InfoScope

01
2010

Customer Magazine of PENTAX LIFE CARE

Technology that gives maximum certainty

Does endoscopy using the Hi Line system really have the same diagnostic potential as chromoendoscopy? Initial data from clinical practice is making people sit up and take notice

Early diagnosis of carcinoma in the gastrointestinal tract:

Prof Raf Bisschops and Dr Silvia Sanduleanu on prevention with PENTAX Hi Line

HIGH-RESOLUTION ENDOSCOPY IS SETTING NEW STANDARDS

Dr Dirk Laval

DEAR READERS,

I am delighted to supply you with the latest issue of the PENTAX InfoScope, which once again offers a variety of fascinating articles.

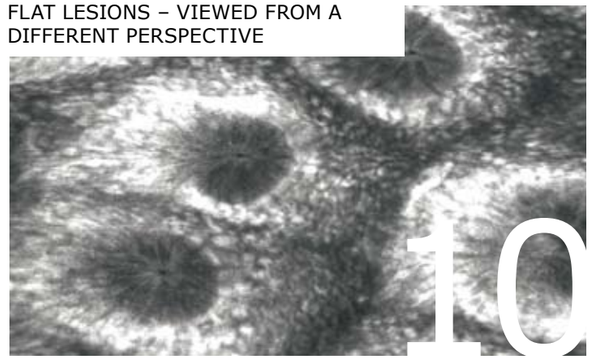
In this issue of the InfoScope we question internationally renowned experts on the subject of colon carcinoma and assemble the latest scientific findings for you. Colon cancer has the second highest mortality rate of all cancers among the world's industrialised nations. Although the current figures are declining slightly, they constitute a depressing reality which could be avoided on such a scale. This is because, particularly in the colon, the opportunity exists for a preventive examination which could avert the incidence and consecutive mortality due to advanced colon cancer.

As a result of the constant technical refinement of endoscopes, gastroenterologists are being challenged to take a good look at the technology available. The latest scientific data shows that the use of high-resolution endoscopes is leading to an improvement in adenoma detection. Small and flat lesions in particular can be better identified. With the Hi Line series, PENTAX provides you with endoscopes enabling you to give your patients the best possible treatment. In addition to excellent image resolution, Hi Line is distinguished by the latest digital filter technology, i-scan modes. In clinical studies i-scan has already proved its potential to increase the adenoma detection rate and to be able to replace traditional chromoendoscopy in the near future. With the i-scan technology PENTAX has set a new standard in high-resolution endoscopy; evidence of which is included in this issue of InfoScope.

PENTAX is not only pushing ahead with the development of the most progressive technologies, but will once again this year be actively supporting the promotion of future oriented projects centred around the early diagnosis of colon cancer. As part of the "Felix Burda Award 2010" we are providing prize money of 10,000 euros for each of the winners of the "Medical Prevention" and "Public Prevention" categories. This investment is being made as we believe it is s important for us to continue increasing awareness of colon cancer prevention among the population.

I hope you enjoy reading this issue of InfoScope.

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



TECHNOLOGY THAT GIVES MAXIMUM CERTAINTY

Excellent illumination, higher resolution with HD+ white light and the i-scan technology of the Hi Line system are increasingly making work easier for endoscopists: suspicious mucosal lesions, especially flat lesions, which have been underestimated for a long time, can be detected and characterised more easily. Initial studies show that in everyday clinical practice HD+ is significantly superior to standard colonoscopy. The increasing use of the system in colon cancer screening could further reduce the incidence and the mortality of colon carcinoma.

"Our data shows that Hi Line is superior to standard endoscopy", explains Dr Arthur Hoffman

Martin K. was lucky: doctors examined his colon as part of a clinical study using a new-generation endoscope. The Hi Line endoscopy system from PENTAX showed conspicuous lesions in three places. Thanks to the i-scan modes, in which the reflected light is processed using special software, the specialists succeeded in characterising the mucosal changes precisely. "With standard endoscopy we might have failed to see the small, depressed lesions", explains Dr Arthur Hoffman, Deputy Head of Interdisciplinary Endoscopy at the University Hospital in Mainz. Using i-scan technology, one change in the tissue turned out to be harmless, two others were classified as conspicuous pit pattern IIIs and IV and were removed.

