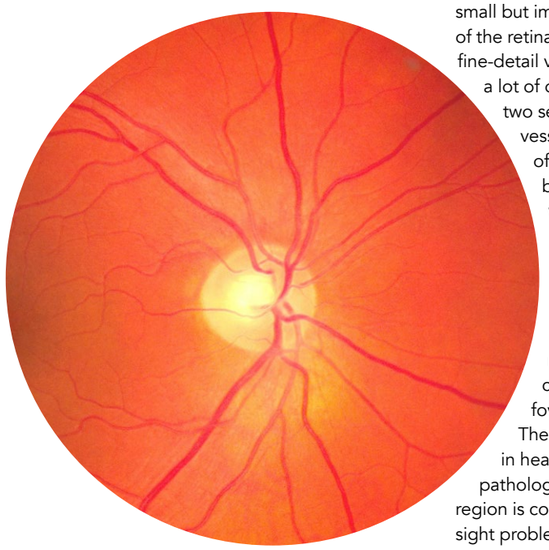
Shining a spotlight on diabetic retinal detachment

Diabetes mellitus affects millions of people globally. Patients are at risk of associated diseases and often encounter problems with their eyesight. Dr Miguel A Quiroz-Reyes, retina specialist at Oftalmologia Integral ABC, Mexico City, Mexico, set out to investigate the outcomes of diabetic patients with advanced complications of the retina. These patients had developed diabetic macula-off tractional retinal detachment, a known risk factor for sight loss. The clinical outcomes of surgical intervention were monitored using the latest tools for visualising the blood vessels within the eye. Dr Miguel A Quiroz-Reyes found that a lack of blood supply is largely responsible for poor visual outcomes in diabetes.

Diabetes mellitus (DM) is a chronic and serious metabolic condition. By 2040 it is estimated that over 642 million people worldwide will have a diagnosis of DM. It is caused by the pancreas not producing enough insulin, or when the body cannot effectively use the insulin it produces. If DM is poorly controlled, blood-sugar levels become very high and over time this leads to serious damage to many of the body's organs including the nerves, eyes, and kidneys. The condition is especially associated with complications of the eye and visual function. If left unmanaged, diabetes can lead to blindness.



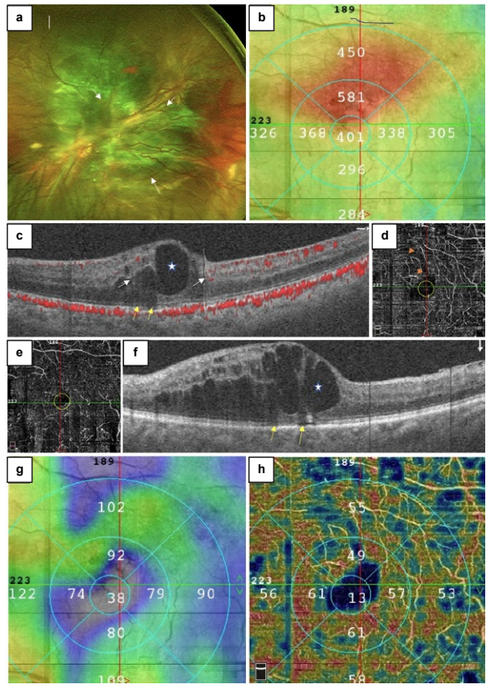
Ophthalmologists are particularly concerned with the retina and macular regions of the eye when assessing problems in DM patients. The human retina is a thin and light-sensitive layer of nerve tissue at the back of the eye and is responsible for visual processing. The macular region is a small but important area at the centre of the retina that bestows central and fine-detail vision. The retina requires a lot of oxygen and is supplied by two separate layers of blood vessels. The innermost part of the retina is supplied by the retinal circulation, while the outer portion is supplied via perfusion through highly specialised choroidal blood vessels. The macular region is supplied by three capillary networks but also has a capillary-free zone called the foveal avascular zone, or FAZ. The FAZ varies in size, even in healthy individuals, though pathological enlargement of this region is commonly associated with sight problems.

