon auto refractor (model KR 800, Topcon, Tokyo, Japan) and comprehensive clinical examination by an optometrist including recording of case history, best subjective correction on Snellen's distance charts, muscle balance, cover test for distance and near, Topcon slit lamp examination, pupil reaction, and intraocular pressuree measurement using applanation tonometry.

Fundus images were obtained for all patients using a nonmydriatic fundus camera (model Topcon Retinal Fundus Camera TRC-NW8F with Accessories) by the fundus photographer. After dark adaptation a single 45^0 digital fundus photograph centered on the macula was taken with the Topcon TRC NW8F camera for both eyes. Noncertified, yet well trained photographers were able to take photographs using auto focus, auto capture features of the hi-end fundus camera. Digital fundus photographs Fig - 30 of the right and left eyes of the patient are acquired under a fixed, predetermined imaging protocol, after 10 minutes of dark adaption, first the right eye followed by 3 minutes of further dark adaption and then the left eye. If the quality of the taken images is found to be poor, then reimaging instruction is given to the fundus photographer. There is make shift dark room with dark cloth at the campsite and patient has to close his eyes and bring about physiological dilation.

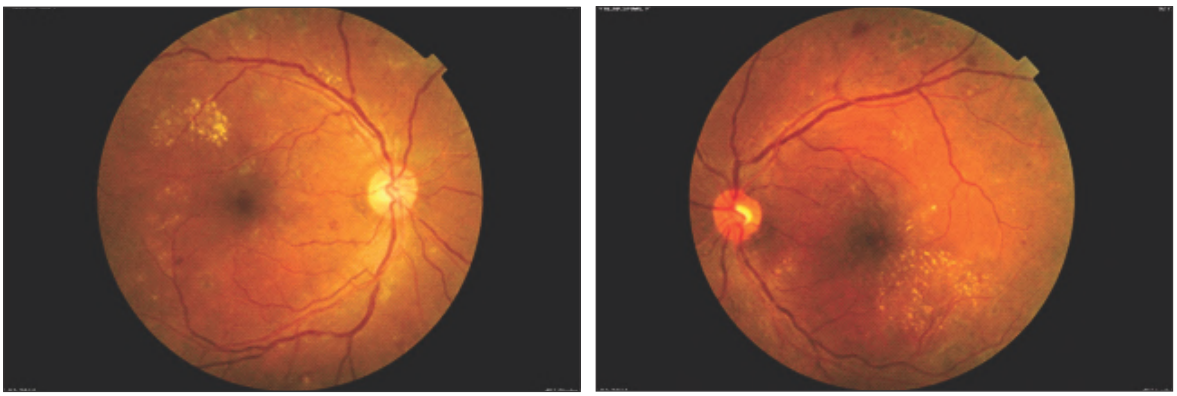

Fig -30 Non Mydriatic fundus photograph from tele camps

The process of teleconsultation

After the initial basic examination by the optometrist, patients requiring teleconsultation were identified. Any patient with loss of vision and any abnormal finding in the fundus image, the patient EMR record and the retinal image was sent to the ophthalmologist at the base hospital (SN) for evaluation by teleconsultation using internet connectivity (data card with laptop). All patient records were converted and stored on the EMR format in the server at the base hospital.

Fig:31 Teleconsultation at campsit

Fig: 32 Teleconsultation at the hospital

The human graders -the general ophthalmologist and fundus photographer read all the digital fundus images. Information on the patient age, sex , duration of diabetes were shared and other details of demographic data and medical records of the patients were withheld from the readers. The reader will be asked to read the images in order. There will be time limit for the reading. A reader will not be allowed to contact others concerning his or her reading. The retinal photographs were stored as JPEG images and viewed in a darkened room on CRT screen. All photographs were deidentified and coded with an identification number and uploaded to a secure database. All digital fundus images, were run through the automated system and were also read by the same general ophthalmologist (Telemedicine expert the 'gold standard') and fundus photographer . The readers will use the same computer and monitor for the grading, and they will be allowed to magnify and move the images, but not modify brightness or contrast. Readers will be allowed to label images as gradable based on their judgment. Over the Two-year study period from Jan 2015 to May 2017, patients with poor quality fundus images were referred to the base hospital for further evaluation.Patients who have been referred to Sankara Nethralaya either for DR or for any investigation or treatment must be noted down in a special register and also issued a patient ID card containing patient name, village name, reason for referral and contact number. These patients must be followed one week later to ensure they have reported to the hospital .The referred patients will avail free treatment at the base hospital.

3. Diabetic Clinics:

Diabetic clinics in and around Chennai, India, were selected.

1) M.V. Hospital for Diabetes & Diabetes Research Centre (Clinic I) at Velachery and Mylapore,-Dr vijay Viswanathan.
2) Dr. Mohan's Diabetes Specialties Centre (Clinic II) at Tambaram, Vellore and Gopalpuram, were chosen

Ethics approval

This study was approved by the Vision Research Foundation Ethics Committee and the research adhered to the tenets of the declaration of Helsinki. Informed consent was taken from all the patients before participation in this study .

This study was performed in an area in chennai with a higher proportions of ophthalmologists than elsewhere in the country. One can speculate that the results observed here might even be more pronounced when density of ophthalmologists is lower, potentially making this screening procedure even more important in other regions, especially in rural areas.

The study was conducted over a period of two year and 6 moths from January 2015 to May 2017, after the approval of the Institutional Ethics Committee.The paramedical staff, fundus photographer and optometrists in diabetic clinics were trained to take fundus photographs with and without dilation using fundus cameras or smartphones.

Patients details ,age ,sex and duration of diabetes was noted in the Microsoft excel sheet 2013 .Diagnosis of DR noted by retinal specialist and Algorithm was also included in the excel sheet . The fundus images were captured at the physician's or diabetologists facility/clinic at the time of a regular diabetic check-up. Patients with already known and newly diagnosed type 2 diabetes were included in the study and underwent retinal imaging with fundus camera (TOPCON TRC-NW300 or FORUS 3nethra or smartphones (android).

Procedure of fundus photography in Diabetic Clinic I -Dr Vijay Viswanathan.

Protocol- Forus 3nethra Classic Fundus Camerawas used. Patients were made to sit for 5 minutes in a darkened room to allow Physiological mydriasis which is achieved in 3 -5mins of dark adaptation by closing the eyes. Further nonmydriatic screening comes along with a higher level of comfort and is less time consuming, with a photography session taking no longer than 10 minutes, compared to mydriatic fundus screening.

A trained paramedical staff took a single undilated 45˚field retinal photograph centred on the macula of each eye. Photographs were taken in a darkened room with no natural or artificial light apart from that produced by the monitor, which faced away from the patient.

On each occasion, the right eye was photographed first and up to 5 minutes was allowed between left eye photograph to allow redilation of the left eye Single /multiple 45 images of the disc and macula of both eyes was taken by trained medical personnel –optometrists /fundus photographer. The imager was allowed to re-image an eye if the imager determined the quality was poor owing to reasons such as patient blink, alignment, or poor fixation.

All images in a given session for each patient was uploaded to the web based Telemedicine platform bundled with 3nethra fundus camera using Broad band connectivity in the diabetic clinic of Dr Vijay viasanathan. Ophthalmologist from sankara nethralaya login to ForusCare to perform various tasks after receiving SMS alerts to their mobile phones Based on the role of the user logging in ForusCare provides different screens. 3nethra Foruscare Uploads diagnosis referrals/reports using client software ForusCareConnect. Doctors log in and report the presence of DR and also grade it . Reports are printed and handed over to the patient. Based on this report patient reports to the ophthalmologists for further treatment.

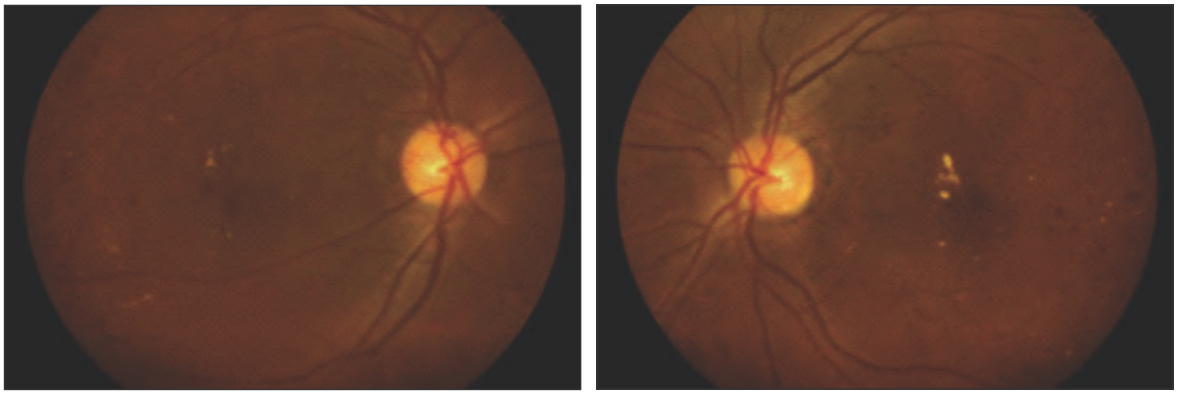

Fig : 33 Non Mydriatic fundus photographs - Diabetic Clinic I – NPDR with DME

The retinal photographs of 1290 patients were stored as JPEG images and viewed in a darkened room on CRT screen. All photographs were coded with an identification number and uploaded to a secure database. All digital fundus images, from the diabetic clinic were reviewed by the same retinal specialist and senior optometrist (grader) from Sankara nethralaya using the same liquid crystal display computer monitor of 1280·800 resolution.

Diagnostic Criteria: Diabetic retinopathy was diagnosed according to the International Clinical Diabetic Retinopathy Disease Severity Scale .Fundus images were also evaluated for gradability. Other incidental fundus photograph findings, other than diabetic retinopathy were also documented

The grading of fundal features by the human graders, retinal specialist and senior optometrist /grader from Sankara nethralaya was done independently. The diagnosis was recorded on Microsoft excel sheet 2013 and was based on retinal features alone (no other clinical information was available to the photograph graders) . Image quality was also assessed by the human graders. The Algorithm assessed the retinal photographs for the presence or absence of DR and gradability of the images. The Sensitivity, specificity, positive and negative predictive values were estimated

Procedure of fundus photography in Clinic II - Dr Mohan Viswanathan .

TOPCON FUNDUS CAMERA–

Protocol- Trained optometrist /Fundus photographer acquired images using a Topcon TRC NW 300 fundus camera. Seven-field images would be obtained after pupillary dilation as per the ETDRS protocol. Such images would be transmitted in real time using broadband connectivity from Tambaran and vellore clinics to Gopalapuram clinic in chennai . The images would be reported by an ophthalmologist within 30 minutes. Images which were not gradable would be taken again on request from the diagnosing ophthalmologist .Patients who are suspected of having Diabetic Retinopathy at a level that requires treatment would be advised to undergo treatment. Such patients would be further examined by the ophthalmologists attached to the Gopalapuram diabetic clinic and treated as per their discretion.

For Mydriatic screening, pupillary dilation alone takes additional 20 to 30 minutes, pupils are dilated with Tropicamide and Drosyn after application /instillation of the eye drops thrice with an interval of 10 minutes Dilation occurs after 20 mins. Furthermore, after pupillary dilation patient has decreased visual function for several hours and has limited access to transport. Dilation requires the presence of optometrists and ophthalmologists to diagnose narrow angles and prevent angle closure glaucoma.

Participants from Vellore diabetic clinic (108 patients) and from Tambaram diabetic clinic (112 patients) underwent fundus photography with Topcon fundus camera , mydriatic seven-field digital retinal colour photography. The 7 fields photographed were the macula, optic disc, superior-temporal, superior nasal, inferior nasal, inferior-temporal and temporal macula fields of each eye. The Topcon TRC-NW300 features a built-in 8 megapixel CCD camera, which gives high quality imaging. All-in-One Design - Auto Focus, Auto Exposure & Auto Shoot and Auto Small Pupil Detection. With advanced software that allows for accurate control of the capturing process, the TRC-NW300 can optimize the exposure settings and lower the flash intensity, thereby increasing patient comfort. The all-in one design is also beneficial for portability of the instrument.

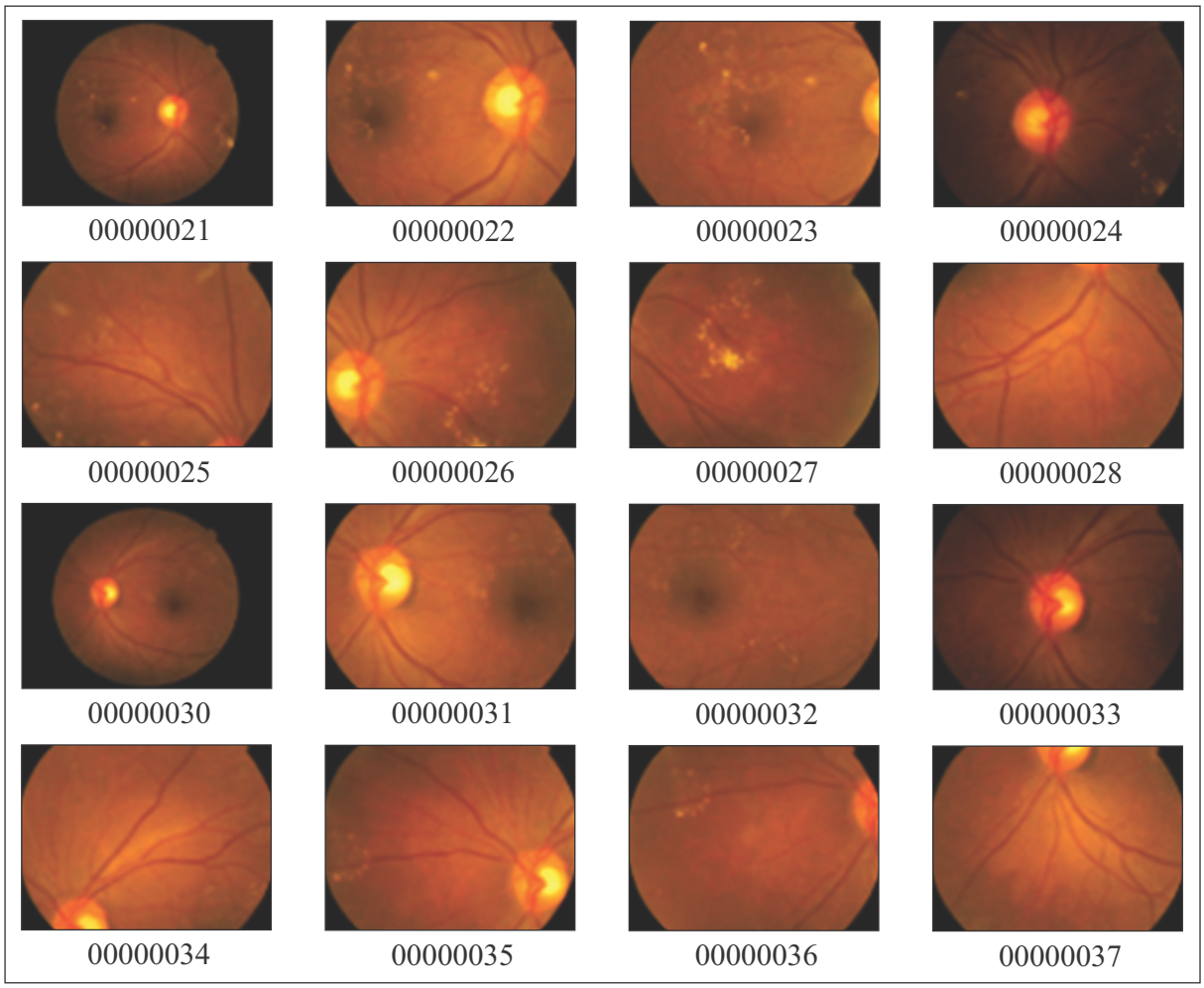

Fig: 34 Mydriatic seven field fundus photographs at diabetic clinic

Diagnostic Criteria Diabetic retinopathy was defined according to the International Clinical Diabetic Retinopathy Disease Severity Scale and severity of diabetic retinopathy was assessed. The minimum criterion for diagnosis of DR was the presence of at least one definite sign of DR in any field of the retina in seven field fundus photographs for each eye. Other incidental fundus photograph findings, other than diabetic retinopathy were also documented.

The grading of fundus features by the human grader- retinal specialist was recorded using the same protocol and was based on retinal features alone (no other clinical information was available to the photograph graders). The Algorithm assessed the retinal photographs for the presence or absence of DR. Sensitivity, specificity, positive and negative predictive values were evaluated.

Smart phone – Material and Methods

55 Participants then underwent fundus photography using the "Fundus on Phone" (FOP) smartphone based retinal imaging system (Remidio Innovative Solutions Pvt Ltd, Bangalore). Retinal Photographs recorded 4 fields which captured the macula, disc and nasal to the optic disc, superior-temporal and inferior-temporal quadrants .

The study period was Jan –Feb 2015 .The smart phone based portable retinal camera has Autofocus and is capable of being used in both clinical set-up and in screening camps . FOP has a 33 mm working distance, a 45 degree field of view, an optical magnification of 2X and +20 to -20 diopter adjustment. The retinal images can be transmitted using the smart phone The Fundus on phone can be fitted on to any standard slit lamp as shown in Fig - 35. Patient data is included in the retinal photographs for reporting process. Archival and retrieval of retinal photographs is done using the stored folder on the phone photos taken with permission from.

Rajalakshmi R, Arulmalar S, Usha M, Prathiba V, Kareemuddin KS, Anjana RM, et al. Validation of smartphone based retinal photography for diabetic retinopathy screening. PLoS One. 2015;10(9):1–10.

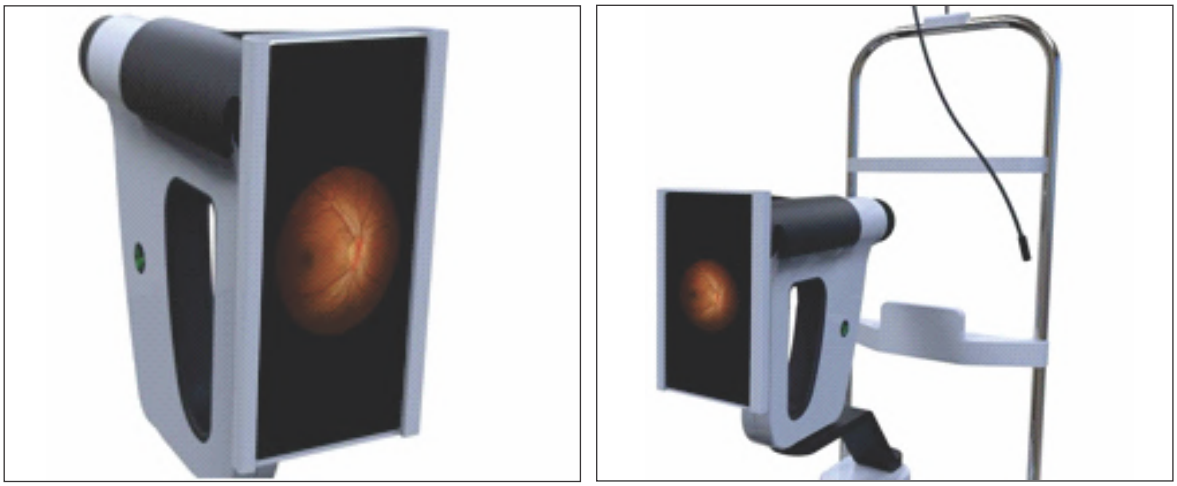

Fig: 35 Fundus on phone

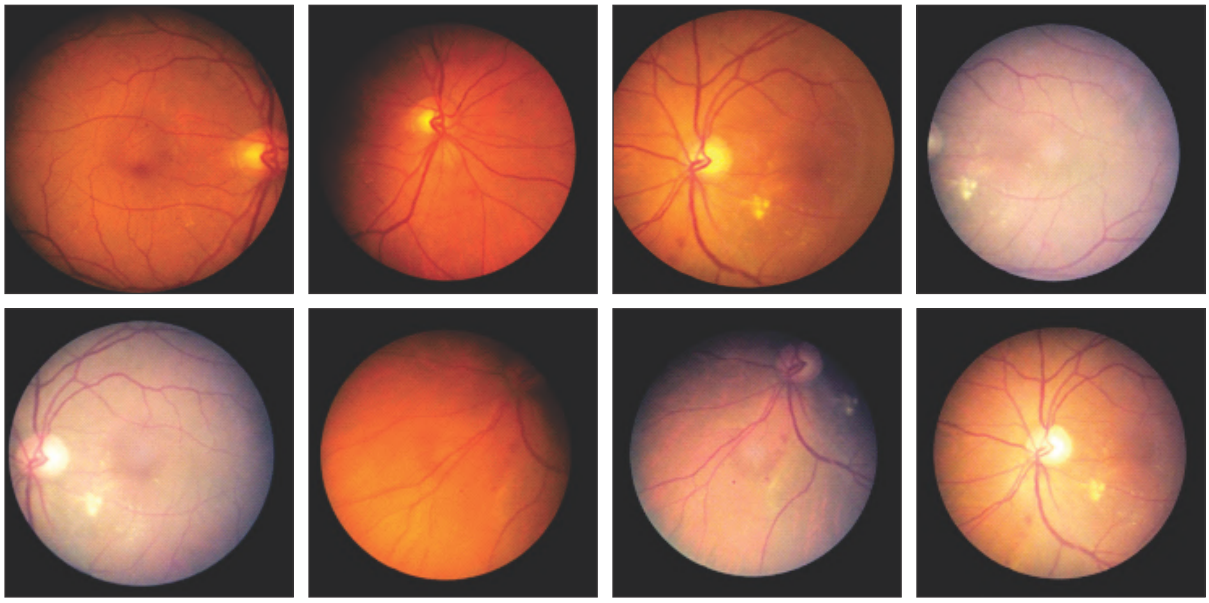

Fig : 36 Mydriatic fundus on phone

All photographs were coded with an identification number and uploaded to a secure database. All digital mydriatic fundus images, from the smart phone were reviewed by the same retinal specialist using the same liquid crystal display computer monitor of 1280·800 resolution. Each eye was assessed separately in a masked manner .

Diagnostic Criteria Diabetic retinopathy was defined according to the International Clinical Diabetic Retinopathy Disease Severity Scale. The diagnosis of diabetic retinopathy was made by the presence of signs of diabetic retinopathy including dot-blot hemorrhage, microaneurysms, cotton wool spots, Hard exudates, and neovascularization. Other incidental fundus photograph findings, other than diabetic retinopathy were also documented The minimum criterion for diagnosis of DR was the presence of at least one definite sign of DR in any field of the retina in the four field photographs for each eye.

The grading of fundal features by the human grader were recorded using the same protocol and was based on retinal features alone (no other clinical information was available to the retinal specialist). All retinal photos were assessed by the Algorithm for each eye separately for presence or absence of DR and gradability. Sensitivity, specificity, positive and negative predictive values were evaluated. "Fundus on Phone is cheaper than the mydriatric and nonmydriatric fundus cameras in India and is user friendly.

Data entry and Statistical analysis

Data Extraction

Before the subject leaves the examination centre, the entire datasheet was doubly checked for any deficiencies and to avoid wrong entries.

Dataset

All data was prepared in the microsoft excel 2013 format with de-identified patients' ID.

1) De-identification of patients' ID with new codes
2) Matching of patients' ID with image ID
3) Patients Age,sex , and duration of diabetes .
4) DR grading system
    a. We converted the DR severity grading based on the International Clinical Diabetic Retinopathy and Diabetic Macular Severity Level
    b. Referable DR was defined as presence of DR in any one field of the fundus photograph for each eye separately
    c. Other incidental fundus photograph findings, other than diabetic retinopathy were also documented

Statistical Analysis:

Evaluation protocol

The design of DR analyzer software as a data-driven system provides specific task-related metrics for evaluation. Performance compared to human expert drives the algorithm refinement process.

Module evaluation: The lesion-level performance of DR analyzer software detectors can be evaluated by comparing algorithm outputs C2 against lesion annotations provided by clinicians. Two methods of evaluation are used:

- FROC analysis (TPR vs FPPI): for lesion detectors, and
- ROC analysis (TPR vs FPR): for normal anatomy detectors and DR referral analytics module.

Metrics used: AUC (area under ROC curve), sensitivity, specificity, precision, accuracy, confusion matrix

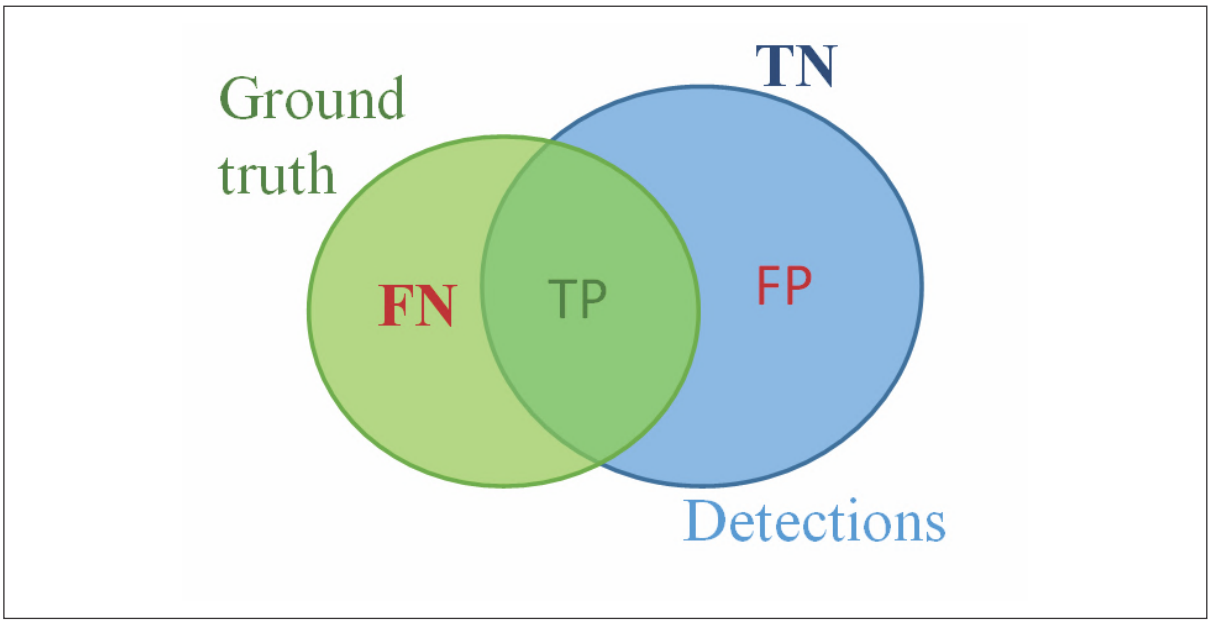

Fig 37

Lesion detection: computed per image

TP: true positive count: number of candidates that are true lesions according to ground truth

FP: false positive count: number of candidates that are not part of the ground truth

FN: false negative count: number of ground truth objects not detected (missed)

TN: true negatives: these are objects that were not detected, and also not part of the ground truth (agreement on negative).

Patient demographics and clinical measures of the eye were summarized for the sample with descriptive statistics.

Continuous variables were presented as mean + standard deviation or median with interquartile range (IQR) and categorical variables were presented as proportions. The algorithm processed the images fed into it using MATLAB software (MathWorks Inc., Natick, MA, USA) and provided numerical outputs for image gradability (image gradability score) and presence of DR (DR score). The image was considered gradable if the image gradability score was >0.1 and DR was considered to be present if the DR score was >0.55.. The cut offs were considered reasonable based on the beta testing during development and pilot testing before undertaking the study. The higher score, the greater was the confidence in gradability and presence of DR .

We determined disease status through undilated fundus examination by a retina specialist at the vitreoretinal outpatient service and the diabetic clinics and by a general ophthalmologist at the tele-camp setting, which served as the reference standard. Wherever possible, we determined the presence of vision threatening diabetic retinopathy (VTDR) defined as presence of severe NPDR or PDR and/or presence of diabetic macular edema as determined by the reference standard.

We estimated the primary outcome, the sensitivity of the algorithm to detect diabetic retinopathy for each camera modality from the three different settings compared to the reference standard, and included 95% Wilson confidence intervals (CI). The specificity, positive and negative predictive value (accuracy and precision respectively) was also estimated. The Area under the Receiver operator curve was also reported with 95% CI. For imaging at each of the three settings, we calculated inter-observer agreement for the primary outcome (presence or absence of DR) as well as a secondary outcome (image gradability) using a kappa statistic. All data was entered in Excel sheets (Microsoft Excel, Version 2010) and all statistical analysis were performed using STATA version 12.1, I/C (STATA Corp, Fortworth, Texas, USA). All P values less than 0.05 was taken as statistically significant.

Results and Analysis

Development of the Algorithm –by HTIC Madras - Results

Diabetic Retinopathy screening decision analytics for algorithm

Given the output of the lesion detection modules and the anatomy detection modules, the screening decision is learnt by training against several manually graded images. The publicly available MESSIDOR dataset and others was used to train the screening analytics module. The area under the curve for receiver operating characteristics (AUC) for DR decision on this dataset was evaluated, and sensitivity and specificity of >80% was achieved.(83% sensitivity at 80% specificity is seen) .

System redesign and Enhancements to a computer-assisted screening technology

Results of Macular edema development

Evaluated on a dataset of 587 retinal images of which 294 images were normal and 293 images contained CSME - clinically significant macular edema and other severe DR signs, the performance of the algorithm is 75% sensitivity at 74% specificity with an area under ROC curve of 0.83

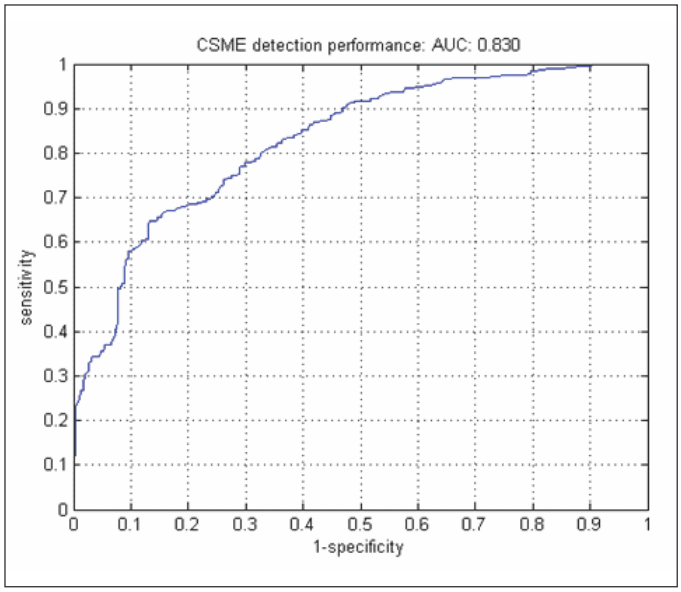

Fig 38: CSME detection performance : AUC: 0.830

Results of image quality assessment

Evaluated in full reference mode with 121 images the sensitivity achieved is 86% at specificity of 88% for image quality .