The top priority of a routine colonoscopy is to detect pre-cancerous and cancerous changes in the colon and to remove them before they metastasise. Here, over the last ten years, the discovery and characterisation of flat and depressed adenoma has become increasingly important. Flat adenoma can be recognised by a slight reddening, a central depression which occurs once in a while, slight differences in colour to the proper mucous membrane and breaks in the capillary vessel network. For a long while, chromoendoscopy using dyes such as methylene blue and indigo carmine was the gold standard for the detection and characterisation of dysplasias. For some time now, PENTAX has provided a high-resolution (HD+, high definition) endoscopy system in which the endoscopes, thanks to enhanced imaging technology, enable a form of virtual chromoendoscopy. Initial clinical studies on the Hi Line system show that the dysplasia discovery rate is significantly higher and that the system, thanks to the i-scan technology, may have the same diagnostic potential as chromoendoscopy. "Our experience in using the Hi Line system leads us to believe that the surface accentuation supported by i-scan technology permits better and easier detection, particularly of small and flat lesions", says Hoffman.

Characterisation of dysplasia supported by i-scan technology

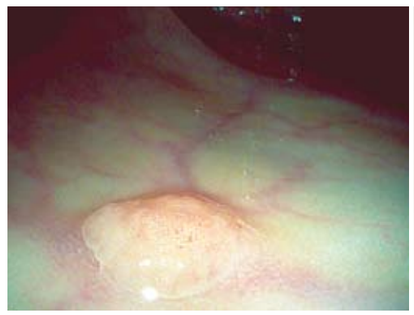
High-resolution endoscopy has been possible since PENTAX implemented a megapixel CCD colour chip into an endoscope. They were the first company to do this. At present, the chip can analyse more than one million pixels per image. An unprecedented attention to detail in the images is leading to an increased discovery rate of conspicuous mucosal lesions. Alongside HD+ image quality, the highly sophisticated i-scan image enhancement technology also contributes to improved detection: i-scan Surface Enhancement (SE) makes it possible to recognize size expansion, patterns and vascularity of the dysplasia even more clearly. "I can isolate suspicious lesions better from their surroundings without the image appearing unnatural", explains Prof Raf Bisschops, Head of the Gastroenterology Department at the University Hospital of Gasthuisberg in Leuven, Belgium. The i-scan Tone Enhancement (TE) mode, which can be activated at the touch of a button, also improve diagnosis: "As a result, even during the examination I am able to characterise lesions more precisely, so that I can carry out the biopsy in a more targeted way".

Promising data for PENTAX Hi Line

Improved detection and characterisation using Hi Line is scientifically proven: in a prospective randomised controlled study submitted to "Endoscopy" and due to be published soon, from which data was presented for the first time at DDW 2009 in Chicago, Hoffman and his colleagues from the University Hospital of Mainz compared standard colonoscopy with Hi Line colonoscopy. "Our data shows that Hi Line is superior to standard endoscopy", explains Hoffman. Thanks to HD+ resolution, the authors discovered significantly more patients with colorectal neoplasia (38 % vs. 13 %). Hi Line was superior, particularly in the detection of difficult-to-recognise neoplastic lesions (80 vs. 16, $p<0.0001$) and flat adenomas (22 vs. 3, $p<0.0001$). The University Hospital of Hamburg Eppendorf (UKE) is currently conducting a similar study together with practice-based colleagues from Hamburg and Berlin. "We will be examining around 1,200 patients either with a unit of the predecessor generation or a Hi Line colonoscope", explains Prof Thomas Roesch, Director of Interdisciplinary Endoscopy at UKE. "The examination will show whether the new device actually leads to a higher detection rate".

Flat lesions: a wolf in sheep's clothing

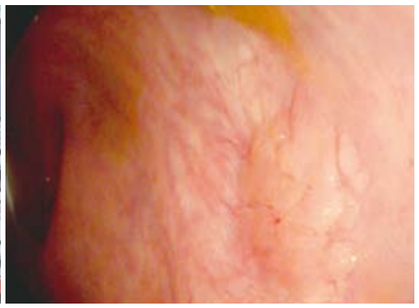
Flat lesions have been neglected for a long time. Reports from Japan in the eighties and nineties suggested that flat lesions are linked with an increased rate of colon carcinoma. However, among Western people there were initially no signs of frequent occurrence. This changed over the years: studies from Sweden, Canada, Great Britain and the USA showed that, where a careful examination technique is used, patients from the Western world also exhibit this form of dysplasia. In 2008, Roy Soetikno and his colleagues from Veterans Affairs Palo Alto Health Care System then published a study with surprising results, for which they had examined just under