DIABETIC COMPLICATIONS

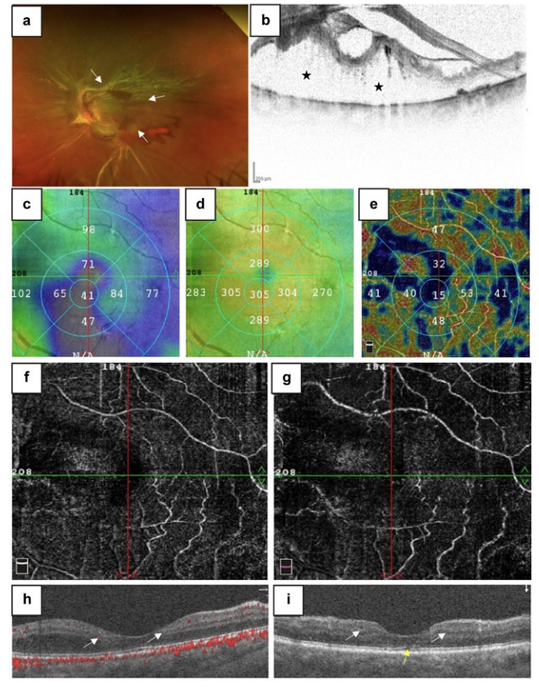
One complication of DM is diabetic retinopathy (DR), which is a leading cause of sight loss in the working-age population in the Western world. Particularly at risk are long-time diabetics with poor control of their blood sugar and poor blood pressure control—prevalent in patients with insulin-dependent diabetes. Dr Miguel A Quiroz-Reyes, MD, and collaborators at the Retina Specialist Unit at Oftalmologia Integral ABC, Mexico, set out to better understand the outcomes of patients with severe eye complications as a result of diabetes.

DR can be categorised into two main types. Non-proliferative diabetic retinopathy is the early-stage of the disease and is less serious. It is defined by early intra-retinal microvascular findings associated with structural damage to the blood vessels. Symptoms can be mild or even non-existent at this stage. For long-term diabetics, DR can become progressive and is known as proliferative diabetic retinopathy (PDR). More serious than DR, PDR is characterised by growth of new retinal vessels that pose a risk for vitreous bleeding, retinal detachment, and neovascular glaucoma.

As Dr Quiroz-Reyes explains, 'PDR can lead to further complications of recurrent vitreous haemorrhages (VH), tractional retinal detachment (TRD), refractory macular edema associated with posterior hyaloid traction, combined traction/rhegmatogenous retinal detachment, and epiretinal membrane (ERM) proliferation'. In addition to PDR related changes, other known causes of visual loss in DM include diabetic macular edema (DMA) and chronic cystic macular edema (CME).



Surgical case 1. a) wide-field colour photo showing extensive tractional retinal detachment (white arrows). b) irregular and severe post-operative macular thickening. c) optical coherence tomography with severe macular thickening and large cystic formation (white asterisk). d) abnormal irregular superficial vascular plexus with abnormal capillary segments, and enlarged foveal avascular zone (yellow circle). e) abnormal vascular deficiencies of the deep vascular plexus, the foveal avascular zone looks smaller with some vessels remodelling (yellow circle). f) severe macular thickening (white asterisk). g) superficial irregular macular partial-thickness topography. h) abnormal vessel density segmentation image over the different macular subfields.



Surgical case 2. a) wide-field colour photo of a left eye with a macula-off diabetic tractional retinal detachment (white arrows). b) abundant subretinal fluid (black asterisks). c) post-operative partial-thickness abnormal superficial macular topography. d) corresponding post-operative full-thickness uniformly thick macular topography. e) abnormal quantitative vessel density. f) very abnormal microcirculation at the superficial vascular plexus. g) deep vascular plexus with many perfusional abnormalities. h, i) abnormal foveal contour and diffuse macular thickening, with disorganisation of retina inner layers (white arrows), and irregularities of the subfovea (yellow arrow). The red dots indicate retinal vessels and the choroidal capillaries.

Typical treatments for long-term DR complications involve surgical vitrectomy—eye surgery that specifically treats problems with the retina and vitreous. Here, the pathological vitreous humor of the eye is removed to enable better access to the retina.

In patients where clinical detection of retinopathy has been delayed, advanced pars plana vitrectomy (PPV) surgery (which removes the vitreous to enable access to the back of the eye) has proven useful. According to Dr Quiroz-Reyes, however, 'We don't yet know enough about the visual outcomes for the patients treated'. Dr Quiroz-Reyes set out to assess visual outcomes using the latest tools for investigating the vasculature of the eye.

We don't yet know enough about the visual outcomes for diabetic patients.