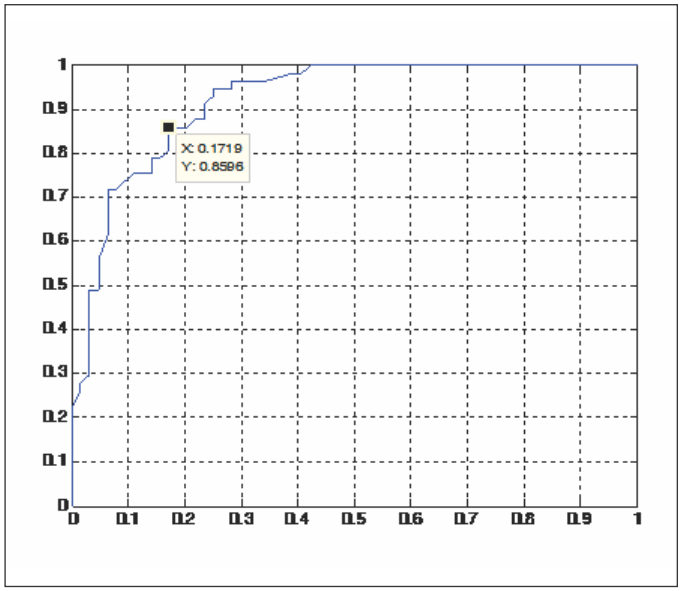

Fig 39: Image quality assessment- AUC

Poor quality image could be due to various factors: improper acquisition due to inadequate skill of the imaging technician, defects in the imaging device, loss during data transmission and storage, or even due to pathological conditions, cataract, bleeding, etc. A low quality image provided to the computer-assisted screening system might result in a misdiagnosis. The general strategy adopted in other works is to have a dedicated module for image quality assessment, and flag all poor quality assessment as abnormal, needing expert review. Having this module in place, which can work for various camera models, and intelligently identify and use only the images found fit for computer-analysis is also very important for the success of computer-assisted screening.

Results of PDR signs detection

The ROC analysis for PDR signs detection was performed on 1052 images, and the area under the ROC curve is 0.89, with a sensitivity of 82% at specificity of 80%. For performing the ROC analysis, a folded cross-validation strategy was used, where 10-folds were used, so that 90% of the images are in the training set and 10% of the images are in the test set. The holdout 10% is randomized and repeated with replacement, so every image gets tested as a result when performing the cross-validation 10 times. The resulting ROC curve is plotted between sensitivity, as the capability to identify PDR cases from the 1052 images, and specificity, which is the false-positive rate (rate of reporting a non-PDR image as PDR). The equal point on the ROC curve is achieved at 81% sensitivity and specificity.

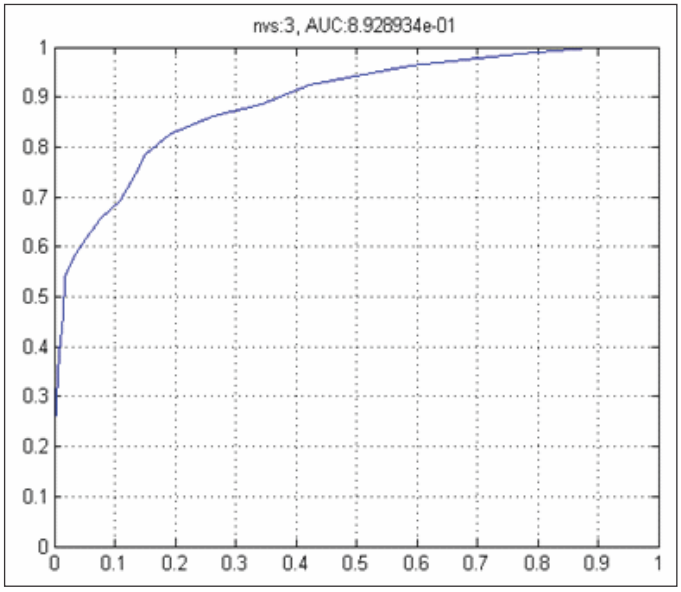

Fig : 40 Proliferative Diabetic Retinopathy- AUC

Performance on 981 patients of SN Dreams :

According to the previous Sankara Nethralaya Diabetic Retinopathy Study, retrospective retinal photographs of 981 patients were analyzed to develop the first version of the software application.The SN-DREAMS dataset using Zeiss FF450 plus fundus camera each imaged with 7 field mydriatic 30 degree imaging in both eyes. The total set has 20177 images, of which 18597 images are marked as gradable.

The number of images graded as DR present by two experts is 2601 out of 20177 (12%) with the rest being DR absent. This dataset represents an epidemiological sampling of a diabetic population in and around Chennai. Thus less than 15% of the images contain DR, and this challenges the algorithm by posing a large data imbalance between the number of normal images and DR positive images. Therefore folded validation was taken up, in order to maximize the chance of the algorithm training with the DR positives.

The performance of the developed algorithm was evaluated with 10 fold cross validation, using 90% of the images for training and the remaining for evaluation. This method is randomized with replacement for the folds, so every image is predicted at least once.The performance with this strategy is observed using Receiver operating characteristics (ROC) analysis, taking the DR confidence scores and computing the sensitivity and specificity at a range of thresholds on the confidence scores.The resulting ROC curve has an area under the curve of 0.786,with the equal sensitivity specificity at 71%..

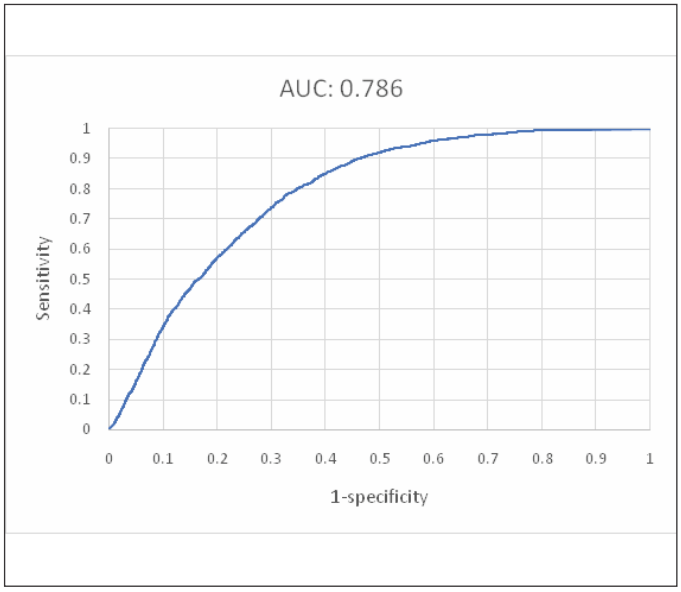

Fig: 41 SN DREAMS 981 PATIENTS ROC CURVE

The system has been built following the same set of principles and technology that drives other well-studied programs such as the Iowa Detection Program, Scottish national DR screening software (D.Fleming, et al., 2010). Such systems have been shown to perform to standards comparable to experts, and reduce screening workload. With sufficient training the HTIC DR screening system shall become capable of addressing the need of automated DR screening in India

Validation of the Algorithm

I. Results from Diabetic retinopathy grading from the Sankara Nethralaya vitreoretinal out – patient department:

A. Demographics and DR status: We enrolled 848 eyes of 485 patients to test the accuracy of the algorithm to detect DR in the outpatient setting of a high volume tertiary referral vitreoretinal clinic. The mean age of participants was 58.2+7.5 years (median=58 years, IQR=53 – 63 years, range=41 – 76) and 68% were men. The mean duration of diabetes in this cohort was 13.1+7.9 years (median=13 years, IQR=7-20 years, range=0.5 – 34 years) and the mean fasting blood sugar was 128+45mg% (median = 120mg%, IQR=100-149mg%, range=70-250mg%).

B. Algorithm Descriptive: The Algorithm successfully graded 634 out of 848 possible images (75%) and diagnosed presence of DR in 583 images.

The mean image gradability score was 0.15+0.06 (median=0.145, IQR= 0.09 – 0.19). The gradeability score for gradable images was 0.17+0.06 in eyes with gradable images compared to 0.08+0.02 for those with ungradable images ($p<0.001$, Wilcoxon test).

The overall DR score was 0.57+0.25 (median=0.63, IQR=0.49-0.73). Eyes with DR had a mean score of 0.71+0.1 and those without DR had a DR score of 0.28+0.2 ($p<0.001$, Wilcoxon test).

C. Algorithm vs. Ophthalmologist:

Table 11 : Gradability

Algorithm Gradability	Ophthalmologist Gradability		Total
	Ungradable	Gradable	
Ungradable	4 (44%)	210 (25%)	214 (25%)
Gradable	5 (56%)	629 (75%)	634 (75%)
Total	9 (100%)	839 (100%)	848 (100%)

Compared to the ophthalmologist (Gold standard), 25% images were ungradable by the algorithm. Overall, the ophthalmologist found only 9 images to be ungradable compared to 214 images by the algorithm. There was only slight agreement in terms of image gradability between the ophthalmologist and algorithm, Kappa= 0.016 (95% CI = -0.013 – 0.044).

Table 12: Sensitivity and Specificity of Algorithm to detect DR compared to Ophthalmologist.

Algorithm DR grading	Ophthalmologist DR grading		Total
	Absent	Present	
Absent	134 (55%)	130 (22%)	264 (31%)
Present	109 (45%)	469 (78%)	578 (69%)
Total	243 (100%)	599 (100%)	842 (100%)

Above is a 2X2 table showing actual DR grading between algorithm and ophthalmologist.

Table 13

Algorithm vs. Ophthalmologist	Value	95% Confidence interval
Sensitivity	78.30%	74.78% to 81.54%
Specificity	55.14%	48.65% to 61.51%
Positive Predictive Value	81.14%	77.71% to 84.25%
Negative Predictive Value	50.76%	44.56% to 56.94%

Table 14: Sensitivity and Specificity of Algorithm to detect DR compared to Ophthalmologist in only images gradable by the Algorithm.

Algorithm DR grading*	Ophthalmologist DR grading		Total
	Absent	Present	
Absent	104 (57%)	94 (21%)	198 (31.4%)
Present	79 (43.2%)	353 (79%)	432 (69%)
Total	183 (100%)	447 (100%)	630 (100%)

*Only Gradable images

Above is a 2X2 table showing actual DR grading between algorithm and ophthalmologist using only gradable images by the algorithm.

Table 15

Algorithm vs. Ophthalmologist*	Value	95% Confidence interval
Sensitivity	78.9%	74.90% to 82.66%
Specificity	56.83%	49.32% to 64.12%
Positive Predictive Value	81.71%	77.74% to 85.25%
Negative Predictive Value	52.53%	45.32% to 59.65%

*Only Gradable images

The sensitivity of the algorithm to detect DR was found to be 79% and specificity was found to be 57% in detecting DR compared to ophthalmologist .

The area under the receiver operator curve was 0.67 (95%CI=0.63 to 0.71).

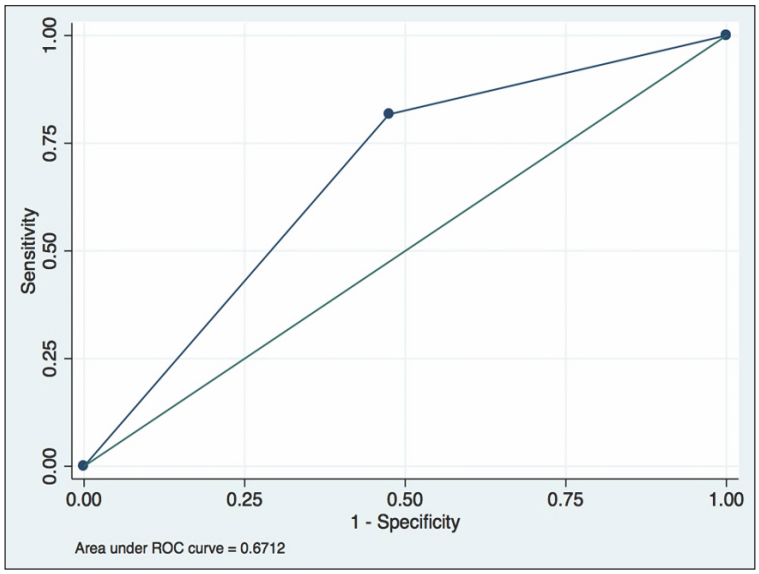

Fig 42

Table 16: Differences in gradability in VTDR compared to non-VTDR.

Algorithm Gradability	Ophthalmologist VTDR		Total
	No VTDR	VTDR	
Ungradable	107 (27%)	107 (24%)	214 (25%)
Gradable	292 (73%)	342 (75%)	634 (75%)
Total	399 (100%)	499 (100%)	848 (100%)

P=0.32, chi square test.
There was no difference in image gradability of the algorithm based on the VTDR status of the eye as graded by the ophthalmologist.

Table 17: Internal validity of the Algorithm grading

Algorithm Gradability	DR status		Total
	No DR	DR	
Ungradable	67 (31%)	147 (69%)	214 (100%)
Gradable	198 (31%)	436 (69%)	634 (100%)
Total	265 (31%)	583 (69%)	848 (100%)

Out of the 214 eyes that were deemed ungradable by the algorithm, 147 (69%) was reported to have DR, showing internal inconsistency of the algorithm.

D. Algorithm vs. Optometrist Grading

Table 18: Gradability

Algorithm Gradability	Optometrist Gradability		Total
	Ungradable	Gradable	
Ungradable	3 (27%)	211 (25%)	214 (25%)
Gradable	8 (73%)	625 (75%)	633 (75%)
Total	11 (100%)	836 (100%)	847 (100%)

Compared to the optometrist, 25% images were ungradable by the algorithm. Overall, the optometrist found only 11 images to be ungradable compared to 214 images by the algorithm. There was only slight agreement in terms of image gradability between the ophthalmologist and algorithm, Kappa= 0.002 (95% CI = -0.024 – 0.028).

Table 19 :Sensitivity and Specificity of Algorithm to detect DR compared to Optometrist.

Algorithm DR grading	Optometrist DR grading		Total
	Absent	Present	
Absent	113 (56%)	150 (24%)	263
Present	89 (44%)	484 (76%)	573
Total	202 (100%)	634 (100%)	836 (100%)

Above is a 2X2 table showing actual DR grading between algorithm and optometrist.

Table 20

Algorithm vs. Optometrist	Value	95% Confidence interval
Sensitivity	76.3%	72.84% to 79.60%
Specificity	55.94%	48.80% to 62.90%
Positive Predictive Value	84.47%	81.24% to 87.34%
Negative Predictive Value	42.97%	36.90% to 49.19%

Table 21: Sensitivity and Specificity of Algorithm to detect DR compared to Optometrist in only images gradable by the Algorithm.

Algorithm DR grading*	Optometrist DR grading		Total
	Absent	Present	
Absent	90 (59%)	108 (23%)	198 (32%)
Present	63 (41%)	364 (77%)	427 (68%)
Total	153	472	625

*Only Gradable images

Above is a 2X2 table showing actual DR grading between algorithm and optometrist using only gradable images by the algorithm.

Table 22

Algorithm vs. Optometrist*	Value	95% Confidence interval
Sensitivity	77.12%	73.06% to 80.83%
Specificity	58.82%	50.59% to 66.71%
Positive Predictive Value	85.25%	81.52% to 88.47%
Negative Predictive Value	45.45%	38.38% to 52.67%

*Only Gradable images

The sensitivity of the algorithm to detect DR was found to be 77% and specificity was found to be 59% in detecting DR compared to Optometrist

The area under the receiver operator curve was 0.63 (95%CI=0.60 to 0.67).

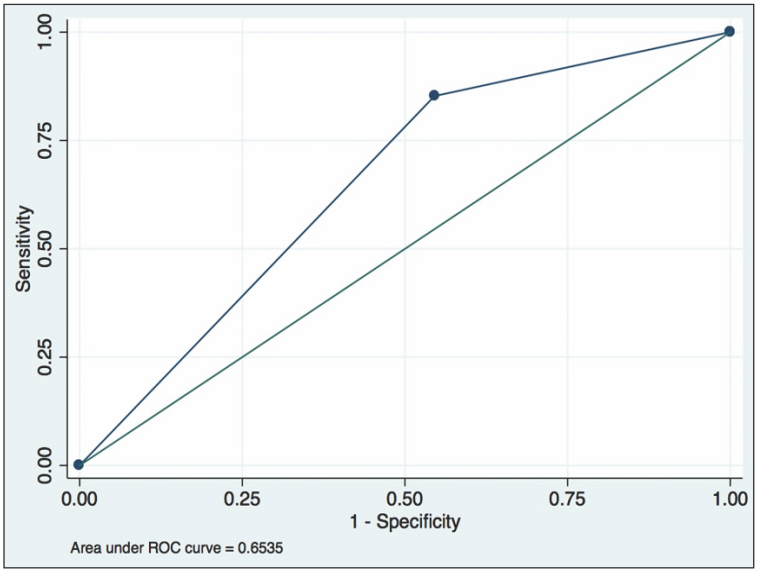

Fig 43

Table 23: Differences in gradability in VTDR compared to non-VTDR.

Algorithm Gradability	Optometrist VTDR		Total
	No VTDR	VTDR	
Ungradable	93 (29%)	120 (23%)	213 (25%)
Gradable	233 (71%)	400 (73%)	633 (75%)
Total	326 (100%)	520 (100%)	846 (100%)

P=0.08, chi square test.

There was no difference in image gradability of the algorithm based on the VTDR status of the eye as graded by the ophthalmologist.

E. Comparison of Ophthalmologist and Optometrist in SN VR OPD

Table 24: Kappa Statistics for agreement

Variable	Optometrist Gradability	
	Kappa	95%CI
Gradability	0.494	0.224 - 0.765
DR Presence (Yes/No)	0.804	0.758 - 0.849
DR status	0.584	0.548 - 0.611
VTDR	0.667	0.617 - 0.71

Table 25: Sensitivity and Specificity of Optometrist to detect DR compared to Ophthalmologist

Ophthalmologist DR grading	Optometrist DR grading		Total
	Absent	Present	
Absent	189 (79%)	13 (2%)	202 (24%)
Present	51 (21%)	582 (98%)	633 (76%)
Total	240 (100%)	595 (100%)	835 (100%)

Above is a 2X2 table showing actual DR grading between optometrist and ophthalmologist.

Table 26

Ophthalmologist vs. Optometrist	Value	95% Confidence interval
Sensitivity	97.81%	96.29% to 98.83%
Specificity	78.42%	72.69% to 83.45%
Positive Predictive Value	91.79%	89.37% to 93.80%
Negative Predictive Value	93.56%	89.25% to 96.53%

The sensitivity of the optometrist to detect DR was found to be 98% and specificity was 78% in detecting DR compared to ophthalmologist.

The area under the receiver operator curve was 0.92 (95%CI=0.91 to 0.94).

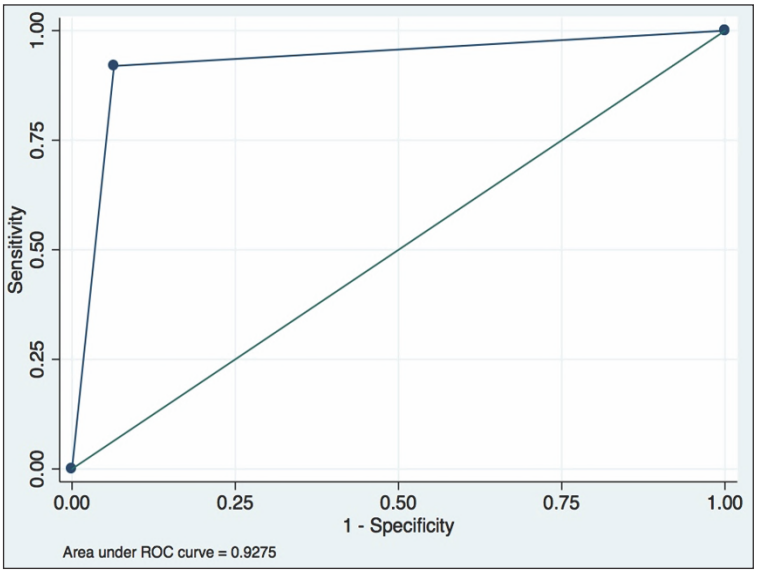

Fig 44

Results summary from use of Algorithm on images obtained from SN VR OPD using non-mydriatic Forus camera:

* 1. The Algorithm is interpreting too many images as ungradable currently compared to both Ophthalmologist (Gold standard) and Optometrist.

* 2. The Algorithm is showing approximately 76 - 78% sensitivity and about 50 - 55% specificity in automated detection of DR

* 3. The Area under the curve is Less than 67% even if only gradable images are taken

* 4. Inconsistency within Algorithm: When image is ungradable by algorithm, still 69% shows DR present. This should be either 100% or ZERO.

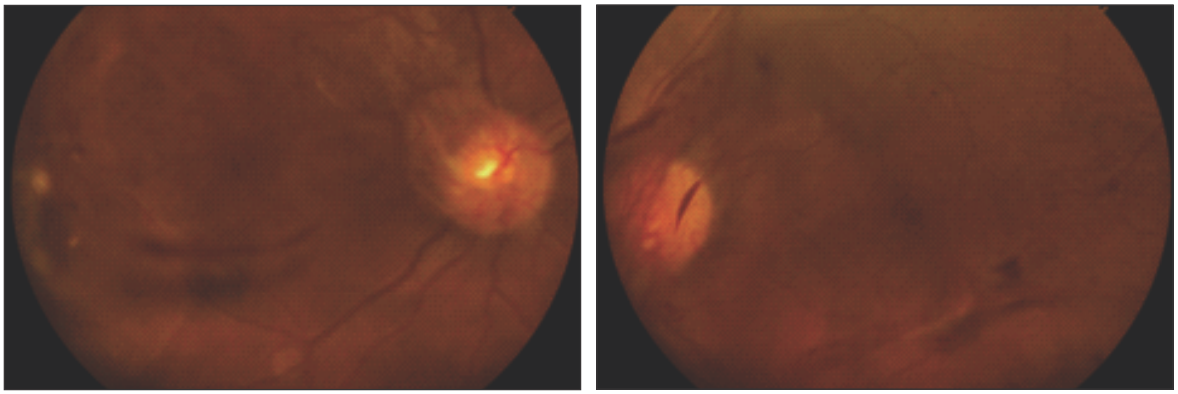

Fig 45 False negative fundus photograph – vitreous haemorrhage

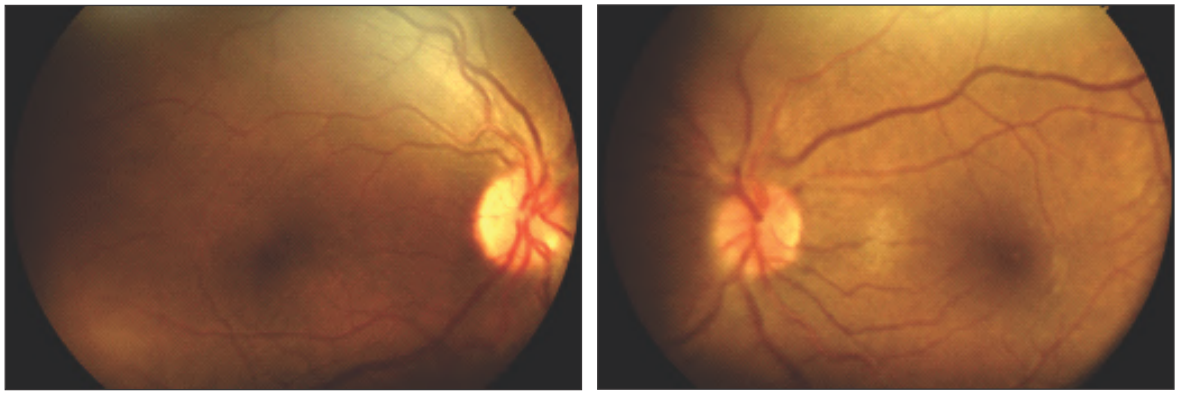

Fig 46 False Positive fundus photograph – Increase in illumination

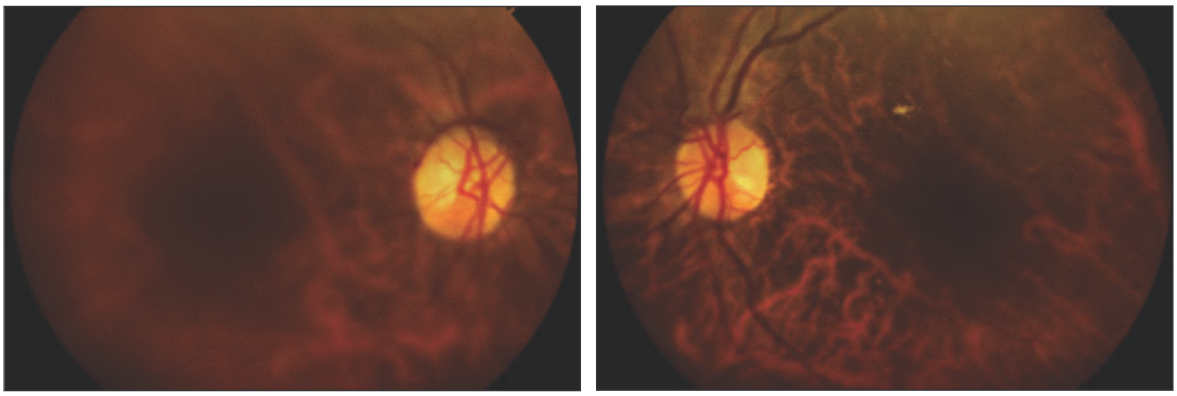

Fig 47 False Positive fundus photograph – Choroidal Sclerosis

Results from Diabetic retinopathy grading from the Tele-ophthalmology camps:

A. Demographics and DR status: We enrolled 939 eyes of 472 patients to test the accuracy of the algorithm to detect DR in the tele-ophthalmology setting. The mean age of participants was 54.5+10.9 years (median=54 years, IQR=47 – 61 years, range=34 – 83) and 66% were men. The mean duration of diabetes in this cohort was 6.9+6.2 years (median=5 years, IQR=2-10 years, range=0.5 – 25 years).

B. Algorithm Descriptive: The Algorithm successfully graded 478 out of 939 possible images (51%) and diagnosed presence of DR in 262 images.

The mean image gradability score was 0.11+0.0 (median=0.103, IQR= 0.03 – 0.17). The gradability score for gradable images was 0.18+0.06 in eyes with gradable images compared to 0.03+0.03 for those with ungradable images ($p<0.001$, Wilcoxon test).

The overall DR score was 0.37+0.28 (median=0.34, IQR=0.12-0.57). Eyes with DR had a mean score of 0.73+0.13 and those without DR had a DR score of 0.22+0.17 ($p<0.001$, Wilcoxon test).

C. Algorithm vs. Ophthalmologist:

Table 27 Gradability

Algorithm Gradability	Ophthalmologist Gradability		Total
	Ungradable	Gradable	
Ungradable	25 (59%)	436 (49%)	461 (49%)
Gradable	17 (41%)	461 (51%)	478 (51%)
Total	42 (100%)	897 (100%)	939 (100%)

Compared to the ophthalmologist (Gold standard), 49% images were ungradable by the algorithm. Overall, the ophthalmologist found only 42 images to be ungradable compared to 461 images by the algorithm. There was only slight agreement in terms of image gradability between the ophthalmologist and algorithm, Kappa= 0.019 (95%CI= -0.008 - 0.046).

Table 28 Sensitivity and Specificity of Algorithm to detect DR compared to Ophthalmologist.

Algorithm DR grading	Ophthalmologist DR grading		Total
	Absent	Present	
Absent	619 (79%)	23 (20%)	642 (72%)
Present	162 (21%)	93 (80%)	255 (28%)
Total	781 (100%)	116 (100%)	897 (100%)

Above is a 2X2 table showing actual DR grading between algorithm and ophthalmologist.

Table 29

Algorithm vs. Ophthalmologist	Value	95% Confidence interval
Sensitivity	80.17%	71.75% to 87.00%
Specificity	79.26%	76.24% to 82.05%
Positive Predictive Value	36.47%	30.55% to 42.70%
Negative Predictive Value	96.42%	94.67% to 97.72%

Table 30: Sensitivity and Specificity of Algorithm to detect DR compared to Ophthalmologist in only images gradable by the Algorithm.

Algorithm DR grading*	Ophthalmologist DR grading		Total
	Absent	Present	
Absent	316 (80%)	10 (15%)	326 (70%)
Present	79 (20%)	56 (85%)	135 (30%)
Total	395 (100%)	66 (100%)	461 (100%)

*Only Gradable images

Above is a 2X2 table showing actual DR grading between algorithm and ophthalmologist using only gradable images by the algorithm.

Table 31

Algorithm vs. Ophthalmologist*	Value	95% Confidence interval
Sensitivity	84.85%	73.90% to 92.49%
Specificity	80.00%	75.71% to 83.83%
Positive Predictive Value	41.48%	33.07% to 50.27%
Negative Predictive Value	96.93%	94.43% to 98.52%

*Only Gradable images

The sensitivity of the algorithm to detect DR was found to be 85% and specificity was found to be 80% in detecting DR compared to ophthalmologist

The area under the receiver operator curve was 0.69 (95%CI=0.65 to 0.73).

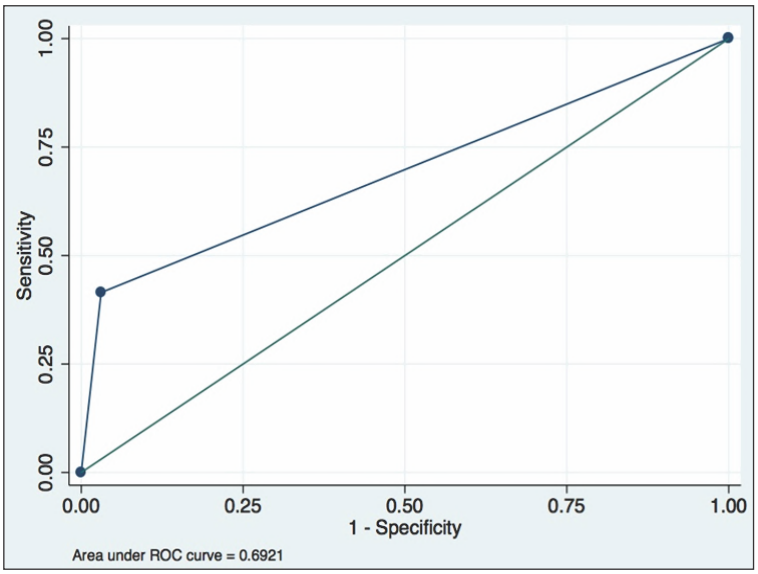

Fig 48

Table 32 : Differences in gradability in VTDR compared to non-VTDR.

Algorithm Gradability	Ophthalmologist VTDR		Total
	No VTDR	VTDR	
Ungradable	423 (49%)	13 (46%)	436 (49%)
Gradable	446 (51%)	15 (54%)	461 (51%)
Total	869 (100%)	28 (100%)	897 (100%)

P=0.81, chi square test.

There was no difference in image gradability of the algorithm based on the VTDR status of the eye as graded by the ophthalmologist.

Table 33: Internal validity of the Algorithm grading

Algorithm Gradability	DR status		Total
	No DR	DR	
Ungradable	338 (73%)	123 (27%)	461 (100%)
Gradable	339 (71%)	139 (29%)	478 (100%)
Total	677 (72%)	262 (28%)	939 (100%)

Out of the 461 eyes that were deemed ungradable by the algorithm, 123 (27%) was reported to have DR, showing internal inconsistency of the algorithm.

D. Algorithm vs Fundus Photographer Grading

Table 34 Gradability

Algorithm Gradability	Photographer Gradability		Total
	Ungradable	Gradable	
Ungradable	25 (50%)	436 (49%)	461 (49%)
Gradable	25 (50%)	453 (51%)	478 (100%)
Total	50 (100%)	889 (100%)	939 (100%)

Compared to the photographer, 49% images were ungradable by the algorithm. Overall, the ophthalmologist found only 50 images to be ungradable compared to 461 images by the algorithm. There was only slight agreement in terms of image gradability between the ophthalmologist and algorithm, Kappa= 0.002 (95&CI= -0.027 - 0.031).

Table 35: Sensitivity and Specificity of Algorithm to detect DR compared to Photographer

Algorithm DR grading	Photographer DR grading		Total
	Absent	Present	
Absent	622 (78%)	22 (24%)	644 (72%)
Present	174 (22%)	71 (76%)	245 (28%)
Total	796 (100%)	93 (100%)	889 (100%)

Above is a 2X2 table showing actual DR grading between algorithm and photographer.

