

## Address by Chairman, Angus Holt

Welcome to the 2009 Annual General Meeting of Optiscan Imaging Limited, my first as a director and Chairman of the Company but my 12<sup>th</sup> as a shareholder. My name is Angus Holt and I have a long history as a shareholder of Optiscan through both personal holdings and via funds with which I am and have been involved. My background is in funds management and private equity with a specific focus on special situations and smaller companies, including start ups. I have significant experience with biotech companies and start ups and am acutely aware of what does and doesn't work in such ventures. I am very pleased with our recent progress and enthusiastic about our future and will now elaborate on where we have been and why and where we need to go now. Before I do that I would like to introduce the other Officers of Optiscan.

Alongside me are my two fellow directors, Vicki Tutungi (CEO) and Peter Delaney (Director of Technology) and also our CFO, Bruce Andrew.

I would also like to welcome Anthony Seyfort from our solicitors, Lander & Rogers, and Don Brumley from our auditors, Ernst & Young. Don will be available to respond to any questions you may have concerning the conduct of the audit and the preparation and content of the Auditor's Report.

As there is clearly a quorum present, I now formally declare the meeting open.

Today's meeting will commence with my review and outlook, I will then hand over to Vicki Tutungi, our CEO, who will provide a review of operations. Following Vicki will be a technical R&D review from Peter Delaney.

We will then move on to the statutory items of business, being the resolutions in the Notice of Meeting. Following completion of those formalities I will open the meeting for questions.

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It was the same day last year that my predecessor Grant Latta addressed the 2008 AGM and conveyed the message of the difficult period the company had recently entered and the risks then confronting the Company. At the time of last year's AGM, while the Company had a somewhat mature and quite superb technology, cash reserves had fallen to a level that could not sustain the operations of the Company beyond mid 2009 (calendar year). Royalty revenues were set to dry up over the coming twelve months and sales levels to Hoya were

highly uncertain, while operating costs continued to track around [\$600,000] per month . Such a parlous financial outlook was exacerbated by the GFC and the consequent lack of availability of capital, particularly for unprofitable biotech companies.

That combination of factors severely narrowed the available avenues for Optiscan to move forward as a Company. As detailed by Grant Latta in his 2008 Address those options included:

- moving forward with a greatly reduced operating capacity but still with a need for near term capital;
- hibernating the company which would result in all activities being parked and all but a few staff being laid off; and
- the laying off of various rights over manufacturing and/or IP via sale or licensing or similar mechanism.

Shortly following the 2008 AGM I intensified my discussions with Grant Latta in order to seek a solution of sorts to the impending doom facing the Company. These highly constructive discussions had as their major focus ways in which the major assets of the Company, being it's IP and key people, could be maintained in an unencumbered and ongoing manner. It was clear that in order to achieve that goal all longer term R&D must cease or be significantly scaled back and that staffing levels be reduced to only essential key players. In addition it was also abundantly clear that a minimum capital injection of \$500,000 was needed in the first half of 2009 (calendar year).

In January 2009 the incumbent Board reduced staffing levels to 23, down from 45 as detailed in the August dated 2008 Annual Report. This downsizing followed a December scale down of the Board to 4 members.

In February this year I was invited by the Board of Optiscan to fill a casual vacancy on the Board, an offer I had sought and clearly accepted. Consistent with my many earlier discussions with Grant Latta, my purpose in joining the Board of Optiscan was to seek ways to allow the Company to move forward without selling or encumbering key assets at a time when such assets had extremely depressed values.

This would involve further cost cuts and a consequent hyper-focussing of activities on the most advanced projects. Indeed all future avenues required significant further cost cuts, such cuts being instituted in the first months following my appointment to the Board. By May this year the Company had 14 staff equating to 12 full time equivalent employees. That core base of staff is considered the optimal number to allow execution of the Company's strategy.

In May, I secured \$500,000 of critical capital for the Company in the form of convertible notes issued to two sophisticated investors. That capital was the final critical element allowing the pursuit of what was the most optimistic avenue available to the Company at the time, removing value crippling outcomes such as IP sales and licensing and hibernation from the table.

As a part of the process of instituting this new strategy, both Grant Latta and Tony Rogers resigned from the Board in May after 7 years of service. On behalf of the Company I thank Grant and Tony for their years of service and I greatly appreciate their support for the new structure. As mentioned earlier the Board now consists of myself as Chairman, our CEO, Vicki Tutungi and our R&D Head, Peter Delaney.

With sufficient capital for another 12 months of operation (May 2009 – May 2010), the Company could now pursue its new hyper focussed strategy at a fraction of its historical cost base. That strategy being to focus on:

- Near term delivery of a smaller, second generation scanner allowing incorporation into high definition endoscopes;
- Continued subsidised (by Zeiss) performance in collaboration with Carl Zeiss in neurology; and
- Virtual zero cost promotion and sale of the Company's own branded research confocal microscope, the Five 1.

While many other applications of the Company's technology have been investigated, some quite intensively, these blue sky opportunities must make way for the more certain and nearer term revenue generating activities of flexible endomicroscopy and funded neurology trials.

At the time of the May restructure two key short term objectives were set that would have a significant bearing on the Company's risk profile, still at the extreme end in May 2009.

Those targets were:

- The finalisation of the terms of settlement with Hoya, following termination of the second generation agreement by Optiscan in March 2009; and
- The successful completion of the clinical grade prototype second generation scanner in a high definition flexible endoscope.

Both of these targets were met within our specified target periods.

On 3 August 2009, Optiscan finalised its going forward position with Hoya, resolving several years of less than optimal relations between the two companies. As well as providing a cash (up front and deferred) settlement of US\$575,000, the agreements reached provide a great

deal of clarity regarding rights to operate in the flexible endomicroscope arena. Previously exclusively the domain of Hoya, Optiscan is now free to sell product into this lucrative market, clearly an event that has the potential to create significant near term value for Optiscan.

On 29 September 2009, Prof. Finlay Macrae successfully completed the first ever dual high definition, endomicroscopy endoscope procedures at Cabrini here in Melbourne. These procedures demonstrated Optiscan's second generation scanner technology, providing tangible evidence of the considerable technological advances it has made with its second generation scanner. It is also tangible evidence of Optiscan's near term ability to have a leading product with which to enter the flexible endoscope market, thus building on the value created by the Hoya agreements of August.

The aforementioned targets removed two major risk factors in the Company's ability to extract value for its scanner technology, being via the flexible endomicroscope market using its second generation technology.

However the Company's financial outlook was still far from secure. As foreshadowed at last year's AGM, royalty revenues would dry up during the course of 2009 and revenue from Hoya would be minimal. Further, sales of Five 1 would be small relative to the Company's operating cost base. Consequently, revenues would not provide financial security in the near term, such security would have to come from further capital.

Following the successful attainment of the Hoya and second generation scanner targets, significant operational de-risking had taken place and there was clear justification for the Company to seek further capital. Given the prevailing buoyant markets, although in my analysis still extremely uncertain, the Board seized the opportunity of a favourable market and a share price more than 2.5 times its lows earlier in the year, to undertake a Share Purchase Plan at 10 cents per share. Ironically the offer took place during the historically bad market month of October and returned a very pleasing result of \$1.175m, inclusive of a placement of \$50,000, surpassing our internal target of \$1m.

The success of the SPP completed what might be classified as Phase 1, the de-risking phase, allowing phase 2, the value extraction phase, to commence with certainty.