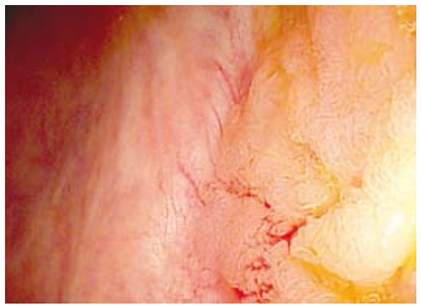


Left: HD+ resolution combined with i-scan Tone Enhancement (TE)

Centre: HD+ resolution combined with i-scan Surface Enhancement (SE)

Right: HD+ resolution





Centre: View of a flat lesion in HD+ white light image

Right: Flat lesion in HD+ resolution with connected i-scan Surface Enhancement (SE)

2,000 predominantly male patients by colonoscopy: using chromoendoscopy, the gastroenterologists observed a prevalence of flat lesions of almost ten per cent – i.e. a rate two to three times higher than previously described. Flat lesions in turn made up 15 per cent of the neoplastic changes.

Gold standard chromoendoscopy: successful, but time-consuming

In conventional standard colonoscopy without colour spray, even trained examiners overlook polypous lesions in 2 to 12 per cent of cases, even if they are 10 millimetres in size or larger. This is in addition to the smaller, flat lesions. It is therefore possible that alongside rapidly growing de novo carcinomas, overlooked or incompletely removed flat lesions are primarily responsible for the majority of interval carcinomas. "Amongst other things, the reason could be the borders of the flat lesions which are difficult to demarcate", says Hoffman. Using chromoendoscopy the borders are revealed more clearly. Chromoendoscopy continues to be regarded as the gold standard for the detection and characterisation of adenomas in the gastrointestinal tract. In particular, the detection of flat and depressed neoplasia has improved decisively as a result of this procedure.

Virtual chromoendoscopy at the touch of a button

During in-vivo chromoendoscopy, individual sections of the colon are coloured with the aid of a spray catheter; complete dyeing of the colon is not practicable. Now, the modern processor technology of the Hi Line endoscopy system offers the possibility of activating image enhancement while the colonoscopy is in progress. This way, the visual impression of the mucosa can be altered without the use of dyes – at the touch of a button in fact – and, unlike chromoendoscopy, is reversible at any time. Using i-scan, surface structures or the vascular pattern of the intestinal mucosa can be shown considerably better just like a digital or virtual chromoendoscopy. In future, the image enhancement technology could supersede the considerably more time-consuming procedure in which, moreover, there is a given uncertainty regarding the concentration of the various dyes. Initial data showed that virtual chromoendoscopy using i-scan is equivalent to in-vivo colouring for the sporadic adenoma and Barrett's esophagus. This proves the great potential benefit of i-scan.

This way Hoffman and his colleagues, using the Hi Line system with HD+ colonoscopy alone, discovered 176 lesions (<5 mm). With i-scan, the discovery rate rose to 335 ($p<0.001$) and with chromoendoscopy to 646 ($p<0.001$). Most of the additional lesions discovered using virtual and conventional chromoendoscopy were flat dysplasia (type IIb, 74 %). However, the number of neoplastic changes did not differ significantly in the three groups examined (HD+: 5, i-scan: 11, chromoendoscopy: 11). Overall, i-scan and chromoendoscopy were better than the standard; thanks to these methods more neoplasias were found.

With the aid of the i-scan modes, chromoendoscopy can therefore be replaced by a virtual colouring and not only with regard to the discovery rate. "i-scan can also improve the overall diagnosis process by supporting the characterisation of the lesions", says Hoffman. At the same time, i-scan technology could clearly have the same diagnostic potential as chromoendoscopy.

Histology in turn can be predicted using i-scan with a high degree of sensitivity (98 %) and specificity (100 %). Surface accentuation using the i-scan modes in combination with HD+ can also improve the detection of flat adenomas.