Table 36

Algorithm vs. Photographer	Value	95% Confidence interval
Sensitivity	76.34%	66.40% to 84.54%
Specificity	78.14%	75.11% to 80.97%
Positive Predictive Value	28.98%	23.38% to 35.10%
Negative Predictive Value	96.58%	94.87% to 97.85%

Table 37: Sensitivity and Specificity of Algorithm to detect DR compared to Photographer in only images gradable by the Algorithm

Algorithm DR grading*	Photographer DR grading		Total
	Absent	Present	
Absent	316 (78%)	9 (18%)	325 (72%)
Present	88 (22%)	40 (82%)	128 (28%)
Total	404 (100%)	49 (100%)	453 (100%)

*Only Gradable images

Above is a 2X2 table showing actual DR grading between algorithm and photographer using only gradable images by the algorithm.

Table 38

Algorithm vs. Photographer *	Value	95% Confidence interval
Sensitivity	81.63%	67.98% to 91.24%
Specificity	78.22%	73.87% to 82.15%
Positive Predictive Value	31.25%	23.35% to 40.04%
Negative Predictive Value	97.23%	94.81% to 98.73%

*Only Gradable images

The sensitivity of the algorithm to detect DR was found to be 82% and specificity was found to be 78% in detecting DR compared to Optometrist

The area under the receiver operator curve was 0.64 (95%CI=0.60to 0.68).

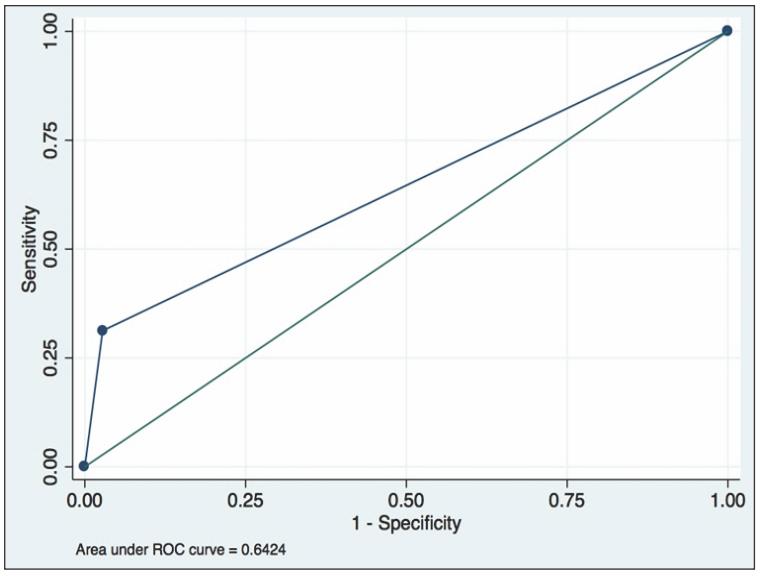

Fig 49

Table 39: Differences in gradability in VTDR compared to non-VTDR

Algorithm Gradability	Photographer VTDR		Total
	No VTDR	VTDR	
Ungradable	424 (49%)	12 (48%)	436 (49%)
Gradable	440 (51%)	13 (52%)	453 (51%)
Total	864 (100%)	25 (100%)	889 (100%)

P=0.92, chi square test.

There was no difference in image gradability of the algorithm based on the VTDR status of the eye as graded by the photographer.

E. Comparison of Ophthalmologist and Photographer in Tele-Ophthalmology

Table 40: Kappa Statistics for agreement

Variable	Photographer Gradability	
	Kappa	95%CI
Gradability	0.292	0.164 - 0.419
DR Presence (Yes/No)	0.903	0.858 - 0.949
DR grade	0.782	0.755 - 0.787
VTDR	0.979	0.938 - 1.000

Table 41: Sensitivity and Specificity of Photographer to detect DR compared to Ophthalmologist

Photographer DR grading	Ophthalmologist DR grading		Total
	Absent	Present	
Absent	754 (99.5%)	15 (14%)	769 (89%)
Present	2 (<1%)	91 (85%)	93 (11%)
Total	756 (100%)	106 (100%)	862 (100%)

Above is a 2X2 table showing actual DR grading between optometrist and ophthalmologist

Table 42

Ophthalmologist vs. Photographer	Value	95% Confidence interval
Sensitivity	85.85%	77.74% to 91.86%
Specificity	99.74%	99.05% to 99.97%
Positive Predictive Value	97.85%	92.45% to 99.74%
Negative Predictive Value	98.05%	96.80% to 98.90%

The sensitivity of the photographer to detect DR was found to be 86% and specificity was 99% in detecting DR compared to ophthalmologist.

The area under the receiver operator curve was 0.98 (95%CI=0.96 to 0.99).

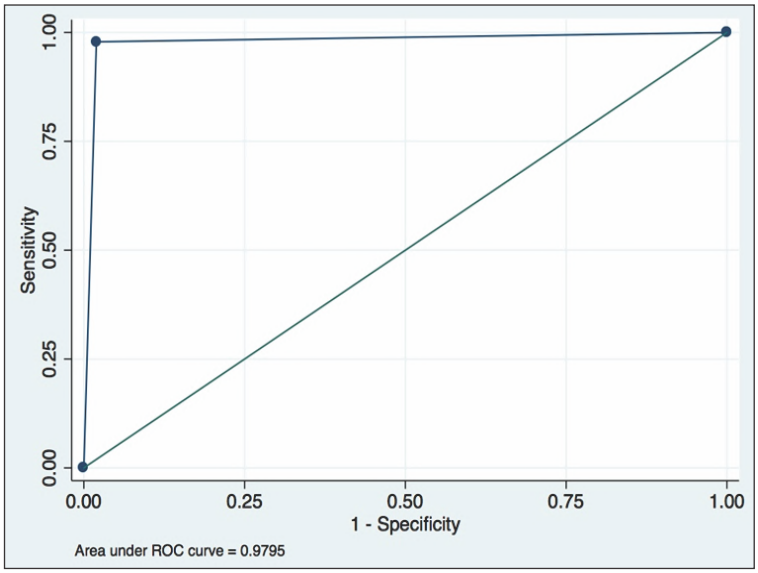

Fig 50

Results summary from use of Algorithm on images obtained from Tele-Ophthalmology camps using non-mydriatic Topcon camera:

* 1. The Algorithm is interpreting too many images as ungradable currently compared to both Ophthalmologist (Gold standard) as well as photographer.

* 2. The Algorithm is showing approximately 76 - 84% sensitivity and about 78 - 80% specificity in automated detection of DR

* 3. The Area under the curve is Less than 70% even if only gradable images are taken.

* 4. Algorithm highly overestimates presence of DR when it can grade the image, this is not seen with the SN VR OPD data

* 5. Inconsistency within Algorithm: When image is ungradable by algorithm, still 27% shows DR present. This should be either 100% or ZERO.

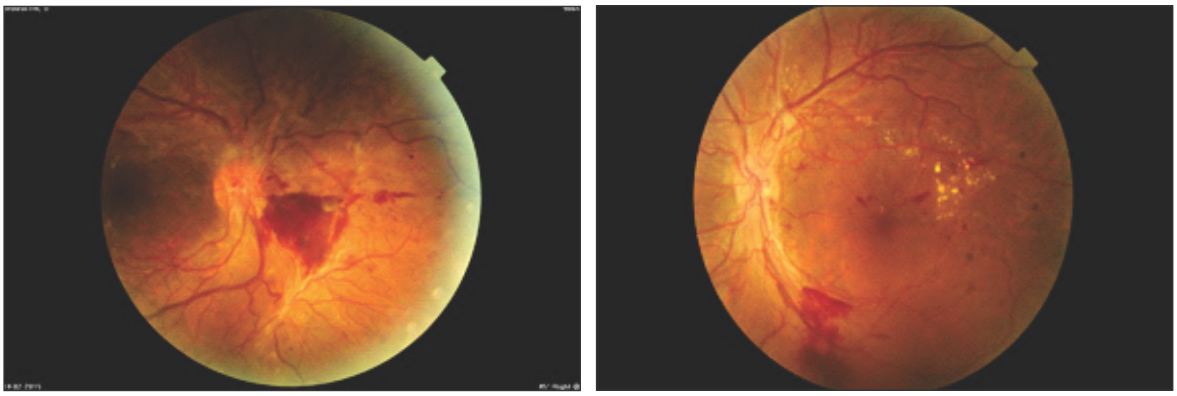

Fig : 51 Tele camps – Algorithm diagnosed DR (PDR)

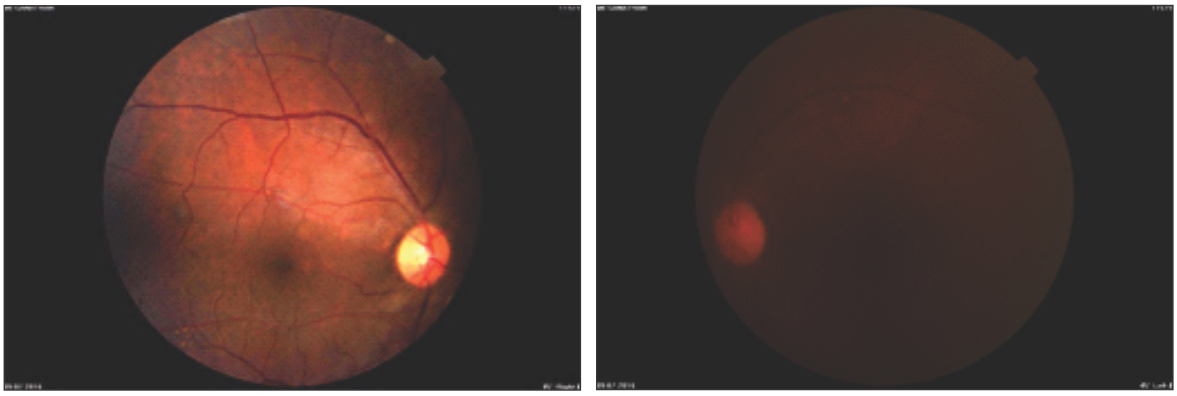

Fig : 52 Tele camps – Cataract changes - ungradable images

Results from Diabetic retinopathy grading from the Diabetic clinics 1 using the non-mydriatic FORUS camera:

A. Demographics and DR status: We enrolled 2526 eyes of 1263 patients to test the accuracy of the algorithm to detect DR in the diabetic clinic setting. The mean age of participants was 54.5+10.6 years (median=55 years, IQR=46 – 62 years, range=34 – 83) and 66% were men. The mean duration of diabetes in this cohort was 8.5+7.3 years (median=7 years, IQR=3-12 years, range=0.5 – 30 years).

B. Algorithm Descriptive: The Algorithm successfully graded 2153 out of 2526 possible images (85%) and diagnosed presence of DR in 594 images.

The mean image gradability score was 0.20+0.10 (median=0.20, IQR= 0.14 – 0.27). The gradability score for gradable images was 0.23+0.08 in eyes with gradable images compared to 0.05+0.03 for those with ungradable images ($p<0.001$, Wilcoxon test).

The overall DR score was 0.29+0.24 (median=0.27, IQR=0.08-0.45). Eyes with DR had a mean score of 0.70+0.12 and those without DR had a DR score of 0.22+0.17 ($p<0.001$, Wilcoxon test).

C. Algorithm vs. Ophthalmologist:

Table 43: Gradability

Algorithm Gradability	Ophthalmologist Gradability		Total
	Ungradable	Gradable	
Ungradable	4 (14%)	369 (15%)	373 (15%)
Gradable	24 (86%)	2129 (85%)	2153 (85%)
Total	28 (100%)	2498 (100%)	2526 (100%)

Compared to the ophthalmologist (Gold standard), 15% images were ungradable by the algorithm. Overall, the ophthalmologist found only 28 images to be ungradable compared to 373 images by the algorithm. There was only slight agreement in terms of image gradability between the ophthalmologist and algorithm, Kappa= -0.001 (95%Ci= -0.019 - 0.018).

Table 44: Sensitivity and Specificity of Algorithm to detect DR compared to Ophthalmologist

Algorithm DR grading	Ophthalmologist DR grading		Total
	Absent	Present	
Absent	1841 (80%)	68 (37%)	1909 (76%)
Present	471 (20%)	116 (63%)	587 (24%)
Total	2312 (100%)	184 (100%)	2496 (100%)

Above is a 2X2 table showing actual DR grading between algorithm and ophthalmologist

Table 45

Algorithm vs. Ophthalmologist	Value	95% Confidence interval
Sensitivity	63.04%	55.63% to 70.03%
Specificity	79.63%	77.93% to 81.25%
Positive Predictive Value	19.76%	16.61% to 23.22%
Negative Predictive Value	96.44%	95.51% to 97.22%

Table 46: Sensitivity and Specificity of Algorithm to detect DR compared to Ophthalmologist in only images gradable by the Algorithm

Algorithm DR grading*	Ophthalmologist DR grading		Total
	Absent	Present	
Absent	1541 (78%)	57 (37%)	1598 (75%)
Present	431 (22%)	98 (63%)	529 (25%)
Total	1972 (100%)	155 (100%)	2127 (100%)

*Only Gradable images

Above is a 2X2 table showing actual DR grading between algorithm and ophthalmologist using only gradable images by the algorithm.

Table 47

Algorithm vs. Ophthalmologist*	Value	95% Confidence interval
Sensitivity	63.23%	55.12% to 70.82%
Specificity	78.14%	76.25% to 79.95%
Positive Predictive Value	18.53%	15.30% to 22.10%
Negative Predictive Value	96.43%	95.40% to 97.29%

*Only Gradable images

The sensitivity of the algorithm to detect DR was found to be 63% and specificity was found to be 78% in detecting DR compared to ophthalmologist

The area under the receiver operator curve was 0.57 (95%CI=0.55 to 0.59).

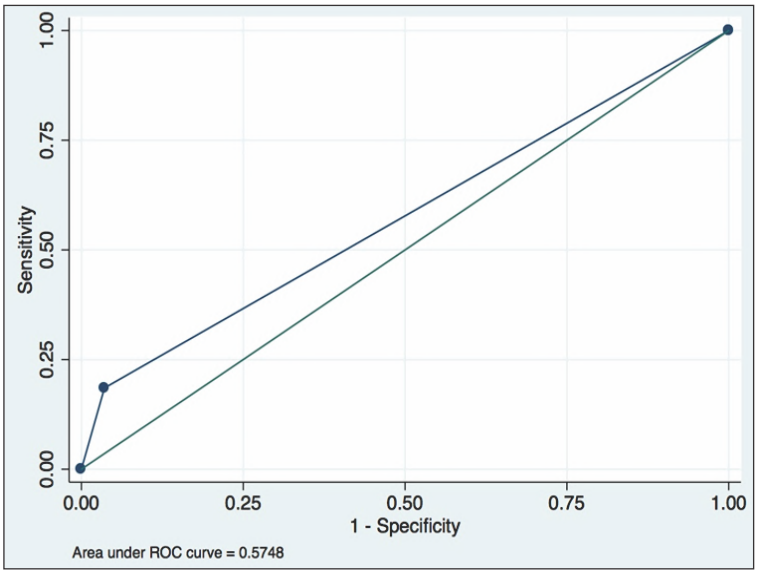

Fig 53

Table 48: Internal validity of the Algorithm grading

Algorithm Gradability	DR status		Total
	No DR	DR	
Ungradable	315 (84%)	58 (16%)	373 (100%)
Gradable	1617 (75%)	536 (25%)	2153 (100%)
Total	1932 (76%)	594 (24%)	2526 (100%)

Out of the 373 eyes that were deemed ungradable by the algorithm, 58 (16%) was reported to have DR, showing some internal inconsistency of the algorithm.

D. Algorithm vs. Optometrist Grading

Table 49: Gradability

Algorithm Gradability	Optometrist Gradability		Total
	Ungradable	Gradable	
Ungradable	5 (19%)	368 (15%)	373 (15%)
Gradable	21 (81%)	2132 (85%)	2153 (85%)
Total	26 (100%)	2500 (100%)	2526 (100%)

Compared to the optometrist, 15% images were ungradable by the algorithm. Overall, the ophthalmologist found only 26 images to be ungradable compared to 373 images by the algorithm. There was only slight agreement in terms of image gradability between the ophthalmologist and algorithm, Kappa= 0.006 (95%CI = -0.014 - 0.026).

Table 50: Sensitivity and Specificity of Algorithm to detect DR compared to Optometrist

Algorithm DR grading	Optometrist DR grading		Total
	Absent	Present	
Absent	1849 (79%)	63 (39%)	1912 (76%)
Present	490 (21%)	98 (61%)	588 (24%)
Total	2339 (100%)	161 (100%)	2500 (100%)

Above is a 2X2 table showing actual DR grading between algorithm and ophthalmologist.

Table 51

Algorithm vs. Optometrist	Value	95% Confidence interval
Sensitivity	60.87%	52.88% to 68.45%
Specificity	79.05%	77.34% to 80.68%
Positive Predictive Value	16.67%	13.74% to 19.93%
Negative Predictive Value	96.71%	95.80% to 97.46%

Table 52: Sensitivity and Specificity of Algorithm to detect DR compared to Optometrist in only images gradable by the Algorithm

Algorithm DR grading*	Optometrist DR grading		Total
	Absent	Present	
Absent	1551 (78%)	51 (38%)	1602 (75%)
Present	446 (22%)	84 (62%)	530 (25%)
Total	1997 (100%)	135 (100%)	2132 (100%)

*Only Gradable images

Above is a 2X2 table showing actual DR grading between algorithm and ophthalmologist using only gradable images by the algorithm.

Table 53

Algorithm vs. Optometrist *	Value	95% Confidence interval
Sensitivity	62.22%	53.48% to 70.42%
Specificity	77.67%	75.77% to 79.48%
Positive Predictive Value	15.85%	12.84% to 19.24%
Negative Predictive Value	96.82%	95.84% to 97.62%

*Only Gradable images

The sensitivity of the algorithm to detect DR was found to be 82% and specificity was found to be 78% in detecting DR compared to Optometrist

The area under the receiver operator curve was 0.56 (95%CI=0.55 to 0.58).

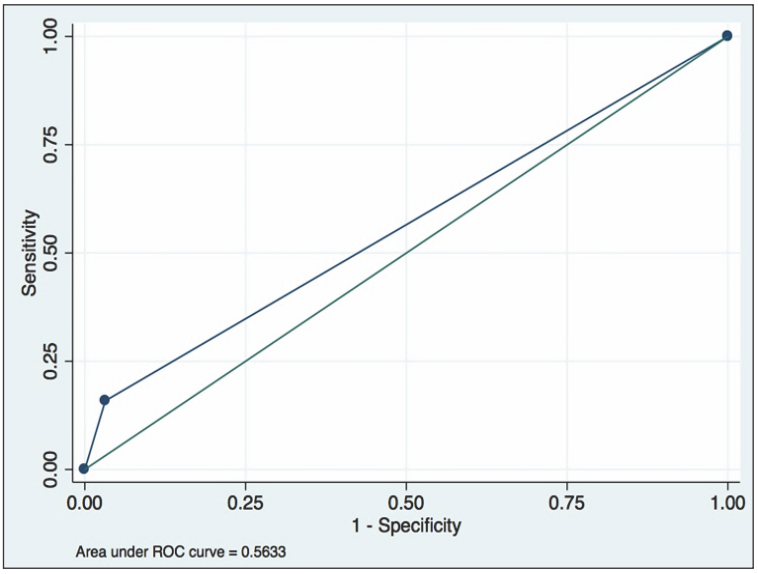

Fig 54

E. Comparison of Ophthalmologist to Optometrist

Table 54: Kappa Statistics for agreement

Variable	Optometrist Gradability	
	Kappa	95%CI
Gradability	0.701	0.561 - 0.840
DR Presence (Yes/No)	0.835	0.813 - 0.854
DR grade	0.835	0.812 - 0.843

Table 55: Sensitivity and Specificity of Optometrist to detect DR compared to Ophthalmologist

Optometrist DR grading	Ophthalmologist DR grading		Total
	Absent	Present	
Absent	2296 (99.5%)	34 (18%)	2330 (94%)
Present	11 (0.5%)	150 (82%)	161 (6%)
Total	2307 (100%)	184 (100%)	2491 (100%)

Above is a 2X2 table showing actual DR grading between optometrist and ophthalmologist.

Table 56

Ophthalmologist vs. Optometrist	Value	95% Confidence interval
Sensitivity	81.52%	75.15% to 86.85%
Specificity	99.52%	99.15% to 99.76%
Positive Predictive Value	93.17%	88.10% to 96.54%
Negative Predictive Value	98.54%	97.97% to 98.99%

The sensitivity of the optometrist to detect DR was found to be 82% and specificity was 99% in detecting DR compared to ophthalmologist.

The area under the receiver operator curve was 0.95 (95%CI=0.93 to 0.97).

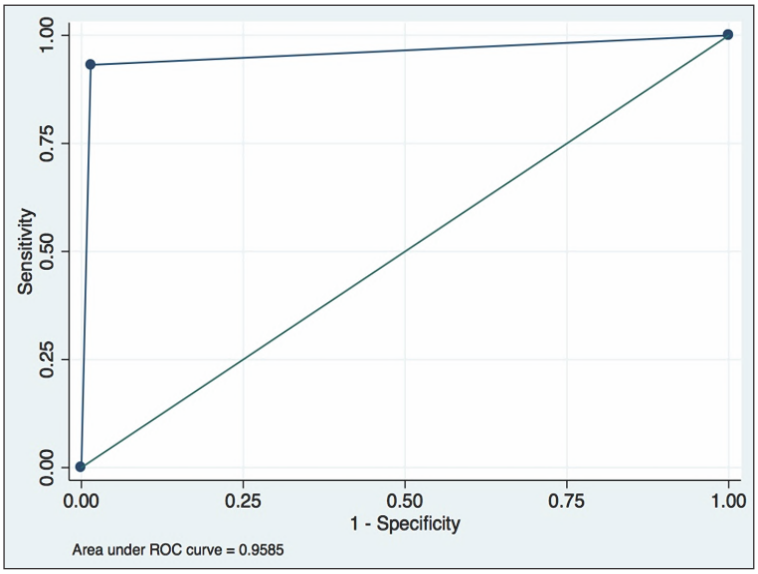

Fig 55 ROC CURVE

Results summary from use of Algorithm on images obtained from Diabetic clinics camps using non-mydriatic FORUS camera:

* 1. The Algorithm is interpreting about 15% as ungradable currently compared to both Ophthalmologist (Gold standard) as well as optometrist. This is an improvement from 49% in Tele-ophthalmology and 25% in SN VR OPD.

* 2. The Algorithm is showing approximately 62% sensitivity and about 77% specificity in automated detection of DR

* 3. The Area under the curve is Less than 57% even if only gradable images are taken.

* 4. Algorithm highly overestimates presence of DR when it can grade the image, This is also seen with Telecamps but not seen with the SNVR OPD data. SNVR OPD has lots of DR compared to the Telecamp and Diabetic clinic which has minimal DR.

* 5. Inconsistency within Algorithm: When image is ungradable by algorithm, still 15% shows DR present. This should be either 100% or ZERO.

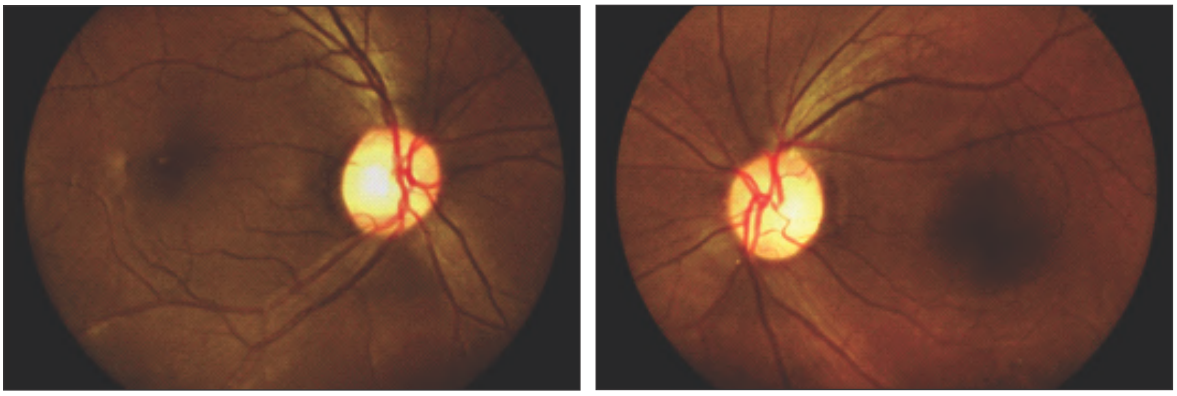

Fig : 56 Diabetic Clinic – 1. Algorithm diagnosis absence of DR in diabetic Patient

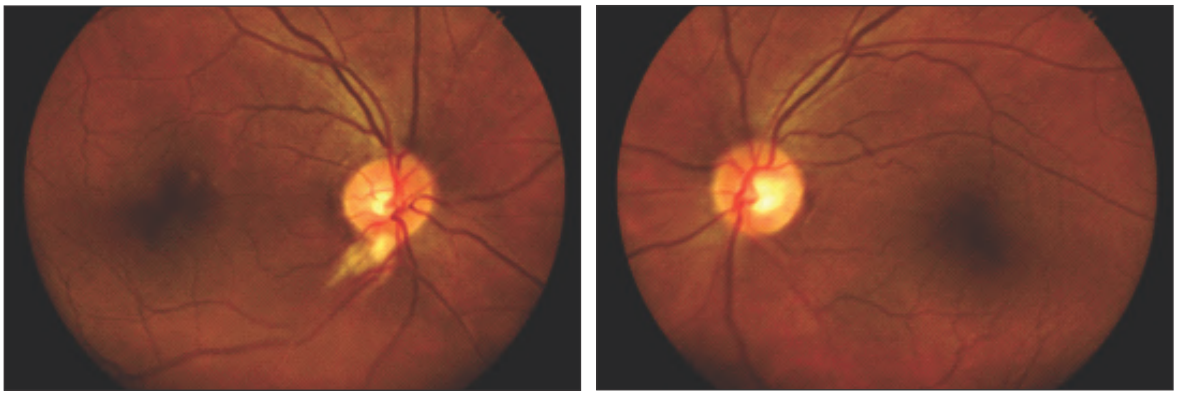

Fig : 57 Diabetic Clinic – 1 Medullated nerve fibre right eye- Algorithm diagnosis as exudate

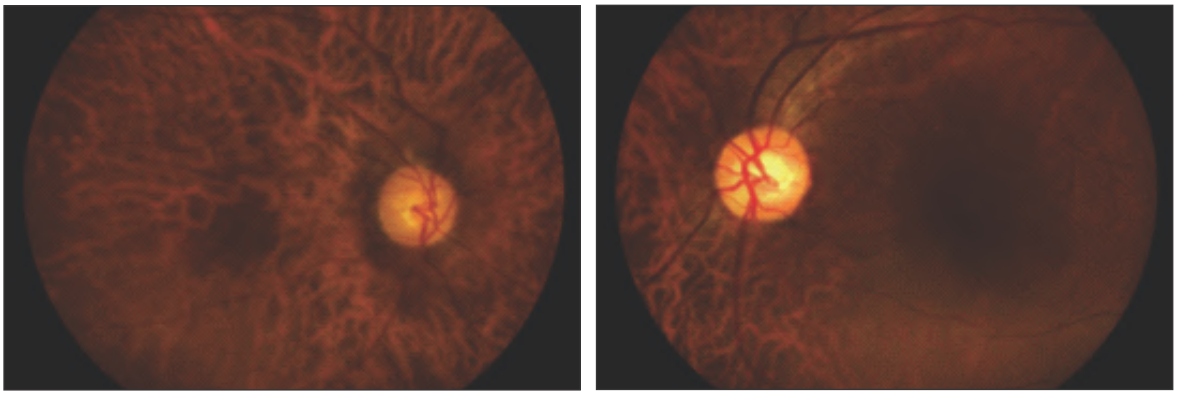

Fig : 58 Diabetic Clinic -1 Choroidal sclerosis- Algorithm misdiagnosis as presence of DR

Results from Diabetic retinopathy grading from the Diabetic clinics using the non-mydriatic FOP camera (smartphone based):

A. Demographics and DR status: We enrolled 110 eyes of 55 patients to test the accuracy of the algorithm to detect DR in the diabetic clinic setting. The mean age of participants was 53.9+10.2 years (median=55 years, IQR=48 – 60 years, range=20 – 82) and 66% were men. The mean duration of diabetes in this cohort was 10.7+6.6 years (median=12 years, IQR=5-14 years, range=1 – 22 years).

B. Algorithm Descriptive: The overall DR score was 0.82+0.16 (median=0.83, IQR=0.73-0.98) in right eye and 0.86+0.16 (median=0.74, IQR=0.58-0.96) in left eye.

C. Algorithm vs. Ophthalmologist:

Table 57: Sensitivity and Specificity of Algorithm to detect DR compared to Ophthalmologist in right eye

Algorithm DR grading	Ophthalmologist DR grading		Total
	Absent	Present	
Absent	1 (50%)	2 (4%)	3 (5%)
Present	1 (50%)	51 (96%)	52 (95%)
Total	2 (100%)	53 (100%)	55 (100%)

Above is a 2X2 table showing actual DR grading between algorithm and ophthalmologist

Table 58

Algorithm vs. Ophthalmologist	Value	95% Confidence interval
Sensitivity	96.23%	87.02% to 99.54%
Specificity	50.00%	1.26% to 98.74%
Positive Predictive Value	98.08%	89.74% to 99.95%
Negative Predictive Value	33.33%	0.84% to 90.57%

The area under the receiver operating curve was 0.65 (95% CI-0.54TO 0.87

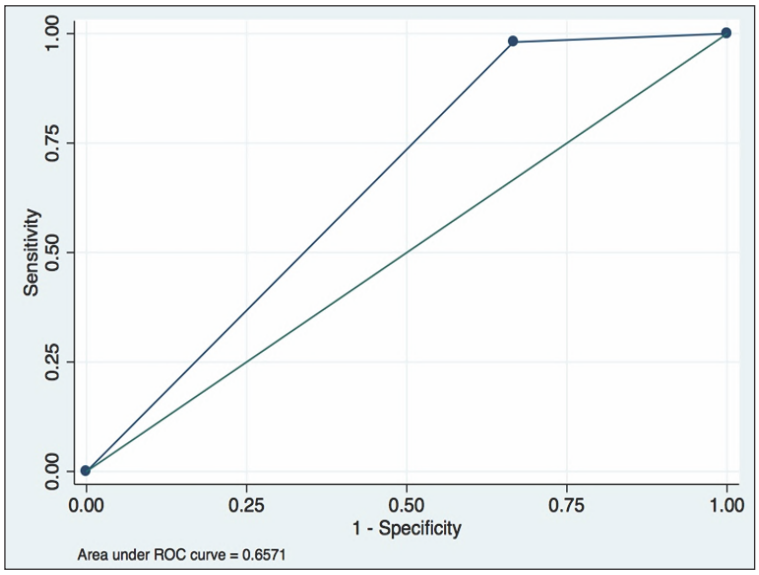

Fig 59 ROC CURVE

Table 59: Sensitivity and Specificity of Algorithm to detect DR compared to Ophthalmologist in left eye

Algorithm DR grading	Ophthalmologist DR grading		Total
	Absent	Present	
Absent	2 (100%)	3 (6%)	5 (9%)
Present	0	50 (94%)	50 (91%)
Total	2 (100%)	53 (100%)	55 (100%)

Above is a 2X2 table showing actual DR grading between algorithm and ophthalmologist

Table 60

Algorithm vs. Ophthalmologist	Value	95% Confidence interval
Sensitivity	94.34%	84.34% to 98.82%
Specificity	0%	–
Positive Predictive Value	100.00%	92.89% to 100.00%
Negative Predictive Value	0.00%	0.00% to 70.76%

The area under the receiver operating curve was 0.50 (95%CI – 0.44 to 0.79)

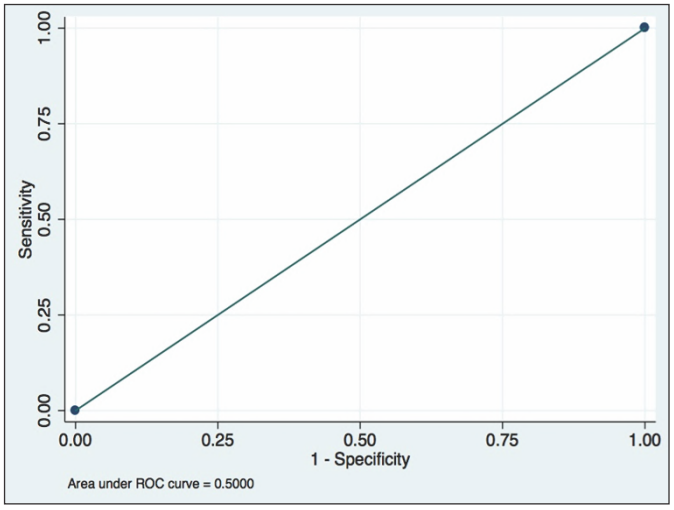

Fig 60 The ROC CURVE

Results summary from use of Algorithm on images obtained from Diabetic clinics camps using non-mydriatic FOP camera:

*1. The algorithm appears to be highly sensitive but not specific for DR detection in images obtained from smartphone based fundus camera.