Phase 1 has been a combination of staff and Board rationalisation, operational hyper focussing, market access and financial security. The results of Phase 1 are:

- Core staffing levels at 12 FTE;
- Monthly costs around \$200,000;
- Certainty around Hoya and flexible scope market access;
- Successful trials of the second generation scanner in an HD endoscope; and

- Financial security in the form of sufficient cash (current balance ~\$2.4m) for the duration of 2010 (calendar year);

In addition to the advances made in phase 1, the Company continues to collaborate with world leader Carl Zeiss in its funded neurology trials and related product development, and also continues to passively pursue sales of the Five 1 research instrument.

Following on from the de-risking phase, the focus will now shift to extracting value in the flexible endomicroscope arena, via our second generation scanner (and box). Sales of the Five 1 research instrument are expected to continue and will be a useful fillip to our cash position but are not expected to directly create significant longer term value. Additionally, the Carl Zeiss collaboration is likely to hit a critical juncture around the middle of 2010 at which time the prospects and value extraction potential will become clearer. Beyond that there are many blue sky opportunities in areas such as endometriosis, prostate, liver and pancreas among others, however the value from this blue sky is only likely to begin to emerge on the back of the successful penetration of the flexible endoscope market.

Optiscan and its technology are well known to all key players (corporate and clinical) presently in the endoscope market, with a growing awareness from emerging players such as China.

It is important to note that the efficacy and clinical value of the Optiscan technology is supported by 100's of quality publications and studies and 1,000's of successful procedures. Our product is in regular use at [7] of the top 10 hospitals in the US, including Johns Hopkins and the Mayo Clinic where we expect to place clinical grade second generation prototypes in the first half of 2010 (calendar year). This experience provides very clear evidence of the economic and clinical benefits and underscores the notion that the Optiscan technology and derivative products have a significant role to play and that such a role should translate to significant economic success for Optiscan. Internal modelling of the present value of Optiscan's technology with regard to the flexible endoscope market only, with assumptions supported by strong empirical clinical evidence, demonstrates that even a moderate penetration into this market would create substantial value.

Our primary objective now is to extract the latent value of our technology in a timely manner, firstly via the flexible endomicroscope arena. Given our success in phase 1, we are well poised to enter the value extraction process and are ready to do business.

Address by CEO, Vicki Tutungi



**Slide 1 – Title**

Good afternoon and thank you for taking the time to come along to the Optiscan Annual General Meeting.

A copy of our presentations will be available on our website.

Gus has provided you with a company overview. I will now go into some detail about the operational activities of the company and Peter will then discuss clinical progress and user group advances.

## Forward Looking Statements

This presentation contains forward-looking statements within the meaning of the United States' Private Securities Litigation Reform Act of 1995. Any statements contained herein that relate to prospective events or developments, including, without limitation, statements made regarding Optiscan's endoscope technology, business and partners are deemed to be forward-looking statements. Words such as "believes," "anticipates," "plans," "expects," "projects," "forecasts," "will" and similar expressions are intended to identify forward-looking statements. There are a number of important factors that could cause actual results or events to differ materially from those indicated by these forward-looking statements, including risks related to our available funds or existing funding arrangements, a further downturn in our customers' markets, our failure to introduce new products or technologies in a timely manner, regulatory changes, risks related to our international operations, our inability to integrate acquired businesses and technologies into our existing business and to our competitive advantage, as well as other factors. Subject to the requirements of any applicable legislation or the listing rules of any stock exchange on which our securities are quoted, we disclaim any intention or obligation to update any forward-looking statements as a result of developments occurring after the date of this presentation.



## Operational Overview

- The smaller scanner in a 'Dual HD scope' was successfully trialled at Cabrini Hospital in Melbourne.
- 2<sup>nd</sup> generation clinical prototypes are now under construction for placement at the Mayo Clinic, Johns Hopkins and Mainz University Hospital and possibly in China.
- Regulatory approval for the 2<sup>nd</sup> generation system will be sought in 2010.
- Hoya is gearing up to manufacture 1<sup>st</sup> generation technology and Optiscan will receive a royalty on all sales.
- The current trial with Zeiss is on track and the results of an earlier successful trial were presented at the American Association of Neurological Surgeons Annual Conference in May.
- The FIVE 1 continues to generate interest through our distributors - so far this financial year sales have been made in Singapore, Australia, China and Canada.



Commercial in Confidence

### Slide 3 – Operational Overview

I would like to focus on the highlights and key milestones for the year.

On the 29 September Professor Finlay Macrae successfully trialled our new smaller scanner in a high definition endoscope on two patients at Cabrini Hospital.

The scope is here today and we are happy to show it to you after the meeting.

I would like to formally acknowledge the support and assistance of Professor Macrae.

Professor Macrae like many of our other opinion leading gastroenterologists has provided his time and expertise to our project free of charge. Thank you Professor Macrae.

On the back of successfully completing this milestone, Optiscan's team of engineers is now working to build 4 clinical grade prototypes of the new generation system and smaller scanner for placement at leading hospitals around the world. This is a critical step in terms of:

- generating interest from the users themselves – market pull from the gastroenterologists
- awareness with the endoscope manufacturers
- de-risking the technology and hence increasing its value

After we have completed the construction of these clinical grade prototypes and have generated some data from their use, we will be filing for regulatory approval of the 2<sup>nd</sup> generation product.

As part of the agreements signed on the 31<sup>st</sup> of July this year, Hoya is now establishing a manufacturing capability for generation 1 technology, and as previously advised when they do start to manufacture and sell, Optiscan will receive a royalty on those sales.

Our project with Zeiss continues to move forward at a satisfactory pace. We are working with Zeiss in neurosurgery, ear nose and throat applications and spinal surgery. Results from


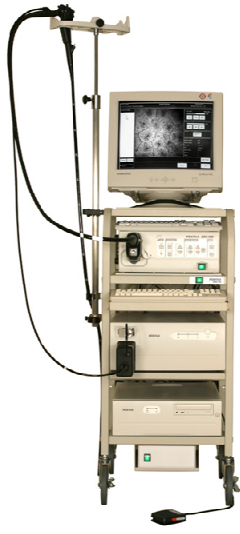


a trial conducted last year appeared at the May Neurological Surgeons Annual Conference and Peter will talk about this in more detail later.

We also continue to receive a steady stream of enquiries about our research product the FIVE 1 and the year has started with a reasonable number of FIVE 1 sales.

## **HOYA PENTAX** ISC 1000

- Optiscan and Hoya entered into new agreements on 31 July 2009. These agreements effectively:
  - Ended Hoya's exclusivity over the technology in gastroendoscopy.
  - Provided Hoya with a license to manufacture the ISC 1000 subject to payment of a royalty back to Optiscan.
- Since signing these agreements Hoya has:
  - Taken receipt of the relevant manufacturing documentation and manufacturing jigs.
  - Undertaken hands on training at Optiscan in manufacturing the product.



#### **Slide 4 – Hoya**

As mentioned, we moved to a new phase of our relationship with Hoya/Pentax on the 31<sup>st</sup> July this year. The key elements of the new relationship are that:

Hoya no longer has any exclusivity over the technology.

Hoya has the right to manufacture the product itself – previously Optiscan supplied product to Hoya.

Hoya has since taken significant steps towards manufacturing.

Hoya has taken receipt of manufacturing documentation and manufacturing jigs and has also sent a team of engineers to Optiscan to learn the manufacturing process.

We will continue to support Hoya and we wish them all the best in this endeavour.

