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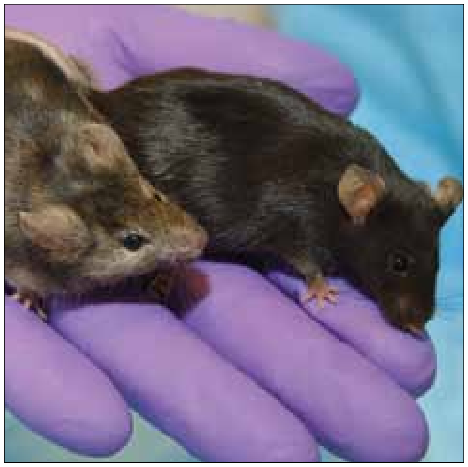
Special Advertising Report: Imaging

Eye research technology focuses on laboratory animals

Much of translational research begins with animals, particularly the laboratory mouse. This research can focus on basic processes, common eye disorders or pharmacological interventions. The mouse is an attractive starting point because researchers can manipulate its genes to produce analogues for a number of human diseases.

And because the retina is an extension of the brain, diseases such as Alzheimer's have been shown to present in the retina. This gives rise to the quest for diagnoses of this neurological disorder through an eye examination. However, advanced technology optimized for eye research using laboratory animals has been minimal.



Retinal imaging microscope

Phoenix Research Laboratories has set out to support such research with advanced technologies. The company first introduced its retinal imaging microscope, the Micron, at the 2009 ARVO Annual Meeting. This system delivered convenient mouse and rat retinal images with four microns resolution, wide field images, and bright field and fluorescent imaging. Fluorescent angiograms show the flow of red blood cells, Evan's blue angiograms are possible, and a host of fluoropores have been imaged, including GFP, CFP, YFP and mCherry.

Phoenix recognized that optimized retinal imaging was just the starting point. At the 2011 ARVO Annual Meeting, the company introduced a slit lamp system for anterior segment imaging, an image-guided focal ERG and an image-guided laser delivery system.

Attachments

These additional modalities are not obtained by stand-alone devices, but through attachments to the Micron camera body. This means labs benefit from substantial cost savings, as they can use existing equipment such as the computer and animal stands. Changing modalities takes only a few minutes. And very importantly, no additional laboratory bench space is required.

"The Micron optics is optimized specifically for the rodent eye, as opposed to offering *ad hoc* adaptations of clinical instruments," explained Bert Massie, PhD, Phoenix chairman. "In order to offer an inclusive set of research modalities, the Micron

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Reinventing the eye exam

ARVO member Alexander Walsh, MD, formerly of Doheny Eye Institute at the University of Southern California, discusses new directions with the use of binocular OCT, particular in the developing world.

Could you expand on the technical advantages binocular OCT offers over other hardware in screening and clinical care?

Outside a handful of revolutionary diagnostic technologies, today's basic eye exam is similar to the one of 50 years ago. Most of its findings — history, review of systems, visual acuity, intraocular pressure, gross visual fields, extraocular motility and alignment, pupillometry, slit lamp biomicroscopy — must be collected manually. They require different instruments, are subjective and/or qualitative, and require manual recording. The major advantage of binoculars is the ease of aligning their optical axes with the eyes. Giving this instrument direct access to the patient's eyes means human operators can be removed from the examination process, thereby reducing costs. Other key benefits include:

- Improved test and re-test reliability, since machines undertake tasks the same way every time;
- Improved accuracy, given the finer measuring capabilities of machines for many tests;
- Increased accessibility with flexible machine placement;

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- Automatic storage and documentation by the instrument, permitting its subsequent review by a human operator.

This final advantage reduces manual charting tasks for physicians and ancillary personnel that are both time consuming and inaccurate. It also ensures exam data can be compared between visits, while enabling more advanced quantification.

Current patient pupil checks rely upon manual recording of a subjective impression of the pupillary reaction. Binocular OCT instruments store images of pupils constricting.

This affords precise quantitative measurements of pupillary diameter, area, latency and acceleration to a millisecond timescale. Furthermore, these images can be reviewed and re-analyzed later, should advances be made in how the pupil works. Good objective data storage begets better quantification, not only in pupillometry but in almost every other test.