* 2. The sample size is exceedingly small and there are not enough cases without DR to draw any meaningful conclusions about the applicability of the algorithm in smartphone fundus photography at present.

Results from Diabetic retinopathy grading from the Diabetic clinics using 7-Field mydriatic retinal imaging using a conventional table-top fundus camera:

A. Algorithm Descriptive: We enrolled 438 eyes with 7-field mydriatic imaging. The overall DR score was 0.85+0.18 (median=0.91, IQR=0.75-1.0) in right eye and 0.85+0.20 (median=0.90, IQR=0.77-1.0) in left eye.

B. Algorithm vs. Ophthalmologist:

Table 61: Sensitivity and Specificity of Algorithm to detect DR compared to Ophthalmologist in right eye

Algorithm DR grading	Ophthalmologist DR grading		Total
	Absent	Present	
Absent	15 (44%)	4 (2%)	19 (9%)
Present	19 (56%)	181 (98%)	200 (91%)
Total	34 (100%)	185 (100%)	219 (100%)

Above is a 2X2 table showing actual DR grading between algorithm and ophthalmologist.

Table 62

Algorithm vs. Ophthalmologist	Value	95% Confidence interval
Sensitivity	91.3%	86.70 % to 94.70%
Specificity	100%	2.50% to 100%
Positive Predictive Value	100%	98.2% to 100%
Negative Predictive Value	5%	0.13% to 24.87%

The area under the receiver operating curve was 0.8472(95%CI – 0.63 to 0.92)

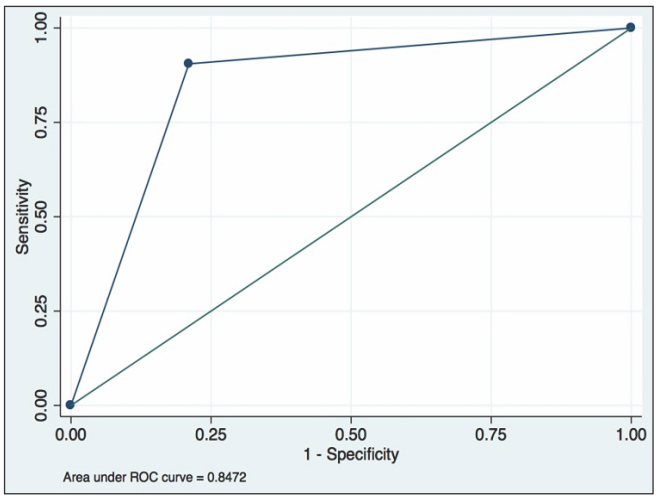

Fig 61 ROC CURVE

Table 63: Sensitivity and Specificity of Algorithm to detect DR compared to Ophthalmologist in left eye

Algorithm DR grading	Ophthalmologist DR grading		Total
	Absent	Present	
Absent	14 (35%)	1 (<1%)	15 (7%)
Present	24 (65%)	180 (99%)	204 (93%)
Total	38 (100%)	181 (100%)	219 (100%)

Above is a 2X2 table showing actual DR grading between algorithm and ophthalmologist

Table 64

Algorithm vs. Ophthalmologist	Value	95% Confidence interval
Sensitivity	93.58%	89.46% to 96.44%
Specificity	100%	2.5% - 100%
Positive Predictive Value	100.00%	98.2% to 100.00%
Negative Predictive Value	6.67%	0.17% to 31.95%

The area under the receiver operating curve was 0.91 (95%CI – 0.81 to 0.97)

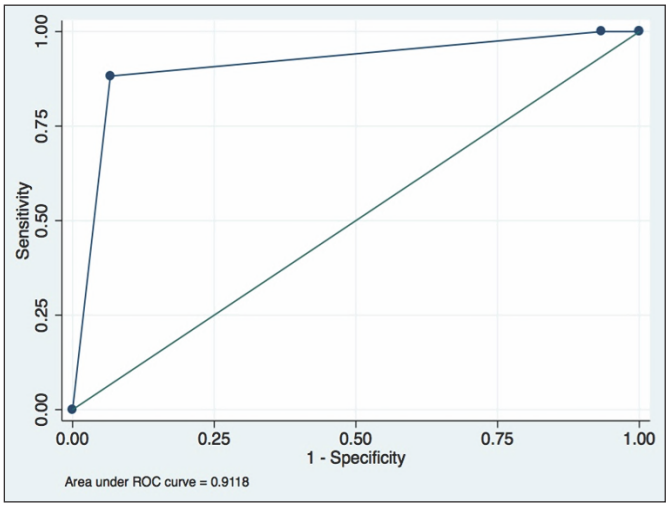

Fig 62 ROC CURVE

Results summary from use of Algorithm on images obtained from Diabetic clinics camps using 7 Field Retinal imaging using table top conventional fundus camera:

*1. The algorithm appears to be highly sensitive and very specific for DR detection in images obtained from 7 Field Retinal imaging using tabletop conventional fundus camera.

* 2. There are very few eyes without DR (17%) to make meaningful comparisons. Yet, this group of images has yielded the best results from the algorithm in terms of sensitivity and specificity in detecting presence/absence of DR.

* 3. This is the only group that had mydriatic imaging from all 7 fields of view in this study. The algorithm showed high sensitivity and specificity in this group as compared to lower sensitivity and specificity in all other sections of the study that obtained non-mydriatic images in different clinical settings. This suggests that the algorithm does not work as well in non-mydriatic image processing, given the fact that the image quality obtained from non-mydriatic imaging is not as good as that obtained with dilated images, though image quality grading was done in this group to substantiate our conclusions.

* 4. This is the only group that acquired images from all 7 fields of view from each eye of more than 200 patients (>400 eyes). The high performance of the algorithm in this group suggests that it is able to pick up pathology in peripheral fields of view where the optic disc and macula may not be visible. Thus anatomic landmarks such as blood vessels and pathologic lesions such as microaneurysms, bleeding spots, cotton wool spots etc. used to develop the algorithm appear to be working well.

* 5. The encouraging results showing high performance of the algorithm in this subgroup may be because the algorithm was initially tested using mydriatic images of high quality from commercially available datasets of images.

The transition to grading non-mydriatic images from different settings has not yet happened and the algorithm needs to be developed further to match results from the mydriatic images when processing non-mydriatic images as well.

A consolidated summary of all the results from various arms of the study with relevant details is presented here.

Table 65: The following is a consolidated table showing results from all arms of the study

Parameter	Clinical setting used to acquire images				
	Ophthal OPD	Telecamps	Diabetic clinic		
Imaging modality	Forus	Topcon	Forus	Topcon	Remidio[$]
Pupil status	Nonmydriatic	Nonmydriatic	Nonmydriatic	Mydriatic	Nonmydriatic
Field of view	45° single	45° single	45° single	7-fields	45° single
Total number of eyes	848	939	2526	438	110
% with DR	71%	13%	7%	84%	96%
% Ungradable by Ophthalmologist	9 (1%)	42 (4%)	28 (1%)	0%	0%
% Ungradable by Algorithm	214 (25%)	461 (49%)	373 (15%)	0%	0%
Sensitivity	78%**	85%**	63%**	91%	96%
Specificity	57%**	80%**	78%**	100%	50%
Positive Predictive Value	81%**	42%**	18%**	100%	98%
Negative predictive value	52%**	97%**	96%**	5%	33%
Area under curve	0.670**	0.69	0.57**	0.84	0.65

** Indices from only gradable images, [$]Smartphone based retinal imaging

Discussion

We used a new computed assisted algorithm for automated detection of diabetic retinopathy in four different clinical settings i.e. ophthalmologists' OPD where non-mydriatic single field images were acquired using a table top camera (Forus, n=848, 71% with DR), outreach telecamps where non-mydriatic single field retinal images were acquired using table top cameras (Topcon, n=939, 13% with DR), diabetic clinics 1 where single field images were acquired using nonmydriatic Forus camera (n=2526 eyes, 7% with DR), diabetic clinics 2 where 7-field dilated retinal imaging was performed using standard tabletop cameras (Carl Zeiss FF450 plus n=438, 84% with DR) and diabetic clinics 2 where four field retinal images were acquired using a smartphone based imaging system (Remidio, n=110, 96% with DR). All four scenarios, totaling 4861 eyes, were included in the study since image quality was expected to be different in these settings and we would be able to assess the ability of the new algorithm in detecting DR in each of these clinical settings. Additionally, we also compared the ability of paramedical staff such as optometrists and trained ophthalmic photographers in detecting presence of DR compared to gold standard grading by ophthalmologists. We found that the computer assisted algorithm showed approximately 76 - 78% sensitivity and about 50 - 55% specificity in automated detection of DR in the Ophthalmologists' OPD setting. The specificity improved to 80% in the tele-camps as well as diabetic clinics using nonmydriatic tabletop fundus camera. However, when used on images from dilated 7-field retinal imaging, the algorithm showed excellent performance with high sensitivity as well as specificity. The algorithm appears to be highly sensitive but not specific for DR detection in images obtained from smartphone based fundus camera. Overall, the Algorithm is interpreting too many images as ungradable currently compared to both Ophthalmologist (Gold standard) and Optometrist in all settings with very low Kappa statistics. We also found inconsistency within the algorithm reporting i.e. when image is ungradable by algorithm, still a substantial number shows DR present i.e. overestimates DR and therefore has low positive predictive value in all three settings.

The deep convolutional neural network (145) computer software designed by Google involved 9963 eyes obtained from EyePACS database in theUnited States, the Messidor-2 data set of images from France and 3 eye hospitals in India (Aravind Eye Hospital,Sankara Nethralaya, and Narayana Nethralaya) from patients presenting for diabetic retinopathy screening and found a much higher sensitivity and specificity compared to our study. While our software is based on image analysis, the Google is based on deep machine learning using neural networks. It is possible that deep machine learning yields better results, as demonstrated by Abramoff et al (153) We also believe that the Google results reported recently are after 5 – 7 years of beta testing of the product involving 1,28,175 images in the developmental phase. Ours is still in beta testing and has yielded close to 80% sensitivity, though specificity is lower. Another major differences between our overall inferior results from that of the Google algorithm is that more than 40% images from the EyePACS and Messidor datasets were acquired after pupillary dilatation. In contrast, more than 90% of our images were non-mydriatic retinal images. On evaluation of our subset of eyes where 7-field mydriatic imaging was employed, we find that the sensitivity and specificity of our algorithm is very similar to that reported from the Google software. However, we had only about 400 eyes with mydriatic imaging as opposed to nearly 10,000 eyes in the validation set used for the Google software. Though premature, it does appear that our new algorithm performs sufficiently well when presented with high quality images after pupillary dilatation, though further study is required to confirm this. The other major difference between ours and the Google study is that higher end table top cameras such as Centervue DRS, Optovue iCam, CanonCR1/DGi/CR2, and Topcon NW using 45 degree fields of view were used to acquire a large number of images in the EyePACS database where as Topcon cameras were exclusively used in the Messidor-2 dataset. In contrast, we have employed locally made Forus camera, a low cost tabletop alternative suitable to our scenario, for obtaining a large number of our images in the ophthalmologists' OPD and diabetic clinic setting. Since image enhancement is part of the initial image processing done by the algorithm, quality of the images obtained may play a role in how well the software is able to detect DR. Since there are no head to head studies comparing the image quality of the Forus camera to Topcon or other established cameras, and assuming image quality to be slightly inferior with the Forus on account of its lower cost, we believe that this may have negatively impacted the performance of our algorithm compared to results from the Google study. Finally, our study was carried out in many different settings outside the ophthalmologists' clinic such as outreach camps and diabetic clinics where control over surroundings, ambient light etc. are difficult as opposed to the controlled office setting used in the EyePACS and Messidor-2 image acquisition. These play a role because ambient light clearly affects pupil size, making them smaller, and therefore difficult to acquire images.

Physiological dilation was followed in SN VR OPD, Telecamps and diabetic clinic 1 and this may also contribute to poor quality of images . Additionally, Indian eyes have darker iris and smaller basal pupillary diameter, greater incidence of cataract and probably more sight threatening DR with vitreous hemorrhage, which can also negatively impact the performance of the algorithm. Overall, we believe that the differences in proportion of mydriatic images, cameras used to acquire images, controlled settings vs. outreach settings and greater proportion of cataract and vitreous hemorrhage have played a role in inferior performance of our algorithm compared to the deep machine learning algorithm designed by Google. It will be interesting to see the yield from the Google algorithm when applied to our set of images. That's will give us a clear idea of the improvements required in our software to better detect DR and its severity.

A screening tool is different from a diagnostic tool and should have much higher sensitivity even at the expense of specificity that we have achieved. This is the first testing of our tool in the real world and based on these results, we will be able to improve the results further in the next versions of the software.

We found that image gardability was similar in our study (75%) compared to the Google developmental series (75%) and validation series (88%) which is an encouraging sign. However, the kappa statistic was very low in our study suggesting very low agreement in terms of DR presence between the graders and the software. Importantly, we found the software to be over – detecting DR by 2 – 3 fold in most of the settings.

In another study by Tufail et al (144) sensitivity and specificity of 4 different automated image analysis software were studied on 1,02,856 images in the UK. Since all these were based on image analysis and not deep machine learning, it may be more appropriate to compare their results with ours.

In this study, authors found a much higher sensitivity and specificity (>90%) using the EyeART (Eyenuk Inc., Woodland Hills, CA) and Retmarker (Coimbra, Portugal). The gradability reporting also shows superior results compared to our outcomes. We also found nearly 80% sensitivity and specificity in the tele – camps and diabetic clinics using non mydritic tabletop cameras. Major differences in the study designs could have contributed to the differences in results. Firstly, the UK study used only mydriatic images where as we have used nonmydriatic images in all our settings. Indian eyes are known to have smaller pupils in scotopic conditions limiting the image quality and thereby compromising the software's assessment capabilities. Secondly, Tufail et al used images obtained inside the ophthalmology clinic settings and images were obtained by trained technicians.

We acquired images in outreach camps where lighting is not entirely under our control as well as in diabetic clinics where technicians are usually fundus photographer and lastly, all the differences mentioned above in comparing our study with the Google algorithm are applicable in this case as well.

In another study by Walton et al (154) published outcomes on the sensitivity and specificity of another new algorithm, the Intelligent Retinal Imaging System (IRIS), was studies on 15,015 eyes from diabetic patients who presented for DR screening. This was a retrospective study and IRIS-based interpretations were compared with manual interpretation. The sensitivity and specificity of IRIS, compared withreading center interpretation, was only 66.4% and 72.8%, respectively, very similar to our results. There are many similarities of this study with our study design. Firstly, the setting for obtaining clinical photographs was a primary care physicians office, similar to the diabetic clinic described in our study. Secondly, all images were entirely nonmydriatic, similar to ours. Our cohort of 2526 eyes that underwent imaging using the Forus camera in diabetic clinics closely resemble the cohort in the IRIS study in that all were nonmydriatic images and baseline patient demographics were similar. Our Algorithm showed 62% sensitivity (vs. 66% in IRIS) and about 77% specificity (vs. 73% in IRIS) in automated detection of DR, figures that are almost identical to that reported by Walton et al using the IRIS algorithm. Both ours, and IRIS are slightly inferior to the results obtained from Google algorithm and the EyeART and Retmarker results presented by Tufail et al (shown above). However, the major difference is that the Google study was used on images obtained from 40% mydriatic images and Tufail et al used all images from dilated pupils.

In another recent study by Abramoff et al (153) they reported on the performance of a new deep-learning enhanced algorithm for automated detection of DR, to the previously published performance of that algorithm, the Iowa Detection Program (IDP)–without deep learning components–on thesame publicly available set of fundus images i.e. Messidor-2 dataset compared with grading by three US Board certified retinal specialists. The deep learning algorithm was found to have a sensitivity of 97% and specificity of 87% No cases of severe NPDR, PDR, or DME were missed and the AUC was 0.980. Authors found that the deep learning algorithm significantly improved specificity of DR detection compared to the previously used Iowa detection program that did not use deep learning.

The Retmarker software has been used to detect DR in Indian eyes by Roy et al (155) Authors analyzed 5780 eyes of 1445 patients through the Retmarker software and found a high sensitivity (>90%) and relatively low specificity (11 – 61%) in detecting DR in Indian eyes with medium to high image quality. In our opinion, our algorithm performs better overall because of its sufficiently high sensitivity and much higher specificity compared to that reported by Roy et al.

Chaum et al (156) presented results from an innovative technique for automated retinal image analysis called content based image retrieval system. Content-based image retrieval (CBIR) is the processof retrieving related images from very large database collections, and matching them by a setof intrinsic features extracted from an image presented to the system. Attributes such as color, texture, shape, and regional structure of the image or of specific objects, are used to detect DR. Chaum et al described that the sensitivity of detection and accuracy for proliferative diabetic retinopathy ranged from 75% to 91.7% and for nonproliferative diabetic retinopathy, ranged from 75% to 94.7% using the CBIR. Similarly, Quellec et al (157) used a similar technique and reported that the interobserver agreement between the most experienced clinicians and the most advanced algorithm was0.592. How the CBIR system fares compared to deep machine learning and other algorithms remains to be seen.

Recently Solanki et al (158) published results from using the EyeART automated image analysis software from mydriatic and nonmydriatic images obtained from the EyePACS database using teleophthalmology. Out of total of 101,710 eyes (54,481 were nonmydriatic), sensitivity of the EyeART was 91%, specificity was 92% and AUC was 0.95. Outcomes from mydriatic imaging was marginally better with improved sensitivity and greater AUC. Comparing this cohort to our cohort of images obtained from telecamps, we observe that our sensitivity and specificity are inferior to the EyeART at present and requires improvements in future iterations. There are very few other reports on applications of automated image analysis software on images obtained from teleophthalmology settings.

In their recent landmark paper on current state of teleophthalmology in the United States, Rathi et al (159) describe applications of teleophthalmology in many diseases including DR. They mention the upcoming role of automated DR screening using various algorithms to ease the human burden on manual DR screening. They conclude by saying that although the findings are encouraging,further work remains to improve the clinical validity of these algorithms.

Authors also state that given the increasing prevalence of diabetic retinopathy, the emergence of automated screening serves as a promisingtool to address this public health issue.

We found that optometrists had an excellent agreement with ophthalmologists in detecting DR, grading DR as well as for image gradability. This is a very relevant finding for resource poor settings like ours. This finding was reproduced in two different settings i.e. ophthalmologists' clinic as well as images obtained from diabetic clinics. Optometrists trained in retinal image grading can be used for reading services to reduce burden of manual grading in the developing world till such time as automated retinal image analysis does not become mainstream. From our experience in telecamps, we also found that trained retinal photographers are able to detect presence/absence of DR and stage DR with satisfactory agreement with ophthalmologists.

This is encouraging because we can consider reporting from photographers in the outreach camps without having to transfer images to the base hospital for DR detection. This will enable screening in very remote areas without internet connectivity .

The large sample size, various different settings and use of different imaging modalities to assess the capabilities of the novel software are the merits of our study. Additionally, training of personnel acquiring images and stringent quality control in grading also added to the robustness of our data. The main drawback of the study are the lack of both mydriatic and nonmydriatic images from the same eye of same patient to assess whether the software performs better when presented with dilated fundus images which are of better quality. However, better performance by using 7-field mydriatic images to the software compared to single field nonmydriatic images does suggest that the software performs better with mydriatic images. To the best of our knowledge, this is the first study analyzing the usefulness of automated image analysis software on images acquired using a smartphone.

Summary & Conclusion

The accepted performance required for reliable use of automated DR screening is above 80% sensitivity and 80% specificity. Our current algorithm is approaching this performance, and specificity of our algorithm needs to be improved. This can be done by initiating further studies in telecamps and diabetic clinics, by which the specificity required can be obtained by training the algorithm. Also more work should be concentrated on achieving highly reliable performance in the cases with sight-threatening DR, so that timely referral and treatment can be initiated.In conclusion, our novel software showed acceptable sensitivity and specificity in teleophthalmology settings, though improved results would be beneficial in improving predictive value and reducing unnecessarily excessive referrals. The main areas that require additional work are the reduction in ungradable images and specifically improve agreement of gradability and DR status with human graders. Optometrists and fundus photographers are as good as the ophthalmologist in detecting DR.

Impact of the Study

HTIC's Eye-PAC platform for ophthalmic image analysis

HTIC has developed a proprietary software platform for ophthalmic image processing, computing and analytics called Eye-PAC. The platform consists of modules for image processing, including algorithms for standardizing images for photometric and subject ethnic variations, enhancing information in regions and structures like illumination correction, haze reduction, glare reduction, vessel enhancement. The platform also contains modules for extracting basic structural information from images, such as location of prominent normal structures, establishing the view captured in the image, sizes, positions, distances and morphometry, and image mosaicking. The analytics modules of Eye-PAC are useful in decision analytics, for arriving at a decision of disease presence, image gradability, comparison of images and reporting.

The modules of Eye-PAC can be integrated to create solutions for diseases. This is a data driven process, requiring algorithmic fine-tuning of the integrated modules, to produce a system that can be used for specific applications.

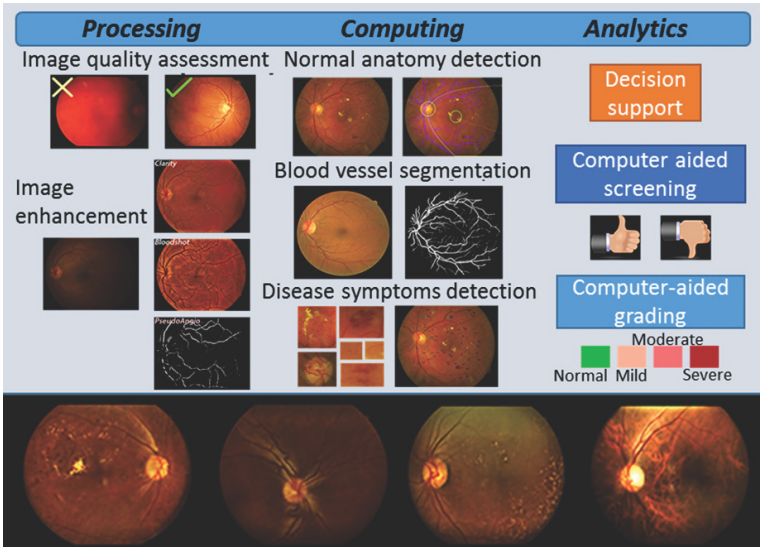

Fig 63 HTIC Eye-PAC platform for DR

The software application development at HTIC Madras will be used as a tool in screening programs for diabetic retinopathy in the Diabetic population . Manual grading is labor intensive and automated retinal image analysis systems is an alternative to detect presence or absence of diabetic retinopathy. Another serviceable metric for quality assurance is the rate of ungradable images, which noted there is no good definition for in the field at present. All the ungradable fundus images should be referred to the ophthalmologists. .

Diabetic macular edema (DME),is the leading cause of vision loss in DR patients. and diagnosed with the identification of retinal thickening, which requires optical coherence tomography (OCT) or stereo imaging.

Retinal thickening, can be assessed by surrogate markers, but noted that surrogate markers and DME (160) are not always correlated. Surrogate markers can be absent or present in DME and DME may be present or absent in the event of surrogate markers. The retinal analyzer and Scanning laser ophthalmoscope can also detect retinal thickening but there are expensive for routine screening in camps. Early detection of Diabetic retinopathy often asymptomatic stages has the potential to significantly reduce the incidence of visual loss in people with diabetes and has a significant impact on the economic and social consequences. Screening diabetic retinopathy saves vision at a relatively low cost.

A valid automated analysis system will need to perform above with 80% sensitivity and 95% specificity set by the World Health Organization for (161) diabetic retinopathy .In a typical DR screening program 78% of screenings have no diabetic retinopathy , Reda et al (162) have suggested and these normal retinal images could be identified and eliminated from the need for manual image reading by an automated analysis system that (163) detects diabetic retinopathy .

Recommendations

Validation of emerging telemedicine practices must be carried as per the American Telemedicine Association's (ATA) standard for validation for DR telemedicine practice . There are 4 different levels, presence of minimal or no DR; presence or absence of vision-threatening DR; an ability to provide clinical recommendations; and an equivalence to Early Treatment DR Study (ETDRS) photograph standard. ETDRS photographs remain "by and large" the gold standard for DR patient evaluation, The validation, programs (164) must establish quality assurance, which includes metrics, like patient satisfaction, follow-up with recommendations for referral, and the efficiency of DR diagnosis.

For automated retinal image analysis to be practiced in India, there is a need to consider regulatory norms, licensure, and costs. For Indian Teleophthalmology there is a need to embrace a culture change " patients have to accept that a computer will diagnose them instead of a doctor and the physician will have to accept that computer will have software programs which will aid in diagnosis of ocular disease. We do need to have further work on adopting a standard guidelines for adopting standard operations for telemedicine and automated retinal analysis.

The current software works sufficiently well when it is able to grade the image, comparing the results from other software applied on nonmydriatic images. However, the ungradability rates are relatively high and the algorithm needs to be improved so that future iterations reduce ungradability and avoid unnecessary patient referrals.

We need medical practitioners and engineers to collaborate and work towards developing and improving new technology which includes intelligent systems and tools that aid in disease identification and diagnosis.

Bibliography - Vancouver style

1. Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes Res Clin Pract. 2010;87(1):4–14.
2. Whiting DR, Guariguata L, Weil C, Shaw J. IDF diabetes atlas: global estimates of the prevalence of diabetes for 2011 and 2030. Diabetes Res Clin Pract. Ireland; 2011 Dec;94(3):311–21.
3. International Diabetes Federation. Eighth edition 2017 [Internet]. 8th ed. 2017. 1-150 p. Available from: http://www.diabetes atlas.org/resources/2017-atlas.html
4. Hu FB. Globalization of diabetes: the role of diet, lifestyle, and genes. Vol. 34, Diabetes care. United States; 2011. p. 1249–57.
5. Anjana RM, Pradeepa R, Deepa M, Datta M, Sudha V, Unnikrishnan R, et al. Prevalence of diabetes and prediabetes (impaired fasting glucose and/or impaired glucose tolerance) in urban and rural India: phase I results of the Indian Council of Medical Research-INdia DIABetes (ICMR-INDIAB) study. Diabetologia. Germany; 2011 Dec;54(12):3022–7.
6. Anjana RM, Shanthi Rani CS, Deepa M, Pradeepa R, Sudha V, Divya Nair H, et al. Incidence of Diabetes and Prediabetes and Predictors of Progression Among Asian Indians: 10-Year Follow-up of the Chennai Urban Rural Epidemiology Study (CURES). Diabetes Care. United States; 2015 Aug;38(8):1441–8.
7. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care. United States; 2004 May;27(5):1047–53.
8. Corcóstegui B, Durán S, González-Albarrán MO, Hernández C, Ruiz-Moreno JM, Salvador J, et al. Update on Diagnosis and Treatment of Diabetic Retinopathy: A Consensus Guideline of the Working Group of Ocular Health (Spanish Society of Diabetes and Spanish Vitreous and Retina Society). J Ophthalmol. 2017; Article ID 8234186, 10 pages https://doi.org/10.1155/2017/8234186

9. Damkondwar DR, Raman R, Suganeswari G, Kulothungan V, Sharma T. Assessing Framingham cardiovascular risk scores in subjects with diabetes and their correlation with diabetic retinopathy. Indian J Ophthalmol 2012;60:45-8
10. Yau JWY, Rogers SL, Kawasaki R, Lamoureux EL, Kowalski JW, Bek T, et al. Global Prevalence and Major Risk Factors of Diabetic Retinopathy. Diabetes Care [Internet]. 2012;35(3):556–64. Available from: http://care.diabetesjournals.org/cgi/doi/10.2337/dc11-1909
11. Namperumalsamy P, Kim R, Vignesh TP et al. Prevalence and risk factors for diabetic retinopathy: A population-based assessment from Theni district, South India. Br J Ophthalmol 2009;93:429-34.
12. Dandona L, Dandona R, Naduvilath TJ, McCarty CA, Rao GN. Population based assessment of diabetic retinopathy in an urban population in southern India. Br J Ophthalmol. England; 1999 Aug;83(8):937–40.
13. Rema M, Premkumar S, Anitha B, Deepa R, Pradeepa R, Mohan V. Prevalence of diabetic retinopathy in urban India: the Chennai Urban Rural Epidemiology Study (CURES) eye study, I. Invest Ophthalmol Vis Sci. United States; 2005 Jul;46(7):2328–33.
14. Ramachandran A, Snehalatha C, Kapur A, Vijay V, Mohan V, Das AK, et al. Diabetes Epidemiology Study Group in India (DESI). High prevalence of diabetes and impaired glucose tolerance in India: National Urban Diabetes Survey. Diabetologia 2001;44:1094-101.
15. Raman R, Vaitheeswaran K, Vinita K, Sharma T. Is prevalence of retinopathy related to the age of onset of diabetes? SankaraNethralaya Diabetic Retinopathy Epidemiology and Molecular Genetic Report No. 5. Ophthalmic Res. Switzerland; 2011;45(1):36–41.
16. Raman R, Gella L, Srinivasan S, Sharma T. Diabetic retinopathy: An epidemic at home and around the world. Indian J Ophthalmol [Internet]. 2016;64(1):69. Available from: http://www.ijo.in/text.asp?2016/64/1/69/
17. Thomas RL, Dunstan FD, Luzio SD, Chowdhury SR, North R V, Hale SL, et al. Prevalence of diabetic retinopathy within a national diabetic retinopathy screening service. Br J Ophthalmol. England; 2015 Jan;99(1):64–8.
18. Gadkari SS, Maskati QB, Nayak BK. Prevalence of diabetic retinopathy in India: The All India Ophthalmological Society Diabetic Retinopathy Eye Screening Study 2014. Indian J Ophthalmol [Internet]. 2016;64(1):38–44.