Not resting on our laurels

There is still a great need for improved colon cancer diagnosis. On the one hand, over the last few years the mortality figures have slowly fallen: between 1990 and 1994 and 2000 and 2004 from 13.4 to 11.5/100,000 in women and from 20.1 to 18.8/100,000 in men. Similar developments can also be observed in North America and Japan. Alongside changes in nutrition, improved early diagnosis may also be a primary contributor to this. On the other hand, approximately one in six people in the Western industrialised countries will suffer from a colon carcinoma, irrespective of their sex. More than a third of patients die – frequently because the tumour is first discovered at an advanced, already metastasised stage and therapeutic measures fail to heal. "This means that bowel cancer is one of the most common causes of cancer death in both sexes", says Roesch.

This ought not to be the case because, just like breast cancer, skin cancer or cervical cancer, the colon carcinoma can be detected at a very early stage and therapy provided. Large randomised controlled studies from the USA, England, Sweden and Denmark proved that a test for occult blood in the stool, carried out annually or every two years reduces colon cancer mortality and incidence. Occult blood tests though react less sensitively to a colon carcinoma (approx. 40 %) if the test is carried out only once. Sensitivity decreases further if there are only relatively small colorectal adenomas.

Many experts therefore favour colonoscopy. "With its colonoscopy screening, introduced in 2002, Germany takes a leading role in Europe", says Bisschops. The acceptance of screening offers among the population is still moderate: just under 600,000 examinations were carried out by endoscopists in 2007. This means that just eleven per cent of those entitled to claim are taking part in the screening programme - an opportunity that many patients fail to take advantage of. At the beginning of 2010 researchers from the German Cancer Research Centre (DKFZ) in Heidelberg were able to show that advanced pre-cancerous stages were present considerably more rarely in people who had already completed a previous colonoscopy, than in study participants who were undergoing a colonoscopy for the first time (6.1 % vs. 11.4 %).

Modern endoscopic imaging procedures such as the Hi Line system from PENTAX could revolutionise colon cancer screening in the future: at any rate, initial data shows that the high-resolution HD+ white light image leads to a far better detection rate and that the connectable i-scan modes enable a diagnosis comparable with chromoendoscopy. "From a scientific viewpoint the biggest task now will be to confirm the advantages of this new technology in a larger patient cohort and to establish the method in everyday clinical practice", says Bisschops.

Modern endoscopic imaging procedures such as the Hi Line system from PENTAX could revolutionise colon cancer screening in the future

HI LINE ADVANTAGES AT A GLANCE ->

High Definition (HD+): better visibility and orientation
- *High resolution and excellent illumination for better orientation and detection*
- *Improved visibility and evaluation of minute lesions*

i-scan Surface Enhancement (SE): supports detection
- *Does not affect natural colour reproduction*
- *Mucous membrane contrasting for better detection of the smallest lesions*

i-scan Tone Enhancement (TE): supports characterisation
- *Targeted imaging technology, fur further assistance in diagnosis*
- *Virtual chromoendoscopy at the touch of a button*

"IN FUTURE HIGH-RESOLUTION ENDOSCOPES COULD REDUCE THE INCIDENCE OF COLON CARCINOMA"

Prof Raf Bisschops is one of the most progressive endoscopists in Europe. He is particularly concerned about the early diagnosis of carcinomas in the gastrointestinal tract. Alongside his interest in innovative technologies, he is actively involved in improving the quality of the training of endoscopists.

InfoScope: *Prof Bisschops, colon carcinoma is still one of the most common cancers. What is the challenge physicians face during diagnosis?*

Bisschops: Well, colon cancer is the third most common cancer in the world. It is true that in the last few years incidence and mortality have decreased, but just in Europe, 400,000 new cases occur every year. Fortunately, colon carcinomas develop very slowly. It takes roughly ten years for adenomas to transform into carcinomas. This gives us the opportunity to discover the disease at an early stage and to treat it effectively. One of our major tasks over the next few years will be to exploit this window of opportunity even better.

InfoScope: *We have been familiar with so-called "flat lesions" for over 30 years and know that they increasingly lead to carcinomas. However, only in the last few years have we begun to understand how important it is to detect these flat lesions at an early stage. Why the delay?*

Bisschops: For a long time we believed that flat and depressed lesions were simply a "Japanese disease". Only when Rembacken published his paper in 2000 in "Lancet" was it clear that flat lesions also occur in the Western population. Incidentally, these changes in the mucous membrane could be seen particularly easily if colonoscopy and chromoendoscopy were combined with one another. Rembacken also recognised that these lesions – especially when they are bigger than one centimetre – have more often turned malignant than a typical polyp. As the significance of flat lesions had not been understood up to that point, little notice had been taken of them in colonoscopic examinations. Today we know that, among others, hereditary non-polyposis colorectal cancer (HPNNC) patients are at risk from flat lesions.