IMAGING TECHNIQUES

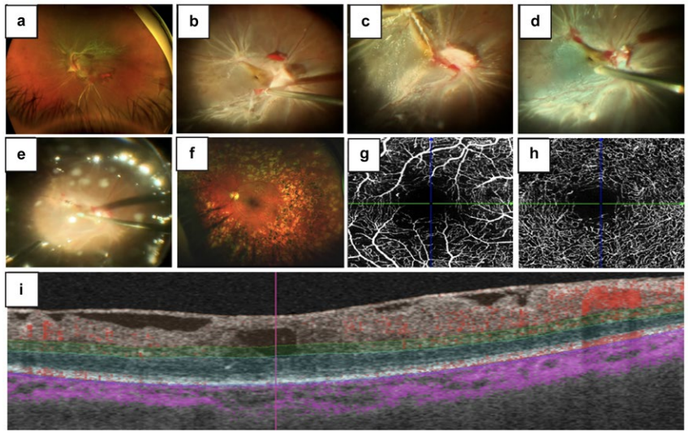
Fluorescein angiography (FA) is an imaging technique used in combination with fluorescent dye, to examine any lack of blood flow to the macular region and assess its significance. It is a key tool for diagnosing how far the disease has progressed by assessing the extent to which changes to retinal blood vessels have occurred. FA does have its limitations, however. Ophthalmologists are unable to see capillaries situated deep within the eye and it cannot be used for clinical assessment and subsequent treatment of the macular region.

Recent research has shown that the problem of restricted blood flow, together with enlargement in the region of the macular known as the FAZ with decrease in the blood flow to the macular region have since been detected in several retinal vascular diseases: diabetic retinopathy (DR), hypertensive retinopathy, retinal vein occlusion, and sickle cell disease.

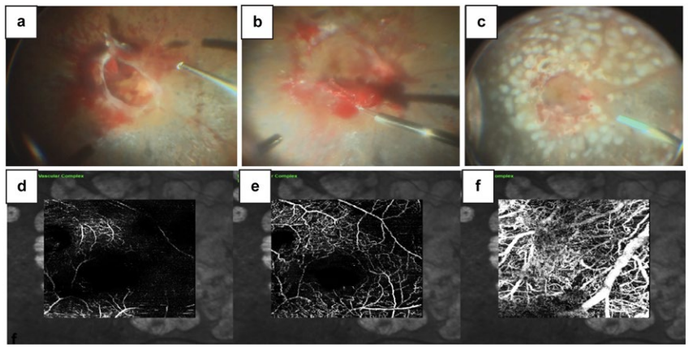
NEWER TECHNIQUES

In the early 1990s a new and complementary technique to FA, optical coherence tomography (OCT), arrived on the scene. This non-contact and non-invasive method completely revolutionised ophthalmological research. Today, this tool facilitates the visualisation of the front (anterior) and back (posterior) segments of the eye and can be used to generate 3D models of the inside of the eye. It can be performed each time a patient visits the clinic.

More recently, a technique known as optical coherence tomography angiography (OCT-A) has also emerged. A non-invasive method for visualising the blood supply to the retina, it does not require the injection of dye. OCT-A is used to assess the density of blood vessels and to quantify blood



Surgical steps and structural findings. a) wide-field colour fundus image of an eye with prolonged type 2 diabetes mellitus and abundant proliferative blood supply that has detached the retina in the macula region. b) surgical image showing severe traction detachment. c) magnified image where the macula is clearly detached, dragged and distorted, d) surgical image using trypan blue dye. e) surgical image where the macula has been released and looks reattached. f) corresponding final long-term photo of the previous images depicting a pale optic nerve, the macula looks attached and there are PRP scars over the entire retina. g) OCT image showing an enlarged foveal avascular zone. h) OCT image of the deep vascular plexus with abnormal capillaries. i) evidence of a central intraretinal cyst, intraretinal haemorrhagic component with traction and macular edema.



Surgical steps. a) transoperative image with diabetic tractional retinal detachment (pars plana vitrectomy). b) transoperative view once the retina has been reattached showing a passive blood aspiration. c) transurgical image showing a nicely reattached retina with PRP laser photocoagulation. d–f) multiple blood flow alterations to the retinal vasculature.

Our study demonstrates that diabetic ischaemia is largely responsible for poor visual outcomes.

flow to the eye. It has been shown to be a crucial tool for assessment of age-related macular degeneration (AMD) and DR.