19. Diabetic Retinopathy Clinical Research Network. DRCRnet Manual of operations Ver 3.0. Tampa, FL: Jaeb Center for Health Research Foundation; April 8, 2005
20. Healy R, Sallam A, Jones V, Donachie PH, Scanlon PH, Stratton IM, et al. Agreement between photographic screening and hospital biomicroscopy grading of diabetic retinopathy and maculopathy. Eur J Ophthalmol 2014;24:550-8.
21. Sallam A, Scanlon PH, Stratton IM, Jones V, Martin CN, Brelen M, et al. Agreement and reasons for disagreement between photographic and hospital biomicroscopy grading of diabetic retinopathy. Diabet Med 2011;28:741-6.
22. Raman R, Gella L, Srinivasan S, Sharma T. Diabetic retinopathy: An epidemic at home and around the world. Indian J Ophthalmol [Internet]. 2016;64(1):69. Available from: http://www.ijo.in/text.asp?2016/64/1/69/
23. Jotheeswaran AT, Lovakanth N, Nadiga S, Anchala R, Murthy G, Gilbert CE. Estimating the proportion of persons with diabetes developing diabetic retinopathy in India: A systematic review and meta-analysis. Indian J EndocrMetab 2016;20:51-8.
24. Chew EY,Ferris FL III. Non proliferative retinopathy. In : Ryan SJ, Hinton DR, Schachat AP, WilkinsonCP, eds, Retina . 4th ed. Philadelphia: Elsevier/ Mosby; 2006: 1271-1284
25. Early Treatment Diabetic Retinopathy Study Research Group.Early photocoagulation for diabetic retinopathy. ETDRS report number 9. Ophthalmology 1991;98:766–85
26. Diabetic Retinopathy Study Research Group. Photocoagulation treatment of proliferative diabetic retinopathy: the second report of diabetic retinopathy study findings. Ophthalmology 1978;85:82–106.
27. Ophthalmology AA of. International Clinical Diabetic Retinopathy and Diabetic Macular Edema Disease Severity Scales Summary. 2002;(October)
28. . Grading diabetic retinopathy from stereoscopic color fundus photographs—An extension of the modified Airlie House classification. ETDRS report number 10. Early Treatment Diabetic Retinopathy Study Research Group. Ophthalmology 1991;98(5 Suppl):786–806
29. Wilkinson CP, Ferris FL 3rd, Klein RE, et al. Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. Ophthalmology 2003;110:1677–1682.
30. GhasemiFalavarjani K, Tsui I, Sadda SR. Ultra-wide-field imaging in diabetic retinopathy. Vision Res. 2017 Oct;139:187-190.
31. Silva PS, Cavallerano JD, Tolson AM. Real-Time Ultrawide Field Image Evaluation of Retinopathy in a Diabetes Telemedicine Program. Diabetes Care. 2015 Sep;38(9):1643-9.

32. Baskin DE. Optical coherence tomography in diabetic macular edema.CurrOpinOphthalmol. 2010 May;21(3):172-7.
33. Taylor HR, Vu HTV, McCarty CA, Keeffe JE. The need for routine eye examinations. InvestigOphthalmol Vis Sci 2004; 45: 2539–2542.
34. Betz-Brown J, Pedula, K., and Summers, K., Diabetic retinopathy — contemporary prevalence in a well-controlled population, Diabetes Care 2003 26(9), 2637-2642
35. Bresnick GH, Mukamel DB, Dickinson JC, Cole DR. A screening approach to the surveillance of patients with diabetes for the presence of vision-threatening retinopathy, Ophthalmology. 2000; 107(1):19–24.
36. Lee DJ, Kumar N, Feuer WJ, Chou C-F, Rosa PR, Schiffman JC, et al. Dilated eye examination screening guideline compliance among patients with diabetes without a diabetic retinopathy diagnosis: the role of geographic access. BMJ Open Diabetes Res Care [Internet]. 2014;2(1):e000031. Available from: http://drc.bmj.com/lookup/doi/10.1136/bmjdrc-2014-000031
37. American Academy of Ophthalmology Retina/Vitreous Panel Preferred Practice Pattern Guidelines, Diabetic Retinopathy, American Academy of Ophthalmology, San Francisco, CA, 2016, November 2016, http://www.aao.org/ppp.
38. Thomas RL, Dunstan F, Luzio SD, Roy Chowdury S, Hale SL, North RV, et al. Incidence of diabetic retinopathy in people with type 2 diabetes mellitus attending the Diabetic Retinopathy Screening Service for Wales: Retrospective analysis. BMJ. 2012;344:e874. [PMCID: PMC3284424] [PubMed: 22362115]
39. Lund SH, Aspelund T, Kirby P, Russell G, Einarsson S, Palsson O, et al. Individualised risk assessment for diabetic retinopathy and optimisation of screening intervals: a scientific approach to reducing healthcare costs. Br J Ophthalmol [Internet]. 2016;100(5):683–7.
40. Leasher JL, Bourne RRA, Flaxman SR, Jonas JB, Keeffe J, Naidoo K, et al. Global estimates on the number of people blind or visually impaired by diabetic retinopathy: A meta-analysis from 1990 to 2010. Diabetes Care. 2016;39(9):1643–9.
41. Tan CS, Chew MC, Lim LW, Sadda SR. Advances in retinal imaging for diabetic retinopathy and diabetic macular edema. Indian J Ophthalmol 2016;64:76-83.
42. Li HK, Hubbard LD, Danis RP, Esquivel A, Florez-Arango JF, Ferrier NJ, et al. Digital versus film fundus photography for research grading of diabetic retinopathy severity. InvestigOphthalmol Vis Sci. 2010;51(11):5846–52.
43. Bernardes R, Serranho P, Lobo C. Digital ocular fundus imaging: A review. Ophthalmologica. 2011;226(4):161–81.

44. Bragge P. Screening for Presence or Absence of Diabetic Retinopathy. Arch Ophthalmol [Internet]. 2011;129(4):435. Available from: http://archopht.jamanetwork.com/article.aspx?doi=10.1001/archophthalmol.2010.319
45. Li HK, Hubbard LD, Danis RP, Esquivel A, Florez-Arango JF, Krupinski EA. Monoscopic versus stereoscopic retinal photography for grading diabetic retinopathy severity. InvestigOphthalmol Vis Sci. 2010;51(6):3184–92.
46. Vujosevic S, Benetti E, Massignan F, Pilotto E, Varano M, Cavarzeran F, et al. Screening for Diabetic Retinopathy: 1 and 3 Nonmydriatic 45-degree Digital Fundus Photographs vs 7 Standard Early Treatment Diabetic Retinopathy Study Fields. Am J Ophthalmol [Internet]. Elsevier Inc.; 2009;148(1):111–8. Available from: http://dx.doi.org/10.1016/j.ajo.2009.02.031
47. Silva PS, Walia S, Cavallerano JD, Sun JK, Dunn C, Bursell S-E, et al. Comparison of Low-Light Nonmydriatic Digital Imaging with 35-mm ETDRS Seven-Standard Field Stereo Color Fundus Photographs and Clinical Examination. Telemed e-Health [Internet]. 2012;18(7):492–9. Available from: http://online.liebertpub.com/doi/abs/10.1089/tmj.2011.0232
48. Williams GA, Scott IU, Haller JA, Maguire AM, Marcus D, McDonald HR. Single-field fundus photography for diabetic retinopathy screening: A report by the American Academy of Ophthalmology. Ophthalmology. 2004;111(5):1055–62.
49. Chin EK, Ventura B V., See K-Y, Seibles J, Park SS. Nonmydriatic Fundus Photography for Teleophthalmology Diabetic Retinopathy Screening in Rural and Urban Clinics. Telemed e-Health [Internet]. 2014;20(2):102–8. Available from: http://online.liebertpub.com/doi/abs/10.1089/tmj.2013.0042
50. Gupta V, Bansal R, Gupta A, Bhansali A. Sensitivity and specificity of nonmydriatic digital imaging in screening diabetic retinopathy in Indian eyes. Indian J Ophthalmol 2014;62:851-6.
51. Ahmed J, Ward TP, Bursell SE, Aiello LM, Cavallerano JD, Vigersky RA. The sensitivity and specifi city of nonmydriatic digital stereoscopic retinal imaging in detecting diabetic retinopathy. Diabetes Care 2006;29:2205-9.
52. Henry P, Stephen J. The Influence of Age , Duration of Diabetes , Cataract , and Pupil Size on. Diabetes Care. 2005;28(10).
53. Murgatroyd H. Effect of mydriasis and different field strategies on digital image screening of diabetic eye disease. Br J Ophthalmol [Internet]. 2004;88(7):920–4.

54. Silva PS, Horton MB, Clary D, Lewis DG, Sun JK, Cavallerano JD, et al. Identification of Diabetic Retinopathy and Ungradable Image Rate with Ultrawide Field Imaging in a National Teleophthalmology Program. Ophthalmology [Internet]. American Academy of Ophthalmology; 2016;123(6):1360–7. Available from: http://dx.doi.org/10.1016/j.ophtha.2016.01.043
55. Tan CSH, Chew MCY, Lim LWY, Sadda SR. Advances in retinal imaging for diabetic retinopathy and diabetic macular edema. Indian J Ophthalmol [Internet]. 2016;64(1):76–83. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26953028
56. Panwar N, Huang P, Lee J, Keane P a., Chuan TS, Richhariya A, et al. Fundus Photography in the 21st Century—A Review of Recent Technological Advances and Their Implications for Worldwide Healthcare. Telemed e-Health [Internet]. 2015;22(AUGUST):150826121255008. Available from: http://online.liebertpub.com/doi/10.1089/tmj.2015.0068
57. Bedard C, Liu S, Patterson C, Gerstein H, Griffith L. Systematic review: Can non-mydriatic cameras accurately detect diabetic retinopathy? Diabetes Res ClinPract [Internet]. Elsevier B.V.; 2017;129:154–9. Available from: http://dx.doi.org/10.1016/j.diabres.2017.04.024
58. Perera CM, Chakrabarti R. A Review of m-Health in Medical Imaging. Telemed e-Health [Internet]. 2015;21(2):132–7. Available from: http://online.liebertpub.com/doi/abs/10.1089/tmj.2013.0330
59. Kim DY, Delori F, Mukai S. Smartphone photography safety. Ophthalmology 2012;119:2200–1. 26
60. Cheng NM, Chakrabarti R, Kam JK. iPhone Applications for Eye Care Professionals: A Review of Current Capabilities and Concerns. Telemed J E Health [Internet]. 2014;20(4):20–2. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24476190
61. Kumar S, Wang E-H, Pokabla MJ, Noecker RJ. Teleophthalmology Assessment of Diabetic Retinopathy Fundus Images: Smartphone Versus Standard Office Computer Workstation. Telemed e-Health [Internet]. 2012;18(2):158–62
62. John S, Arun V, Katti N, Appukuttan B, Pearlson, Badrinath SS. Are smartphones comparable to laptops for image diagnosis in teleophthalmology? In: Studies in Health Technology and Informatics. 2013. p. 1065.
63. Russo A, Morescalchi F, Costagliola C, et al. Comparison of smartphone ophthalmoscopy with slit-lamp biomicroscopy for grading diabetic retinopathy. Am J of Ophthalmology. 2015;159(2):360-364e1

64. Ryan ME, Rajalakshmi R, Prathiba V, Anjana RM, Ranjani H, Narayan KMV, et al. Comparison among methods of retinopathy assessment (CAMRA) study: Smartphone, nonmydriatic, and mydriatic photography. Ophthalmology [Internet]. Elsevier Inc; 2015;122(10):2038–43. Available from: http://dx.doi.org/10.1016/j.ophtha.2015.06.011

65. Bolster NM, Giardini ME, Bastawrous A. The Diabetic Retinopathy Screening Workflow: Potential for Smartphone Imaging. J Diabetes SciTechnol [Internet]. 2015;10(2):318–24. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26596630%5Cnhttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC4773975

66. Giardini ME, Livingstone AT, Jordan S, et al. A smartphone based ophthalmoscope. In: Proceedings of the 36th Annual International Conference IEEE Engineering in Medicine and Biology Society. Red Hook, NY: Curran Associates; 2014:2177-2180

67. Bastawrous A, Giardini ME, Bolster NM, et al. Agreement of a smartphone based ophthalmoscope (Peek Retina) with standard fundus cameras for optic nerve imaging in a large Kenyan cohort. JAMA Ophthalmol. In press 2015

68. Micheletti JM, Hendrick AM, Khan FN, Ziemer DC, Pasquel FJ. Current and Next Generation Portable Screening Devices for Diabetic Retinopathy. J Diabetes SciTechnol [Internet].2016;10(2):295–300.

69. Maamari RN, Keenan JD, Fletcher DA, Margolis TP. A mobile phone-based retinal camera for portable wide field imaging. Br J Ophthalmol [Internet]. 2014;98(4):438–41. Available from: http://bjo.bmj.com/lookup/doi/10.1136/bjophthalmol-2013-303797

70. Tran K, Mendel TA, Holbrook KL, et al. Construction of an inexpensive, hand-held fundus camera through modification of a consumer “point-and-shoot” camera. Invest Ophthalmol Vis Sci 2012;53:7600–7

71. American Diabetes Association. Standards of medical care in diabetes. J ClinAppl Res Educ 2015;38:1–94

72. Hazin R, Barazi MK, Summerfield M. Challenges to establishing nationwide diabetic retinopathy screening programs. CurrOpinOphthalmol 2011;22:174–179

73. Revisiting Diabetes 2000: Challenges in Establishing Nationwide Diabetic Retinopathy Prevention Programs AJO November 2011 Volume 152, Issue 5, Pages 723–729

74. Sheppler CR, Lambert WE, Gardiner SK, Becker TM, Mansberger SL. Predicting adherence to diabetic eye examinations: Development of the compliance with Annual Diabetic Eye Exams Survey. Ophthalmology 2014;121:1212–1219.

75. Hussain R, Rajesh B, Giridhar A, Gopalakrishnan M, Sadasivan S, James J, et al. Knowledge and awareness about diabetes mellitus and diabetic retinopathy in suburban population of a South Indian state and its practice among the patients with diabetes mellitus: A population-based study. Indian J Ophthalmol [Internet]. 2016;64(4):272. Available from: http://www.ijo.in/text.asp?2016/64/4/272/182937
76. Vashist P, Singh S, Gupta N, Saxena R. Role of early screening for diabetic retinopathy in patients with diabetes mellitus: an overview. Indian J Community Med [Internet]. 2011;36(4):247–52. Available from: http://www.ijcm.org.in/text.asp?2011/36/4/247/91324%5Cnhttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3263142&tool=pmcentrez&rendertype=abstract
77. Murthy GV, Gupta SK, Bachani D, Tewari HK, John N. Human resources and infrastructure for eye care in India: Current status. Natl Med J India. 2004;17:128–34. [PubMed: 15253398]
78. Das T, Pappuru RR. Telemedicine in diabetic retinopathy: Access to rural India. Indian J Ophthalmol 2016;64:84-6.
79. Resnikoff S, Felch W, Gauthier TM, Spivey B. The number of ophthalmologists in practice and training worldwide: A growing gap despite more than 200 000 practitioners. Br J Ophthalmol. 2012;96(6):783–7.
80. Gilbert C, BabuRg, Gudlavalleti AV, Anchala R, Shukla R, Ballabh P, et al. Eye care infrastructure and human resources for managing diabetic retinopathy in India: The India 11-city 9-state study. Indian J EndocrinolMetab [Internet]. 2016;20(7):3. Available from: http://www.ijem.in/text.asp?2016/20/7/3/179768.
81. Raman R, Gupta A, Sharma T. Telescreening for Diabetic Retinopathy. Retin Fifth Ed. 2012;2:1006–11.
82. Kolomeyer AM, Szirth BC, Shahid KS, Pelaez G, Nayak N V, Khouri AS. Software-Assisted Analysis During Ocular Health Screening. Telemed E-Health. 2013;19(1):2–6.
83. Chasan JE, Delaune B, Maa AY, Lynch MG. Effect of a Teleretinal Screening Program on Eye Care Use and Resources. JAMA Ophthalmol [Internet]. 2014;132(9):1045.
84. Zimmer-Galler IE, Kimura AE, Gupta S. Diabetic retinopathy screening and the use of telemedicine. CurrOpinOphthalmol. 2015;26(3):167–72.
85. Klein R, Klein BE, Moss SE, Davis MD, DeMets DL. The Wisconsin epidemiologic study of diabetic retinopathy. VI. Retinal photocoagulation. Ophthalmology 1987;94:747–753

86. Hudson SM, Contreras R, Kanter MH, Munz SJ, Fong DS. Centralized reading center improves quality in a real-world setting. Ophthalmic Surg Lasers Imaging Retina 2015;46:624–629.
87. Shi L, Wu H, Dong J, Jiang K, Lu X, Shi J. Telemedicine for detecting diabetic retinopathy: a systematic review and meta-analysis. Br J Ophthalmol [Internet]. 2015;99(6):823–31. Available from: http://bjo.bmj.com/lookup/doi/10.1136/bjophthalmol-2014-305631
88. Tsui I, Havunjian MA, Davis JA, Giaconi JA. Snapshot of Teleretinal Screening for Diabetic Retinopathy at the West Los Angeles Medical Center. Telemed J E Health [Internet]. 2016;22(10):1–4.
89. Park DW, Mansberger SL. Eye Disease in Patients with Diabetes Screened with Telemedicine. Telemed J E Heal [Internet]. 2016;21(2):21
90. Maa AY, Patel S, Chasan JE, Delaune W, Lynch MG. Retrospective Evaluation of a Teleretinal Screening Program in Detecting Multiple Nondiabetic Eye Diseases. Telemed e-Health [Internet]. 2017;23(1):41–8. Available from: http://online.liebertpub.com/doi/10.1089/tmj.2016.0039
91. Mansberger SL, Gleitsmann K, Gardiner S, Sheppler C, Demirel S, Wooten K, Becker TM. Comparing the effectiveness of telemedicine and traditional surveillance in providing diabetic retinopathy screening examinations: A randomized controlled trial. Telemed J E Health 2013;19:942–948
92. Zapata MA, Arcos G, Fonollosa A, Abraldes M, Oleñik A, Gutierrez E, et al. Telemedicine for a General Screening of Retinal Disease Using Nonmydriatic Fundus Cameras in Optometry Centers: Three-Year Results. Telemed J E Health [Internet]. 2017;23(1):30–6. Available from: http://online.liebertpub.com/doi/10.1089/tmj.2016.0020%5Cnhttp://www.ncbi.nlm.nih.gov/pubmed/27228051
93. Kumar S, Tay-Kearney M-L, Chaves F, Constable IJ, Yogesan K. Remote ophthalmology services: cost comparison of telemedicine and alternative service delivery options. J TelemedTelecare. 2006;12(May 2005):19–22.
94. Valikodath NG, Leveque TK, Wang SY, Lee PP, Newman-Casey PA, Hansen SO, et al. Patient Attitudes Toward Telemedicine for Diabetic Retinopathy. Telemed e-Health [Internet]. 2017;23(3):205–12. Available from: http://online.liebertpub.com/doi/10.1089/tmj.2016.0108

95. Mohan V, Deepa M, Pradeepa R, Prathiba V, Datta M, Sethuraman R, et al. Prevention of diabetes in rural India with a telemedicine intervention. J Diabetes SciTechnol [Internet]. 2012;6(6):1355–64.

96. Importance of telemedicine in diabetes care: Relationships between family physicians and ophthalmologists wjo 2015 july Pedro Romero-Aroca, Ramon Sagarra-Alamo, Alicia Pareja-Rios, Maribel López

97. O'Hare JP, Hopper A, Madhaven C, Charny M, Purewell TS, Harney B, et al. Adding retinal photography to screening for diabetic retinopathy: a prospective study in primary care. BMJ [Internet]. 1996;312(7032):679–82. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2350501&tool=pmcentrez &rendertype=abstract

98. Gulliford MC, Dodhia H, Sivaprasad S, Ashworth M (2010) Family Practices' Achievement of Diabetes Quality of Care Targets and Risk of Screen-Detected Diabetic Retinopathy. PLoS ONE 5(4): e10424. doi:10.1371/journal.pone.0010424

99. Salti H, Cavallerano JD, Salti N, Jawhari DJ, Haddad S, Sun JK, et al. Nonmydriatic retinal image review at time of endocrinology visit results in short-term HbA1c reduction in poorly controlled patients with diabetic retinopathy. Telemed J E Health [Internet]. 2011;17(6):415–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21675867

100. Roser P, Kalscheuer H, Groener JB, Lehnhoff D, Klein R, Auffarth GU, et al. Diabetic retinopathy screening ratio is improved when using a digital, nonmydriatic fundus camera onsite in a diabetes outpatient clinic. J Diabetes Res. Hindawi Publishing Corporation; 2016;2016.

101. The OPHDIAT program (France),[5] Massin P, Chabouis A, Erginay A, Viens-Bitker C, Lecleire-Collet A, Meas T, et al. OPHDIAT: A telemedical network screening system for diabetic retinopathy in the Ile-de-France. Diabetes Metab. 2008;34:227–34. [PubMed: 18468470

102. PadmajaKumari R, Raman R, Sharma T. Physicians, pharmacists, and people with diabetes in India. Pharm World Sci. 2008;30(6):750–2.

103. Coronado AC, Zaric GS, Martin J, Malvankar-Mehta M, Si FF, Hodge WG. Diabetic retinopathy screening with pharmacy-based teleophthalmology in a semiurban setting: a cost-effectiveness analysis. C Open [Internet]. 2016;4(1):E95–102. Available from: http://cmajopen.ca/cgi/doi/10.9778/cmajo.20150085

104. John S, Sengupta S, Reddy SJ, Prabhu P, Kirubanandan K, Badrinath SS. The SankaraNethralaya mobile teleophthalmology model for comprehensive eye care delivery in rural India. Telemed J E Health [Internet]. Mary Ann Liebert, Inc. 140 Huguenot Street, 3rd Floor New Rochelle, NY 10801 USA; 2012;18(5):382–7. Available from: http://online.liebertpub.com/doi/abs/10.1089/tmj.2011.0190

105. Mohan V, Prathiba V, Pradeepa R. Tele-diabetology to Screen for Diabetes and Associated Complications in Rural India: The Chunampet Rural Diabetes Prevention Project Model. J Diabetes SciTechnol [Internet]. 2014;8(2):256–61. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24876575

106. Murthy KR, Murthy PR, Kapur A, Owens DR. Mobile diabetes eye care: Experience in developing countries. Diabetes Res ClinPract [Internet]. Elsevier Ireland Ltd; 2012;97(3):343–9. Available from: http://dx.doi.org/10.1016/j.diabres.2012.04.025

107. Qureshi B, Al-Rajhi A, Eckert K, Ravilla T, Khanna R, Mansur R, et al. Best practice eye care models. Indian J Ophthalmol. 2012;60(5):351.

108. Kovai V, Rao GN, Holden B. Key factors determining success of primary eye care through vision centres in rural India: patients' perspectives. Indian J Ophthalmol [Internet]. 2007;60(5):487–91. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3491281&tool=pmcentrez&rendertype=abstract

109. Raman R, Rani PK, ReddiRachepalle S, Gnanamoorthy P, Uthra S, Kumaramanickavel G, et al. Prevalence of Diabetic Retinopathy in India. SankaraNethralaya Diabetic Retinopathy Epidemiology and Molecular Genetics Study Report 2. Ophthalmology [Internet]. American Academy of Ophthalmology; 2009;116(2):311–8. Available from: http://dx.doi.org/10.1016/j.ophtha.2008.09.010

110. Agarwal S, Raman R, Paul PG, Rani PK, Uthra S, Gayathree R, et al. SankaraNethralaya-Diabetic Retinopathy Epidemiology and Molecular Genetic Study (SN-DREAMS 1): study design and research methodology. Ophthalmic Epidemiol [Internet]. 2005;12(2):143–53. Available from: http://www.ncbi.nlm.nih.gov/pubmed/16019696

111. Agarwal S, Raman R, Kumari RP, Deshmukh H, Paul PG, Gnanamoorthy P, et al. Diabetic retinopathy in type II diabetics detected by targeted screening versus newly diagnosed in general practice. Ann Acad Med Singapore. 2006;35(8):531–5.

112. Raman R, et al. Influence of glycosylated hemoglobin on sight-threatening diabetic retinopathy:Apopulationbased study. Diab Res ClinPract (2011), doi:10.1016/j.diabres.2011.01.006

113. Das T, Raman R, Ramasamy K, Rani PK. Telemedicine in diabetic retinopathy: Current status and future directions. Middle East Afr J Ophthalmol 2015;22:174-

114. KanagasingamYogesan, Leonard Goldschmidt. Digital Teleretinal Screening. Teleophthalmology in practice.2nd edition 2011. pg. 135-142.

115. Saumya Pal S, Raman R, Ganesan S, Sahu C, Sharma T. SankaraNethralaya Diabetic Retinopathy Epidemiology and Molecular Genetic Study (SN--DREAMS III): study design and research methodology. BMC Ophthalmol [Internet]. BioMed Central Ltd; 2011;11(1):7.

116. Raman R, Mahajan S, Rani PK, Agarwal S, Sharma T. eHEALTH INTERNATIONAL Telehealth Program for Diabetic Retinopathy in Rural South India : A Pilot Study. 2005;

117. Raman R, Rani PK, Mahajan S, Paul P, Gnanamoorthy P, Krishna MS, et al. The tele-screening model for diabetic retinopathy: Evaluating the influence of mydriasis on the gradability of a single-field 45 degrees digital fundus image. Telemed J E Health 2007;13:597-602.

118. Kumari Rani P, Raman R, Manikandan M, Mahajan S, Paul PG, Sharma T. Patient satisfaction with tele-ophthalmology versus ophthalmologist-based screening in diabetic retinopathy. J TelemedTelecare 2006;12:159-60.

119. Knowledge of diabetes and diabetic retinopathy among rural populations in India, and the influence of knowledge of diabetic retinopathy on attitude and practice

120. Rachapalle SR, Frick KD, Ph D, Raman R, Rani PK, Sharma T, et al. eHEALTH INTERNATIONAL Mobile Teleophthalmology : A cost effective screening tool for diabetic retinopathy in rural south India. http://www.ehealthinternational.net/

121. Rani PK, Raman R, Sharma V, Mahuli S V., Tarigopala A, Sudhir RR, et al. Analysis of a comprehensive diabetic retinopathy screening model for rural and urban diabetics in developing countries. Br J Ophthalmol [Internet]. 2007;91(11):1425–9. Available from: http://bjo.bmj.com/cgi/doi/10.1136/bjo.2007.120659

122. American telemedicine Association- American telemedicine Associationhttp://www.americantelemed.org/files/public/standards/DiabeticRetinopathy_withCOVER.pdf
Telehealth Practice Recommendations for Diabetic Retinopathy, Second Edition Helen K. Li, Mark Horton, Sven-Erik Bursell, Jerry Cavallerano, Ingrid Zimmer-Galler, Mathew Tennant, Michael Abramoff, Edward Chaum, Debra Cabrera DeBuc, Tom Leonard-Martin, Marc Winchester Telemedicine and e-Health. December 2011: 814-837.

123. Mookiah MRK, Acharya UR, Chua CK, Lim CM, Ng EYK, Laude A. Computer-aided diagnosis of diabetic retinopathy: A review. Computers in Biology and Medicine. 2013 Dec;43(12):2136–55.
124. Antal B, Hajdu A, Maros-Szabó Z, Török Z, Csutak A, Peto T. A two-phase decision support framework for the automatic screening of digital fundus images. Journal of Computational Science. 2012 Sep;3(5):262–8.
125. Saleh MD, Eswaran C. An automated decision-support system for non-proliferative diabetic retinopathy disease based on MAs and HAs detection. Computer Methods and Programs in Biomedicine. 2012 Oct;108(1):186–96.
126. Roychowdhury S, Koozekanani DD, Parhi KK. Screening fundus images for diabetic retinopathy. In: Signals, Systems and Computers (ASILOMAR), 2012 Conference Record of the Forty Sixth Asilomar Conference on [Internet]. IEEE; 2012 [cited 2015 Jan 27]. p. 1641–1645.
127. Quellec G, Lamard M, Abràmoff MD, Decencière E, Lay B, Erginay A, et al. A multiple-instance learning framework for diabetic retinopathy screening. Medical Image Analysis. 2012 Aug;16(6):1228–40.
128. Pires R, Jelinek HF, Wainer J, Goldenstein S, Valle E, Rocha A. Assessing the Need for Referral in Automatic Diabetic Retinopathy Detection. IEEE Transactions on Biomedical Engineering. 2013 Dec;60(12):3391–8.
129. Roychowdhury S, Koozekanani DD, Parhi KK. DREAM: Diabetic Retinopathy Analysis Using Machine Learning. IEEE Journal of Biomedical and Health Informatics. 2014 Sep;18(5):1717–28.
130. Venkatesan R, Chandakkar P, Li B, Li HK. Classification of diabetic retinopathy images using multi-class multiple-instance learning based on colorcorrelogram features. In: 13. Engineering in Medicine and Biology Society (EMBC), 2012 Annual International Conference of the IEEE [Internet]. IEEE; 2012 [cited 2015 Jan 27]. p. 1462–1465.
131. Niemeijer M, Van Ginneken B, Russell SR, Suttorp-Schulten MSA, Abràmoff MD. Automated detection and differentiation of drusen, exudates, and cotton-wool spots in digital color fundus photographs for diabetic retinopathy diagnosis. InvestigOphthalmol Vis Sci. 2007;48(5):2260–7.
132. Philip S, Fleming AD, Goatman KA, Fonseca S, McNamee P, Scotland GS, et al. The efficacy of automated “disease/no disease” grading for diabetic retinopathy in a systematic screening programme. Br J Ophthalmol. 2007;91:1512–7. [PMCID: PMC2095421] [PubMed: 17504851]

133. Messidor 1200 -Web URL: http://messidor.crihan.fr/index-en.php
134. DRIVE dataset Web URL: http://www.isi.uu.nl/Research/Databases/DRIVE/
135. ARIAWeb URL: http://www.eyecharity.com/aria_online.html
136. Abràmoff MD, Folk JC, Han DP, Walker JD, Williams DF, Russell SR, et al. Automated analysis of retinal images for detection of referable diabetic retinopathy. JAMA ophthalmology. 2013;131(3):351–357.
137. Fleming AD, Goatman KA, Philip S, Prescott GJ, Sharp PF, Olson JA. Automated grading for diabetic retinopathy: a large-scale audit using arbitration by clinical experts. Br J Ophthalmol. 2010;94:1606–10
138. Scotland GS, McNamee P, Fleming a D, Goatman K a, Philip S, Prescott GJ, et al. Costs and consequences of automated algorithms versus manual grading for the detection of referable diabetic retinopathy. Br J Ophthalmol. 2010;94(6):712–9.
139. Abra`moff MD, Reinhardt JM, Russell SR. Automated early detection of diabetic retinopathy. Ophthalmology. 2010;117:1147–1154
140. Soto-Pedre E, Navea A, Millan S, Hernaez-Ortega MC, Morales J, Desco MC, et al. Evaluation of automated image analysis software for the detection of diabetic retinopathy to reduce the ophthalmologists' workload. ActaOphthalmol. 2015;93(1).
141. Looker HC, Nyangoma SO, Cromie DT, Olson JA, Leese GP, Philip S, et al. Predicted impact of extending the screening interval for diabetic retinopathy: The Scottish 13. Diabetic Retinopathy Screening programme. Diabetologia. 2013;56:1716–25. [PMCID: PMC3699707] [PubMed: 23689796]
142. Goh JKH, Cheung CY, Sim SS, Tan PC, Tan GSW, Wong TY. Retinal Imaging Techniques for Diabetic Retinopathy Screening. J Diabetes SciTechnol [Internet]. 2016;10(2):282–94. Available from: http://journals.sagepub.com/doi/10.1177/1932296816629491
143. Valverde C, Garcia M, Hornero R, Lopez-Galvez MI. Automated detection of diabetic retinopathy in retinal images. Indian J Ophthalmol 2016;64:26-32
144. Tufail A, Rudisill C, Egan C, Kapetanakis VV, et al. Automated Diabetic Retinopathy Image Assessment Software: Diagnostic Accuracy and Cost-Effectiveness Compared with Human Graders. Ophthalmology 2017;124:343-351
145. Gulshan V, Peng L, Coram M, Stumpe MC et al. Development and Validation of a Deep Learning Algorithm for Detection of Diabetic Retinopathy in Retinal Fundus Photographs. JAMA. 2016 Dec 13;316(22):2402-2410.

