

Endomicroscopy: See more

Histology in vivo: the fascinating possibilities of endomicroscopy meet with an enthusiastic response world-wide.

Report on the "2nd International Endomicroscopy Meeting"

Endomicroscopy: On the way to becoming a part of the clinical routine

Prof Mimi Canto and Dr Christian Bojarski explain areas of application and perspectives



ENDOMICROSCOPY: SEE MORE

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A NEW HORIZON IN ENDOSCOPY

DEAR READERS,

We are pleased to present the latest issue of the PENTAX InfoScope, which is available in English for the first time. Our subject this time is also very special: it's all about the innovative and exciting technique of confocal endomicroscopy.

PENTAX is the only manufacturer to offer this technology built into the distal end of its endoscopes. Endomicroscopy assists the experienced examiner in reducing the number of biopsies necessary for certain indications such as inflammatory bowel diseases. This not only reduces the complication rate in patients, it also cuts overall health care costs.

The fact that endomicroscopy has become well established throughout the world was strikingly evident at the "2nd International Endomicroscopy Meeting". The world's best experts in this field met in Mainz, Germany, and presented their scientific research. The clinical benefits of endomicroscopy were demonstrated to all attending participants through highly interesting live demonstrations.

Discover new horizons in endoscopy and gain some inspiration from this InfoScope. Read about the beginnings of confocal endomicroscopy, which owes its breakthrough not least to the pioneering work of Prof Ralf Kiesslich in Mainz. Find out more from Dr Christian Bojarski about current clinical and scientific indications for endomicroscopy and its potential use outside university institutions. Learn from Prof Mimi Canto of the renowned Johns Hopkins Hospital in Baltimore how confocal endomicroscopy has become an established part of her medical routine.

You can also find detailed information on the new online platform for endomicroscopy, where you can discover many interesting endomicroscopy case studies.

As you can see, there is plenty of fascinating information in this issue. I hope you all enjoy reading it.

Sincerely yours,

Dr Dirk Laval, Project Manager Scientific Relations, PENTAX LIFE CARE



Dr Dirk Laval

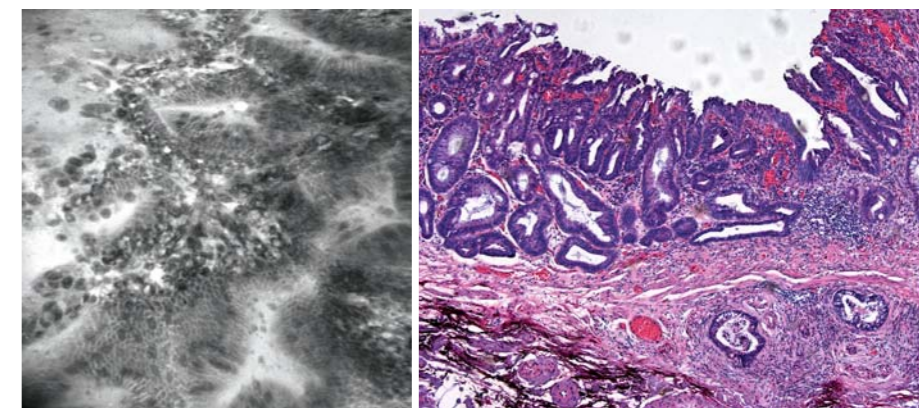
FASCINATING INSIGHTS WITH DIRECT CONSEQUENCES FOR CLINICAL PRACTICE

by Prof Ralf Kiesslich, Congress President "2nd International Endomicroscopy Meeting"

Six years ago, in 2003, we tested the first endomicroscopy system at the I. Medical Department of Mainz University Hospital. I can still remember very clearly the first patient, whose intestinal mucosa was analysed using the confocal laser technique. We found a colonic carcinoma, five adenomas as well as three hyperplastic polyps. The examination lasted about two hours and we took hundreds of endomicroscopic images.

Specialists from all over the world discuss the latest research results

From the very first examination, endomicroscopy opened up fascinating insights into human intestinal mucosa. And this fascination continues to this day. Barely six years after the first application, the "2nd International Endomicroscopy Meeting" took place in September 2009 in Mainz. More than 120 experts and interested physicians discussed the latest results of research in endomicroscopy. During the two-day conference, three hours of live demonstrations were transmitted from the I. Medical Department of Mainz University Hospital to the conference center. Specialists from around the world examined patients with Barrett's esophagus, inflammatory bowel diseases and suspected adenomas in the colon. They verified their macroscopic impressions with endomicroscopic images. Thus clearly defined target structures, such as goblet cells in the region of the lower esophagus, provide evidence of Barrett's esophagus. This diagnosis means an increased risk of cancer and indicates monitoring endoscopies. Each of the live demonstrations only lasted 20 minutes on average.