## Size of the Flexible Endoscopy Market

- BCC Research, *Gastrointestinal Endoscopy Equipment: Global Markets, 2009*

*"The overall gastrointestinal endoscopy market was measured at revenues of approximately US\$2.9 billion in 2005..."*

Breaking that down further into treatment and diagnostic equipment:

*"The gastrointestinal diagnostic equipment market was measured at revenues of US\$1.71 billion in 2005, rising approximately 23.7% to \$2.12 billion in 2007, an additional 12.2% to \$2.38 billion in 2008, and projected to rise to \$2.4 billion in 2009. The gastrointestinal diagnostic equipment market is forecast to reach revenues of approximately \$3.3 billion in 2014..."*



### Slide 5 – Size of the Flexible Endoscopy Market

Hoya's interests are in flexible endoscopy, and I think it is worth recapping the size of that market.

We have talked in round terms of a market worth \$3B, and the overall gastrointestinal endoscopy market was measured at US\$2.9B in 2005.

But BCC Research in their Global Market Report of 2009 have provided a more detailed breakdown of the the gastrointestinal endoscopy market. That report identifies 3 sectors:

Diagnostic equipment

Treatment equipment

And veterinary equipment

Our endomicroscope falls within the diagnostic equipment sector of the market. This sector is expected to be worth US\$2.4B this year and over US\$3.3B by 2014.

Clearly, a significant subsector of the overall global endoscopy market.

## Interest in China

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- Along with the recent sale of a FIVE 1 in China a number of enquiries have been coming from this significant market.
- The Chinese endoscopy market is estimated to be worth over US\$150M in sales annually. (Merchant Research and Consulting Ltd)
- Growth is being driven by China's large ageing population, increasing buying power, improving healthcare, rising demand for high quality medical equipment, and increasing incidence of chronic disease and cancer.



### Slide 6 – Interest in China

Staying on market size for a moment.

We have recently received significant interest in the endomicroscope from China.

The Chinese endoscopy market is growing strongly and is being driven by a number of factors:

- Ageing population
- Increasing buying power
- Improving health care
- Rising demand for quality medical equipment
- Increasing incidence of chronic disease and cancer

This is potentially a significant development for Optiscan and we will continue to investigate the opportunity.

**OptiScan | FIVE (1) Research Instrument**

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- Singapore - research into mouth cancer
- Canada - research into lung tissue
- China – translational research Shanghai Shugang Hospital



**Slide 7 – FIVE 1**

We continue to receive interest from the global research community in our FIVE 1 product. So far this financial year we have sold product into Singapore, Canada and China.

We have also quoted on a second system into China, a local system here in Australia and a couple of systems into the US.

Whilst this market is not significant in terms of size, it is strategic.

Many of the researchers that purchase a FIVE 1 system use it for translational research.

Translational research, is research directed at turning an early stage investigational research project into a recognised medical treatment.

This by its very nature is an opportunity for the identification and development of new medical applications for our technology and as such something that we will continue to foster.





- 2007 agreement to co-develop an endomicroscope with the Carl Zeiss Group.
- Zeiss is an exclusive partner in this field.
- The field covers neurosurgery, ENT and spinal surgery.
- Initial results are promising and were presented to the American Association of Neurological Surgeons Annual Conference in May 2009.
- The abstract of the presentation is available at the AANS website, and Peter will talk about outcomes shortly.:

<http://www.aans.org/library/article.aspx?ArticleId=54813>



**Slide 8 – Zeiss**

As previously mentioned, our collaboration with Zeiss continues to progress very satisfactorily.

It is safe to say that both Zeiss and Optiscan are pleased with the trial results to date. But I will leave, it to Peter to discuss those results with you in detail.

## The New Smaller Scanner

- Optiscan has developed a second generation scanner for its endomicroscope technology.
- The scanner is 70% smaller in volume and was trialled at Cabrini in September.

New Scanner Model

Current Scanner Model



### Slide 9 – The Smaller Scanner

Probably the most significant advance made during the course of the year, in terms of creation of value, was the completion of the development of the smaller scanner. We have bought along the flexible endoscope incorporating the smaller scanner that was used in the Cabrini trial

## Advantages of the New Scanner

- The advantages of the new scanner include:
  - The smaller size which makes it suitable for more applications including:
    - use in all major endoscope brands and in more models.
    - use in the FIVE 1 - 80% of all research is on small animals.
    - Use in a smaller rigid endoscope/laparoscope.
  - The scanner is more robust than the existing model.
  - The scanner is cheaper to build.



### Slide 10 – Advantages of the New Scanner

The advantages of the smaller scanner over the existing technology are many and significant:

Rather than being designed for one brand of endoscope, this smaller scanner is suitable for use in all major brands of endoscopes and more endoscope models. This of course, opens up the potential to capture more of that US\$3B market that I spoke about earlier.

Over 80% of all animal research is conducted on small animals, we believe that by incorporating the smaller scanner into the FIVE 1 product, more of the animal research market will be opened up to us.

From a manufacturing perspective, the scanner is more robust than the 1<sup>st</sup> generation model and it is cheaper to manufacture.

From an intellectual property perspective, Optiscan has a number of new patent applications that relate to this new technology which of course increases the value of Optiscan's intellectual property portfolio.

And Optiscan retains exclusive rights to this technology in that US\$3B gastroenterology endoscopy field.

## The New Processor Unit

- Optiscan's new processor has been successfully prototyped.
- Completion of software engineering and mechanical engineering is now underway for clinical grade prototypes to be constructed.
- The advantages of the new processor include:
  - Enables rapid customized hardware reconfiguration for efficient access to new applications and markets.
  - New digital interfaces have been used that will allow more extensive integration with other medical systems.
  - Cheaper to assemble.
  - Improved serviceability.
  - ROHS compliant design.



### Slide 11 – The New Processor Unit

Along with the development of the new smaller scanner has been the development of the new processor.

We have bought it along today and will demonstrate it after the meeting.

The new processor also offers a number of different advantages over the old technology.

It too is cheaper to manufacture and has improved serviceability.

Importantly it is also ROHS compliant – this is a regulatory change that all medical device manufacturers are required to make, ensuring that their products are lead solder free.

But, the new processor also provides a number of features for the future.

The digital interface allows more extensive integration with other medical systems. For instance, patient images could be stored on the patients electronic file at the hospital.

The system has also been designed for rapid customisation for new applications. This should significantly reduce the development time required for new medical applications of the system.



## Corporate Structure Post SPP

- Ordinary shares on issue: 128.8 Million
- Market capitalisation (20/11/09) A\$12.5 Million
- Cash at bank(post SPP): A\$2.4 Million
- Average Net Operating Cash Burn 09/10: A\$200K p.mth.



### Slide 12 – Corporate Structure Post SPP

After issuing the shares allocated under the SPP, Optiscan now has 128.8 million shares on issue.

As of close of business Friday our market cap was \$12.5M

Our cash at bank post SPP is \$2.4M and

Our average net operating burn rate for the financial year to date is about \$200K per month.

## Next Steps

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- Complete construction of 4 clinical grade prototypes.
- Insert smaller scanner into the endoscope of choice of the gastroenterologist (Pentax, Olympus, Fujinon and Other)
- Conduct testing and validation necessary for ethics approval.
- Obtain ethics approval to run trials at Mainz, Johns Hopkins, Mayo and in China(possibly Beijing).
- Run short trial at each site.
- Conduct demonstration at some/all sites to raise commercial profile and generate interest.
- Complete documentation for regulatory approval.



### Slide 13 – Next Steps

Let me now turn to the future:

As I have mentioned, our nearest term milestone, is to complete the 4 clinical grade prototypes for placement at key hospitals around the world.