146. Sánchez CI, Niemeijer M, Dumitrescu A V., Suttorp-Schulten MSA, Abràmoff MD, van Ginneken B. Evaluation of a Computer-Aided Diagnosis System for Diabetic Retinopathy Screening on Public Data. InvestigOpthalmology Vis Sci [Internet]. 2011;52(7):4866. Available from: http://iovs.arvojournals.org/article.aspx?doi=10.1167/iovs.10-6633

147. Kauppi T, Kämäräinen J-K, Lensu L, Kalesnykiene V, Sorri I, Uusitalo H, et al. Constructing Benchmark Databases and Protocols for Medical Image Analysis: Diabetic Retinopathy. Comput Math Methods Med [Internet]. 2013;2013. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3703800/

148. Winder RJ, Morrow PJ, McRitchie IN, Bailie JR, Hart PM. Algorithms for digital image processing in diabetic retinopathy. Comput Med Imaging Graph. 2009 Dec;33(8):608–22

149. John S, Ram K, Sivaprakasam M, Raman R. Assessment of Computer-Assisted Screening Technology for Diabetic Retinopathy Screening in India - Preliminary Results and Recommendations from a Pilot Study. Stud Health Technol Inform. 2016;231(41):74–81.

150. M. U. Akram, S. Khalid, A. Tariq, and M. Y. Javed, "Detection of neovascularization in retinal images using multivariate m-mediods based classifier," Computerized Medical Imaging and Graphics 2013 ; 37, (5) 346–357

151. Oloumi F, Rangayyan RM, Ells AL. Computer-aided diagnosis of proliferative diabetic retinopathy via modeling of the major temporal arcade in retinal fundus images. J Digit Imaging. 2013;26(6):1124–30.

152. Lee J, Zee BCY, Li Q. Detection of neovascularization based on fractal and texture analysis with interaction effects in diabetic retinopathy. PLoS One. 2013;8(12).

153. Abràmoff MD, Lou Y, Erginay A, Clarida W, Amelon R, Folk JC, et al. Improved automated detection of diabetic retinopathy on a publicly available dataset through integration of deep learning. InvestigOphthalmol Vis Sci. 2016;57(13):5200–6.

154. Bennett Walton, Robert B. Garoon, Christina Y. Weng, Jacob Gross, Alex K. Young, Kathryn A. Camero, Haoxing Jin, Petros E. Carvounis, Robert E. Coffee, Yvonne I. Chu. Evaluation of Automated Teleretinal Screening Program for Diabetic Retinopathy. JAMA Ophthalmol. 2016;134(2):204–209.

155. Roy R, Lob A, Pal BP, Oliveira CM, Raman R, Sharma T. Automated diabetic retinopathy imaging in Indian eyes: A pilot study. Indian J Ophthalmol 2014;62:1121-4

156. Chaum E, Karnowski TP, Govindasamy VP, Abdelrahman M, Tobin KW. Automated diagnosis of retinopathy by content-based image retrieval. Retina. 2008;28:1463–77

157. Quellec G, Lamard M, Cazuguel G, Bekri L, Daccache W, Roux C, et al. Automated assessment of diabetic retinopathy severity using content-based image retrieval in multimodal fundus photographs. InvestigOphthalmol Vis Sci. 2011;52(11):8342–8.
158. Kaushal Solanki, MalavikaBhaskaranand, ChaithanyaRamachandra, Sandeep Bhat, Muneeswar Gupta Nittala, Srinivas R Sadda, Jorge Cuadros; Validation of EyeArt Automated Diabetic Retinopathy Screening System on large cohort of mydriatic and non mydriatictelescreening data from EyePACS. Invest. Ophthalmol. Vis. Sci. 2017;58(8):3775.
159. SiddarthRathi, , Edmund Tsui, Nitish Mehta, et al The Current State of Teleophthalmology in the United States Ophthalmology 2017;124:1729-34
160. Litvin T V., Weissenberg CR, Daskivich LP, Zhou Q, Bresnick GH, Cuadros JA. Improving Accuracy of Grading and Referral of Diabetic Macular Edema Using Location and Extent of Hard Exudates in Retinal Photography. J Diabetes SciTechnol 2016; 10: 262–270
161. World Health Organisation, Diabetes care and research in Europe: The St. Vincent Declaration. Diabetes mellitus in Europe: A problem for all ages in all countries. A model for prevention and self care, St. Vincent (Italy), 1989.
162. Reda,E.,Dunn,P.,Straker,C.,etal.,Screeningfordiabeticretinopathyusing the mobile retinal camera: The Waikato experience, New Zealand Medical Journal, 116(1180), 562, 2003.
163. Bhaskaranand M, Ramachandra C, Bhat S, Cuadros J, Nittala MG, Sadda S, et al. Automated Diabetic Retinopathy Screening and Monitoring Using Retinal Fundus Image Analysis. J Diabetes SciTechnol [Internet]. 2016;10(2):254–61. Available from: http://journals.sagepub.com/doi/10.1177/1932296816628546
164. Trucco E, Ruggeri A, Karnowski T, Giancardo L, Chaum E, Hubschman JP, et al. Validating Retinal Fundus Image Analysis Algorithms: Issues and a Proposal Validating Retinal Fundus Image Analysis Algorithms. Invest Ophthalmol Vis Sci. 2013;54(5):3546–59.

LIST OF ABBREVIATIONS

DR	Diabetic Retinopathy
NPDR	Nonproliferative Diabetic Retinopathy
DME	Diabetic Maculopathy
CSME	Clinically Significant macular edema
PDR	Proliferative diabetic retinopathy
HTIC	Healthcare Technology Innovation Center
SN	Sankara Nethralaya
ETDRS	Early Treatment Diabetic Retinopathy Study
ICDR	International Classificatoin of Diabetic Retinopathy

CERTIFICATE FOR ANTI PLAGIARISM CHECK

This is to certify that this dissertation work titled **"TO COMPARE THE ACCURACY OF COMPUTER AIDED GRADING FOR PRESENCE OR ABSENCE OF DIABETIC RETINOPATHY FOR TYPE 2 DIABETIC PATIENTS IN A TELE-SCREENING PROGRAM"** of the candidate Dr Sheila John with registration Number .: ACI(2)/53775/2012 for the award of Ph.D. in the branch of Ophthalmology . I personally verified the urkund.com website for the purpose of plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows 3 percentage off plagiarism in the dissertation.

Guide & Supervisor sign with seal
Dr Jyotirmay Biswas
Director of UVEA & Ophthalmic Pathology
Medical Research Foundation

[URKUND] Confirmation | Home - URKUND

Secure | https://secure.urkund.com/account/#317143/0/0

URKUND

Help | Upload documents | SHEILA JOHN

Analysis Address : sheilajohn24.mgrmu@analysis.urkund.com

sheilajohn24.mgrmu@analysis.urkund.com (1) | New folder | Settings | 1/1

3%	D34189558	SYN THESIS 13.pdf	Antiplagiarism certificate	3 MB	30386 word(s)	SHEILA JOHN	12/23/2017 9:42 AM

[Urkund] 2% similarity - | D34189558 - SYN THESIS | Home - URKUND

Secure | https://secure.urkund.com/view/33701464-146582-981006#DcgxDoMwEEXBu7h+inb/rm3gKhFFhAJyERrKKHcPzRTzLZ+rLE/HDb8NPPGKd+RIKFCihu6ZCMJJKo3OvFKucZxjH9vr3N5IsYfJ5gyvypp9smj6/QE=

URKUND | SHEILA JOHN (sheilajohn24)

Document: SYN THESIS 13.pdf (D34189558)
Submitted: 2017-12-23 14:12 (+05:0-30)
Submitted by: SHEILA JOHN (sheilajohn24@gmail.com)
Receiver: sheilajohn24.mgrmu@analysis.urkund.com
Message: Antiplagiarism certificate Show full message

3% of this approx. 62 pages long document consists of text present in 12 sources.

Sources | Highlights

Rank	Path/Filename
	https://www.duo.uio.no/handle/10852/34723
	100960622028-TS.pdf
	DR-MATHIEW TRANSFORMATION PAPER.docx.doc
	http://www.pitt.edu/~super7/46011-47001/46191.ppt
	http://messidor.crihan.fr/index-en.php
	http://www.isi.uu.nl/Research/Databases/DRIVE/
	http://www.adcis.net/en/DownloadThirdParty/EOphtha.html

1 Warnings | Reset | Export | Share

TITLE: To compare the accuracy of Computer Aided grading for presence or absence of diabetic retinopathy for type 2 diabetic patients in a Tele-screening program. INTRODUCTION The prevalence of Diabetes Mellitus in the world is estimated to be 439 million by 2030 (1) out of which 80% reside in Asia(1–3) and more than 60 million are in India and this is expected to increase to more than 100 million (3,4) by 2030.The first national study conducted by the Indian Council of Medical Research (India Diabetes study(5) for people <20 years, determined the prevalence of pre -diabetes (impaired fasting blood glucose, and impaired glucose tolerance) and diabetes to be 77.2 million and 62.4 million people respectively. The conversion rate of pre-diabetes to diabetes was 58.9% and for normal persons the conversion rate to dysglycemia was 45% in the 10 year follow up of patients in the Chennai Urban Rural Epidemiology Study (CURES). (6) Based on the reports of the international federation of diabetes (IFD) (3) there will be 629 million people(3) with diabetes aged (20-79 years) by 2045.12% of global expenditure is spent on diabetes.Three quarters of the people

65% # 1 Active

is a chronic disease that occurs either when the pancreas does not produce enough insulin (type 1) or when the body

cannot effectively use the insulin it produces (type 2). Insulin is a hormone that regulates blood sugar by enabling the glucose from food to enter the body cells and be used as a source of energy. Hyperglycemia, is a common effect of uncontrolled diabetes and leads to serious damage to many of the body's organs. Long-term complications of diabetes develop gradually, depending on the duration and glycemic control and are macrovascular and microvascular (8) in nature. Microvascular complications include diabetic neuropathy, nephropathy and retinopathy. 1)Macrovacular - Blood vessel (vascular disease) damage: Diabetes dramatically increases the risk of various cardiovascular problems, (9) including hypertension, heart attack, and stroke. 2) Nerve damage (neuropathy) and foot damage: Excess sugar can injure the walls of the tiny blood vessels (capillaries) that nourish the nerves, especially in the foot region and this could lead to loss of all sensation in the affected limbs and foot ulcers. 3) Kidney damage (nephropathy): The kidneys have millions of tiny blood vessel clusters (glomeruli) that filter waste from the blood. Hyperglycemia can damage this delicate filtering system and can lead to kidney failure or irreversible end-stage kidney disease, which may require dialysis or a kidney transplant.

Urkund's archive: Anna University, Chennai / DR-MATHIEW TRANSFORMATION PAPER.docx.doc 65%

The contents of the source document cannot be displayed!

Possible reasons:

1. The document is stored in the URKUND Partner section and is listed as inaccessible. If you do not own this book already, you need to purchase it from the vendor.

2. The document has been exempted as a viewable source in the URKUND Archive by the author

Submitter and Receiver information is available by hovering the mouse pointer on the source name above.

Informed Consent Form for Research Study

To compare the accuracy of Computer Aided grading for presence or absence of diabetic retinopathy in type 2 diabetes patients in a telescreening program.

Principal Investigator: **Dr Sheila john**
Consultant Ophthalmologist and
Head of Teleophthalmology dept.
Sankara Nethralaya
Chennai -600 006

Our studies are aimed at establishing feasibility of Computer aided software applications for diagnosis for the presence or absence of diabetic retinopathy in Telescreening programme. Specifically, we are seeking logistical and clinical support for testing the effectiveness and efficacy of Computer Aided software applications for the "Presence or absence of" Diabetic Retinopathy with the existing manual system of grading done by ophthalmologist/optometrist in a Telescreening program.

Our studies entail taking fundus photographs of patients who come to the diabetic clinic,Telecamps, and Sankara Nethralaya Eye Hospital to have a medical / eye examination in order for the physician and ophthalmologist to diagnose and advise them on their ailments. The fundus photograph will form a part of your routine examination. The study will in no way influence the plan of care/treatment of your disease condition.

CONFIDENTIALITY

The results of the study may be published in a medical book or journal, or presented at meetings for educational purposes. Neither your name, nor any other personal health information that specifically identifies you, will be used in those materials or presentations. The study doctor or the imager will photograph your eyes as part of the examination. Such photographs may be used for educational purposes or published in medical or scientific publications. No personal health information that specifically identifies you will be disclosed without your permission.

CONSENT STATEMENT

I have read or this form has been read to me and I have had an opportunity to discuss and ask questions about the information describing this medical research study in this consent form. The study doctor or study staff have explained this information and answered all of my questions to my satisfaction. I voluntarily consent to take part in this study.

I understand that my participation in this study may involve the photographing of my eyes, specifically the back portion - Retina. I also understand that my identity will not be disclosed and such photographs will be used for educational purposes or published in medical or scientific publications.

I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s). I agree to take part in the above study.

_____

Name of Participant /patient with MRD NO:

_____ _____

Signature of Participant Date

_____

Name & Designation of Person Obtaining Consent

_____ _____

Signature of Person Obtaining Consent Date

_____

Name of Witness

_____ _____

Signature of witness Date

VISION RESEARCH FOUNDATION

[Regd. Under Act XXI of 1860]
New No.41, Old No.18, College Road, Chennai - 600 006

Dr. H. N. MADHAVAN, M.D. Ph.D. President
Mr. R. RAJAGOPAL Vice-President
Dr. TARUN SHARMA, MD., FRCS Ed., MBA. Hony. Secretary
Mr. R. S. FALOR Treasurer

Dr. RONNIE JACOB GEORGE, D.O., DNB., MS
Director - Research

Comments

Comments by Ethics Subcommittee Member :
Queries were raised by the members and Dr. Sheila John replied to the comments. The proposal was approved.

The Ethics Committee is working according to ICH-GCP and applicable laws and regulations.

26.02.2013
Date of Issue

Hon. Justice S Mohan
Chairman, Ethics Sub-Committee

Ethics Committee Membership List

Name	Profession	Affliation	Voting during the meeting	Member of the study
Hon. Justice Mohan S	Former Judge	Outside Member	✓ Yes / No	Yes / ✓ No
Dr. Ronnie Jacob George	Ophthalmologist	Sankara Nethralaya	✓ Yes / No	Yes / ✓ No
Dr. S Krishnakumar	Ophthalmologist	Sankara Nethralaya	✓ Yes / No	Yes / ✓ No
Dr. Tarun Sharma	Pathologist	Sankara Nethralaya	✓ Yes / No	Yes / ✓ No
Dr. H N Madhavan	Microbiologist	Sankara Nethralaya	✓ Yes / No	Yes / ✓ No
Dr. T S Surendran	Ophthalmologist	Sankara Nethralaya	✓ Yes / No	Yes / ✓ No
Dr. Bakulesh M Khamar	Ophthalmologist	Outside Member	✓ Yes / No	Yes / ✓ No
Dr. K P Misra	Cardiologist	Outside Member	✓ Yes / No	Yes / ✓ No
Dr. Santha Devi T	Thoracic Physician	Outside Member	✓ Yes / No	Yes / ✓ No
Dr. Manjula Dutta	Epidemiologist	Outside Member	✓ Yes / No	Yes / ✓ No
Dr. Rama Shanker Verma	Biotechnologist	Outside Member	✓ Yes / No	Yes / ✓ No
Prof. N Veezhinathan	Theologist	Outside Member	✓ Yes / No	Yes / ✓ No
Lion G V Raman	Social Service	Outside Member	✓ Yes / No	Yes / ✓ No
Mrs. Radhika Krishnan	Advocate	Outside Member	✓ Yes / No	Yes / ✓ No
Mrs. Sujatha Viswanath	Common Person	Outside Member	✓ Yes / No	Yes / ✓ No

Phone : 2827 1616, 4227 1500, Fax : 91 - 44 - 2825 4180
INTERNET e-mail : drhnm@snmail.org, nanu@snmail.org
WEB : http://www.sankaranethralaya.org

VISION RESEARCH FOUNDATION

[Regd. Under Act XXI of 1860]
New No.41, Old No.18, College Road, Chennai - 600 006

Dr. H. N. MADHAVAN, M.D. Ph.D. President
Mr. R. RAJAGOPAL Vice-President
Dr. TARUN SHARMA, MD., FRCS Ed., MBA. Hony. Secretary
Mr. R. S. FALOR Treasurer

Dr. RONNIE JACOB GEORGE, D.O., DNB., MS
Director - Research

Name and Address of Ethics Committee :	Ethics Sub-Committee (Institutional Review Board) Vision Research Foundation New No.41, Old No.18 College Road Chennai 600 006.

Ethics Committee Decision

Study Code :	350-2012-P
Study Protocol Title :	To compare the Accuracy of Computer Aided grading for presence or absence of diabetic retinopathy in type 2 diabetes patients in a telescreening program
Principal Investigator(s) :	**Dr Sheila John,** Vision Research Foundation Sankara Nethralaya, New No.41, Old No.18 College Road Chennai 600 006.
Name of Trial Site(s)	Vision Research Foundation, Sankara Nethralaya New No.41, Old No.18 College Road Chennai 600 006.

The Ethics Committee has reviewed the following documents related to the above study :

To compare the Accuracy of Computer Aided grading for presence or absence of diabetic retinopathy in type 2 diabetes patients in a telescreening program

Review and Approval

21.02.2013 & Chennai
Date and Place of Decision

The study / Study documents
- ✓ are approved
- are not approved
- Require modification prior to approval

An explanation / Comments are provided in comments
- ✓ Yes
- No

Phone : 2827 1616, 4227 1500, Fax : 91 - 44 - 2825 4180
INTERNET e-mail : drhnm@snmail.org, nanu@snmail.org
WEB : http://www.sankaranethralaya.org

Driving Reform: Digital Health is Everyone's Business
A. Georgiou et al. (Eds.)

doi:10.3233/978-1-61499-558-6-139

A Pilot Study to Improve Access to Eye Care Services for Patients in Rural India by Implementing Community Ophthalmology through Innovative Telehealth Technology

Sheila JOHN [a,1], M PREMILA [a], Mohd JAVED [a], Vikas G [a] and Amol WAGHOLIKAR [b]
[a] *Department of Teleophthalmology, Medical Research Foundation, Sankara Nethralaya, Chennai, India*
[b] *The Australian e-Health Research Centre, CSIRO, Brisbane, Australia*

Abstract. Objective: To inform about a very unique and first of its kind telehealth pilot study in India that has provided virtual telehealth consultation to eye care patients in low resource at remote villages. **Background:** Provision of Access to eye care services in remote population is always challenging due to pragmatic reasons. Advances in Telehealth technologies have provided an opportunity to improve access to remote population. However, current Telehealth technologies are limited to face-to-face video consultation only. We inform about a pilot study that illustrates real-time imaging access to ophthalmologists. Our innovative software led technology solution allowed screening of patients with varying ocular conditions. **Methods:** Eye camps were conducted in 2 districts in South India over a 12-month period in 2014. Total of 196 eye camps were conducted. Total of 19,634 patients attended the eye camps. Innovative software was used to conduct consultation with the ophthalmologist located in the city hospital. The software enabled virtual visit and allowed instant sharing of fundus camera images for assessment and diagnosis. **Results:** About 71% of the patients were found to have Refractive Error problems, 15% of them were found to have cataract, 7% of the patients were diagnosed to have Retina problems and 7% of the patients were found to have other ocular diseases. The patients requiring cataract surgery were immediately transferred to city hospital for treatment. Software led assessment of fundus camera images assisted in identifying retinal eye diseases. **Conclusion:** Our real-time virtual visit software assisted in specialist care provision and illustrated a novel tele health solution for low resource population.

Keywords. Telehealth, Ophthalmology, Mobile Eye care services, remote population, low resource settings

Introduction

Approximately 285 million people worldwide live with visual impairment [1]. Of these, 39 million people are blind (defined as best corrected vision of less than 3/60 in the

[1] Corresponding Author: Sheila John, D.O., Department of Teleophthalmology, Sankara Nethralaya, Medical Research Foundation, New No. 41, Old No. 18, College Road, Chennai 600006, India; Email: sheilajohn24@gmail.com.

better eye), and low vision in approximately 117 million people is due to uncorrected refractive errors [2]. 80% of global blindness is avoidable. One in every three treatable blind people in the world is an Indian. The number of blind persons in India is currently over 18 million and this estimate is 50% more than the figure of 12 million from a decade ago. It amounts to approximately one-fourth of all the blind people worldwide making the Indian blind population account for 20% of blindness [3]. Cataract is still the major cause of avoidable blindness in India. Taking the existing prevalence rate into account, it may be difficult to achieve total elimination of blindness in India by 2020. The recent epidemiological surveys have shown that Cataract, diabetic retinopathy, glaucoma, and childhood blindness have started to cause increased number of blind people in India. Hence, ophthalmology in India needs to be more holistic and medical initiatives towards all eye diseases should be taken. The high magnitude of avoidable blindness in India is concentrated in the rural areas mainly due to the lack of trained ophthalmologists being present in villages, underutilisation of public health services for the eye due to lack of awareness, lack of capital (from both government and public sector) for introducing facilities in the rural areas that can provide primary and secondary care for the eye and lack of adequately trained manpower. These problems can be addressed effectively by mobile, comprehensive and sustainable eye care systems easily accessible to the rural people in villages. Sankara Nethralaya (SN), a unit of Medical Research Foundation, is a tertiary eye care center in South India and is committed to patient care, ophthalmic research, and training at all levels for over three decades. With the aim of providing comprehensive and quality eye care to the rural population, a unique program implementing a mobile tele-ophthalmology unit was designed at SN and launched in 2003 [4]. SN conducts eye care camps in villages of South India. These remote outreach camps must ensure quality, especially in terms of screening vision threatening diseases, referral services, and affordable, rapid rehabilitation. However, subsequent interventions and follow up visits require the same medical records at multiple camp locations. To facilitate this, SN has implemented recording clinical data on electronic medical records (EMR). Teleophthalmology and EMR thus have unleashed a new frontier in ophthalmology for screening and recording of common ophthalmic diseases [5].

Teleophthalmology can reduce the need for travel for both the patient and ophthalmologist. The advances in internet technology and growth of internet across India's population have provided a tremendous opportunity to develop innovative Telehealth solutions [6, 7]. The trend of using video conferencing software solutions for tele-consultation is commonly observed [8]. However, these solutions require higher bandwidth and they also cannot provide real-time image sharing for point-of-care clinical diagnosis and treatment decision making. Therefore, the quality of Telehealth experience does not meet requirements for a clinical-grade consultation. We have addressed this very major limitation in the current state-of-the-art facility by developing an innovative Telehealth consultation service.

Our innovative software enabled service provides real-time fundus image sharing and annotation which allows a specialist ophthalmologist in the city hospital to examine and assess eye anomalies of patients in remote villages that have inadequate internet bandwidth. In this paper, we inform the results of our unique pilot study involving virtual visits during eye camps in low resource settings in villages in South India. Our pilot study suggests that improving access to eye care may facilitate in reducing the incidence of blindness in underserved as well as urban communities.

1. Methods

1.1. Identification of Remote Villages for Eye Camps

Remote Villages in Kanchipuram and Thiruvallur districts with a population of one million from the state of Tamil Nadu were chosen to provide comprehensive eye examination under the directives of the head of the department of Teleophthalmology at SN. The inclusion criteria for the villages considered factors such as distance from the base hospital being an important one (within150km to 200km) of the base hospital in Chennai, Prevalence of district-wise blindness as published by the District Blindness Control Society (DBCS) of India and Economic feasibility of the camp site. After the districts and villages were identified, the permission of the head of the DBCS was obtained in all states. The geographic locations of the villages are shown in Figure 1.

Figure 1. Eye camp locations and eye camp bus.

1.2. Conduct of Eye Screening Camps

This pilot study was conducted in eye screening camps in rural villages near Chennai, Tamilnadu from January 2014 until December 2014. The participating patients were from villages without adequate access to eye care services. The eye screening camps were conducted by a team composed of optometrists, social workers, administrative staff, ophthalmologists as well as information technology experts. This team travelled to the eye camp sites in a bus equipped with fundus camera, slit lamps and other instruments required for conducting eye screening examination. The patients underwent comprehensive eye examination by the team members to determine the prevalence of any ocular conditions. A hospital-based ophthalmologist advised patients through Tele consultations for further treatment. The specialist ophthalmologist consultation was carried out over video conferencing using data card and web-based

communication tools. A detailed ocular assessment was recorded using Electronic Medical Records. The work flow at the eye screening camps is shown in Figure 2.

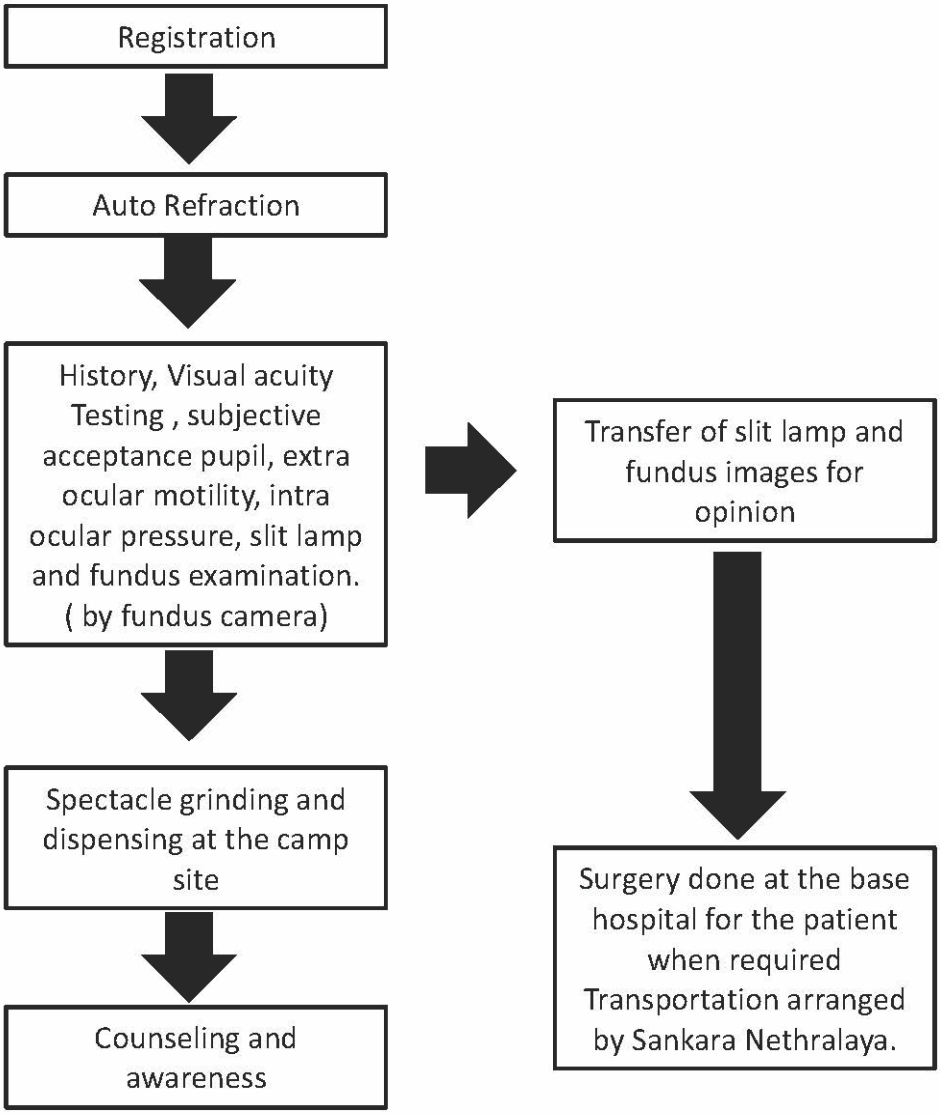

Figure 2. Tele Consultation flow chart.

1.3. Virtual Visit

An innovative software was used to share the fundus camera images in real-time. Since the software used accurate application-level sharing, there was no necessity to transfer images. A schematic representation and implementation of our solution used to conduct virtual visits is shown in Figure 3.

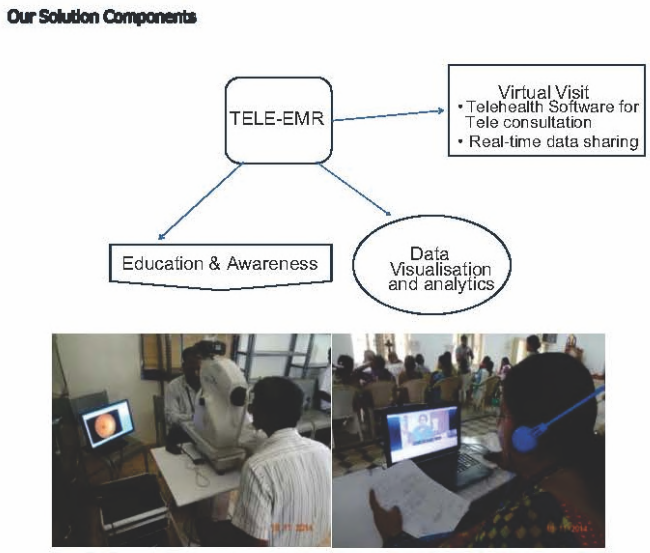

Figure 3. Schematic representation and implementation of our real-time virtual visit solution.

The ophthalmologist based at the city hospital could provide an immediate advice in real-time through the virtual consultation visit. All the patient records in the Tele-EMR were updated with the fundus camera images. The diagnosis of eye diseases is mainly based on eye images generated by the fundus camera. Therefore, automatic integration of the eye images with clinical notes at every visit and storing them into EMR will be very useful, especially in chronic diseases such as glaucoma, diabetic retinopathy and macular degeneration. Our solution enables seamless storing the eye images in the EMR and hence these images can be analysed for management of chronic eye diseases. The virtual visit component of our solution enabled sharing of fundus images with the ophthalmologist in the city hospital. The image sharing was implemented with a simple "click and share" feature. An exact replica of the fundus camera image appeared on the ophthalmologist's computer screen. The software's unique capability enabled real-time sharing of images in low bandwidth setting with weaker internet connectivity. Our solution thus addressed the limitations of technology infrastructure in rural regions of India where only allows satellite-based tele-connectivity is available with its implementation challenges. Our solution also simplified the work flow for telehealth consultation. The solution also required very little training to the eye camp site operators. The commercial-grade software was implemented without any development cost. Thus our model offers a cost-effective and efficient telehealth solution.

2. Results and Discussion

From January 2014 to December 2014 we have conducted 196 camps and a total number of 19,634 patients were examined. In our study 10073 males and 9561 females underwent comprehensive eye examination. The study shows a slightly higher percentage presence of male patients. About 51.3% of the patients in this study were males and 48.7% of them were females. The analysis of the results is shown in Figure 4.

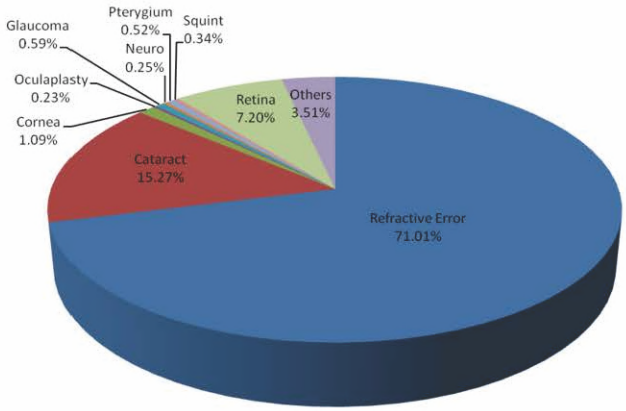

Figure 4. Analysis of patient diagnosis.

About 71% of the patients were having Refractive Error problems, 15% of them were found to have cataract, and 7% of the patients were detected with Retina problems [9] of which about 4% had diabetic retinopathy [10]. Seven (7) % of the patients had other ocular diseases and some of them were referred to the base hospital to undergo specific tests to confirm the diagnosis. Refractive errors included myopia, hyperopia and presbyopia for which glasses were dispensed at the eye camp location, as a corrective measure, with the help of mobile refraction van. All patients with significant cataract and other disorders requiring surgical intervention or other investigations as deemed fit after tele-consultation [11] were issued registration slips and advised to attend the appropriate subspecialty clinics at the base hospital at no cost. The software led diagnosis assisted in proactive assessment of patient's eye condition and resulted into immediate intervention to avoid any further deterioration of their eye health. About 1950 patients were referred to main hospital for cataract surgery during the study period and those patients underwent cost free state of art cataract surgery successfully at the SN community hospital. Our solution thus illustrates promising results for further development into a regular health service that can assist specialist clinicians with the ultimate benefit to the underserved population.