The endomicroscopic image (left) clearly shows malignant cells. In the histological preparation of the endoscopically performed mucosa resection (right) a sunken early carcinoma (3.2 mm) was confirmed.

Histology in vivo

The fundamental difference between endomicroscopy and all further new endoscopic imaging techniques is obvious: histology is not predicted, but rather it is displayed directly in vivo. In this way the endoscopist can analyse cellular and sub-cellular components directly. For example, in one patient with a long-standing case of ulcerative colitis, the examiners detected a small, depressed lesion in the region of the lower sigma. It could barely be detected macroscopically. Even after chromoendoscopy with methylene blue, one half of the conference participants was not certain whether it was a neoplastic or non-neoplastic lesion. Only endomicroscopy clearly revealed malignant cells. The mucosa was then resected and an early carcinoma, 3 millimetres in size, was discovered, which had already infiltrated the upper third of the submucosa (see figure).

The huge progress of endomicroscopy was noticeable throughout the conference. Up to now experts have come out with more than 100 publications

associated with endomicroscopy. During the conference the international faculty presented excellent summaries of these and their own data. It remains necessary to conduct systematic studies of this new imaging technique and to develop endomicroscopic diagnostic criteria and training standards for endomicroscopy.

Technology of the future

Endomicroscopy, with its abundance of diagnostic possibilities, can no longer be held back. It will inevitably change and shape our clinical routine. Read this issue of InfoScope and get caught up in the enthusiasm of the conference participants.

LOOK INTO THE DEPTHS

In mid-September endoscopists from all over the world met in Mainz to report on current research results in endomicroscopy and discuss the importance of the new technology. Once integrated into the clinical routine, the method could facilitate faster diagnoses with shorter waiting times for patients. Examination procedures and diagnostic criteria should now be standardised for this purpose.



After he had taken the first in vivo endomicroscopic images of the patient's intestine, he immediately went to his students in the cafeteria. He showed them the images and asked whether they could recognise what sort of tissue it was. Yes, quite clearly, intestinal villi. "I knew straight away that we had a revolutionary technique, if even the inexperienced eyes of a student could make such a diagnosis", remembers Prof Ralf Kiesslich, head of interdisciplinary gastrointestinal endoscopy at the I. Medical Department of Mainz University Hospital, about the beginnings of endomicroscopy.

Six years have passed since then, and this once little-known technology has now developed into a valuable diagnostic procedure: endomicroscopy – the synthesis of endoscopy and confocal microscopy. In simple terms, a microscope was incorporated into the distal end of an endoscope. To obtain

the images, the examiner focuses blue laser light onto the suspect tissue area. The laser light stimulates contrast agents such as fluorescein that have previously been injected intravenously. A special confocal lens detects the fluorescent light. This results in microscopic images of the mucosa down to a depth of 250 microns.

Comparable with histopathology

In comparison with conventional histopathology, endomicroscopy can make accurate statements about tissue architecture, inflammatory cell infiltrates, malignant cell changes and mucosal changes. The advantage of the procedure: the examiner receives all the information during the ongoing procedure. "This is how unnecessary biopsies and multiple examinations can be prevented", explains Prof Ralf Kiesslich. Simultaneously, it is now possible for the first time to observe physiological and pathophysiological processes in vivo, such as the migration of bacteria and immune cells. Kiesslich even says that new histopathological characteristics have emerged for various indications which are quite specific to endomicroscopy. This does not mean, however, that classic histopathology is losing its significance: it is the only way to detect risk factors for neoplasia, such as the cell-nucleus-cytoplasm ratio or the infiltration of lymphocytes into vessels and submucosal layers.



Better detection rate despite fewer tests

Prof Mimi Canto of Johns Hopkins Hospital in Baltimore presented data of 46 patients with Barrett's esophagus and associated neoplasias that had been evaluated in a randomised cross-over study. All participants were examined and biopsied selectively with endomicroscopy ("smart biopsy") and randomly with 4-quadrant biopsy. Confocal endomicroscopy doubled the hit rate for neoplasia (33.7% vs. 17.2%, $p=0.03$). In addition, only half as many biopsies were necessary for the Baltimore endoscopists to reach a definitive diagnosis (10.8% vs. 28.4%, $p=0.004$). In two thirds of the patients the examiners were even able to dispense entirely with taking biopsies. Endomicroscopy thus not only improved the diagnostic accuracy, but the procedures were also significantly less invasive. A multicenter study in Germany and the U.S. is now being conducted to show whether the benefits of the method can also be transferred to a larger group of patients. Recruitment of patients has started and the first results are expected in 2010/2011.

