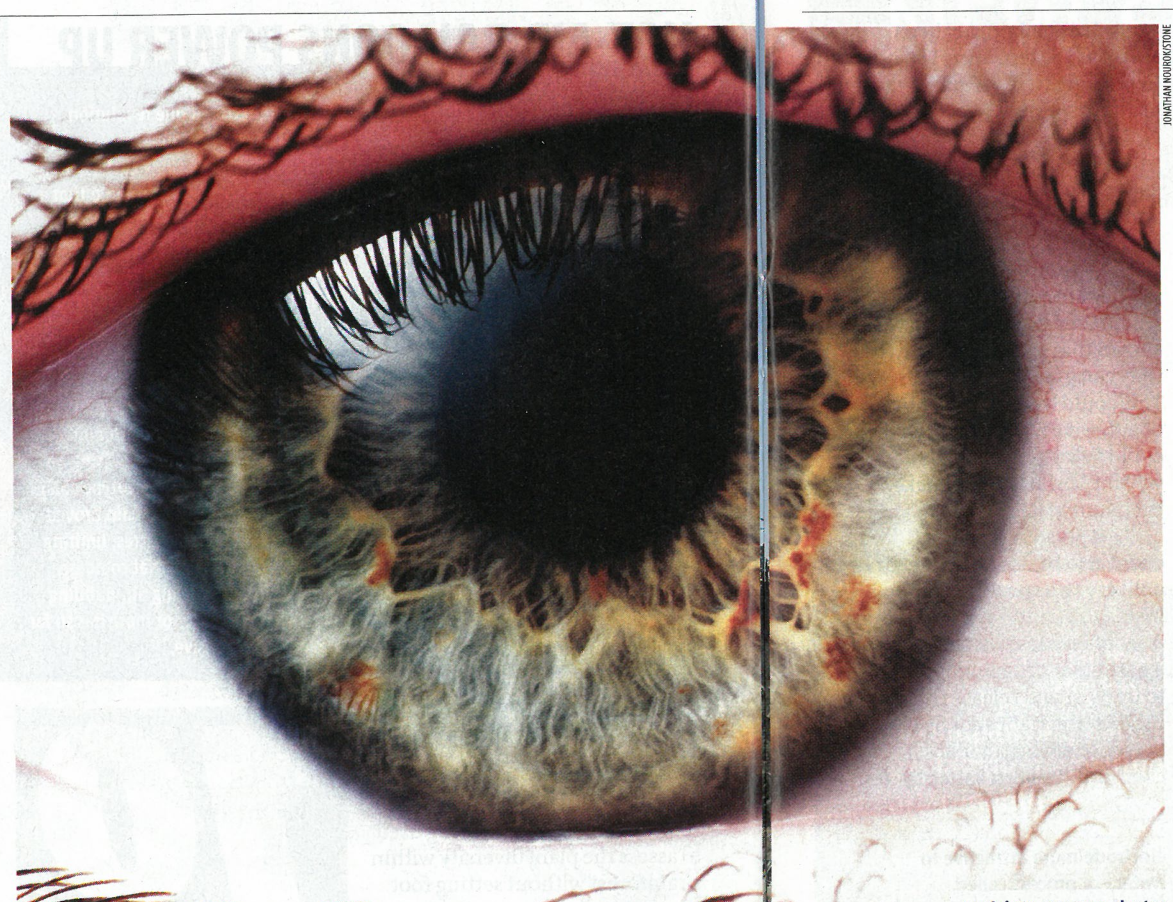
Eyes wide open, please, let's look into your brain


Look into my eyes, doctor

A laser version of ultrasound identifies brain tumours and neurodegenerative diseases from your eyes only

DUNCAN GRAHAM-ROWE

THE eyes may be the windows to the soul, but they also make pretty good peepholes into the brain. Thanks to an optical version of ultrasound, it is becoming possible to locate and monitor the growth of brain tumours, and to track neurodegenerative conditions like multiple sclerosis, Alzheimer's and Parkinson's disease – all by peering into the eye.