Binoculars can examine both eyes simultaneously, an important feature in functional tests that measure the brain's ability to integrate visual stimuli. It also saves time, with some tasks completed simultaneously.

Decreasing operational costs while increasing efficiency seems a win-win outcome. How would you balance product quality and performance with marketplace viability?

Most instruments require a human operator, something which incurs an on-going, annual salary cost over the life of the machine: an instrument costing $40,000 may require a $40,000 pa operator for five years, resulting in a $200,000 additional outlay on labor costs. Purchasing less expensive instruments has little impact, without the operator being removed from the equation. Making the instrument operational by the patient achieves this, delivering an immediate impact upon the cost of running a practice. Combining many instruments can also reduce operational costs: smart phones have incorporated the functions of music and video outputs, at the same time delivering a superior and cheaper telephone function.

Many devices in an eye clinic use the same components to perform different tasks: power supply, light source, a visual target for the subject to focus upon, a method of obtaining feedback or patient input, a recording device and so on.

Well constructed diagnostic systems such as smart binocular devices should contain the capacity to perform all of these functions in a single machine: vision testing, autorefraction, intraocular pressure measurements, quantitative pupillometry, alignment and motility testing, OCT biomicroscopy, etc.

Alexander Walsh, MD

This amalgamation of functions is intended to reduce both capital equipment and labor costs. This can be augmented by replacing a large proportion of slit lamp examinations with OCT biomicroscopy, which is completed by the patients themselves in the waiting room. Such a move would enable the doctor either to see more patients or spend additional quality time with existing ones.

What particular challenges do you face in promoting this device across the developing world?

A key feature of the developing world is its inexpensive labor, which reduces the advantage of self-operated instrumentation. However, the lack of skilled labor means a machine that performs the full range of tests consistently could prove extremely useful to doctors in the developing world. Furthermore, most developing world doctors live in cities, while their patients inhabit more rural areas.

Therefore, a patient-operated instrument that can be taken to remote areas to collect findings for a complete eye examination should advance the development of true telemedicine. Indeed, these instruments could help standardize the conduct of eye exams around the world, regardless of where they are performed.

One of the biggest challenges in entering developing world markets lies in designing for extreme affordability. At the outset of this process, my aim was to introduce a $1 eye exam throughout rural India.

The constructed business model enabled us to practically give the instrument away for free, rather like a cell phone, while generating good revenues on the high patient volumes within the developing world.

The cross-subsidization of developing world markets with revenue earned from the developed world formed a central plank of this business model. Yet despite traveling the world for almost two years in search of foundations and wealthy individuals to support this venture, no one was willing to take the risk.

The result is that we continue to construct fragile and expensive binoculars for the developed world, only for them to subsequently undergo makeshift redesigns for the developing world. This represents a lost opportunity to introduce innovative instruments into a poorly served marketplace.

The automated teller machine provides an apposite analogy. The complex equation of human tellers, check books, deposit slips and time has been distilled into a convenient, objective, accessible and inexpensive device. The future of ophthalmology must envisage doctors being equipped with multi-functional instrumentation, delivering better diagnoses, faster, and at a lower cost. For the reasons I mentioned above, I do think it's possible.

For more details, see Walsh's 2009 article "Reinventing the Eye Exam" at http://goo.gl/np3ei. ■

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was redesigned to provide these additional features through attachments to the basic body. The result is that each modality is an incremental investment, use of limited laboratory space is minimized and the research team can quickly move from one modality to another, eliminating the need for separate animal sessions."

Massie said that the company has so far delivered over 90 systems into Asia, Europe and North America. Users come from pharmaceutical companies, universities and research centers.

Significant reported research with the Micron includes observation of β Amyloid plaques in the eyes of Alzheimer's mice and the use of the focal ERG to observe stem cell rescue of damaged retina.

Phoenix continues to emphasize technical progress. The company is currently developing an optical head for larger animals, such as rabbits, and plans to introduce additional modalities soon. ■