A start-up spreads its wings

Although it is not even ten years old, the UK-based start-up company Michelson Diagnostics is already making a big name for itself through its patented advanced imaging technology, Optical Coherence Tomography (OCT). Able to provide ultrahigh resolution images of just about every epithelial tissue in the body, OCT has many applications. For the moment Michelson Diagnostics is focussing on dermatology, where promising results are being generated in clinical trials. We wanted to know what makes Michelson Diagnostics tick and where the company is headed, so we spoke to Jon Holmes, CEO of the company.

With a background in industrial applications of laser scanning and image processing, Jon Holmes is a co-founder of MIchelson Diagnostics and has been CEO since its creation in 2006. Since then, Jon has successfully piloted the company through several financing rounds and the associated milestones.

Q. *Michelson Diagnostics is about eight years old. What's the story behind its creation?*

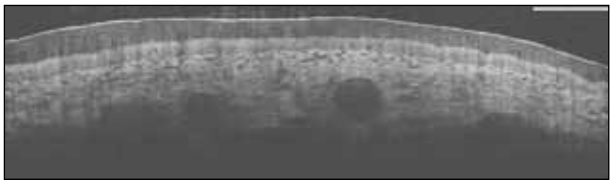
Yes it seems like yesterday but in fact it was in 2006 that, with a couple of colleagues, we founded Michelson Diagnostics. Our backgrounds and expertise were in industrial applications of laser scanning and image processing, principally in the world of factory automation. For example, we used advanced technological approaches in applications such as automatic quality control and inspection of products as diverse as silicon chips and plate glass. On the face of it, therefore, a field that seems far from the medical imaging area where we are now active. However I really saw an opportunity to apply our expertise in scanning technologies to the biomedical field and came across this wonderful field of Optical Coherence Technology (OCT), which was a perfect match between our skill sets and the clinical need of high resolution images of sub-surface objects. We could see that there was a gap in terms of image quality and came up with an idea to address that image quality gap. OCT still underpins our company, and is our unique technology, albeit one with many, many clinical applications.

Q. *Well before we go much further maybe you'd better give a short description of the OCT technique itself and the principles behind it.*

Originally developed by Prof Fujimoto in MIT as far back as the early 1990s, OCT is an optical signal acquisition and processing method, founded on the well-known physical principles of optical interferometry. OCT enables the generation of 3D images of very high resolution — at the micrometer level, that is some 10 to 20 times higher resolution than typical ultrasound images. A trade-off with respect to the extremely high resolution is the fact that the penetration in the tissue being imaged is only a few millimeters. (Although various tricks can be used to squeeze some more depth of image, this always comes at the price of lower resolution). The low penetration of the technique means that it is mainly suitable for examination of epithelial surfaces. Indeed one of the first applications of OCT was in the analysis of the surface of the retina. Literally tens of millions of cases have by now been scanned with OCT. The method has become almost the technique of choice in the analysis of several eye diseases and is used on a global basis to make clinical decisions regarding blinding diseases such as macular degeneration, diabetic retinopahy and glaucoma.

Q. *If OCT is already well established, what does Michelson Diagnostics bring to the party?*

We bring our proprietary variant of the method which is the use of multi-beam as opposed to single-beam technology. In our implementation we use four separate beams of laser light, each of which is focussed at a different depth. These are then scanned separately and a compound mosaic image generated. With our multi-beam technology, which was originally developed by Prof Yang from the University of Toronto in Canada, we get even higher resolution (in fact twice) than with single beams. We use a sophisticated diode laser operating at 1300 nm, i.e. in the Near Infrared Region. We have a rapid wavelength sweep at 20 000 times per second on either side of the central 1300 nm wavelength, from 1250 nm to 1350 nm. This approach is one that is used regularly in the telecommunications industry for the monitoring of the quality of fiber-optic cables. This makes the whole approach more affordable.



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Q. *Is this high resolution really needed clinically?*

The straight answer to that is yes. Of course as I said there are many potential applications of OCT each with their own particularities, but in the one that we have decided to focus on, namely the analysis of skin cancers such as non melanoma skin cancer (NMSC), the higher the resolution the better. This is so that the dermatologist can identify the critical morphological features of the tissue underlying the skin.

Q. *You mentioned that you have decided to focus on dermatological applications. Why?*

It's true that there are many more possible applications of OCT than in the analysis of dermatological cancers. I've already mentioned the well-established ophthalmological applications, but there are many others, such as measurement of atherosclerotic plaque in the coronary arteries, analysis of oral cancers, etc. — by the way the potential of OCT in imaging oral cancers seems especially interesting.

But back to dermatology. This area seems particularly intresting to us since there is an ever-increasing number of patients with suspect lesions needing to be analyzed to determine whether they are malignant or not. Epidemiologically the increase in the number of NMSC cases is probably due to the aging of the once "golden" generation of the baby boomers who exposed themselves immoderately to the sun. The cumulative effect over time of many hours of exposure to sunshine with no skin protection is certainly partly responsible for the current huge increase in the number of cases. Although the deadly malignant melanoma gets a lot of the headlines, in fact there are nearly twenty times more cases of non-melanoma skin cancer (NMSC) .

The clinical priority is to determine as reliably as possible whether the lesion is malignant or not. For this, the gold standard is biopsy/histology. Apart from the obvious discomfort for the patient, the biopsy approach is time-consuming and costly, all the more so when there are many lesions to be looked at.