Vascular architecture as a diagnostic criterion

Although the incidence of stomach cancer is indeed decreasing in Western countries, malignancy is often diagnosed very late. The 5-year survival rate is less than 5 percent, which is why scientists are searching for a better method of early detection. A very promising

method is endomicroscopic visualisation of the mucosa which is suspected of being cancerous, explained Prof Yan-Qing Li of Shandong University in Jinan, China. In their study, Li et al. examined 21 patients with early-stage stomach cancer and 40 patients with intraepithelial neoplasia of the stomach. Under endomicroscopic visualisation, the vascular structure of malignant and healthy gastric mucosa differed considerably in shape, diameter, number and leakage. The Chinese also determined that the degree of differentiation of the carcinoma has a crucial influence on the vascular structure. While the undifferentiated gastric carcinoma was shown to be hypovascular with short branched vessels, the vessels in the differentiated carcinoma are dilated and increasingly coiled. Thus, it should be possible to detect cellular changes at a very early stage with the assistance of endomicroscopy – which in the final analysis could lead to an improved survival rate.

Early detection for at-risk patients

In the future, colorectal cancer patients could also benefit from gentle early detection using endomicroscopy. According to Dr Silvia Sanduleanu of the Maastricht University Medical Center in the Netherlands, finetuning of surveillance programmes in patients at-risk for CRC can be obtained in the future using this technique. Patients with prior history of colorectal cancer, Lynch syndrome, or a family

Left: Experts and interested parties discussed their experiences with endomicroscopy in lectures and in personal discussions.

Right: Live examinations were transmitted to the conference center from the Mainz University Medical Center.

»» "For many years we were only able to diagnose and treat on the basis of superficial observations. Now for the first time we can look beneath the surface with a thousand-fold magnification – and the possibilities are endless", according to Prof Ralf Kiesslich.



history of colon cancer are the focus of their research. Numerous biopsies could be avoided by endomicroscopically differentiating between high-risk adenomas and those with a low risk, according to Sanduleanu. In a recent study (Clinical Gastroenterology and Hepatology, 2009), the Dutch group examined 44 patients with high-grade dysplasias and 16 with low-grade dysplasias. Endomicroscopy differentiated with high specificity (93.7%) and high sensitivity (97.7%) the degree of differentiation of the low- and high-grade adenomas. It would therefore be a good idea to create a standardised monitoring program using endomicroscopy and make it available for high-risk patients, explained Sanduleanu.

"Killer applications" for endomicroscopy

However, neoplasias and metaplasias are not the only things that can be diagnosed using endomicroscopy. Non-malignant diseases are also an interesting area of application: "Celiac disease and microscopic colitis are considered to be killer applications for endomicroscopy", says Prof Ralf Kiesslich in Mainz. Due to the fact that these diseases leave no macroscopically detectable traces behind, it used to only be possible to identify them using random biopsies. Endomicroscopy can now target biopsies in diffuse patchy diseases such as Celiac disease. In the world's first prospective validation study, Dr Rupert Leong from Sydney, Australia demonstrated that the features of villous

atrophy (≤ 5 villi/high power field view) and crypt hypertrophy (≥ 1 crypt/high power field) in Celiac disease was representative of conventional histological changes. Furthermore, endomicroscopy was able to detect minor changes of Celiac disease in patients undergoing treatment with a gluten-free diet not detected by histology. "Minor changes of Celiac disease may indicate inadequate treatment or inadvertent gluten in the diet," said Leong "and this may result in ongoing immunological attack of the small bowel. It is therefore important to pick up mild abnormalities missed by conventional biopsies." Dr Leong also proved that changes in the mucosa are most likely to occur in the duodenal bulb, and not in the descending part of the duodenum as had long been assumed. "The proximal part of the duodenum is the site that had the highest yield of Celiac disease findings."

The cause of microscopic (collagenous) colitis remains unknown. Experts have discussed bacterial and viral infections, non-steroidal anti-rheumatics as well as a genetic predisposition. Affected patients complain about watery diarrhoea along with upper abdominal discomfort, fatigue and meteorism. An essential histological sign is increased subepithelial deposits of collagen. Up to now this could only be detected using endoscopic step biopsies. However, different working groups have since been able to detect well defined sheathing of the crypts under endomicroscopic visualisation,

which correlates with the thickened subepithelial collagen band in the histological examination.

Imagine the future, make it happen

It is possible to image morphological situations in vivo using contrast agents such as fluorescein. In the future the confocal technology could also play an important role in molecular imaging using marked antibodies, DNA probes and signal peptides, by providing information about the functionality of tissue structures. How do the cells react to therapy? What immunological processes occur?