InfoScope: *So a precise eye is needed for detecting flat lesions?*

Bisschops: Flat lesions must be removed exactly like other conspicuous tissue structures. Studies show that the discovery rate, particularly of small lesions, can be increased by 20–25 per cent using a few simple techniques. Therefore if screening programmes offering preventive polypectomies are already taking place, as many suspicious lesions as possible should also be detected and removed. I am sure that through high-resolution endoscopy with its high degree of attention to detail this problem can increasingly be solved – and, in future, colon cancer will occur less frequently thanks to better prevention.

InfoScope: *So how can the discovery rate be improved?*

Bisschops: Naturally this includes measures such as a well prepared bowel. In addition, enough time should remain for the second phase of the examination, the withdrawal of the endoscope. This extra six or seven minutes can really increase the discovery rate, we know this from various studies. For a simple colonoscopy without a polypectomy I allow a quarter of an hour, in high-risk patients I reckon with 30 to 45 minutes. The aim must not simply be to get through a dozen colonoscopies in an afternoon.

InfoScope: *What role do new technologies play in the detection rate?*

Bisschops: With the increasing use of high-resolution endoscopes a new era has begun in diagnosis – comparable with the switch from fibreglass endoscopes to video technology. In the next few years these older systems will all be replaced by HD technology. The image quality of the equipment is outstanding. With HD resolution we can actually detect smaller lesions more easily. Thanks to the image enhancement technology, the demarcation of healthy tissue and the classifying of the lesions is even easier.

InfoScope: *In your opinion, would it be ideal if colon cancer screening was done with the help of virtual chromoendoscopy, also known as an endoscopy with digital colour filters?*

Bisschops: Yes, exactly. We know that colonoscopy with polypectomy reduces the incidence of colon carcinoma. And, when fewer people fall ill, it results in fewer deaths. The faecal occult blood test (FOBT) of course also has its legitimacy. However, the difference between the stool test and endoscopic methods is that the stool test – exactly like the newer blood tests incidentally – only works when the carcinoma already exist. As a result of a colonoscopy using high-resolution endoscopes and connected colour filters we can discover precursor lesions. This means we are practising prevention. The carcinoma simply doesn't develop in the first place.

InfoScope: *To what extent can HD technology change colonoscopy?*

Bisschops: Our goal must be to detect even more relevant tissue changes. To date we have been satisfied with discovery rates of 15 per cent in women and 25 per cent in men. In his trial with Hi Line, Arthur Hoffman found almost 40 per cent. Douglas Rex discovered as many as 60 to 65 per cent. The higher the rates, the more carcinomas we can hopefully prevent.

InfoScope: *You have been using the PENTAX Hi Line system since 2008. To what extent has this changed your clinical work and how do you go about an examination?*

Bisschops: You get used to the exceptional image quality quite quickly. It is quite an adjustment for me every time I have to work with an older endoscope. As we have not yet equipped all the rooms with the new devices, I mainly examine at-risk patients with the high-resolution Hi Line endoscope, i.e. HNPCC patients, those with Ulcerative Colitis or people who come in for a follow-up of Barrett's esophagus. When inserting the endoscope, to begin with I work only with HD+ white light. Then, for contrast and structure amplification, I activate the i-scan image enhancement feature. With the i-scan Surface Enhancement (SE) mode, suspicious lesions can be found more easily; I can also demarcate them better within their environment. The i-scan Tone Enhancement (TE) mode assists me in characterising lesions during the examination itself, so that I can take biopsies in a very targeted way for instance in Ulcerative Colitis patients.

InfoScope: *Are you planning any studies using the Hi Line technology?*

Bisschops: Yes, we are presently recruiting patients with Ulcerative Colitis for a randomised study in which we will be comparing the discovery rate of conventional chromoendoscopy with that of virtual chromoendoscopy. If the figures are comparable – which we assume will be the case – we would no longer have to use colour spray. It would be much more efficient simply to press the relevant button on the Hi Line endoscope – and still achieve a result which is exactly as good. But for that we will first have to wait for the data.