In contrast, OCT, through use of a small hand-held optical scanner, generates immediately high quality and high resolution images of the sub-dermal tissue micro-structure, Thus it is quick and painless to the patient.

And then if after confirmation that the lesion is indeed malignant, the monitoring of the subsequent surgical procedures can also be significantly improved by use of OCT technology. In cases of malignant skin cancers, the aim is to excise the malignancy as completely as possible, with excision of as little as possible of the surrounding normal tissue. Frequently, to be as sure as possible that all cancerous cells are removed the excision area is made as large as possible, with the consequent disadvantage that a cosmetically disfiguring scar on normal tissue remains.

An alternative is the so-called Mohs approach, which is often used to treat common types of skin cancers, especially in the United States. Basically the procedure is a microscopically controlled surgery, during which, after each removal of tissue, and while the patient waits, a pathologist examines the tissue specimen there and then for cancer cells. The results of this histology examination inform the surgeon where next to remove tissue.

Although the success rate is generally high, the obvious downside is that, depending on how many iterations are involved, the procedure can take a long time. It is clear that a rapid analysis by OCT of the cellular structure of the remaining tissue has the potential of saving a significant amount of time. The approach has several advantages, such as being quick and painless, being able to immediately determine whether the lesion is shallow enough to be treated by non-invasive mans such as creams. In addition the response of the lesion to the treatment can be easily monitored.

Q. *In practice how are your evaluations of the technique in dermatology getting on?*

These are going well. The OCT instrument that we have developed Vivosight OCT was selected for use in a recently completed multi-centre, prospective clinical trial for the diagnosis of basal cell carcinoma. In the study, over 250 patients with clinically suspicious lesions for basal cell carcinoma were scanned at six centres in Germany. In each case, diagnosis using VivoSight OCT was compared

Designed for easy disinfection, the probe is comfortable both for the clinician and the patient.

The Vivosight system produced by Michelson Diagnostics.

with the gold standard of biopsy and histological analysis. The clinicians involved in the trial, Prof J Welzel, and Dr M Ulrich have just presented the results at the recent American Acacademy of Dermatology's annual meeting. Dr Ulrich concluded in her presentation that: "VivoSight enabled a statistically significant improvement in the specificity and Negative Predictive Value (NPV) of Basal Cell Carcinoma diagnosis over both clinical and dermoscopy on this cohort of challenging pink patches. Thus many biopsies can be avoided with VivoSight OCT, and patients can instead be treated non-invasively." The full data will be published later this year, but already we are encouraged that the preliminary results support our contention that OCT can be used to significantly reduce the need for biopsies. More broadly we believe that our system has the potential to become the standard of care for the non-invasive diagnosis and monitoring of certain diseases and conditions that affect the skin, and in particular non-melanoma skin cancers.

Q With all these exciting results, let's get back to the company itself. How are you structured to support the trials that are being carried out on your system. What about funding? regulatory issues? Reimbursement?

Yes we have to keep our feet on the ground in the midst of these exciting results. We are still a small start-up, albeit one with highly qualified people on board. We have a total head-count of 19, most of whom are based in our facilities in Orpington, Kent in southern England. In addition we have sales offices in Munich, Germany and also in the United States.

'Regarding regulatory status, our Vivosight system has the CE mark and 510 (k) clearance in the United States. It is also registered with TGA in Australia'.

Our major marketing focus is at the moment on Germany, United States and in Australia. Regarding re-imbursement, the technique is already re-imbursed in Germany for patients within the private health insurance system.

As for financing, so far we have successfully negotiated several funding rounds, mainly from venture capital companies and have met the associated deadlines.

In addition to all this we were recently awarded a EUR 2.3 million grant from the EU under the EU's framework programme. This was for a collaborative development project — known as Advance (**A**utomatic **D**etection of **VA**scular **N**etworks for **C**ancer **E**valuation) in which Michelson Diagnostics is the lead partner. The aim of the three-year project is to use OCT technology to determine the extent of vascular networks underlying certain skin cancers. The hope is that the measurement of such vascular networks could be an early indication of malignancy. Since OCT is the first technology available that can visualize the 3D vascular network in and around the skin tumors within the tissue, *in vivo* and in real time the device should enable not just the identification of the tumor but also its stage of development and aggressiveness.

Looking further down the road, we recognise that, as we accumulate more and more data from clinical trials supporting the use of OCT technology, we will have to expand our marketing and support infrastructure. One way to do this could be via arrangements under which we would license our technology to the well-established medical imaging companies, who up until now do not have OCT as one of their main imaging modalities.

But that's for the future. In the meantime we are dealing with the exciting present.

Book review

ABC of Dermatology, 6th Edition
Ed by Rachael Morris-Jones 240
240 pages Pub. by Wiley Blackwell BMJ books, May 2014

With over 450 full colour images, ABC of Dermatology is a practical guide to identification, recognition, treatment and management of common dermatological conditions encountered within primary care, walk-in centres, and the emergency room and within patients admitted to hospital with medical/surgical conditions.

Fully updated with new developments and treatments, this sixth edition provides expanded coverage of psoriasis, eczema, inflammatory dermatoses and drug photosensitivity. It also includes improved coverage of the management of onychomycosis, scabies and lice, and hair and scalp, and new content on biological treatments, lymphoedema, community acquired MRSA, pityriasis rosea, immune reconstitution syndrome and antifungal drugs.