"Complex pathophysiological processes can only be reproduced to a limited extent in vitro", said Dr Martin Goetz from the I. Medical Department of Mainz University Hospital in explaining the interest in molecular imaging. Using an animal model, the scientists in Mainz have already succeeded in detecting colon dysplasias in vivo using targeted fluorescein-marked antibodies and endomicroscopy. In the future the hope is to also obtain a better understanding of the development and treatment of cancer and inflammatory diseases in humans. "We can visualise processes at the cellular level with endomicroscopy. This helps us to identify new disease markers for bowel diseases such as certain receptors on immune and cancer cells", according to Goetz. Two potential markers are EGFR and VEGF, which play an important role in molecularly targeted tumour therapy. Both have already been studied in Mainz. Prof Markus Neurath, Director of the Clinic for Gastroenterology, Pneumology and Endocrinology at the University of Erlangen, summarised the potential benefits by stating "the developments in the area of molecular imaging are heading in the direction of a therapy tailored to the patient."

Solid data for a simplified diagnosis

More than 100 endomicroscopic studies with more than 1,000 patients have already been published in renowned journals such as Nature Medicine, Lancet, and Gastroenterology. They show that confocal endomicroscopy is

increasingly finding its place in clinical practice. In addition to typical diseases of the gastrointestinal tract, such as neoplasias, reflux or inflammatory bowel diseases, rarer indications are also attracting attention: Dr Christian Bojarski of the Charité University Medical Department in Berlin reported on improved early detection of graft versus host reactions following bone marrow transplants, which are expressed as diarrhoea. Here endomicroscopy can quickly and clearly identify specific changes in the intestinal mucosa in vivo. This enables prompt therapeutic intervention. In addition, the non-invasive technique reduces gastrointestinal bleeding and could thus prevent infectious complications.

Red flag and endeavours for a consensus

In order to integrate endomicroscopy into the clinical routine even more, the search is on for a "red flag" or some other aid to scan the mucosa over a large area and visually mark suspected dysplasias. In the near future a consensus for the application of endomicroscopy also needs to be reached based on the available data. Which at-risk patients are especially suited to the technique? Which indications are worthwhile? According to which algorithm should an endomicroscopic examination be performed? "Within a few years we have been able to determine specific characteristics for the individual diseases", said Kiesslich. The time has therefore come to increasingly incorporate endomicroscopy into the clinical routine for reliable diagnosis.

»» *Indications for endomicroscopy: Barrett's esophagus, non-erosive reflux disease, neoplasias of the gastrointestinal tract, Celiac disease, ulcerative colitis, amyloidosis, microscopic colitis.*

ADVANTAGES OF ENDOMICROSCOPY ->

- Real time: real time images
- "Smart" biopsy: targeted biopsies
- In vivo: during the ongoing procedure
- Subsurface imaging: look into the depths of the mucosa

"YOU DON'T NECESSARILY NEED A PATHOLOGIST"

Prof Mimi Canto is considered to be one of the most active minds on the international endoscopy scene. At the "2nd International Endomicroscopy Meeting" in Mainz she spoke exclusively with InfoScope about how endomicroscopy has changed her work as a gastroenterologist and why women are better endoscopists.

InfoScope: Prof Canto, how did you actually get into endomicroscopy?

Prof Mimi Canto: I had met Ralf Kiesslich at various endoscopy conferences and at some stage we became friends. So in 2003 when he gave the first lectures on endomicroscopy and presented his images, I immediately thought to myself: this is exciting, I want to do this, too. And so in 2005 I came to Mainz for the first time. I have since been back a few more times and each time I examined 10-15 cases together with him using endomicroscopy. After examining about 30 patients with him I started to feel confident that I could do it on my own at the Johns Hopkins Hospital. Since then I have been training people myself in Baltimore.

InfoScope: How exactly did you proceed in your training phase?

Prof Mimi Canto: The best way to learn endomicroscopy is to practice it over and over again. In other words, learning by doing. I have compared my diagnoses with those of the pathologists, looked at images that my colleagues had made and researched cases. And I have spent a lot of time with our pathologist. Together we have figured out which structures require special attention during the examination.

It is interesting to note that the colon is easiest to examine, while the stomach is a bit more difficult and imaging the esophagus requires the most patience of all because of the respiratory movements of the patient. But as an endoscopist, you're not reinventing the wheel, even if you're performing your first endomicroscopic examination.

InfoScope: How much does endomicroscopy influence your daily work? And what has changed as a result of the new technology?