As part of that project we will insert the smaller scanner into the endoscope of choice of the gastroenterologist for use in a trial and demonstration. We currently anticipate that we will test the smaller scanner with at least 3 of the leading brands of endoscopes.

In order to trial the new scanner and new processor we must conduct the necessary testing and validation for hospital ethics approval. These results may also be used in the regulatory approval submissions to be made later in the year.

We then hope to run short trials at each of the key hospitals and conduct demonstrations of the technology to raise commercial interest and interest from the broader community of gastroenterologists.

With the completion of successful trials we will then be in a position to complete the regulatory documentation and submit it for regulatory approval of the new product.

## 2009-2010 Key Milestones

- Prototype of smaller scanner complete - Qtr 3 2009 
- Human trial of smaller scanner in HD Scope - Qtr 3 2009 
- Complete clinical grade prototypes - Qtr 1 2010 **On track**
- Gen 2 Demonstrations - 4 units placed at Mayo, Johns Hopkins, Mainz and China - Qtr 2 - 2010 **On track**
- Fulfilment of Zeiss trial agreement - Qtr 3 2010 **On track**
- Regulatory Approval for Gen 2 system - Qtr 4 -2010 **On track**

### Slide 14 – Key Milestones

Our key milestones relate to our 2 major projects:

Fulfilment of the trial agreement with Zeiss; and

Completion of the trials of the gen 2 systems and submission of documentation for regulatory approval.

## Address by Director of Technology, Peter Delaney

As both Gus and Vicki have detailed, this was a year in which financial constraints and the market environment required decisive prioritisation and extreme focus. As a result, many of the longer range clinical programs and product developments were parked while we focused on core technology for our most advanced applications, predominantly in gastrointestinal or GI endoscopy.

Despite this GI focus, our established base of rigid surgical instruments and relationship with Zeiss saw important progress in rigid applications. A notable body of user driven studies effectively elected the lead areas of rigid development on our behalf. This market pull and the emergence of the first key publications of clinical rigid surgical applications will serve as an important foundation for future product development opportunities. It also represents further validation as to the worth and broader applicability of Optiscan's technologies.

In overview, today I would like to explain the importance of our new 2<sup>nd</sup> generation endomicroscopy and what it means for users in real applications.


I will then cover the ongoing growth in the Gi endoscopy application, the now clear business case for healthcare adoption supported by the latest studies, and the importance of our 2<sup>nd</sup> generation technology in capturing the growth in medical acceptance.

I will also outline the status of rigid applications, including those pursued with Carl Zeiss,

### New 2<sup>nd</sup> Generation Technology

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- New platform for all future products
- New features driven by clinical experience
- Extends functional capabilities for users
- Better integration with clinical environments
- Improved workflow in established applications
- Easier system to learn for new users



It is very important to recognise that while staffing and budget reductions certainly limited our R&D capacity for running parallel projects for most of the term, we have not compromised our core capabilities for core activities. The result is that 2<sup>nd</sup> generation

technology has emerged as a new platform for future products, with potential well beyond its initial deployment in GI endoscopy.

You have heard from Vicki the commercial and operational advantages, but I want to add an explanation of what the new technology means for users, medical workflows and product desirability.

The first generation system has been in clinical use for over 5 years now. The new platform supports a raft of features that are drawn directly from the experience and observations of our users over that time as applications have matured.

Such features extend the functional capabilities in practical ways that will make the system more streamlined, efficient and enjoyable to use.

The configuration is overall more flexible, catering for more user preferences in the ways different users like to setup their procedure rooms.

Even in applications where the first generation system is proven to work, we all know that users of new technology expect improvement and ongoing innovation - the new platform will realise improved workflow and ease of use that will make it the system of choice for both new and experienced endomicroscopists.

Taking a look in slightly more detail, the two main developments are the new smaller scanner and the new confocal processor box...



Several of the advantages of the new scanner are immediately obvious from looking at it – it takes up only 30% of the volume of the old scanner and this enables completely new configurations not possible before.

For example, taking up less room in the end of a flexible endoscope leaves more space to package it up with larger neighbouring components such as high definition cameras and large biopsy channels – like the dual HD system I will talk about a bit later.

Alternatively, coupling with other very small components can enable an overall smaller diameter endomicroscope such as bronchoscopes for imaging the airways or paediatric scopes for very young children.

In these examples the shorter rigid length also allows the devices to be more flexible and easier to navigate through tight bends inside the body.

Naturally, the smaller diameter also enables rigid endomicroscopes to have a smaller bore, allowing access into the body via smaller incisions for less invasive surgery, or access to small animals in the case of the FIVE1 market.

Despite this feat of miniaturisation, though, the new generation scanner functionally outperforms its larger predecessor. Optically, it has higher resolution than that first generation scanner – it produces cleaner images of a single layer of cells at a time without overlapping layers.

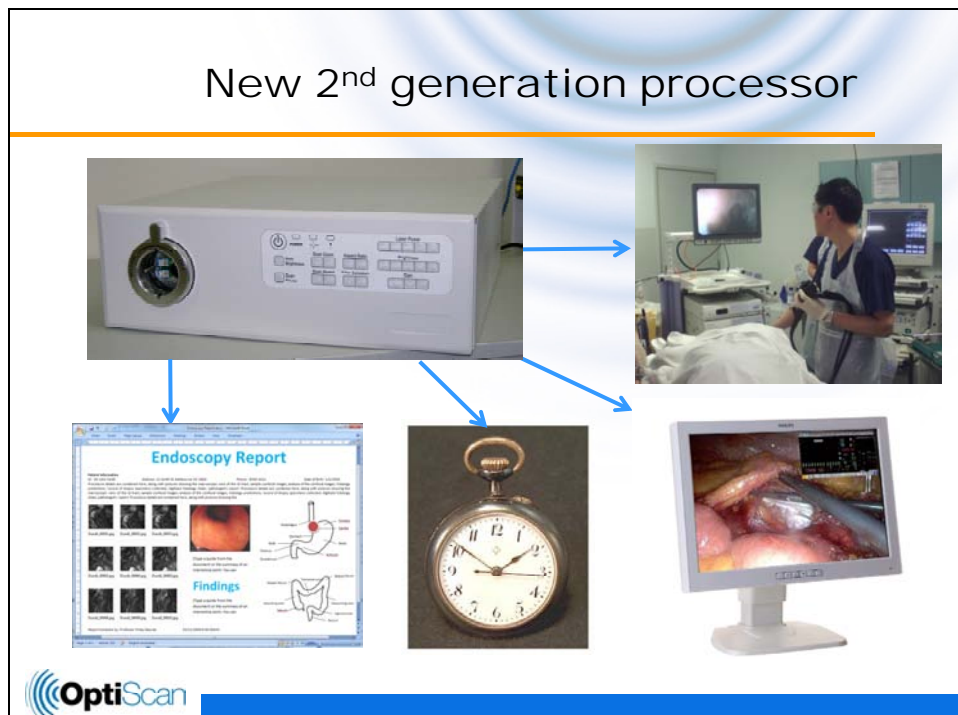
It has more scan modes, such as full HD 1080p microscopic scanning, and has more precise actuation mechanisms, allowing features like automated “virtual biopsies”.

But one of the most significant enhancements is the speed, taking the imaging experience from about 1-2 scans per second right up to interactive near video rates, as shown in the following video.

In this video, we start with a recording of the old system scanning at 1-2frames per second, While quite usable, you can see that moving the probe smears the image and waiting for stable images limits how much tissue you can look at in a short space of time.