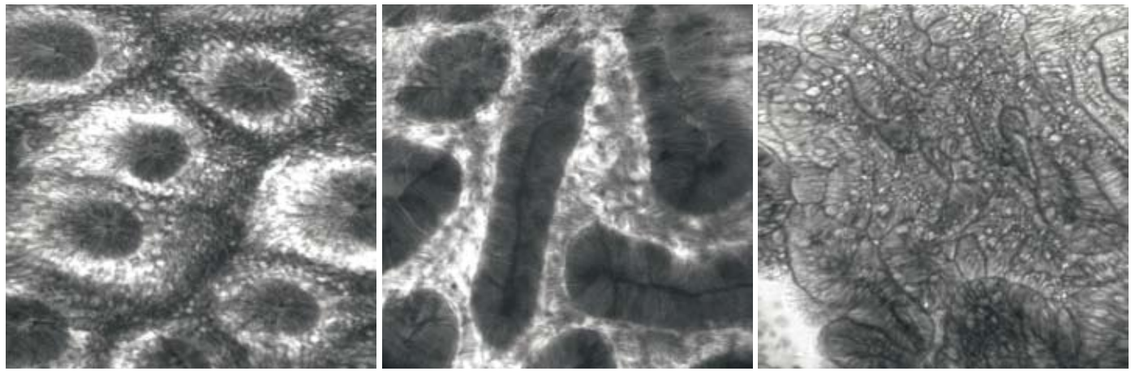
InfoScope: *Thank you very much for the interview.*

The interview was conducted by the science journalist Constanze Löffler.

PERSONAL DETAILS ->

Prof Raf Bisschops studied medicine at the Catholic University of Leuven (Belgium). Following his studies he trained there as a gastroenterologist. During this period he acquired his doctorate with a manuscript in the field of neurogastroenterology. Since 2006 Bisschops has been associate head of the Gastroenterology Department at the University Hospital of Gasthuisberg in Leuven and has been Associate Professor of Gastroenterology at the Catholic University of Leuven. His great interest lies in new endoscopic imaging procedures, in particular the endoscopic treatment of Barrett's Esophagus and reflux. As a clinical researcher he is concerned with endoscopic imaging designed to discover pre-cancerous lesions of the gastrointestinal tract. Bisschops has received several awards for his scientific work and publishes regularly in distinguished specialist journals.

Prof Raf Bisschops



Confocal endomicroscopy images **Left:** normal colonic mucosa showing regular crypt architecture and vascular pattern (fluorescein 10 %) **Centre:** tubular adenoma with low-grade dysplasia showing slightly irregular crypts (fluorescein 10 %) **Right:** tubulo-villous adenoma with high-grade dysplasia showing crowding of crypts and enlarged, round nuclei (white dots highlighted after using acriflavin hydrochloride 0.05 %)

FLAT LESIONS – VIEWED FROM A DIFFERENT PERSPECTIVE

Dr Silvia Sanduleanu reports on the detection of flat lesions with the aid of confocal endomicroscopy, thus shedding light on a further innovative examination method.

Conventional colonoscopy is the gold standard screening modality for the detection of colorectal neoplasia. Therefore, legitimate concern was raised when a few recent studies demonstrated that, in everyday practice, protection against colorectal cancer (CRC) offered by colonoscopy is still limited. Colonoscopy decreases the risk of subsequent CRC in the left-sided colon, but it seems to offer insufficient protection against right-side located cancers (Baxter, Ann Int Med 2008). For a long while, endoscopists and pathologists alike were at a loss to explain the origin of interval cancers – CRCs detected within 3 years after a negative colonoscopy – and hence were unable to modify their practice. Increased clinical awareness over the past years in conjunction with technological advances allowed us to consciously improve our practice, to ultimately optimise the prevention of CRC.

The following questions confront clinicians and scientists today:

Why is it important to accurately diagnose and classify non-polypoid colorectal neoplasia (NP-CRN)?