Prof Mimi Canto: I see 12-14 patients each day and one quarter of them comes because of Barrett's esophagus. I almost always use the endomicroscope on the Barrett's patients. I use this technique especially for second opinions and to clarify difficult cases: is it really a case of Barrett's esophagus or not? Does the patient need to be monitored closely? Is therapy necessary? Because of this method we have become much more certain and faster in such diagnoses. Thanks to endomicroscopy, for example, I do not have to ask my patient to come back in two weeks when the pathology results will be available, but rather I can normally send him home with a definitive diagnosis. And of course I can also remove intraepithelial neoplasias straight away.

Thus, endomicroscopy enables me to reach a diagnosis and administer treatment in a single session.

InfoScope: What further advantages does endomicroscopy offer?

Prof Mimi Canto: Well, diagnostics has a lot to do with classifying patients into certain risk groups. Currently we can do this based on morphological criteria, gene tests or careful history taking. In the future we hope to be able to detect molecular changes at the cellular level with the aid of endomicroscopy and suitable markers. The hope is that this will enable us to predict, for example, whether someone will contract intestinal cancer and must be screened regularly or rather not.

InfoScope: Your lecture here at the "2nd International Endomicroscopy Meeting" was about the improved early detection of Barrett's esophagus with endomicroscopy. Can you tell us about your experiences? And what advantages does the method offer for this indication?

Prof Mimi Canto: As I already said, we can diagnose Barrett's esophagus more easily and clearly. In our study we had a higher hit rate in the detection of relevant metaplasia than was the case with conventional quadrant biopsy. And we

PERSONAL DETAILS ->

Prof Marcia (Mimi) Canto, M.D. and M.H.S., completed her medical studies in 1985 at the University of the Philippines. She specialised in internal medicine at the State University of New York Health Sciences Center in Brooklyn, New York. After completing another specialisation as gastroenterologist/hepatologist at Johns Hopkins Hospital and gaining a master's degree in clinical epidemiology at the Johns Hopkins School of Hygiene and Public Health, she underwent further training for three years as an endoscopist at Case Western Reserve University in Cleveland. Prof Canto has been back at Johns Hopkins Hospital since 1996, where she has been head of clinical research in the endoscopy department for three years. She is considered an international expert on the diagnosis and treatment of Barrett's esophagus and pancreatic cancer. Prof Canto is the author of numerous publications in renowned journals and a highly respected speaker at national and international endoscopy and gastroenterology conferences.



Prof Mimi Canto

required fewer biopsies overall. So we are able to work less invasively and save money, because the pathologist has less work. Cost consciousness is becoming more and more important in the health system.

InfoScope: During DDW 2009 in Chicago, U.S., you received the Takeda Endoscopic Research Award, one of the ASGE Chrystal Awards. Why was the award given?

Prof Mimi Canto: We will use the money connected with the award for a new study on Barrett's esophagus. The study that I have just described included only 41 patients in only one clinic. Now we can undertake a multicenter study with the same design, but at four clinics in Germany and the U.S., in which around 200 patients will participate.

InfoScope: For which indications does endomicroscopy offer the greatest advantages?

Prof Mimi Canto: Oh, that depends on what exactly you need or are looking for. I personally think it's great that my work with Barrett's patients has become so much easier. Other gastroenterologists, who are concerned more with colon cancer or inflammatory bowel diseases, could also provide you with a list of their

advantages. For the first time we are able to diagnose several diseases, such as Celiac disease or microscopic colitis, using endomicroscopy, without having to take biopsies. In the lectures here at the symposium we have also heard about rarer indications, such as the graft versus host reaction. Indeed, I can use the method for any question concerning changes in the mucosa.

InfoScope: Prof Canto, you are one of the few successful women on the endoscopy scene. You are Associate Professor of Medicine and Oncology and head of endoscopy at Johns Hopkins Hospital – one of the most renowned clinics in the U.S. How did you become so successful?

Prof Mimi Canto: For the record, I gave up the head of endoscopy position some time ago. It involved too much administrative work for me. Perhaps that is part of the recipe for success: I concentrate on what is essential. Perhaps women can do this better. So I have focussed my efforts on my research on Barrett's esophagus and pancreatic cancer. The combination of scientific work with publications in a specialised area and constant continuing education are absolutely essential for success. As a very traditional university oriented toward research, Johns Hopkins Hospital provides me with ideal conditions.

I discovered my passion for endoscopy during my training as a gastroenterologist. Back then there were hardly any women practicing endoscopy. But this did not put me off. Then I applied to one of the best programmes in the U.S., run by John Vargo at the Cleveland Clinic Foundation. At that time I was actually the very first woman to take part in the training. When endomicroscopy came on the scene years later, I threw myself into it. Neither the first shaky images nor the long journeys to Mainz could hold me back.