Compare this to the new system – as you can see here as I image the inside of my cheek, the image is completely interactive in real time. As you move the probe, you are able to follow the structures across the surface without smearing and cover much more tissue in just a few seconds.

This will allow endoscopists and surgeons to look around larger areas of interest much more quickly in the search for relevant disease or margins to guide surgical removal of tissue. The fast scanning is a joy to use and requires less concentration to “hold still” while looking for microscopic detail.



Equally important are the features of the new processor. This is a much smaller unit than its predecessor, having condensed two larger boxes into one.

In a crowded endoscopy room or operating theatre, space is precious. Whereas the first gen system would generally need to be wheeled into the room on a dedicated trolley tower, the new unit will require only a single shelf and is more likely to be accommodated on existing trolleys and shelves.

The system has also been designed to support a wide array of display formats to use existing screens in procedure rooms, including full screen display in SD, HD and widescreens.

The system is also designed to consider the requirements of endoscopy and theatre nurses who must handle and setup the equipment – a new plug and play interface allows rapid disconnection and reattachment of different endoscopes without re-initialising the system, saving time and therefore contributing to cost effectiveness.

The software architecture is much more open than the first generation system, with digital connectivity to enable streamlined capture of images into external software systems, such as electronic medical records.

Overall, the features of the new box and scanner combine to deliver a very inobtrusive instrument that will be very easy to learn, setup and put to effect within the time pressured workflow of medical procedures.



I will now take you through the current status and this year's progress in clinical applications and market development starting with gastrointestinal (or GI) flexible endoscopy. To appreciate the our current status of it is important to also understand how the endoscopy market itself is progressing how we align with that progress...



## Medical Need in GI Endoscopy

- The goal for endoscopy is to find disease and treat it in a single procedure.
- From the original Olympus “microfilm” endoscopes, to fibre optic endoscopes, to modern video scopes, visualisation has improved dramatically .
- With better visualisation, there has been tremendous growth in therapeutic procedures to remove disease endoscopically
- Despite all these advances, the dream of “see & treat” remains limited because even the best macroscopic visualisation is just a “camera”
- Confirmation of disease from cellular information only comes from biopsies, days after the procedure.
- Accuracy of endoscopic findings with biopsy is also limited – finding the best biopsy sites where established disease exists can be problematic



The goal for modern endoscopy is to find disease, especially early cancer or pre-cancer and preferably to treat it in a single procedure.

Things have come a long way since the invention flexible of endoscopy. Olympus first invented an insertable “microfilm” camera (like a tiny spy-cam). There was no image interaction – the film was developed afterwards and if the pictures revealed something big, it was off to surgery for the patient.

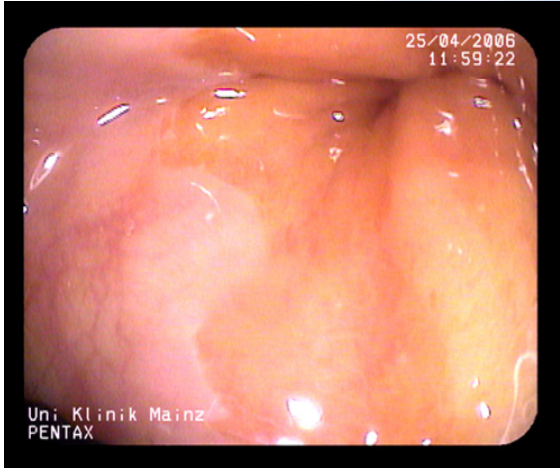
Then fiber optics enabled direct view fibrescopes which could be combined with channels for taking biopsies or resecting small lesions. Visualisation was quite poor and only advanced disease tended to be found, unless the endoscopist was lucky with randomly placed biopsies.

As fibrescopes were replaced by video scopes having CCD camera chips with more accurate colour and more pixels, the sensitivity of endoscopy became much better, and the field progressed to develop more therapeutic interventions, especially for early disease. But this transition only occurred through the 1980’ and 90’s, so this is a still quite a young field. Video scopes have improved tremendously, further supporting a shift in endoscopic practice from being a diagnostic to a therapeutic procedure – or so called “see and treat”.


However, despite all these advances, the dream of totally effective “see & treat” remains elusive in many cases because of two limitations – firstly, even the best CCD image is just a “camera” - while lesions might be observed, confirmation of disease from cellular information only comes from biopsies, days after the procedure. Therapy then requires a separate endoscopy or surgery.

Secondly, accuracy of endoscopic findings with biopsy is also limited – finding the best biopsy sites where established disease exists can be problematic

### Challenges in endoscopy



Which site contains an early, curable, but life threatening cancer?



8

This is best illustrated with an example. This is the CCD camera or conventional endoscopic view (using the Pentax endomicroscope) of the lower oesophagus in a patient with Barrett's oesophagus (the reddish area across the whole right hand side of the image, which in a normal patient would all be the more white colour at the left). We are looking here at the region about where you experience heartburn, which sometimes causes this Barrett's oesophagus..

This tissue actually looks quite healthy overall, but the condition of Barrett's oesophagus) is known to carry a risk of progressing to an aggressive cancer that is very hard to see endoscopically.

Now I will tell you in advance there is an early cancer here, but where would be the best place to take a biopsy to find out? It is very difficult for the endoscopist - there is really no clue from this view, so the standard approach is to biopsy randomly, and hope the biopsies find any disease.

## Multiple endoscope developments have been driven by this need

---

- Great efforts have been made to improve visualisation
  - Improved resolution of the camera (eg HD)
  - Light filtering techniques (eg NBI)
  - Image processing (eg iScan, FICE)
  - Autofluorescence imaging
- At best, these techniques improve detection of lesions, however, they do not contain the cellular information required to determine pathology
- Endomicroscopy is the first and only technology to offer cellular information at the time endoscopy – the “virtual biopsy”



Great efforts have been made to improve visualisation to achieve this same result by improving the CCD camera image. These include things like:

Improved resolution of the camera (eg HD);

Light filtering techniques (eg NBI);

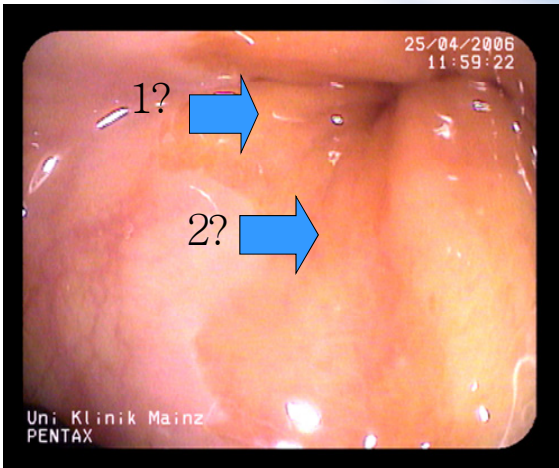
Image processing (eg iScan, FICE);

Autofluorescence imaging


At best, these techniques improve detection of lesions, however, studies repeatedly find that they do not contain the cellular information required to determine pathology accurately.