3. Conclusion

We conducted a pilot study that illustrated application of software led telehealth implementation to screen patients in low resource settings. Our pilot study showed that Virtual visit based eye care services can assist in identifying causes of blindness and avoidable blindness can be treated. A large scale commercial rollout of our solution can be considered for future implementation.

Acknowledgement

This pilot study has been supported by Sankara Nethralaya (SN), a unit of Medical Research Foundation with appropriate ethics approval. The author(s) sincerely thank Sankara Nethralaya and Medical Research Foundation for their support.

References

[1] Vision 2020 global initiative for the elimination of avoidable blindness: Action plan 2006–2011. Available at www.who.int/blindness/en/index.html (last accessed September 21, 2011).
[2] Dandona L, Dandona R. What is the global burden of visual impairment? BMC Med 2006;4:6.
[3] Online News Article, http://www.deccanherald.com/content/240119/india-accounts-20-per-cent.html, ^ April 2012.
[4] John S, Sengupta S, Reddy SJ, Prabhu P, Kirubanandan K, Badrinath SS. The Sankara Nethralaya Mobile Teleophthalmology Model for Comprehensive Eye Care Delivery in Rural India. Telemedicine and e-Health. 2012; 18: 382 – 7.
[5] Williams F, Boren SA. The role of the electronic medical record (EMR) in care delivery development in developing countries: a systematic review. Inform Prim Care. 2008; 16:139-45
[6] McKinsey & Company, Report, India's Internet opportunity, March 2013, Viewed online, May 2014.
[7] McKinsey & Company, Report, Online and upcoming: The Internet's impact on India, December 2012, Viewed Online, May 2014.
[8] Xiao, D., Vignarajan, J., Lock, J., Frost, S., Tay-Kearney, M.-L., & Kanagasingam, Y. (2012). Retinal image registration and comparison for clinical decision support. The Australasian Medical Journal, 5(9), 507–512. doi:10.4066/AMJ.2012.1364.
[9] Gupta A, Raman R, Sharma T Evaluation of the effectiveness of diagnostic & management decision by teleophthalmology for retinal diseases.. Indian J Med Res. 2014 Jun;139(6):954-5.
[10] Surendran TS, Raman R, Teleophthalmology in Diabetic Retinopathy, J Diabetes Sci Technol. 2014 Mar 17; 8(2):262-266
[11] Paul PG, Raman R, Rani PK, Deshmukh H, Sharma T, Patient satisfaction levels during teleophthalmology consultation in rural South India. Telemed J E Health. 2006 Oct; 12(5):571-8

HiNZ
Health Informatics New Zealand

This is to certify that

Sheila John

attended

HiNZ 2016 + NZNIC-16 + GT 2016 + SFT-16

HiNZ Conference, NZ Nursing Informatics Conference, Global Telehealth, Successes & Failures in Telehealth

- [ ] 31.10.2016 | EMRAM workshop | 3 hours
- [ ] 31.10.2016 | Continuity of Care workshop | 3 hours
- [ ] 31.10.2016 | HSAG workshop | 5 hours
- [ ] 31.10.2016 | Universal Health Coverage workshop | 3 hours
- [x] 01.11.2016 | HiNZ + SFT + GT plenary day | 6.5 hours
- [x] 02.11.2016 | HiNZ + SFT + GT plenary day | 6.5 hours
- [x] 03.11.2016 | HiNZ + SFT + GT plenary day | 5.5 hours
- [ ] 03.11.2016 | NZNIC conference | 6 hours
- [x] Speaker

HEALTH INFORMATICS NEW ZEALAND · WWW.HINZ.ORG.NZ · HiNZ

Signed

Kim Mundell
HiNZ Chief Executive

ABSTRACTS

The 7th International Conference on Transforming Healthcare with Information Technology, and The 21st Conference of the International Society for Telemedicine and eHealth
Chennai, India
20 -22 October 2016

Index by Session
(Hyperlinked session titles – mouse-over and [ENTER] to navigate; to locate an author – [CTRL][F], type in the surname, [ENTER])

Session 8: **Industry Bytes**

- Cloud Computing In Health Care: A Game Changer. UK Ananthapadmanabhan
- Drones in Healthcare : A Global and National Perspective. K Ramachandra
- Deploying Technology In Preventing NCDs: Lessons From the Arogya World mDiabetes Program. S Venkataraman
- Evidence Based Clinical Decision Support – An Enabler For Clinicians In The 21st Century. L Singh
- Role of Predictive Analytics In Improving Healthcare Effectiveness. GGK Tech, India

Session 9: **Clinical Applications of HCIT**

- How To Improve Large Scale Emergency Management By Introducing Modern ICT. O Eielsen, JS Moy, B Nordboe
- A Telemedicine's New Step Ongoing : Transatlantic Teleconsultation. A Petitet, J Cinqualbre, D Uhlrich, S D'hardiville, G Menand, E Cloche, S Widmer, C Bronner
- The Global Trend of eHealth: Focusing On Regional Health Information Networks. M Tsuji
- ePharmacy and ePrescription: Present and The Future. E Reddy

Session 10: **Special addresses**

- Delivering HCIT. R Branzell
- Quality Health Care: Technology and Data Drive Improvement. S Lieber
- Heathcare Apps – What We Should Look Out For. A Joshi
- Implementing A Strategy Building A Secure And Resilient Critical Information Infrastructure. M Tiwari
- Role of ICT in Medical Research. S Swaminathan

Session 10a: **HCIT Spectrum**

- Enhancements to a Computer-Assisted Screening Technology For Diabetic Retinopathy: System Redesign Based On Our Pilot Study In Indian Setting. S John, S Kulasekaran, S Mulay, Ki Ram, M Sivaprakasam, R Raman, SS Badrinath
- Evaluating the Feasibility of Virtual Mentoring Connecting an Academic Centre to District Health Professionals From Bihar In Providing Quality Care For Alcohol Use Disorders. M Jayant, S Lekhansh, A Ashfaq, KSunil, N Sinha, AK Shahi, C Prabhat, K Arun, S Lakshmanan,[1] P Murthy, V Benegal, M Komaromy, S Arora
- Virtual Knowledge Network Nimhans Echo: Innovative Tele-Mentoring Model For Skilled Capacity Building In Addiction And Mental Health. P Chand, K Arun, M Jayant, S Lakshmanan, S Manjula, R Lakshmi, N Kubenthiran, V Benegal, P Murthy, M Komaromy, S Arora
- Is HIE Enough For Care Coordination? A Jain
- Personalized Mobile Applications in HealthCare. B Upadhya
- The Pitfalls To Achieving The Standardisation And Interoperability Of Clinical Data. RQ Siddiqui, F Siddiqui, S Pachauri, S Ali
- The Use Of Web Offline Seminars By Brazilian Physical Therapists. D De Mello Florentino, KM Silva, M I De Castro E Souza.
- Cloud Applications on Airborne and Allergy Diseases Vulnerability. SK Sharma, P Rahi
- Implementation Of Online Safety Incident Reporting System In A Tertiary Care Teaching Hospital. B Johnson, MS Arun, G Somu

getting the basics right matters. By basics, I mean the fundamental principles of good infrastructure management—know your network, guard your perimeter, and keep systems up to date.

Many IT organizations overlook fundamental security measures in their haste to adopt the latest cybersecurity solution being pushed by the press or marketed by vendors. In most cases they fail to utilize the existing features built into the products that they have already bought. In many cases, organizations fail to even implement their IT infrastructure as recommended by the OEMs and also best practices. However, a persistent adversary requires an informed and persistent defense. Security professionals must take a life-cycle approach to cybersecurity as the foundation of their strategy and organizations formulate and implement a Digital Transformation Strategy with a three or five year vision.

A life-cycle model of cybersecurity identifies the people, processes, and technology needed to protect systems, detect intrusions, respond to security events, and recover systems. Through proactive assessment, planning, and preparation each step of the way, your organization can mitigate the risks associate with cyber threats and improve its strategy going forward in a cycle of continuous improvement.

The session is intended to cover some of the forgotten fundamentals of Information Security, sharing from experience the common mistakes made in the conduct of IT Risk Assessments and application of security controls.

Back to Contents

ROLE OF ICT IN MEDICAL RESEARCH

Soumya Swaminathan
Secretary of Health Research, Govt of India and Indian Council for Medical Research

Back to Contents

MODERATOR'S OVERVIEW

Sangita Reddy
Apollo Hospital Group, India

Back to Contents

The 7th International Conference on Transforming Healthcare with Information Technology

HCIT Spectrum

ENHANCEMENTS TO A COMPUTER-ASSISTED SCREENING TECHNOLOGY FOR DIABETIC RETINOPATHY: SYSTEM REDESIGN BASED ON OUR PILOT STUDY IN INDIAN SETTING

Sheila John, S Kulasekaran, Supriti Mulay, Keerthi Ram, Mohanasankar Sivaprakasam, Rajiv Raman, SS Badrinath

Background: Diabetes related vision loss is a major risk among 50 million diabetics in India, and diabetic retinopathy (DR) is identified as a leading cause of preventable vision loss in working age population. The current clinical protocols especially tele-screening for early detection, are well-amenable to augmentation by computer-assisted screening technology, for providing cost-effective large-scale deployment and preventive eye care for diabetics. We had developed a DR screening system based state of art image analytics technology, and conducted a pilot study of our system in a retrospective setting, to assess the applicability and value add in large prospective studies and routine telescreening. Though the performance of our system

was at par with international systems, our experiment indicated the need for 3 specific capabilities to be incorporated in the system in order to succeed in Indian settings.

Methods: Our DR image screening system was developed based on images from publicly available retinal image datasets (about 2000 images) from around the world. The pilot study included 200 cases sampled uniformly from an epidemiological study to represent various levels of pathology. The data and the system outputs showed the need for a strong module examining image quality, specific analysis for clinically significant macular edema, and analytics for fail-safe recognition and flagging of proliferative (late-stage) DR. A dataset of 587 images was constructed from our study to develop these modules.

Results: The developed system for image quality examination uses machine learning to rank the quality of an image, and bypass further analysis if details in the image are scarce (could be due to advanced pathology or auxiliary complications). The second module localizes the macula, identifying macular edema (exudative clusters, proximity to macula, and intensity) and grades clinically significant macular edema. The third important module for proliferative DR examines neovascularity and provides a heat-map of the different regions of retina which could be having proliferative vascular abnormality and retinal detachment. All the 3 new modules involve novel indigenously developed image analytics, since prior art which is applicable the Indian scenario was found to be scarce.

Conclusion: Learnings from our pilot study of computer-assisted DR screening were used to develop new computational modules specific to needs in Indian scenario. The developed systems are data driven, and can iteratively be refined to provide quality-assured DR screening capability, and empower more technicians to participate in the care delivery process, enabling outreach at national scale.

Back to Contents

EVALUATING THE FEASIBILITY OF VIRTUAL MENTORING CONNECTING AN ACADEMIC CENTRE TO DISTRICT HEALTH PROFESSIONALS FROM BIHAR IN PROVIDING QUALITY CARE FOR ALCOHOL USE DISORDERS

M Jayant,[1] S Lekhansh, [1] A Ashfaq, KSunil,[2] Narendra Sinha,[2] AK Shahi [2] C Prabhat,[1] K Arun,[1] S Lakshmanan,[1] Pratima Murthy,[1] Vivek Benegal, [1] Miriam Komaromy,[3] Sanjeev Arora[3]

[1] Centre for Addiction Medicine, NIMHANS, [2] ECHO Institute USA, [3] State Health Society Bihar

Introduction: The State Health Society, Government of Bihar approached NIMHANS to develop a model to equip non-specialist primary health physicians and counsellors in the management of alcohol use disorders (AUDs), a serious public health problem in India.

Methods: A two week on-site training followed by an online fortnightly virtual tele-mentoring based on NIMHANS ECHO model was employed. Multi-point videoconferencing was used by the 'HUB' (NIMHANS) to conduct tele-health sessions and share best practices with the 'SPOKES' (i.e. physicians and counsellors from nine districts of Bihar). A baseline questionnaire repeated before and after three months of tele-mentoring was used to assess the participants' knowledge, skills and level of expertise. Primary measures to assess the impact of training included a monthly report of the total number of AUD cases seen, admitted for inpatient care and retained in follow-up.

Results: Of the 28 doctors and counsellors who attended the onsite training program, 18 regularly attended the online component and provided feedback at three months. Significant improvements were reported in knowledge, and competence to assess and treat alcohol use disorders .The relative contribution of the online tele-mentoring and handholding component in these improvements was perceived by the participants as 72%. Over three months, 2143 cases were screened across all the centres, of whom 709 (33%) had an AUDIT score greater than 16, indicating harmful use or dependence. The follow up rate was noted to be 49.1%. Only 76 (3%) cases required referral to specialists.

Conclusion: The tele-mentoring model was found to be effective in training non-specialist physicians and counsellors to provide health care for AUDs as reflected by the number of patients seeking treatment, retained in the treatment and a significant decrease in the need for specialist referral. The main barrier for regular participation was internet connectivity.

Back to Contents

Global Telehealth 2015: Integrating Technology and Information for Better Healthcare
G. Gillis et al. (Eds.)

doi:10.3233/978-1-61499-505-0-95

Governance and Management of National Telehealth Programs in Asia

Alvin MARCELO [a,1] Jai GANESH [b], Jai MOHAN [c], DB KADAM [d], BS RATTA [e], Gumindu KULATUNGA [f], Sheila JOHN [g], Andry CHANDRA [h], Oscar PRIMADI [i], Athika Abdul Sattar MOHAMED [j], Muhammad Abdul Hannan KHAN [k], Abul Alam AZAD [l], Portia MARCELO [a]

[a] *University of the Philippines Manila,* [b] *Sri Sathya Sai Central Trust, Prasanthi Nilayam, Andhra Pradesh, India,*
[c] *International Medical University, Malaysia,* [d] *Telemedicine Maharashtra India,* [e] *Telemedicine Society of India,* [f] *Suwasariya, Ministry of Health, Sri Lanka,* [g] *Medical Research Foundation, Sankara Nethralaya, Chennai, India,* [h] *Directorate Ancillary and Health Facility, Ministry of Health Indonesia,* [i] *Center of Data & Information, Ministry of Health Indonesia,* [j] *Ministry of Health Maldives,* [k] *GIZ Bangladesh,* [l] *Ministry of Health, Bangladesh*

Abstract. Telehealth and telemedicine are increasingly becoming accepted practices in Asia, but challenges remain in deploying these services to the farthest areas of many developing countries. With the increasing popularity of universal health coverage, there is a resurgence in promoting telehealth services. But while telehealth that reaches the remotest part of a nation is the ideal endpoint, such goals are burdened by various constraints ranging from governance to funding to infrastructure and operational efficiency. Objectives: enumerate the public funded national telehealth programs in Asia and determine the state of their governance and management. Method: Review of literature, review of official program websites and request for information from key informants. Conclusions: While there are national telehealth programs already in operation in Asia, most experience challenges with governance and subsequently, with management and sustainability of operations. It is important to learn from successful programs that have built and maintained their services over time. An IT governance framework may assist countries to achieve success in offering telehealth and telemedicine to their citizens.

Keywords. Telehealth, telemedicine, IT governance, management, framework

Introduction

Telehealth and telemedicine have been practiced in Asia for quite some time [1,2] but only recently has there been accessible documentation to evaluate public funded national programs. The Telemedicine Development Center of Asia [3] has extensively documented experience providing regional support to countries' need for remote medical education. Innovative private-sector-led programs also abound [4] but largely

[1] Corresponding author: alvin.marcelo@gmail.com.

operate through internal funding. Telehealth programs working nationally with public funds are often unpublished.

The Asia eHealth Information Network (www.aehin.org) is a group of four hundred plus eHealth advocates composed of representatives from ministries of health, ministries of information technology, academe, and non-government sectors with an interest in promoting eHealth in the region and within their respective countries. Since its inception in 2012, the AeHIN has embarked on strengthening the capacity of countries for designing and implementing national-scale health information systems. Recently, it co-organized a conference on measuring and achieving universal health coverage with information and communications technology [5]. In this conference (and in a previous one [6]), telehealth and telemedicine were cited as key technology-dependent activities that can contribute greatly to realizing the benefits of universal health care (UHC). IT governance was also listed as an important enabler for successful national eHealth systems.

Telehealth and telemedicine are complex processes that are dependent on even more complex underlying information technologies. Without an organizing framework like IT governance, implementers of these programs (health and IT professionals) succumb to this complexity and often encounter failure. Adding to the challenge is the lack of experience of many implementers with the sophistication required by systems that need to be deployed nationally.

Many citations can be obtained about telehealth and telemedicine practice in Asia but only a few programs are actually operating (or were designed to operate) at national scale with support and funding from government. This paper aims to collate public funded, national telehealth programs and assess their governance and management systems using an industry-accepted IT governance framework.

COBIT5 is an IT governance framework developed by the Information Systems Audit and Control Association (www.isaca.org). It is considered a best practice framework created and maintained by a global group of experts with experience in governing and managing complex IT environments. The framework is available for free at www.isca.org/cobit .

ISO/IEC 38500 *Information technology – Governance of IT for the organization* is an international standard on corporate governance of IT released by the International Organization for Standardization Organization (ISO) and the International Electrotechnical Commission (IEC). It is a framework for the effective governance of IT at the highest levels of the organization. The standard is downloadable at www.iso.org for a fee. As the two frameworks are comparable, COBIT5, which is freely downloadable, will be used for this study.

A key principle of COBIT 5 is to separate **governance** from **management**. This separation serves to clarify the lines of accountability (governance) and responsibility (management) for key processes in the whole enterprise information technology program. Governance requires "evaluating stakeholder needs; setting direction through prioritization and decision making; and monitoring performance, compliance and progress against plans" [7]. Management on the other hand, takes the "results, guidance and output from these governance activities, and plans, builds, runs and monitors activities (PBRM) to ensure alignment with the direction set by the governance body". This alignment of governance and management is aimed at achieving the enterprise objectives. The hypothesis is that when strategy is aligned with operations, then stakeholder needs will be met.

1. Objectives

The objectives of this article are: to enumerate the various national telehealth programs in Asia, assess their underlying governance and management structures, and identify factors that may contribute to their success or failure from the governance and management perspectives.

2. Methodology

A search of Pubmed for *"national telehealth programs"* AND *"Asia"* was conducted followed by specific searches per country (replacing *"Asia"* with *"country name"*). Requests for information were also released in the AeHIN general mailing list. A Google search was also performed for the same query strings. Regional telehealth activities such as those conducted by the Telemedicine Development Center of Asia (TEMDEC), which are beyond national scope, were excluded. Programs that have reached national-scale but not yet formally endorsed by the ministry of health were also excluded from the study.

3. Results

The search yielded a total of nine national/state-wide telehealth programs from seven countries (Table).

3.1. National Telehealth Programs

Seven countries have national telehealth programs collected from the review of literature and from the request for information.

A review of the state of governance and management of these national telehealth programs was done from the following sources: published articles, official websites, and personal communications with key informants. Where possible, information was obtained from the focal point of the management body of the national telehealth program.

Table 1. State of governance and management of publicly funded national telehealth programs in Asia

Country (program)	Governance	Management	Reference
Bangladesh (Health Information System, e-Health and Medical Biotechnology)	Ministry of Health and Family Welfare	Management Information System, Director General of Health Service	www.dghs.gov.bd/index.php/en/data/84-english-root/ehealth-eservice/490-telemedicine-service
India (ISRO Telemedicine Program)	Development and Education Communication Unit (DECU)	Devolved to inter-institutional-level coordinators	isro.gov.in/applications/tele-medicine
India (Sankara	Sankara	Department of	www.sankaranethralaya.org

Nethralaya Teleophthalmology Program (SNTOP)*	Nethralaya	Teleophthalmology	
India (Telemedicine Maharashtra)*	Byramjee Jeejeebhoy Government Medical College and Sassoon General Hospitals, Pune	Telemedicine Department	www.bjmcpune.org
Indonesia (National Telemedicine Program)	Ministry of Health	Directorate of Ancillary Services, Ministry of Health	buk.depkes.go.id
Malaysia (Telekesihatan)	Ministry of Health	Telehealth Division, Ministry of Health	telekesihatan.moh.gov.my
Maldives (Telemedicine Kiosks Project)	National eHealth Steering Committee	Ministry of Health	
Philippines (National Telehealth Service Program)	National eHealth Steering Committee	UP Manila National Telehealth Center	one.telehealth.ph
Sri Lanka (Health Net [Suwasariya])	Ministry of Health	Health Education Bureau, Ministry of Health	suwasariya.gov.lk

* state-wide

Either the Ministry of Health (MOH) alone or a multi-sector group led by MOH governs the national telehealth programs listed. Of the nine programs, formal units within the MOH structure manage six, academic institutions manage two, and a non-government organization operates one.

4. Discussion

Varghese and Scott [8] had conducted a survey on telehealth policies in 2004 and discovered wide variance in policy maturity and readiness of countries in the region. Ten years after, these policies have evolved into concrete implementations as summarized in this paper. This paper's high-level analysis, which focused on governance and management, revealed several interesting facets about national telehealth programs in Asia.

Governance has been cited in the literature as an important factor in successful telehealth programs [9,10].

COBIT5 emphasizes, as a matter of principle, the importance of separating governance from the management of enterprise IT [11]. They claim that with this separation, there is an easier check and balance between the two domains resulting in better performance for both.

In this study, while most telehealth programs claim that they have governance and management structures, a few admit that their governance bodies have not been as active as desired. These admissions are further corroborated by the lack of accessible

websites to obtain references about the activities of the governance body or even how to access telehealth services.

These websites are sensitive indicators of the state of governance and management, as they serve as mechanisms for disseminating information about the programs as well as portals to the actual telehealth services. These are important knowledge products especially if the target audience is the general public.

Realizing that most members of the highest decision-making body of a national telehealth program may not have the comprehensive knowledge about IT, COBIT5 emphasizes five processes that they should own to empower the rest of the complex processes underneath them to move in accordance with their desired strategy and directions.

The five key processes for the governance bodies of national telehealth programs are: "ensure governance framework setting and maintenance, ensure benefits delivery, ensure risk optimization, ensure resource optimization, ensure stakeholder transparency." [12]

4.1. Ensure Governance Framework Setting and Maintenance

From all the sites studied, there were no explicit statements about any overarching IT governance framework being adopted by the national telehealth program. Although this lack of information does not mean that there is no underlying framework, its absence on program websites suggests that it is not being communicated explicitly to the stakeholders. In such cases, there is practically no governance framework being maintained.

In the Philippines, while the National eHealth Steering Committee had adopted COBIT5 as their governance framework [13], the National Telehealth Service Program has not yet formally aligned with it.

Ensuring governance framework setting is a leadership function that triggers the rest of the framework into action.

4.2. Ensure Benefits Delivery

Where available, the programs expressed similar benefits: access to quality health information, good governance, equity, and improved health outcomes [14]. Many of the countries have formally expressed aspirations for UHC and cited telehealth as an important tool to achieve that. Key performance indicators (KPIs) however are not evident in most programs and are difficult to elicit from their official websites. With IT governance, these KPIs are ideally formalized at the outset and are publicly announced.

4.3. Ensure Risk Optimization

Risks were not explicitly mentioned in the program websites although some have mentioned privacy, confidentiality, and sustainability in scientific publications describing the program. Risk registers are often proprietary and it is usual for most enterprises not to divulge them due to the sensitive nature of their contents. However, high-level statements on key risks (privacy and confidentiality) are indications of the programs' awareness of these risks and of their efforts to take a proactive stance to prevent these risks from converting into problems.

4.4. Ensure Resource Optimization

All of the programs reviewed are funded by the national government through public funding. Financial statements were not readily accessible from the programs but a few had cited the difficulty of sustaining their efforts without a guarantee of constant regular resources from national government. In general, most programs are challenged by the lack of funds to sustain their programs which may suggest poor resource optimization.

4.5. Ensure Stakeholder Transparency

In the review of official documents, websites, and key informant interviews, stakeholder transparency is still implicit and is not formally expressed. While some programs have clear published organizational structures, most do not explicitly inform the public about their prevailing governance mechanisms, minutes of meetings, or formal agreements.

Governance is ideally established by the highest decision-making body in the country which takes accountability for evaluating the needs of stakeholders, for setting directions, and for monitoring progress. Aside from defining the expected benefits from the national telehealth program, they also determine acceptable risks and provide the necessary resources to operate it. Since most benefits will redound to the health sector, the ministry of health is the natural leader of the national telehealth program. But because risks and resources are often shared with other agencies (e.g., ministry of ICT, national health insurance agency, clinical professional associations, health providers, sub-national governments, academe, etc.), a multi-sector structure is the ideal form for governance. Unless this structure is created and its members perform their governance tasks, the national telehealth program will be confronted with obstacles often beyond management's ability to surmount, resulting in failure.

Management on the other hand requires a thorough understanding of the benefits, risks, and resources set forth by the governance structure. Aside from ensuring smooth operations, they also constantly communicate with the decision-makers on the state of the program and provide feedback that all components needed to deliver the benefits are operating as expected. The lack of websites for some programs indicates that their core governance process of stakeholder transparency has not yet been activated.

Conclusions

National telehealth programs are one of the most complex enterprise information systems around the world due to the number of stakeholders and components involved in its design and operation. Such complex systems can benefit tremendously from the systematic organization offered by IT governance frameworks. Although the maturity and sophistication of each program studied varied widely, they all shared in the vision of better access to health information towards an empowered and healthier citizenry. A clear vision is a good starting point for the application of IT governance for national telehealth programs. But in order to concretize this vision into actual benefits to relevant stakeholders, alignment of governance and management is required.

The lack of clarity on the state of governance for the national telehealth programs suggests that most of the threats they face such as sustainability and stakeholder

adoption are rooted on this problem. Unless addressed explicitly through the application of IT governance frameworks, these programs will continue to be susceptible to the challenges posed by their complex environments.

References

[1] Durrani H(1), Khoja S. A systematic review of the use of telehealth in Asian countries. J Telemed Telecare. 2009;15(4):175-81. doi: 10.1258/jtt.2009.080605.

[2] Dadlani R(1), Mani S(2), Jai Ganesh AU (3), Mohan D(4), Rajgopalan N(4), Thakar S(4), Aryan S(4), Hegde AS(4). The impact of telemedicine in the postoperative care of the neurosurgery patient in an outpatient clinic: a unique perspective of this valuable resource in the developing world--an experience of more than 3000 teleconsultations. World Neurosurg. 2014 Sep-Oct;82(3-4):270-83. doi: 10.1016/j.wneu.2014.05.027. Epub 2014 Jun 2.

[3] Shimizu S(1), Kudo K, Antoku Y, Hu M, Okamura K, Nakashima N. Ten-year experience of remote medical education in Asia. Telemed J E Health. 2014 Nov;20(11):1021-6. doi: 10.1089/tmj.2014.0018. Epub 2014 Oct 1.

[4] Joshi R, Thatte U. Dynamic Intelligent Blood Donor Network. http://aehin.hingx.org/1512 last accessed January 31, 2015.

[5] Proceedings from the Measuring and Achieving Universal Health Coverage with Information and Communications Technology. http://bit.ly/uhcict last accessed January 31, 2015.

[6] Proceedings from the Second General Meeting of the Asia eHealth Information Network. http://aehin.hingx.org/1819 last accessed January 31, 2015.

[7] COBIT5 Principles: Where did they come from? ISACA, 2014. http://www.isaca.org/Knowledge-Center/Research/Documents/Cobit-5-Principles_whp_Eng_0714.pdf Last accessed January 31, 2015

[8] Varghese S1, Scott RE. Categorizing the telehealth policy response of countries and their implications for complementarity of telehealth policy. Telemed J E Health. 2004 Spring;10(1):61-9.

[9] Lluch M(1), Abadie F. Exploring the role of ICT in the provision of integrated care--evidence from eight countries. Health Policy. 2013 Jun;111(1):1-13. doi: 10.1016/j.healthpol.2013.03.005. Epub 2013 Apr 12.

[10] Villalba E(1), Casas I, Abadie F, Lluch M. Integrated personal health and care services deployment: experiences in eight European countries. Int J Med Inform. 2013 Jul;82(7):626-35. doi: 10.1016/j.ijmedinf.2013.03.002. Epub 2013 Apr 12.

[11] COBIT5 Enabling Processes. http://www.isaca.org/COBIT/Documents/COBIT5-Ver2-enabling.pdf Last accessed January 31, 2015.

[12] Governance and Management for the Philippine eHealth Strategic Framework and Plan. http://bit.ly/ehealthgovernance last accessed January 31, 2015.

[13] Mohan J, Suleiman AB. E-Health Strategies for Developing Nations. IMIA Yearbook of Medical Informatics 2005.

[14] Mohan J, Yaacob R. The Malaysian Telehealth Flagship Application: a national approach to health data protection and utilisation and consumer rights. International Journal of Medical Informatics, 73, 217-227, 2004.

SERUM INSTITUTE OF INDIA PRESENTS

Telemedicon

13th International Conference 2017

9th - 11th November 2017

Theme : Digital Health - Shaping The Future Of Healthcare

TELEMEDICON 2017 SOUVENIR

www.telemedicon2017.com

Abstracts

Prospective Validation of Computer Graded Diagnosis of Diabetic Retinopathy Screening Tool

Authors: Sheila John, Sangeetha Srinivasan, Keerthi Ram, Supriti Mulay, Mohanasankar Sivaprakasam.

Objective:

To validate a computer-assisted software to identify the presence of diabetic retinopathy (DR) from single-field retinal images in comparison to that of an optometrist andophthalmologist (retinal specialist).

Materials & Methods:

467 patients (or 786 eyes) underwent nonmydriatic posterior pole 45-degree retinal photography. Images were then processed through the software, and independently graded by the optometrist, ophthalmologist - retina specialist (reference standard). Kappa scores (κ), areas under the receiver operating characteristic curves (AUCs), sensitivity and specificity were determined.

Results:

Mean±SD of age of patients was 58.2±7.5 years, with a mean diabetes duration of 13.2±7.9 years; 70% being men.Out of 786 eyes, 576 eyes (72.9%) have been marked as DR present by ophthalmologist, whereas 607 eyes (76%) have been marked DR present by optometrist. The algorithm predicted 584 eyes (73.92%) as DR present.

Discussion:

The inter-rater agreement (Cohen's kappa) found between algorithm to ophthalmologist is 0.3506, and the kappa between algorithm to optometrist is 0.321. The kappa between ophthalmologist to optometrist is 0.412. The algorithm achieves sensitivity of 83.15% at specificity of 51.1%, with a prediction accuracy of 82%. The area under the ROC curve achieved by the algorithm as compared with ophthalmologist is 0.7502.

Conclusion:

The algorithm for identifying DR presence has been validated in a prospective manner in a tertiary care setup and the algorithm achieves good agreement, accuracy and sensitivity to ophthalmologist. The algorithm can serve as a decision support for optometrists augmenting their capability to provide a referral decision for timely disease management.

Telemedicon
13th International Conference 2017

Grant Medical Foundation
Ruby Hall Clinic

13th International Conference of Telemedicine Society of India "Telemedicon 2017", Pune India

9th - 11th November 2017

THEME : DIGITAL HEALTH - SHAPING THE FUTURE OF HEALTHCARE

Certificate of Participation

This is to certify that

Dr Sheila john

Presented an Oral Paper on

Prospective validation of computer graded diagnosis of diabetic retinopathy screening tool

during the **13th International Conference of Telemedicine Society of India - Telemedicon 2017,**
held on 9th - 11th November 2017 at Pune.