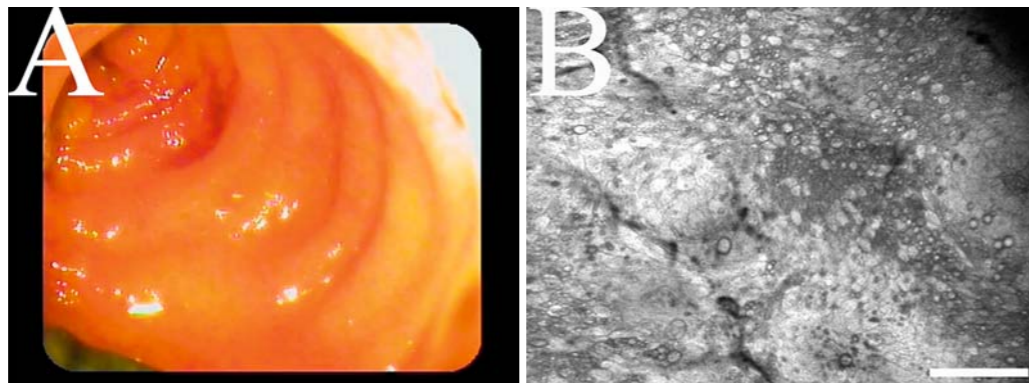
InfoScope: Prof Canto, thank you very much for this interesting discussion.

The economic journalist Constanze Löffler conducted the interview.

ENDOMICROSCOPY – THE TECHNOLOGY OF THE FUTURE EVEN OUTSIDE UNIVERSITY AND RESEARCH SETTINGS?

Dr Christian Bojarski reports on current clinical and scientific indications for endomicroscopy and discusses its use outside university institutions.

Endoscopy (A) and endomicroscopy (B, bar=100 µm) in a patient with acute graft versus host disease. A merely moderate inflammation (in A) is compared with a severe crypt architectural irregularity with almost complete destruction of the crypts (crypt drop-out) (in B).



During an endoscopy of the gastrointestinal tract, confocal laser endomicroscopy facilitates the performance of in vivo microscopy by visualising cellular and sub-cellular structures with the most exceptional optical resolution to date. With the endoscope and confocal laser microscope combined into one device, there is no need to change endoscopes. The microscope can be "switched on" as often as necessary during the examination. The histological images are displayed in real time on an additional monitor. Currently, the following two endomicroscopes are available: the EG-3870CIK is recommended as a gastroscope for examining the upper gastrointestinal tract, while the lower gastrointestinal tract can be examined with the colonoscope (EC-3870CIFK), which is longer but equipped with the same specifications.

A total of 40 hospitals in Europe and over 60 around the world meanwhile work with the endomicroscopy system. At first, "visible" endoscopic lesions, such as polyps and carcinomas in the upper and lower gastrointestinal tract, were selectively examined endomicroscopically in order to obtain an idea of how gastrointestinal pathology can be visualised endomicroscopically and how these findings can be delimited from a normal finding. In recent years, the largely "invisible" gastrointestinal pathologies (collageneous colitis, Celiac disease, intestinal GvHD, DALM lesions in ulcerative colitis, etc.) have increasingly become the focus of endomicroscopy. For the endomicroscope to visualise something that is "invisible", however, further chromoendoscopic procedures such as classic or virtual chromoendoscopy may be required under certain

circumstances to locate a pathological lesion with subsequent targeted biopsy. The basic advantage of endomicroscopy can be described using the term "smart biopsy". In the future, the central challenge for endomicroscopy with respect to molecular imaging will be to target pre-neoplastic lesions and delineate them from inflammatory mucosal changes.

Confocal endomicroscopy was initially evaluated by university researchers for its benefits in scientific studies and clinical trials. After being evaluated for more than five years, endomicroscopy is now definitely ready to be used outside university settings – especially where the focus is on the treatment of chronic inflammatory bowel diseases. Surveillance colonoscopy for ulcerative colitis is an excellent example of this. Taking around 40–50 individual samples from the colon (quadrant biopsy, 4 biopsies every 10 cm) is considered mandatory (Ulcerative colitis guideline, DGVS, 2004). The use of spray dyes in chromoendoscopy can provide assistance in better delineating flat lesions (Colorectal cancer guideline, DGVS, 2008). Endomicroscopy in ulcerative colitis with quadrant microscopy and biopsy of the abnormal mucosal areas takes no longer than a classic surveillance colonoscopy with 50 biopsies being taken. Endomicroscopy helps to save taking biopsies from normal intestinal sections while ensuring that high-quality surveillance of the entire colon remains unchanged.

Even though there is currently no reimbursement for endomicroscopy itself, the enormous cost-saving potential of the technology can already be estimated based on surveillance colonoscopy for ulcerative colitis.