This method can also be used to accurately detect a range of other clinically important changes to the eye, including neovascularisation (new blood vessel growth), retinal branch vein occlusion (BVO) retinal artery occlusion (RAO), vessel abnormalities, non-perfused areas of the different subregions of the retina, and anterior segment neovascularisation.

INVESTIGATING DIABETIC MACULA-OFF TRACTIONAL RETINAL DETACHMENT

Using OCT-A, Dr Quiroz-Reyes specifically investigated diabetic macula-off tractional retinal detachment. This condition occurs in long-term diabetics who experience complications of PDR and are thereby at risk of sight loss.

Dr Quiroz-Reyes set out to investigate post-surgical outcomes for visual acuity in those who had successfully undergone up-to-date perfusion-control PPV for tractional retinal detachment. Using this multi-modal imaging tool, Dr Quiroz-Reyes obtained detailed images deep into the retinal tissues including the vasculature. During follow-up, perfusional, structural, and functional post-surgical outcomes were assessed, and compared to fully resolved TRD. The study included a total number of 30 eyes in 27 patients.

The serial post-operative OCT-A imaging highlighted abnormal microcirculation patterns, both at the superficial level and in deep vascular areas. Multiple micro-abnormalities typical of FAZ were observed, capillary dropouts with an irregular and enlarged perifoveal capillary network, and different but distinct areas of non-perfused macula regions according to the flow deficiencies in macular blood flow were evaluated. There was evidence of disorganisation of the retinal inner layers (DRIL) and chronic ischaemic macular edema in 82% of the cases examined—an outcome which explains the levels of poor visual recovery seen with this condition.

As Dr Quiroz-Reyes says: 'our study demonstrates that diabetic ischaemia is largely responsible for poor visual outcomes. Technology has improved over the past decade, improving the surgical treatment of retinal detachment involving the macula. However, the outcomes of surgical treatments for diabetic patients have not undergone a similar change.'

This study expands our understanding of OCT-A for detailed imaging and the presence of DRIL in successful cases of surgical treatment of the eye. Further research is now needed to determine the optimum time for surgical intervention in patients with TRD threatening or involving the macular region.

Behind the Research

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Research Objectives

Professor Miguel A Quiroz-Reyes, MD, investigates the long-term post-operative outcomes in the sight-threatening condition, diabetic macula-off tractional retinal detachment.

Detail

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Bio
Miguel A Quiroz-Reyes, MD was born in Mexico City. He did his postgraduate studies at the National Autonomous University of Mexico, Institute of Ophthalmology, Eye Research Schepens Foundation, Massachusetts Eye and Ear Infirmary, and Retina Associates, Boston, MA, USA. He is former president of The Mexican Retina Society, and retina surgeon at the Institute of Ophthalmology and Retina Specialist Unit at Oftalmologia Integral ABC Institution, a medical and surgical non-profit organisation.

Funding
Retina Specialists Unit at Oftalmologia Integral ABC

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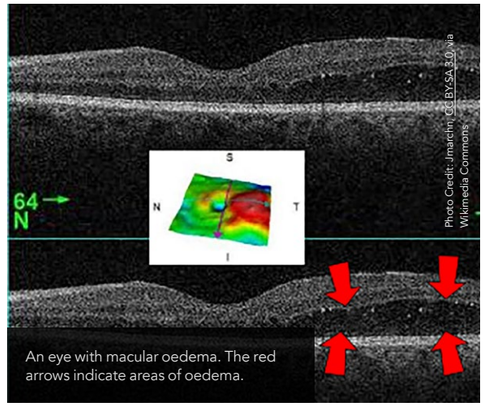

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An eye with macular oedema. The red arrows indicate areas of oedema.

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Personal Response

Do the current imaging modalities available enable ophthalmologists to entirely visualise the vasculature of the eye?

"Recently, OCT-A has particularly evolved in favour of the study of patients with ocular vascular alterations caused by a wide variety of mainly systemic diseases with secondary repercussion at the retinochoroidal level. From spectral domain OCT angiography we have gone to Swept Source OCT angiography with greater definition, field of visualisation, and better penetration at the tissue level—allowing us to assess practically all the vascular layers of the eye at the same time. Even the deepest vascular layers of the eye can be visualised with this new non-invasive imaging technology. Consequently, we are better prepared to diagnose in a timely manner and treat serious retinal vascular entities, such as diabetic retinopathy, that potentially cause blindness."