The brain is connected to each eye by an optic nerve, so any degeneration of the brain caused by such diseases can also damage cells along the nerve and in the retina, says Helen Danesh-Meyer, an eye surgeon and neuro-ophthalmologist at the University of Auckland Medical School in New Zealand. Indeed, a loss of visual function is one of the first symptoms in many people with a neurodegenerative condition.

Although evidence of a link between degeneration of the optic nerve and diseases such as Alzheimer's has been around since the late 1980s, without instruments capable of measuring the retinal changes accurately it is only recently that this knowledge could be put to use, says Danesh-Meyer.

The accuracy of ophthalmological tools has greatly improved in the last few years. Developments include a type of laser-camera technique called Heidelberg retina tomography (HRT), and a laser device called GDx, both of which can be used to scan the shape and thickness of optical nerve fibres at the back of the eye.

Both tools are now widely used to manage glaucoma, but in 2006 Danesh-Meyer became one of the first researchers to use them to study neurodegenerative diseases by looking at the region of the retina where ganglion cells meet to form the optic nerve – a region known as the optic nerve disc (OND). In a trial involving 40 Alzheimer's patients and 50 healthy volunteers, she was able to show that people with Alzheimer's had a distinctive enlargement to a cup-shaped part of their OND and a progressive thinning of the retinal nerve fibres within the disc.

> "People with Alzheimer's have a distinctive shape to the disc of their optic nerve"

Following this discovery, researchers have been using even more accurate instruments to track degenerative changes in the OND to monitor the progression of diseases like Alzheimer's, Parkinson's and MS. But it has been the emergence of optical coherence tomography (OCT) that appears most promising: it became commercially available in 2006 and is fast becoming a standard tool for the management of glaucoma and diabetic retinopathy. When applied to the OND, it produces highly detailed two and three-dimensional images of the subsurface retinal tissue, says Denise Valenti at Boston University, who has been using OCT to study Parkinson's and Alzheimer's.

The technique works very much like ultrasound, but bounces light off the tissue instead of sound waves. One beam of light is fired at the tissue and another at a reference mirror. When the reflected beams have travelled an identical distance, interference will make their combined beam brighter than if the distances are different. So by reflecting one beam off of different layers of tissue, and moving the reference mirror until the combined reflected beam is brightest, the technique can measure the depths of each section of tissue and build up a detailed image of its structure. It has proved particularly useful in ophthalmology because the semi-transparent nature of retinal tissue makes it possible for OCT to penetrate to greater depths – up to several millimetres. When applied to the OND it can give information about both the shape and thickness of retinal nerve fibres, allowing even subtle changes to be tracked.

Such changes can be used to monitor the progression of diseases non-invasively and relatively cheaply. Unlike MRI, which is expensive and can require patients to remain still for an hour or more, OCT is increasingly available in clinics and can be carried out in a few minutes. "It's extremely inexpensive compared to other tests," says Valenti.

One possibility is to use OCT to monitor the effectiveness of treatments for neurodegenerative diseases, says Danesh-Meyer: "These drugs can have a lot of side effects, so if they are not having a benefit then you won't want to continue with them."

Laura Balcer, a neurologist at the University of Pennsylvania School of Medicine in Philadelphia, has been using OCT on patients taking part in MS drug trials to try to establish if the system can accurately gauge drug efficacy. Such an objective tool would allow symptoms to be picked up that might otherwise go unreported, she says. For example, OCT has already shown that even in people with MS whose eye function is normal, there are marked differences in OND shape and fibre thickness compared with healthy people. "MS researchers are very excited about OCT," she says.

The technology is also proving its value as a tool for monitoring brain tumours, which can affect vision by pressing on the optic nerve. Such pressure will cause damage to different parts of the OND, depending on where in the brain the tumour is located, says Danesh-Meyer. What's more, the extent of the thinning of the nerve-disc fibre can also reveal whether vision will be restored upon removal of the tumour.