PERSONAL DETAILS ->



Dr Christian Bojarski

Dr Christian Bojarski studied medicine in Berlin. After completing a DFG scholarship programme for basic research (subject: influence of apoptosis on tight junction proteins) he returned to clinical gastroenterology and has been working at the Central Endoscopy Department of the Benjamin Franklin campus of the Charité, Berlin since 2003. Endomicroscopy has been in use there since March 2006. The technology is currently being used to focus on patients with chronic inflammatory bowel diseases, Celiac disease and graft versus host disease.

What are the limitations for the use of endomicroscopy outside university settings?

- >> The detection, assessment and conclusive evaluation of normal and pathological endomicroscopic changes in the gastrointestinal tract require special training (1–3 days) as well as a learning curve of around 50 examinations to ensure the safe performance of the procedure and reliable interpretation of findings. Cooperation with a pathology institution is essential.
- >> An intravenous contrast agent (fluorescein 2.5–5 ml) must be administered for each endomicroscopic procedure. The currently approved medical fee schedule (GOÄ, number 344; 5.83 euro, single rate; applicable for Germany) practically covers the costs of its procurement and administration.
- >> The "savings potential" of endomicroscopy currently consists of avoiding unnecessary biopsies for special clinical symptoms. However, the examination is not yet being reimbursed appropriately.

What opportunities exist for the use of endomicroscopy outside of university settings?

- >> Every hospital can identify a niche based on innovative endoscopic procedures and thereby influence referrals and/or patient volumes.
- >> In the ideal case, lively interdisciplinary discussion/co-operation can develop with the pathology institution. Endomicroscopy is not competing with pathology but instead helps to supply better tissue for pathological diagnosis.
- >> The spread of in vivo histological procedures further enhances the highly specialised endoscopic diagnostic procedures currently in use and may create the basis for appropriate reimbursement.



EXCELLENT PERSPECTIVES IN MEDICAL EDUCATION



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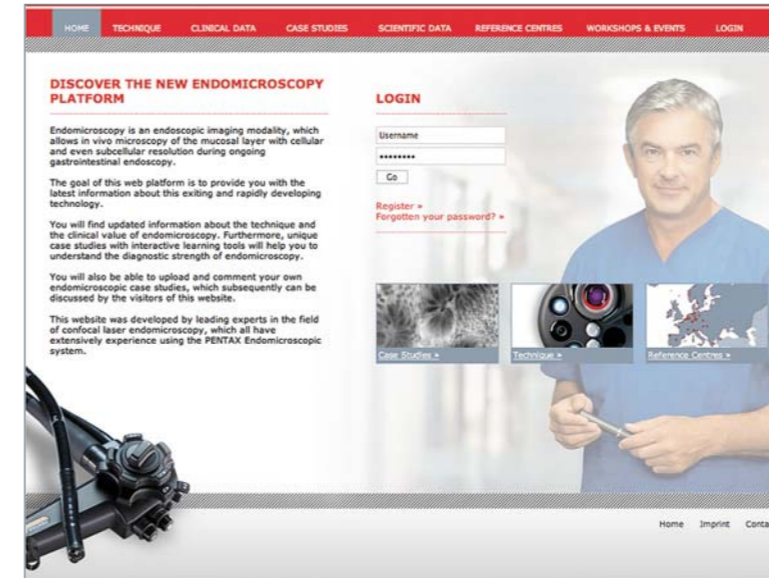
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Simply register directly with the contact persons stated above. The number of participants per training course is limited, so please register early to ensure your participation.

EXPERIENCE INTERESTING FEATURES OF THE NEW ONLINE PLATFORM FOR ENDOMICROSCOPY

In co-operation with leading experts in the field of endomicroscopy, PENTAX has developed a new online platform for endomicroscopy. Interesting topics and interactive learning elements ensure lively, international discourse.



All important details, case studies and areas of application: www.endomicroscopy.info offers an abundance of relevant information for the user. You can also upload your cases and receive a fascinating DVD or book on the subject of endomicroscopy.



Assess case studies from clinical practice and find out valuable information about the technology and the wide-ranging areas of application for endomicroscopy.

Ina Klocke,
Marketing Communications
PENTAX LIFE CARE

By logging on to www.endomicroscopy.info visitors now have the opportunity to become thoroughly acquainted with the specialised technology and special features of endomicroscopy; they can also learn in detail about the clinical applications. Illustrations of an endomicroscope depict the differences between such a device and conventional endoscopes. The "Anatomy" section provides a readily understandable description of how individual regions of the body are endomicroscopically imaged.

Examples of endomicroscopy being used in clinical practice

An interesting database of interactive case studies, covering the upper to the lower gastrointestinal tract by section, is the centerpiece of the website.