In the early ’80s Japanese endoscopists pioneered the field of new image-enhanced endoscopy techniques. Technological advances and a comprehensive practice of endoscopy resulted in the first description of flat carcinomas, the so-called ‘phantom carcinomas’. It became clear that NP-CRNs are prone to underdetection using conventional techniques, are more challenging to remove, and some of them may contain advanced histopathology. That is why NP-CRNs are considered to be one of the ‘main culprits’ responsible for the occurrence of interval cancers. Several studies demonstrated that especially Paris type II-b (flat) and II-c (depressed) lesions frequently harbour advanced histopathology. Although these lesions are relatively uncommon, it seems reasonable that with increasing screening, ageing and technological progress, such lesions will be more frequently unmasked.

This message seemed to be breaking new ground as it spread endemically from Japan to the rest of the world. An important step forward in our understanding of epidemiology and the clinical relevance of NP-CRN in the Western population was brought about by the work of Soetikno (Jama 2008), who estimated the prevalence of NP-CRN in a population of US veterans as being 10 % to 15 %. However, NP-CRNs were 10-fold more likely to contain in-situ or submucosal invasive carcinomas than polypoid lesions.

Currently, a large inception cohort of 2,600 patients has been built up at the University Hospital of Maastricht to address epidemiology, clinicopathological and molecular features of NP-CRN in a Dutch population and potential implications for CRC screening (DDW 2010).

What is the role of image-enhanced endoscopy techniques in the diagnosis and classification of CRN?

Chromoendoscopy, either traditional, dye-based or newly emerged digital-based techniques, are valuable diagnostic tools in everyday practice. These technologies provide useful information for detection and especially characterisation and classification of colorectal neoplasia. An alternative endoscopic modality is confocal laser endomicroscopy (CLE), which allows in-vivo diagnosis of colorectal lesions (Kiesslich, Gastroenterology 2004). In a study of 72 patients at high risk for CRC, as a cause of Lynch syndrome, familial CRC, or prior history of CRC, our group applied chromoendoscopy in conjunction with CLE to describe differential features between adenomatous and non-adenomatous colorectal polyps. Using fluorescein in combination with acriflavine, both general tissue architecture and cyto-nuclear alterations were described. In addition, we defined the ‘adenoma dysplasia score’ as a simple instrument which enables in-vivo differentiation of high-grade dysplasia from low-grade dysplasia with high accuracy (96.7 %). In 7 (22 %) of cases, CLE resulted in the upgrading of histological diagnosis. This data highlights the need for uniform and objective criteria to facilitate the dialogue between endoscopist and pathologist. The key message is that accurate diagnosis and classification of colorectal neoplasia are important, especially in high-risk groups, as this may help to reclassify patients into higher or lower risk categories, and thereby fine-tune surveillance programmes.

What are the implications for GI training?

After some decades of controversy, the role of NP-CRN in colorectal carcinogenesis is now largely accepted. Studies on epidemiology and clinicopathological features of NP-CRN contributed in fact to raising community awareness, especially regarding the importance of quality colonoscopy and the need for systematic training to adequately detect and manage these lesions. A few issues need to be addressed in the near future: firstly, educational programmes should be developed in this field. ‘Training the trainers’ and ‘Training the trainees’ are of equal importance in this process. Fortunately, a plethora of training modalities is currently available, among them tele-teaching, video training etc. Secondly, special attention should be paid to achieving optimum bowel preparation, standardising withdrawal techniques and, when necessary, applying selective chromoendoscopy to clarify the borders of these lesions prior to removal. It remains to be shown whether the detection rate of NP-CRN should be regarded as an indicator for quality colonoscopy in the future.

In short, recent technological advances have not only improved our knowledge on new facets of colorectal carcinogenesis but have also enabled new applications that are gaining a foothold in everyday clinical practice as adjuncts or replacements of the traditional techniques.

PERSONAL FACTS ->

Dr Silvia Sanduleanu is a gastroenterologist, and has been a staff member at the Department of Gastroenterology & Hepatology of the Maastricht University Medical Centre (MUMC), in the Netherlands since 2006 s. Her main clinical and research field of interest is GI oncology. After completing her PhD on the diagnosis of gastric pre-cancerous lesions (topic: ‘Atrophic gastritis during acid-suppressive therapy, with focus on ECL-cell hyperplasia and intragastric bacteria’, 2001), her research work focused on screening for CRC in average and high-risk groups. She is presently involved in studies addressing the role of non-polypoid mechanisms in colorectal carcinogenesis and the potential use of new image-enhanced endoscopy techniques in the diagnosis and classification of colonic lesions. Confocal endomicroscopy has been in use at the MUMC since April 2007. This technology is currently being applied in patients at high risk for CRC, e.g. patients with hereditary forms of colorectal cancer and patients with inflammatory bowel diseases.