Endomicroscopy is the first and only technology to offer cellular information at the time endoscopy – the “virtual biopsy”

### Challenges in endoscopy

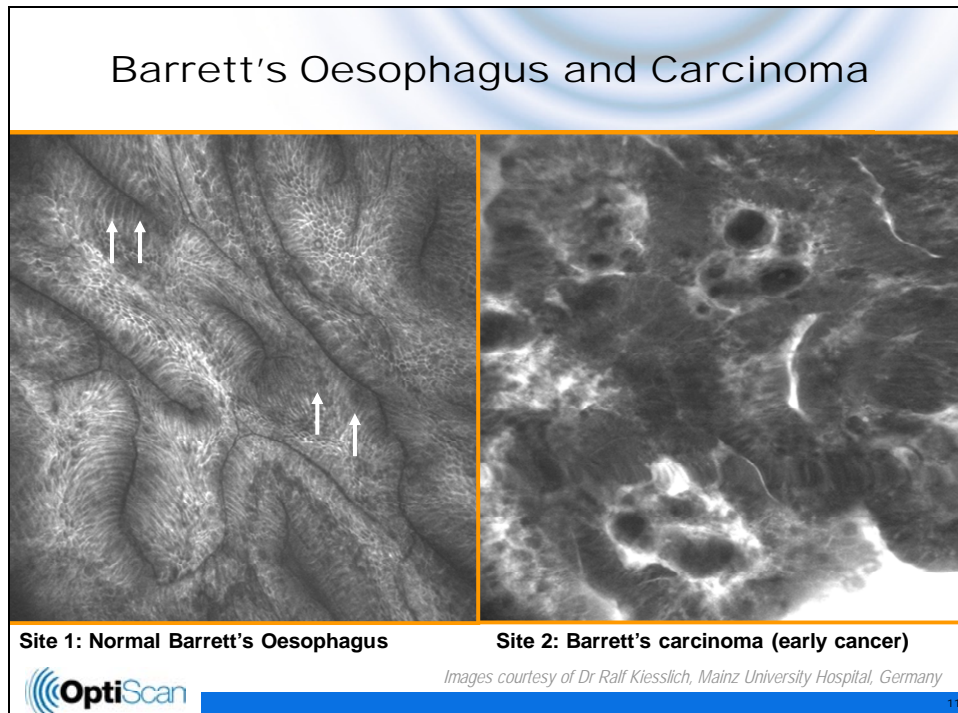


Which site contains an early, curable, but life threatening cancer?

 10

So coming back to our example, where would have been the best place to biopsy?

Well, employing the endomicroscope scanner in that scope, these two sites provided microscopic images in real time during the procedure. These would have appeared in real time on a separate screen alongside the view I showed before.



Here are images - The pattern on the left from site 1 was normal Barrett's esophagus, with no signs of cancerous progression, whereas the image on the right from site 2 was an early, treatable, but potentially life threatening cancer, and this was known before the end of the procedure, allowing targeted biopsy to this site with confidence of having found something important, or alternatively, in some cases of early disease, it could have been treated during the same procedure.

Over 100 published studies published  
see bibliography at [www.optiscan.com](http://www.optiscan.com)

**Scientific Papers**

**Clinical**

2009 - Clinical

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Endomicroscopy has now been very well studied and consistently produces positive data. There are over 100 studies published, up significantly from last year. There are also literally countless conference presentations and multiple book chapters and training guides, including online at [www.endomicroscopy.org](http://www.endomicroscopy.org). This extensive and growing bibliography is available at our website [www.optiscan.com](http://www.optiscan.com), and we try hard to keep this up to date in the face of a rapid rate of publication.

# Flexible applications now cover most major gastrointestinal disorders

**Confocal endomicroscopy**  
Kerry Dunbar and Marcia Canto

**Purpose of review**  
Confocal laser endomicroscopy is an emerging field of endoscopic imaging allowing gastroenterologists to obtain in vivo histology of the gastrointestinal mucosa. The present review will address the most recent advances in confocal laser endomicroscopy and discuss its future.

**Recent findings**  
Interest in confocal laser endomicroscopy and in vivo diagnosis of gastrointestinal disorders has increased in the last few years. Confocal laser endomicroscopy can studies an epithelial mucosa in three channels: color and multi-angle 'pseudo' mucosal biopsy when combined with chromoendoscopy. Confocal laser endomicroscopy may currently diagnose neoplasia (metaplasia, adenoma, adenocarcinoma) and the duct. Moreover, in vivo visualization of morphology, epithelial abnormalities, such as mucosal hyperplasia and 'open' gaps in the gut, may increase understanding of the possible pathogenic mechanisms of disease. Fluorescent peptide markers that target receptors are also being developed as a complementary approach to visualization of in vivo histopathology.

**Summary**  
Confocal endomicroscopy is a developing area of gastrointestinal endoscopy with expanding clinical and research applications. The present review focuses on recent advances in confocal endomicroscopy.

**Keywords**  
endoscopy, confocal endomicroscopy, fluorescence, microscopy, novel imaging, performance, observation, sensitivity, specificity

**Introduction**  
Confocal laser endomicroscopy (CLE) can provide high-resolution in vivo assessments of mucosal histology. The present review describes available CLE imaging systems and contrast agents and reviews the CLE literature from 2007 and 2008, including CLE applications throughout the gastrointestinal tract, modes of the emerging uses of CLE, and targeted contrast agents.

**Confocal endomicroscopy systems**  
There are two confocal endomicroscopy systems currently in use. The Pentax EC-3000, with the EC-3000 confocal endomicroscopy processor (Pentax, Tokyo, Japan) and Optiscan Pro (Le, Nanning, CH, Vietnam), installed in a conventional endoscope with a miniature confocal microscope on the tip. The system provides in vivo image capture and the ability to use the standard endoscope accessory channel. Images can be collected by scanning fibers through the mucosa

- Barrett's esophagus and Barrett's Cancer
- Oesophageal squamous cell carcinoma
- Non-erosive reflux disease
- Reflux esophagitis
- H.pylori
- Gastritis
- Gastric intestinal metaplasia
- Gastric cancer
- Celiac disease
- Ulcerative Colitis
- Colorectal Cancer surveillance
- Microscopic colitis
- Graft Versus Host Disease (GVHD)
- Pouchitis (in colectomy patients)
- Paediatrics

Dunbar K, Canto M. Confocal endomicroscopy. *Curr Opin Gastroenterol* 2008; 24(5): 631-637.



Endomicroscopy is thus very well tested in clinical studies. The weight of data is varied for different applications, but there exists positive clinical data in many of the major conditions encountered in modern GI endoscopic procedures. This is listed in this slide and was also very recently reviewed in the displayed review article published this year in Current Opinions in Gastroenterology by the lead users at Johns Hopkins Hospital in Baltimore, USA. The diversity of applications which benefit from the use of endomicroscopy speaks to the widespread applicability of the technique in virtually any endoscopy setting.

Recall that last year I reported that a landmark randomised clinical trial out of Mainz, Germany measuring the benefit of endomicroscopy in patient with longstanding ulcerative colitis, which I will re-visit in moment. This year, a second randomised clinical trial from Johns Hopkins in the US reinforced the evidence for use of endomicroscopy for improving diagnostic yield, this time in patients with Barrett's Oesophagus. Together, and due to the excellent design of the studies enabling direct comparison of the outcome of the two types of endoscopic procedure alongside un-altered standard of care procedures, these data represent a weight of evidence that supports a tangible business case and health economic advantage to adoption of endomicroscopy.