Following a brief introduction and description of the clinical case, users can access endoscopic, endomicroscopic and histological images. Distinctive and abnormal areas are annotated with expert comments through the exact placement of arrows directly on the images. This allows the user to make an "initial" diagnosis – with the comments hidden – and then simply click on the screen to display a short explanation of the diagnosis for comparison. Take advantage of this unique opportunity to benefit from the experience of endomicroscopy users and learn how reliable and accurate a diagnosis can be with the assistance of endomicroscopy.

If you are already successfully using endomicroscopy in your hospital, you can even post your own cases to the website. A user-friendly interface enables you to easily upload and annotate cases in the personal log-in area. You can even upload short video sequences to the website. As soon as you have posted a case study to the website you will be able to benefit from the lively discourse on the website and solicit feedback from other endomicroscopy users.

Pool of scientific publications on endomicroscopy

In addition, all scientific publications on endomicroscopy are listed on the website. More than 100 have been published to date. You can browse through the publication database easily – by author, title and date of publication. If you are interested in further information about a certain paper, you can retrieve the relevant abstract by clicking on the associated link. Of course the database is updated on an ongoing basis, ensuring that your information is always up to date.

Under the "Reference Centers" menu item you can see all the places in the world where endomicroscopy is used, as displayed on an animated map of the world. By clicking on the relevant continent you can see all the hospitals in which endomicroscopy is currently being used.

If you are an endomicroscopy user yourself, you can also have your reference center displayed on the map in the personal area and include your contact details.

If you would now like to experience endomicroscopy as it is used in practice, you can find information about the PENTAX Medical Education Centers in the "Events" info area and register directly to participate in a course.

The new website can be viewed as the most important platform for opinion leaders and those interested in the field of endomicroscopy. Log on and experience the interactive features of this website at www.endomicroscopy.info.

Upload your own endomicroscopic case studies to www.endomicroscopy.info – it's worth it!

Registering with www.endomicroscopy.info is definitely worth it – post three endomicroscopic case studies, including images, to the website and as an acknowledgement you will receive the fascinating DVD "Endomicroscopy Live 2009" with three highly interesting and detailed examination sequences, recorded at the Mainz University Medical Center. As an alternative you can select the book "Atlas of Endomicroscopy". We will contact you as soon as you have posted your case studies – and then you can let us know which you prefer.

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FUTURE OF ENDOMICROSCOPY

Endomicroscopy not only enables significantly more patient-friendly diagnosis. Above all, it improves the diagnostic rate during cancer and inflammatory disease development and therapy. Conclusion of the conference: this technology will vastly improve clinical procedures.

VIEWS ON THE CONFERENCE

>> *"What a fascinating event. I cannot wait to report back to my colleagues at home and for us to apply all the new knowledge."*

Prof Hanns-Ullrich Marschall, Department of Medicine,
Karolinska University Hospital Huddinge, Stockholm

>> *"In the near future endomicroscopy will prevent the untargeted removal of tissue samples in special diseases of the GI tract."*

Dr Christian Bojarski, Charité University Medical Center Berlin

>> *"Outstanding lectures, exciting cases in the live broadcast, intensive discourse with colleagues from all around the world – I am already looking forward to the next endomicroscopy meeting."*

Prof Joseph Sung, Department of Medicine and Therapeutics,
Kings of Wales Hospital, The Chinese University of Hong Kong

>> *"The future belongs to endomicroscopy. We are currently standing on the cusp of this technological development."*

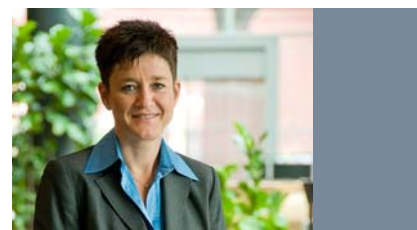
Prof Markus Neurath, Clinic for Gastroenterology, Pneumology and Endocrinology,
University of Erlangen

>> *"All of us feel newly inspired after this event. There is simply still so much to discover and to examine."*

Prof Ralf Kiesslich, Head of Interdisciplinary Gastrointestinal Endoscopy
of the Mainz University Medical Center

>> *"It is wonderful to see how a new generation of endoscopists is coming of age with this powerful technology."*

Prof Jean-Paul Galmiche, CHU University Hospital, Nantes, France



>> *The range of the clinical indications for endomicroscopy is really fascinating – and inspiring: for us the scientific discourse with international experts is essential for the continuing technological development of endomicroscopy. Here, the continuous improvement of patient care is our core concern.*

Jenny Adebahr, European Manager
Marketing & Product Management,
PENTAX LIFE CARE

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