Dr K Selvakumar President Telemedicon - 2017	Dr B S Ratta Organizing Chairperson Telemdicon - 2017	Dr Prachee Sathe Org. Secretary Telemedicon - 2017	Dr Nirmal Gupta Secretary Telemedicon - 2017

The Promise of New Technologies in an Age of New Health Challenges
A.J. Maeder et al. (Eds.)

doi:10.3233/978-1-61499-712-2-74

Assessment of Computer-Assisted Screening Technology for Diabetic Retinopathy Screening in India – Preliminary Results and Recommendations from a Pilot Study

Sheila JOHN[a,1], Keerthi RAM[b], Mohanasankar SIVAPRAKASAM[b] and Rajiv RAMAN[a]
[a]*Sankara Nethralaya, Chennai, India*
[b]*Healthcare Technology Innovation Centre, IIT Madras, India*

Abstract. *Background* Diabetic retinopathy (DR) is regarded as a major cause of preventable blindness, which can be detected and treated if the cases are identified by screening. Screening for DR is therefore being practiced in developed countries, and tele screening has been a prominent model of delivery of eye care for screening DR. *Aim* Our study has been designed to provide inputs on the suitability of a computer-assisted DR screening solution, for use in a larger prospective study. *Methods* Computer-assisted screening technology for grading diabetic retinopathy from fundus images by a set of machine learning algorithms. *Results* The preliminary recommendations from a pilot study of a system built using the public datasets and retrospective images, showed a good sensitivity and specificity. *Conclusion* The machine learning algorithms has to be validated on a larger dataset of a population level study.

Keywords. Screening, computer-assisted, algorithms, diabetic retinopathy

Introduction

More than 50 million people in India are at risk of developing sight threatening eye diseases. Blindness due to chronic eye disease such as diabetic retinopathy (DR), can be averted if detected early through regular eye check-up. Early identification by screening is the key step in addressing treatable blindness, in the face of India's dual challenge of huge population and limited availability of experts.

The gold standard in DR screening is digital photography of the retina, and image-based tele screening methods such as ophthalmologist-based and ophthalmologist-led [1] have been used for epidemiological studies to find the prevalence of DR in India. Such studies have identified around 5-6% of diabetic population needing sight-threatening, treatable DR. An ophthalmologist-led telescreening has been considered as a suitable and cost-effective model for India.

[1]Corresponding Author: Dr Sheila John, Department of Teleophthalmology, Sankara Nethralaya, a Unit of Medical Research Foundation, New No:41, Old No:18 College Road, Chennai – 600 006, India
Email: sheilajohn999@gmail.com

The advancement expected in telescreening includes introduction of improved equipment, better communication infrastructure, and introduction of computer-assisted screening technology. The images acquired during different screening models can be digitally processed and analysed using image computing – and there has been good amount of research to create computer-assisted screening technology in developed nations [2][3][4]. Introduction of computer-assisted image analysis for screening can enable wider deployment and empower minimally skilled technicians to participate in the care delivery process, thereby auguring greater penetration with existing telescreening setups, and outreach at a national scale.

This study reports an assessment of computer-assisted technology by building a DR screening software based on methods selected from the known art, and provides analyses from a pilot study of the system in a retrospective assessment conducted to assess the applicability and value of such technology for introduction in a larger prospective study, and steps towards incorporating such technology in routine telescreening in India.

1. Research on computer assisted DR screening

The technology for screening and grading diabetic retinopathy from fundus images is driven by a set of machine learning algorithms. These algorithms detect normal anatomical structures and clinical pathological signs in the given retinal image. The typical sequences of operations within an algorithm are pre-processing, image segmentation, feature extraction and pattern classification. Pre-processing is used to normalize image brightness, perform correction for non-uniformity in the image, reduce noise, and reduce image artifacts. Segmentation identifies candidate objects of interest (lesions, anatomical structure and others). Feature extraction computes quantitative information such as size, appearance, color, texture from the segmented candidates.

A categorized review of techniques used in digital color fundus image processing in Diabetic Retinopathy is presented in [5] under 5 categories: 1) Image enhancement, 2) Localization and segmentation of optic disc, 3) segmentation of retinal vasculature, 4) localization of fovea and macula, 5) Localization and segmentation of retinopathy.

Diabetic retinopathy referral decision is produced by two broad approaches. The first is a rule-based system, where in the number and location of detected lesions is used, and a set of rules are applied to provide the decision/grade of the image. E.g. the minimum requirement for performing grading according to American Academy of Ophthalmology ICDR scheme requires the count of micro aneurysms, hemorrhages in different quadrants, and exudative lesions, with respect to fovea position. Though this approach is intuitive and simpler to implement, it is not grounded on sample statistics and relies on the accuracy of lesion detection algorithms. Further, this approach might not provide parameters for controlling the sensitivity and specificity of the decision.

The second approach uses machine learning algorithms that learn the referral decision based on several samples provided along with expert annotation. This approach is more popular, since several frameworks are available to train the system, and the system can be improved by increasing the training set.

1.1. Publicly available datasets for system development and evaluation

For the purpose of this study a computer-assisted DR screening system was built, adhering to the data-driven approach, comprising of modules for determining gradability, normal anatomy detection, pathological signs detection, and analysis for computing the screening decision. The block diagram of the system is shown below:

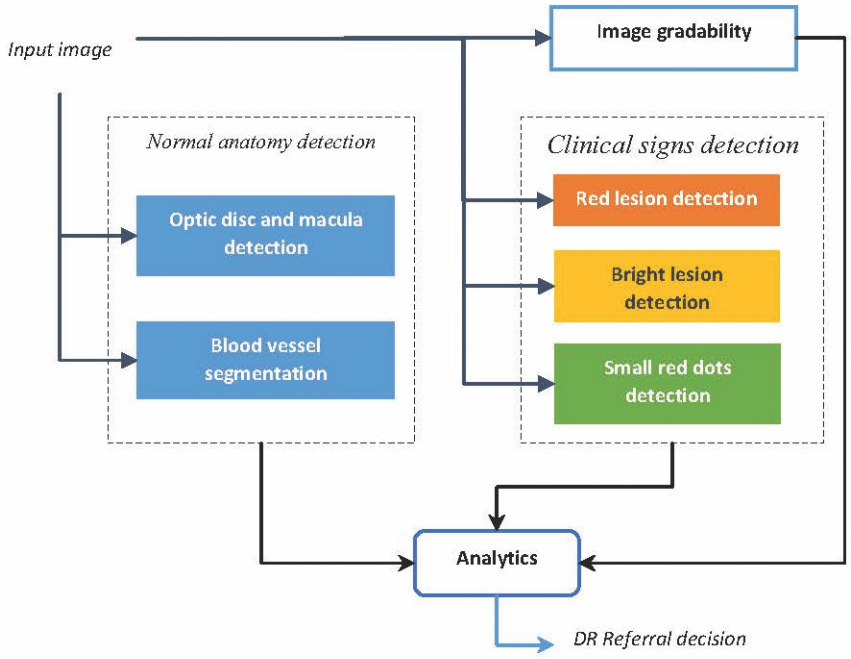

Figure 1. Block diagram of system for diabetic retinopathy screening from fundus images

The image gradability module determines parameters like image clarity, illumination uniformity, blur and provides a numeric score of gradability. Low gradability images would generally not succeed in further processing steps. Also blurred images and images with unclear media might indicate other conditions such as cataract and bleeding. Such cases might need referral. Hence the gradability score is vital during the DR decision analytics.

Normal anatomy detectors localize the 3 main anatomical structures: optic disc, blood vessels and fovea. These regions in the image are to be processed differently: e.g. optic disc should be disregarded by bright lesion detection algorithm. Blood vessels need to be suppressed for red lesion detection algorithm. The position of fovea, macula and temporal arcade structure are important for the DR decision analytics.

Three main categories of lesions have been handled in the system: small red dots (including micro aneurysms and dot hemorrhages), red lesions (blot hemorrhage, flame hemorrhage, pre-retinal hemorrhage), and bright lesions (small hard exudates, circinate exudates, cotton wool spots, ischemic zones). Each of the detectors finds lesions and assigns a confidence score for the detected lesion at every detected position. This provides a control parameter for selecting the sensitivity of each detector. Sensitivity

can be increased by selecting a low confidence threshold and specificity increases at higher confidence thresholds.

Given the output of the lesion detection modules and the anatomy detection modules the screening decision is learnt by training against several manually graded images.

In order to develop these modules and verify the functionality of the modules, publicly available retinal fundus image datasets have been used. Table 1 gives the names and details of the public image databases used for developing the corresponding modules. The two classes of information available in the public datasets are lesion-level manual annotations of various individual signs (such as DiaretDB) and image level readings which provide the screening and grading ground truth for each image (such as Messidor).

Table 1. Public datasets used for developing and verifying the modules of the system. The references are given in numbers and indicate the source of the data.

Module	Databases	Number of Images	Description of dataset
Image gradability	HRF[6]	36	Folder of good and bad quality images
Optic disc and macula detection	Stare[7]	81	Location of optic disc
	ReviewDB[8]	99	
Blood vessel segmentation	Drive[9]	40	Manual segmentation of blood vessels
	Stare[7]	20	
	Aria[10]	143	
Red lesion detection	DiaretDB[11]	89	Location of lesions
Bright lesion detection	Hei-Med[12]	169	Location of lesions, regions of exudates
	DiaretDDB[11]	89	
Small red dots detection	ROC[13]	100	Location of lesions
	DiaretDB[11]	89	
DR referral decision	Messidor[2]	1200	4 grades of DR severity

It is known that publicly available datasets have been acquired in clinical settings and therefore might not capture population level statistical distribution of DR prevalence. Therefore the study included a first pass observation of performance of the developed system on a selected set of images sampled from an epidemiological study followed by refinement of the algorithms to adapt to observations in Indian images, and a pilot study to evaluate the system on limited scale field data from Indian settings.

1.2. Objective of the study

The study has been designed to provide inputs on the suitability of a computer-assisted DR screening solution for use in a larger prospective study. Two specific outcomes from this study are:

- Identification of protocol to be used for prospective study
- Recommendations on capabilities needed in computer-assisted solutions for successful deployment in screening setups in India.

2. Study design

The first pass study of the designed system was done with retrospective images selected uniformly from an epidemiological study. The sample size selected was 100

cases where each case has images of one or both eyes captured in multiple fields. The subject details were anonymized and images were renumbered so that the file names indicate the field of view captured. The images selected were acquired using mydriasis, with 45 degree magnification and had been jpeg-compressed with quality factor ranging from 75% to 95%. Images with media opacity, severe pathology hindering imaging and low quality of capture were earmarked and included to observe the performance of the image gradability step in the system. The gold standard grading performed in the epidemiological study was taken as is, and it consists of consensus readings classifying each image into 5 levels of DR severity grades, and an image gradability flag. For the purpose of the study, an image was considered as referable if a consensus reading of 'moderate', 'severe' or 'proliferative DR' was given.

2.1. Anatomical and lesion level annotations

A resident clinical expert performed annotation of DR lesions in the selected set of images using a specially developed tool, based on marking of hand-drawn polygons and small regions of interest for lesions. The types of lesions annotated are:

- Red structures: small red spots, blot, flame, vitreous haemorrhage, neovascularization
- Blood vessels: up to 3rd order branching – this was done on normal images
- Bright structures: optic disc, cup, small hard exudates, confluent plaque, soft exudates, ischemic areas
- Indication of presence of IRMA, fibrous proliferation

2.2. Evaluation metrics

The design of DR analyzer software as a data-driven system provides specific task-related metrics for evaluation. Performance compared to human expert drives the algorithm refinement process.

Module evaluation: the lesion-level performance of DR analyzer software detectors can be evaluated by comparing algorithm outputs against lesion annotations provided by clinicians. Two methods of evaluation are used:

- FROC analysis (TPR vs FPPI): for lesion detectors and
- ROC analysis (TPR vs FPR): for normal anatomy detectors and DR referral analytics module.

Metrics used: AUC (area under ROC curve), sensitivity, specificity, precision, accuracy, confusion matrix

3. Study outcomes

The performance of the built system for different modules was observed. The image gradability module showed a sensitivity of 85.9% at specificity of 83%.

The performance of anatomy detectors was also evaluated against the prepared annotations and is given in the figures 2.a and 2.b.

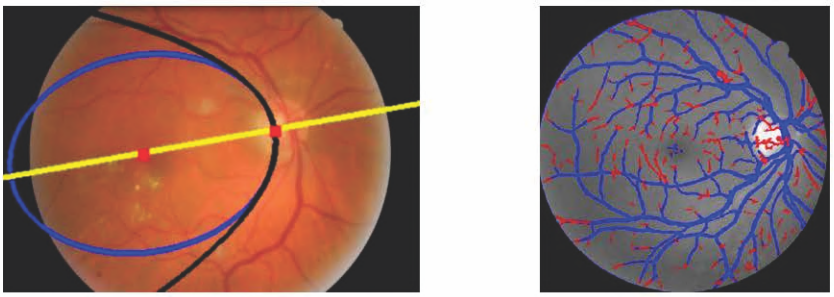

Figure 2.a. Outputs from the normal anatomy detectors. **2.b.** Output of blood vessel segmentation

The image-level performance observed on the Messidor public dataset is shown in Fig.3a. The performance of 83% sensitivity at 80% specificity is seen in this dataset. However direct evaluation on Indian data showed a reduction in performance to 70% sensitivity and specificity. This shows the need for refinement of the system for Indian data. After refinement, a high level of specificity is attained as shown in Fig. 4. Inspection of the DR severity scores reported by the system indicates that images of advanced stages of the disease receive higher severity scores.

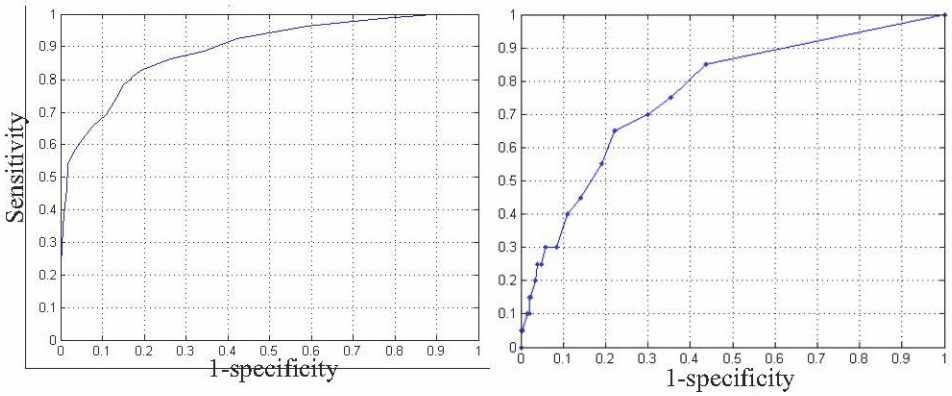

Figure 3.a. Image level decision performance on MESSIDOR dataset, and **3.b** cross-validation in selected Indian data from epidemiological data

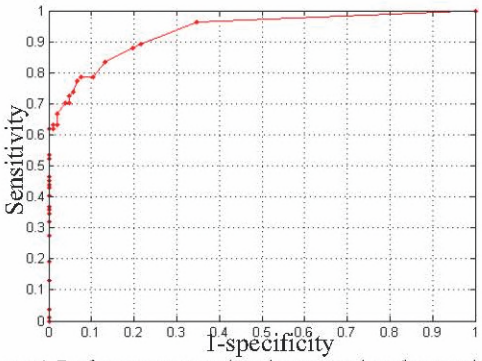

Figure 4. Performance curve (receiver operating characteristic curve) after refinements

The software system has been developed and evaluated using mydriatic imaging with 45 degree magnification and 7 field photography, which adheres to the globally accepted protocol [14].

Conclusion and recommendations for prospective study

The computer-assisted DR screening system has been shown to perform at a satisfactory level of sensitivity and specificity on the limited study and hence similar protocol would need to be followed for a prospective study.

The prospective study could have the following aspects for study:

- Inclusion of non-mydriatic imaging: The performance of the system on images acquired with a non-mydriatic camera for the same subjects could be included, which will help in studying if enough information can be derived by the software from non-mydriatic images, having the mydriatic images for comparison.
- Inclusion of separate analytics for diabetic macular edema: expert reading of macular edema should be taken and a separate module should be built which provides a grade of severity of diabetic macular edema.
- Analysis of treated DR images: Though the prospective study is intended to find new cases of DR the software should have the capability to identify treatment indications such as laser marks. Also advanced stages of DR such as neovascularization and fibrous proliferation should be treated as highly critical and separate modules in the system should be designed for identifying these. Though the prevalence of these in screening population is expected to be few these are signs for which a false or negative could be unacceptable.
- Study of the grading capability of the system and evaluation of observer variability between system outcome of grade and expert grading.

Based on this limited scale experiment the performance of the DR screening system on epidemiological data has been studied and the need for image quality check and pre-filtering for dust particles in software has been identified. The system is a data-driven system and the current performance is comparable to state of art methods showing that the technology used in the software is verifiable and needs to be validated on larger data with the inclusion of non-mydriatic images.

References

[1] Sharma, T., Raman, R., John, S. and Badrinath, S. "Telescreening for diabetic retinopathy in South India," in *Digital Teleretinal Screening*, 2012, pp. 137-142.

[2] Dupas, B., Walter, T., Erginay, A., Ordonez, R., Deb-Joardar, N., Gain, P., Klein, J-C. and Massin, P. "Evaluation of automated fundus photograph analysis algorithms for detecting microaneurysms, hemorrhages and exudates, and of a computer-assisted diagnostic system for grading diabetic retinopathy," *Diabetes & Metabolism,* 2010.

[3] Fleming, A.D., Goatman, K., Philip, S., Prescott, G.J., Sharp, P.F. and Olson, J.A. "Automated grading for diabetic retinopathy: a large-scale audit using arbitration by clinical experts," *BJO,* pp.

1606-10, 2010.

[4] Abràmoff, M.D., Folk, J.C., Han, D.P., Walker, J.D., Williams, D.F., Russell, S.R., Massin, P., Cochener, B., Gain, P., Tang, L. and Lamard, M. "Automated analysis of retinal images for detection of referable diabetic retinopathy," *JAMA Ophthalmology,* 2013.

[5] Winder, R.J., Morrow, P.J., McRitchie, I.N., Bailie, J.R. and Hart, P.M. "Algorithms for digital image processing in diabetic retinopathy," *Computerized medical imaging and graphics,* 2009.

[6] Köhler, T., Budai, A., Kraus, M., Odstrcilik, J., Michelson, G. and Hornegger, J. "Automatic No-Reference Quality Assessment for Retinal Fundus Images Using Vessel Segmentation," in *IEEE Internatioal Symposium on Computer-Based Medical Systems*, 2013.

[7] Hoover, A. and Goldbaum, M. "Locating the optic nerve in a retinal image using the fuzzy convergence of the blood vessels," *IEEE Trans. Medical Imaging,* vol. 22, pp. 951-958, 2003.

[8] Lowell, J., Hunter, A., Steel, D., Ryder, B. and Fletcher, E. "Optic nerve head segmentation," *IEEE Trans. Medical Imaging,* vol. 23, no. 2, 2004.

[9] Staal, J.J., Abramoff, M.D., Niemeijer, M., Viergever, M.A. and Ginneken, B. "Ridge-based vessel segmentation in color images of the retina," *IEEE Trans. Medical Imaging,* vol. 3, pp. 501-509, 2004.

[10] Bankhead, P., Scholfield, C.N., McGeown, J. and Curtis, T.M. "Fast retinal vessel detection and measurement using wavelets and edge location refinement," *PLoS One,* vol. 7, no. 3, 2012.

[11] Kauppi, T., Kalesnykiene, V., Kamarainen, J.K., Lensu, L., Sorri, I., Raninen, A., Voutilainen, R., Uusitalo, H., Kalviainen, H. and Pietila, J. "DIARETDB1 diabetic retinopathy database and evaluation protocol," in *Proc. Medical Image Understanding and Analysis*, 2007.

[12] Giancardo, L., Meriaudeau, F., Karnowski, T.P., Li, Y., Garg, S., Tobin, J.K.W. and Chaum, E., "Exudate-based diabetic macular edema detection in fundus images using publicly available datasets," *Medical Image Analysis,* vol. 16, no. 1, pp. 216-226, 2012.

[13] Niemeijer, M., Ginneken, B. v., Cree, M.J., Mizutani, A., Quellec, G., Sanchez, C.I., Zhang, B., Hornero, R., Lamard, M., Muramatsu, C., Wu, X., Cazuguel, G., You, J., Mayo, A., Li, Q., Hatanaka, J., Cochener, B., Roux, C., Karray, F., Garcia, M. and F, H. "Retinopathy Online Challenge: Automatic Detection of Microaneurysms in Digital Color Fundus Photographs," *IEEE Trans. Medical Imaging,* vol. 29, no. 1, pp. 185-195, 2010. T. r. c. o. ophthalmologists, "Diabetic retinopathy Guidelines," 2012.

[14] Antal, B., Hajdu, A., Marcos-Szabo, Z., Torok, Z., Csutak, A. and Peto, T. "A two-phase decision support framework for the automatic screening of digital fundus images," *Journal of Computational Science,* 2012.

[15] Abramoff, M.D., Viergever, M.A., Niemeijer, M., Russell, S.R., Suttorp-Schulten, M. and Bram van Ginneken, "Evaluation of a system for automatic detection of diabetic retinopathy from color fundus photographs in a large population of patients with diabetes," *Diabetes care,* pp. 193-198, 2008.

[16] MD, Abramoff., MK, Garvin. "Retinal imaging and image analysis" *IEEE Reviews in biomedical engineering,* pp. 169-208, 2010.

[17] Pires, R., Jelinek, H.F., Wainer, J., Goldenstein, S., Valle, E. and Rocha, A. "Assessing the need for referral in automatic diabetic retinopathy detection," *IEEE Trans. Biomed. Engg,* 2013.

[18] Quellec, G., Lamard, M., Abràmoff, M.D., Decencière, E., Lay, B., Erginay, A., Cochener, B. and Cazuguel, G. "A multiple-instance learning framework for diabetic retinopathy screening," *Medical image analysis,* 2012.

[19] Raman, R., Rani, P.K., Rachepalle, S.R., Gnanamoorthy, P., Uthra, S., Kumaramanickavel, G. and Sharma, T. "Prevalence of diabetic retinopathy in India: Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetics Study Report 2," *AAO J.Ophthalmology,* pp. 311-318, 2009.

MEDINFO 2013
C.U. Lehmann et al. (Eds.)

doi:10.3233/978-1-61499-289-9-1065

Are Smartphones Comparable to Laptops for Image Diagnosis in Teleophthalmology?

Sheila John[a], Vikram Arun[c], Nahush Katti[c], Bindu Appukuttan[b], Pearlson[a], Sengamedu S Badrinath[a,b]

a.Department of Teleophthalmology, Medical Research Foundation, Sankara Nethralaya, Chennai, India
b.Medical and Vision Research Foundation, Sankara Nethralaya, Chennai, India
c.Rockbridge High School, USA

Abstract:
Objective: To assess the reliability and accuracy of smartphones in diagnosing transmitted fundus images in comparison with a laptop. Materials and Methods: Fundus images captured with a Topcon NW 200 camera were transferred onto a conventional laptop and a smartphone and given to ophthalmologists for diagnosis.The smartphone and the laptop diagnosis were compared with the actual face to face diagnosis statistically to assess their diagnostic accuracy.Results: Fundus images of 228 eyes of 114 patients(mean age 47 years,73.6% males) were included in the study. 92.5% eyes were correctly diagnosed by both smartphones and laptop. Smartphone analysis revealed 98% sensitivity,57% specificity and kappa value of 0.62 in comparison to laptop, suggessting substantial interrater agreement.Conclusions: Smartphones are as effective as the laptop in diagnosing fundus pathologies and hold promise for teleophthalmology in future.

Key words: smartphone, ophthalmology

Introduction

Smartphones are the new wave of telemedicine technology which provide more feasible access to the doctor compared to conventional laptops. Smartphones differ from laptops in being more handy, better wireless internet connectivity, smaller screen size ,advanced image viewing capabilities and a different operating system. Ophthalmology's need for image quality requirement is high. As laptops or conventional computer screens are routinely used for teleconsultation purposes, at our centre, we conducted a pilot study to compare the diagnostic ability and reliability of smartphone in comparison to laptop in posterior segment conditions, to assess its suitability for teleophthalmology.

Methods

Hundred and twenty patients presenting to the fundus photography clinic of an ophthalmic tertiary care centre were randomly selected. Patients below 10 years and those with media opacities were excluded. A detailed history and visual acuity assessment by a trained optometrist was recorded on Electronic Medical Records (EMR). The examining ophthalmologist recorded the *actual diagnosis* on the EMR. After obtaining an informed consent and pupillary dilatation, a single 45^0 digital fundus photograph centered midway between the centre of the macula and the disc was captured with Topcon NW200 3.1 megapixel camera using the Imagenet software and stored onto the computer in the JPEG format. The fundus images and the EMR were downloaded onto a smartphone (HTC Sensation) and a laptop (Sony notebook with diagonal screen size :15.6', display resolution 1024 x 768 pixels). The data was compressed to zip folders on the HTC sensation and transmitted via 3G network to a LG Optimus G2X phone (android version 2.3.4 ,4'multi touch display screen with resolution of 480x800 pixels and a 50% brightness contrast ratio of 982) with another ophthalmologist at a distant centre.The ophthalmologists reviewed the brief history and images on the smartphone and laptop and recorded it as the *smartphone and laptop diagnosis* respectively. All the three ophthalmologists had the same years of clinical experience and were experienced with teleconsultation. The diagnosis was labeled as 'correct' or 'incorrect' in concordance with the face to face examination and statistical analyses done using statistical software (SPSS for Windows version 13.0; SPSS Science, Chicago, IL).

Results

The study included 228 eyes of 114 informed consenting patients(mean age 47 years,73.6% males,26.4% females) with 61 (26.5%) diabetic retinopathies, 56 (24.3%) macular diseases, 22 (9.5%) retinal vasculopathies, 19 (8.2%) optic nerve head and 31(13.4%)miscellaneous conditions and 39(16.9%)normal eyes. The diagnosis was correctly diagnosed by both smartphone and laptop in 211(92.5%) eyes, incorrectly diagnosed in 8(0.03%) eyes, while correctly on smartphone but incorrectly on laptop in 6(0.02%) eyes and vice versa in 3(0.01%) eyes.The sensitivity of smart phone was 98%(95% CI:95-99%) while specificity was 57%(95% CI:25-81%) and the kappa value was 0.62($p<0.05$) suggesting substantial interrater agreement .

Conclusion

Thus smartphones would be technically feasible in areas where access to computers with internet connectivity is unreliable or insufficient and with further innovations like imaging with 20D lens or incorporating a flash in the smartphone camera would also alleviate the need for carrying bulky equipment to the camp site.

Address for correspondence:

Dr Sheila John,Department of Teleophthalmology, Medical Research Foundation, , No 18 College Road,Nungambakkam Chennai ,Tamil Nadu. India -600 006.Phone: +91 – 44 – 28271616 Fax: +91 – 44 – 28254180. Email: sheilajohn999@gmail.com

MEDINFO 2013
C.U. Lehmann et al. (Eds.)

doi:10.3233/978-1-61499-289-9-1065

Are Smartphones Comparable to Laptops for Image Diagnosis in Teleophthalmology?

Sheila John[a], Vikram Arun[c], Nahush Katti[c], Bindu Appukuttan[b], Pearlson[a], Sengamedu S Badrinath[a,b]

a.Department of Teleophthalmology, Medical Research Foundation, Sankara Nethralaya, Chennai, India
b.Medical and Vision Research Foundation, Sankara Nethralaya, Chennai, India
c.Rockbridge High School, USA

Abstract:
Objective: To assess the reliability and accuracy of smartphones in diagnosing transmitted fundus images in comparison with a laptop. Materials and Methods: Fundus images captured with a Topcon NW 200 camera were transferred onto a conventional laptop and a smartphone and given to ophthalmologists for diagnosis.The smartphone and the laptop diagnosis were compared with the actual face to face diagnosis statistically to assess their diagnostic accuracy.Results: Fundus images of 228 eyes of 114 patients(mean age 47 years,73.6% males) were included in the study. 92.5% eyes were correctly diagnosed by both smartphones and laptop. Smartphone analysis revealed 98% sensitivity,57% specificity and kappa value of 0.62 in comparison to laptop, suggessting substantial interrater agreement.Conclusions: Smartphones are as effective as the laptop in diagnosing fundus pathologies and hold promise for teleophthalmology in future.

Key words: smartphone, ophthalmology

Introduction

Smartphones are the new wave of telemedicine technology which provide more feasible access to the doctor compared to conventional laptops. Smartphones differ from laptops in being more handy, better wireless internet connectivity, smaller screen size ,advanced image viewing capabilities and a different operating system. Ophthalmology's need for image quality requirement is high. As laptops or conventional computer screens are routinely used for teleconsultation purposes, at our centre, we conducted a pilot study to compare the diagnostic ability and reliability of smartphone in comparison to laptop in posterior segment conditions, to assess its suitability for teleophthalmology.

Methods

Hundred and twenty patients presenting to the fundus photography clinic of an ophthalmic tertiary care centre were randomly selected. Patients below 10 years and those with media opacities were excluded. A detailed history and visual acuity assessment by a trained optometrist was recorded on Electronic Medical Records (EMR). The examining ophthalmologist recorded the *actual diagnosis* on the EMR. After obtaining an informed consent and pupillary dilatation, a single 45^0 digital fundus photograph centered midway between the centre of the macula and the disc was captured with Topcon NW200 3.1 megapixel camera using the Imagenet software and stored onto the computer in the JPEG format. The fundus images and the EMR were downloaded onto a smartphone (HTC Sensation) and a laptop (Sony notebook with diagonal screen size :15.6', display resolution 1024 x 768 pixels). The data was compressed to zip folders on the HTC sensation and transmitted via 3G network to a LG Optimus G2X phone (android version 2.3.4 ,4'multi touch display screen with resolution of 480x800 pixels and a 50% brightness contrast ratio of 982) with another ophthalmologist at a distant centre.The ophthalmologists reviewed the brief history and images on the smartphone and laptop and recorded it as the *smartphone and laptop diagnosis* respectively. All the three ophthalmologists had the same years of clinical experience and were experienced with teleconsultation. The diagnosis was labeled as 'correct' or 'incorrect' in concordance with the face to face examination and statistical analyses done using statistical software (SPSS for Windows version 13.0; SPSS Science, Chicago, IL).

Results

The study included 228 eyes of 114 informed consenting patients(mean age 47 years,73.6% males,26.4% females) with 61 (26.5%) diabetic retinopathies, 56 (24.3%) macular diseases, 22 (9.5%) retinal vasculopathies, 19 (8.2%) optic nerve head and 31(13.4%)miscellaneous conditions and 39(16.9%)normal eyes. The diagnosis was correctly diagnosed by both smartphone and laptop in 211(92.5%) eyes, incorrectly diagnosed in 8(0.03%) eyes, while correctly on smartphone but incorrectly on laptop in 6(0.02%) eyes and vice versa in 3(0.01%) eyes.The sensitivity of smart phone was 98%(95% CI:95-99%) while specificity was 57%(95% CI:25-81%) and the kappa value was 0.62($p<0.05$) suggesting substantial interrater agreement .

Conclusion

Thus smartphones would be technically feasible in areas where access to computers with internet connectivity is unreliable or insufficient and with further innovations like imaging with 20D lens or incorporating a flash in the smartphone camera would also alleviate the need for carrying bulky equipment to the camp site.

Address for correspondence:

Dr Sheila John,Department of Teleophthalmology, Medical Research Foundation, , No 18 College Road,Nungambakkam Chennai ,Tamil Nadu. India -600 006.Phone: +91 – 44 – 28271616 Fax: +91 – 44 – 28254180. Email: sheilajohn999@gmail.com