In the case of one patient who was 24 weeks pregnant following several IVF attempts, OCT monitoring allowed surgeons to hold off on removing her brain tumour until well into the third trimester, when the fetus had a better chance of survival. The usual treatment would have been to operate immediately to prevent permanent vision loss, but this would have risked inducing premature labour. By monitoring the compression on the optic nerve to ensure it did not reach the point at which permanent damage was inevitable, Danesh-Meyer was able to keep tabs on the tumour's growth and delay the surgery. As a result, the baby was born safely and the patient kept her vision.

The ultimate aim for many using OCT is to diagnose diseases before symptoms arise. The difficulty with this is that the thickness of retinal nerve fibres can vary from person to person, says Danesh-Meyer, so there is not always a clear baseline from which to compare patient scans.

Eventually though, the low cost and simplicity of the technology may make it feasible for people to be given an OCT scan of each eye at a young age, to give doctors a record of their healthy retinal nerve, says Danesh-Meyer. With regular screening, some neurological conditions could be spotted incredibly early. "We're really just at the cusp of knowing where this is all going." ●

Virtual double flexes your muscles

A SYSTEM that creates a virtual body double of a person's skeleton and muscles could help fitness fanatics or people trying to regain movement after an illness by showing them how well they are exercising.

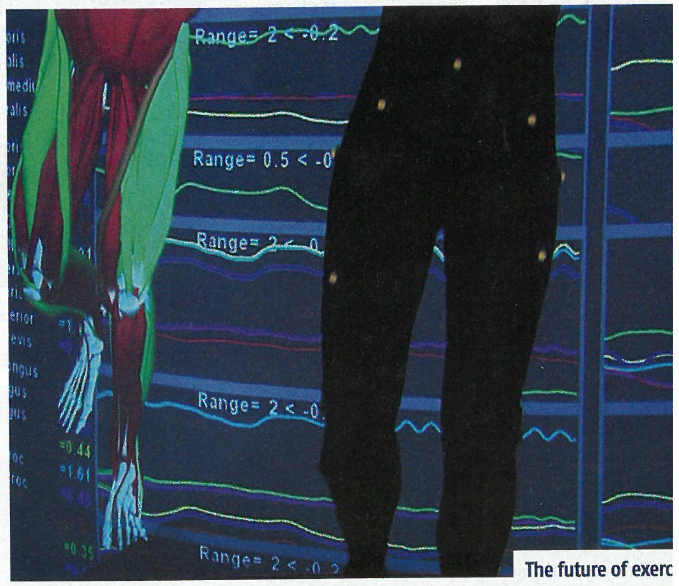
The Human Body Model, developed by Motek Medical in Amsterdam, the Netherlands, uses a virtual double to show which muscles a person is using by highlighting them in green (see image). The force being generated is shown by the intensity of the colour. "It allows you to see the muscle groups you are using in real time, and even the forces they are creating, which are usually invisible," says Motek's founder Oshri Even-Zohar. The user's on-screen output is not a direct measure of their muscle activity, but is based on existing models of the anatomy and physics of the human body and is intended as a tool to help the patient.

Users carry out exercises, such as running on a treadmill, while wearing a suit with 47 reflective markers placed in the positions of specific muscles. While the person runs, infrared strobe lights, flashing several hundred times a second, help eight cameras to track the markers. Sensors on the floor of the treadmill can also be used to measure the force applied to the ground by the user's feet to give more information on their muscle output and the load on their joints.

The final stage is to feed this information into computer models, which help create the detailed on-screen display of the user.

The software used to help create the double was trained by directly measuring the force generated by people's muscles while recording their motion and the electrical activity of their muscles. This could only be done for some movements and forces, though, such as pushing against weights. "There is no tool in medical science that allows you to measure all the muscle forces in motion," says Even-Zohar.

The system is being tested at Sheba Hospital in Tel Aviv, Israel, where it is helping people regain movement after a stroke. Researchers at the Cleveland Clinic in Ohio are also using the system to study gait and locomotion in healthy, active people. Tom Simonite ●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