<p><b>Ulcerative Colitis – A randomised prospective blinded trial</b> (Johannes Gutenberg Univ, Germany)</p> <ul style="list-style-type: none"> <li>• 161 patients randomised into 2 groups – confocal vs std procedure</li> <li>• Confocal guided biopsy found 4.75 fold more early cancer</li> <li>• Actual biopsies taken halved           <ul style="list-style-type: none"> <li>• 42 in std procedure group</li> <li>• 21 in confocal group</li> </ul> </li> <li>• Based on real-time diagnosis, only 4 biopsies per patient was required</li> <li>• Now advanced to multicentre study</li> </ul> <p><small>Kiesslich R, Goetz M, Lammersdorf K, Schneider C, Burg J, Stolte M, Vieth M, Nafe B, Galle PR, Neurath MF. Chromoscopy-guided endomicroscopy increases the diagnostic yield of intraepithelial neoplasia in ulcerative colitis. <i>Gastroenterology</i> 2007; 132: 874-882.</small></p>	<p><b>Barrett's Oesophagus – A randomised prospective blinded crossover trial</b> (Johns Hopkins Hospital, USA)</p> <ul style="list-style-type: none"> <li>• 52 patients randomised into 2 groups – confocal vs std procedure</li> <li>• Patients received alternate procedure 6 weeks later</li> <li>• Diagnostic yield doubled by endomicroscopy guided biopsy</li> <li>• Actual biopsies taken halved</li> <li>• Zero biopsies were taken in 67% patients in confocal group</li> <li>• Now the subject of ASGE funded multicentre study</li> </ul> <p><small>Dunbar KB, Okolo P, Montgomery E, Canto MI. Confocal laser endomicroscopy in Barrett's esophagus and endoscopically inapparent Barrett's neoplasia: a prospective, randomized, double-blind, controlled, crossover trial. <i>Gastrointest Endosc</i> 2009; 70(4): 645-654.</small></p>
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Firstly, the colitis study, conducted at Johannes Gutenberg University in Mainz, Germany: This was a randomised prospective blinded trial, meaning that just before their endoscopy, the patient is assigned randomly and without bias to have either the standard of care endoscopic procedure or the endomicroscopy guided procedure.

161 patients (considered large population for an endoscopy trial)

Confocal guided biopsy found 4.75 fold more early cancer

The actual number of biopsies taken was halved

42 in std procedure group

21 in confocal group

Based on real-time diagnosis recorded at the time of observation, only 4 biopsies per patient was required to achieve the full improvement in detection.

This has been a very impactful result and the trial design is also now the subject of a larger multicentre study that will replicate and compare the effect across multiple countries.

Secondly, and more recently, the Barrett's study by Dr Marcia Canto at Johns Hopkins Hospital in Baltimore, USA:-

This study in 52 patients with Barrett's oesophagus was also a randomised design, but was also a crossover design. This means that after being randomised to either the conventional or endomicroscopy procedure, the patient comes back some weeks later for the opposite – this is very powerful because you can measure if either technique detects something missed by the other.

The results werethat:

Diagnostic yield was doubled by endomicroscopy guided biopsy;


The number of actual biopsies taken was halved



Zero biopsies were taken in two thirds of patients in confocal group  
This was a very impressive result and has been advanced to a multicentre study. Notably, the multicentre study has been funded independently by the American Society for Gastrointestinal Endoscopy (the ASGE) acknowledging its importance in the field.

## Business Case

- Using Ulcerative colitis as a single example application:
  - Mainz data supports an average reduction of 20 biopsies per patient (conservative use of endomicroscopy)
  - Surveillance programme of 200 procedures pa saves 5,000 biopsies pa
  - Cost for processing 2 biopsies per pot = €120 euro
  - Savings due to reduced biopsies = €240K pa
- Likewise, a compelling case can be derived for Barrett's oesophagus, using the same equipment.
- The above repays instrument purchase in less than one year
- "See & Treat" procedures can also eliminate the cost of a follow-up procedure
- Early detection also eliminates downstream curative medical costs



Just as important as the medical benefit of these two study outcomes is the quantification it provides of costly biopsy reductions. This enables a business case to be modelled by hospitals in support of applications to acquire endomicroscopy systems.

For example, from the Mainz ulcerative colitis study the following business case can be constructed:

Conservative utilisation of endomicroscopy achieves an average reduction of 20 biopsies per patient

Consider a surveillance programme of 200 procedures pa saves 5,000 biopsies pa

Cost for processing 2 biopsies per pot = €120 euro

Savings due to reduced biopsies = €240K pa

The above repays instrument purchase in less than one year.

To further bolster the business case for a system purchase:

A compelling case can also be derived for Barrett's oesophagus, using the same equipment base costs.

The business case for "See & Treat" procedures can also eliminate the cost of a follow-up procedure. Although this has not yet been quantified

Early detection also eliminates downstream curative medical costs

Thus, we can state with conviction that based on these studies, and in any modern healthcare environment that see reasonable numbers of patients with Barrett's oesophagus

and ulcerative colitis (both prevalent and growing in most western populations), it is more costly to continue current standard practice than to adopt endomicroscopy.

## The Future of Endomicroscopy – combination with HD endoscopes

- Confocal endomicroscopy is not a standalone technology
- The conventional functions of the endoscope are required to navigate to sites of interest and identify suspicious areas
- The conventional view of the endoscope has recently improved from standard definition video to High Definition, just like TV.
- HD reveals more lesions, but has high false positive rates, requiring many more biopsies for a modest increase in detection.
- HD is thus a perfect match for endomicroscopy for finding areas to interrogate with non-invasive microscopic imaging
- The first generation Pentax endomicroscopes only have SD video, limiting some of the value of endomicroscopy



So amidst this progress towards adoption, what is the significance of Optiscan's new generation with HD endoscopes, and what does this mean?

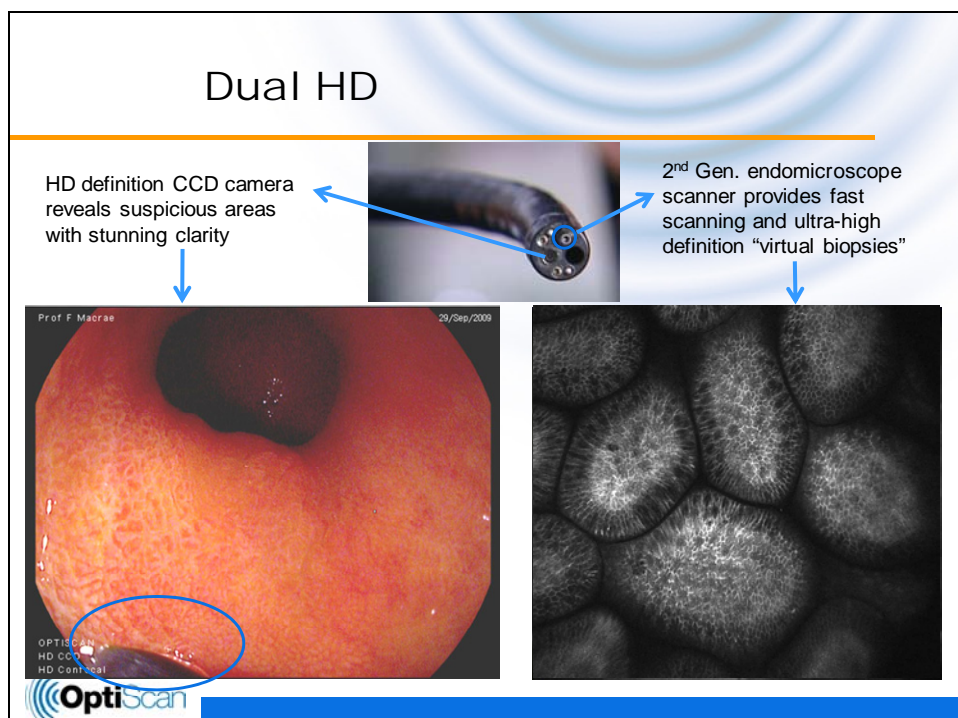
Well firstly, note confocal endomicroscopy is not a standalone technology - the conventional functions of the endoscope are required to navigate to sites of interest and identify suspicious areas.

The conventional view of the endoscope has recently improved from standard definition video to High Definition, just like TV.

And just as HDTV let's you see more defects or blemishes on the skin of a news presenter, HD endoscopy reveals more lesions in the gut. However, most of these are not serious and this observation is not diagnostic – in fact, it has such a high false positive rate that it leads to many more biopsies to convert the extra observed blemishes in the gut to a modest increase in detection of relevant disease.

HD is thus a perfect match for endomicroscopy, revealing blemishes which can then be immediately interrogated with non-invasive microscopic imaging.

The first generation Pentax endomicroscopes only have SD video, limiting some of the value of endomicroscopy. The reason is that the HD CCD chip, the camera in the tip of the endoscope, is larger, and will not fit with the first generation scanner. Our new smaller scanner overcomes this problem.



But as reported recently, we have successfully incorporated our new scanner into an HD endoscope with a large therapeutic biopsy channel, as pictured here, and completed the first procedures in patients in September.

The advantage to the workflow is clear from this example –

The HD CCD, or camera, shows the overall structure of the tissue in stunning detail. Many small irregularities are seen on the surface on the left in this example indicating an increased chance of serious abnormality. While the view shows a large area very clearly, and is thus useful for finding such areas, it is not good enough for diagnosis as there is no cellular detail.

But by targeting the inbuilt endomicroscope scanner onto this area, which is easy because the scanner, shown circled in both views, is visible from the HD view.

Once on the relevant site, ...

...the new endomicroscope produces interactive cellular views as shown here. From this video, you can appreciate the interactivity offered by the fast scanning, and ultimately, super high resolution cellular images from various depths are captured as digital images, as shown here. In this case there is no cellular abnormality, despite some architectural change, so no biopsy at this site is warranted. I would comment though that in this patient, some sites of pre-cancer were found later during the procedure, just around the other side, indicating therapy was required.

We are very excited about the combination of these two views, and as Vicki mentioned, are presently building scopes based on several different brands of HD endoscopes for use in trials at international sites. We will work closely with these sites for rapid trial activity to measure the benefit of this combination in terms of additional efficacy, reduced procedure time, and user preference.

**Now onto rigid surgical applications, and firstly our Zeiss collaboration.**

Vicki has already described the commercial framework under which we continue to work with Zeiss. Importantly, the first data from the Zeiss funded studies was presented at AANS, the American Association for Neurological Surgeons, in Chicago, USA in April.

The authors noted in their published abstract (which is available at the website shown above) that:

“Exquisite images were acquired, and correlated well with corresponding histology”

“Imaging was distinguished between tumor and non-tumor tissue, including infiltrative tumor margins”

“Margins were easily identified by observers without prior neuropathology training after minimum experience with the technology”

Furthermore, the presenting author received an award from the Journal of Neuro Oncology for the work, making the study a featured presentation at the AANS.


A second publication in this applications area using Optiscan’s technology by Schlosser et al noted “...On a cellular level, [endomicroscopy] could contribute to ensuring that as much tissue is excised as necessary and as little as possible – which would be beneficial for patients suffering from brain tumour...”. (Schlosser *et al*, Confocal Neurolasermicroscopy in Human Brain –

Perspectives for Neurosurgery on a Cellular Level. *Cen Eur Neruosurg*, 2009.

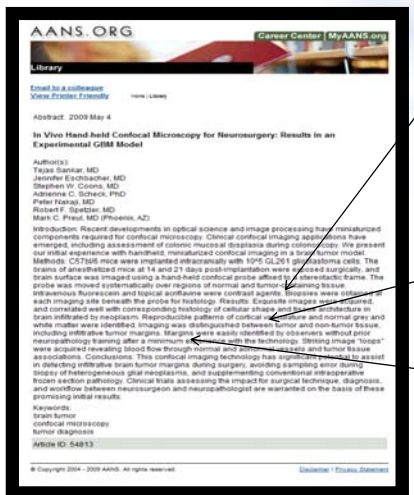
We are excited about the potential of this application area and continue to work very closely with Zeiss on their trial program.

## Rigid Surgical Trial Activity

- Women's health – ongoing single centre study
- Robotic – proof of principle trial completed
- Pancreatic resection – Investigator driven at 3 sites (Australia, Germany, UK)
- Liver laparoscopy – investigator driven at 2 sites (Germany, UK)
- Neurosurgery – publications emerging
- ENT – investigator driven at 2 sites (Singapore, Germany)
- Rigid Thoracoscopy Lung Cancer Study – investigator driven (Australia)




- The abstract of the presentation is available at the AANS website:  
<http://www.aans.org/library/article.aspx?ArticleId=54813>



*...Results: Exquisite images were acquired, and correlated well with corresponding histology....*

*...Imaging was distinguished between tumor and non-tumor tissue, including infiltrative tumor margins...*

*...Margins were easily identified by observers without prior neuropathology training after minimum experience with the technology...*



Women's health – ongoing trial activity is limited to a single centre study in endometriosis with only very preliminary data. However, expansion of this into a larger scale pursuit has been parked pending better resourced times.

Likewise, the robotic assisted prostatectomy surgery application has been parked, although we did allow the proof of principle trial to come to a successful natural completion during the year.

Pancreatic resection surgery has received ongoing interest since publication the first trial at Bankstown Hospital. Although we are not sponsoring further trial, work continues in investigator driven studies using our instruments at 3 sites (Australia, Germany, UK). One of these sites fully funded and commissioned a clinical prototype system for their studies.

Liver laparoscopy continues, also investigator driven at 2 sites (Germany, UK)

Neurosurgery was reviewed previously in the Zeiss update.

ENT studies continue, investigator driven, at 2 sites (Singapore, Germany)

A investigator driven rigid thoracoscopy lung/thoracic malignancy study recently began in Melbourne, Australia.

Amidst this ongoing work in rigid surgical applications of our technology, early clinical work across multiple applications also appeared in peer prestigious medical journals:

Our early trials in cervical cancer were published in the renowned British Journal of Obstetrics and gynaecology. Our first open surgical application, pancreatic cancer resection surgery, was published in the Annals of Surgery. The first study imaging human airways was accepted by the journal CHEST. The first liver laparoscopy trial was published in Hepatology, and as mentioned already, the first neurosurgery data was also published.

These publications will raise significant awareness in each of the relevant clinical specialist communities as the applications are advanced under investigators own steam as outlined.

## Summary and Outlook

- Medical evidence and business case for GI endomicroscopy are strong.
- User feedback has defined key improvements for enhanced efficiency and popularity
- Optiscan has the new technology to deliver these benefits to a wider market
- The Zeiss collaboration has progressed the neurosurgery application significantly
- Multiple rigid endoscope applications are being progressed steadily by our user base
- The maturity and growth in the above applications represents a strong base from which to extract value.



So in summary,  
The medical evidence and business case for adoption of GI endomicroscopy are strong.

User feedback has given us a clear definition of key improvements for enhanced efficiency and popularity of our systems

Optiscan has the new technology to deliver these benefits to a wider market

The Zeiss collaboration has progressed the neurosurgery application significantly

Multiple rigid endoscope applications are being progressed steadily by and enthusiastic user base

The maturity and growth in the above applications represents a strong base from which to extract value.

Thank you all very much for your attention.