Dr Silvia Sanduleanu

THE ENDOSCOPY DEPARTMENT AT JULIUSSPITAL WUERZBURG – INNOVATIVE, MODERN, COMMITTED

For two years, a team of doctors at the Gastroenterology Department at Juliusspital in Wuerzburg has been working with the PENTAX Hi Line endoscopy system. During this time the team has carried out several hundred examinations with the new generation of equipment. This is precisely the right time to take stock.

"In my opinion, in the medium-term HD+ endoscopy will be accepted, as the diagnostic standard", says Prof Scheppach

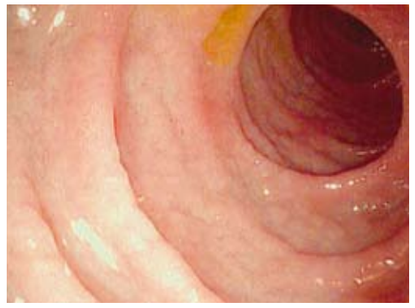
Anyone entering the Endoscopy Department at Juliusspital in Wuerzburg may not at first detect anything unusual, but when you take a second look a wealth of diagnostic equipment is revealed which we usually only find in full-service hospitals: in the four rooms, besides standard examinations, the clinic's lead clinician, two senior gastroenterological physicians and an internist carry out modern diagnostic procedures such as double balloon enteroscopy, mini-laparoscopy and high-end sonography including contrast medium enhancement. All endoscopy workstations have been equipped with Hi Line systems since the beginning of 2008; two years therefore, since Juliusspital made its entry into the world of innovative high-definition endoscopy (HD). "In my opinion, in the medium-term HD+ endoscopy will be accepted as the diagnostic standard", says Prof Wolfgang Scheppach, head clinician at the Medical Clinic specialising in gastroenterology/rheumatology at Juliusspital in Wuerzburg. "The high image resolution makes the detailed detection of mucous membrane changes possible in a way that didn't exist before".

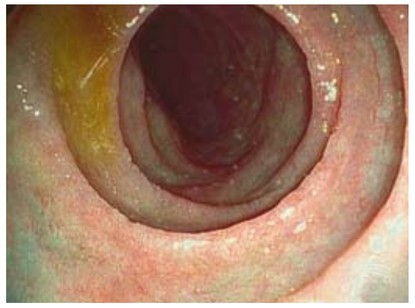
Better view, easier diagnosis?

130,000 people live in Wuerzburg, and roughly as many in the surrounding area. For their treatment they can choose between three large hospitals. In the meantime the good reputation of the modern and efficient endoscopy department at Juliusspital has spread among referring doctors and patients alike. Tina M. was also sent there by her GP for clarification. For months the 45 year-old had been suffering from chronic diarrhoea with protein deficiency oedema. "Even when the endoscope was being inserted, in white light a clearly recognisable 'scalloping' of the Kerckring folds was apparent", explains Scheppach. Here conventional videoendoscopes would only have shown a shadowy surface structure. "The mucosal changes became even clearer and more plastic when we activated the i-scan modes." The mosaic-like rutting of the duodenal mucosa is an expression of villous atrophy and is regarded – alongside other, rarer diseases – as an indicator of Celiac Disease. The histopathological examination confirmed the suspected diagnosis: Celiac Disease, Marsh IIIa stage.

Left:
Celiac Disease in the white light image with HD+ resolution

Right:
Celiac Disease in HD+ resolution combined with i-scan Tone Enhancement (TE)





Improved diagnosis not yet clear

In agreement with hospital management, Scheppach had opted for the Hi Line endoscopy system because its cost-benefit ratio turned out to be the most attractive. Furthermore, the head clinician believes that patients want to know in ever greater detail what the respective department offers them: "Quite a few people enquire beforehand about the generation of equipment we work with and how experienced our examiners are", says Scheppach. "It was the correct decision to equip the department with PENTAX devices". The Hi Line endoscopes have a pixel resolution many times higher than conventional equipment. Besides a positive initial verdict, the examiners report a subjectively better view and sharper contouring of the mucosa, with the result that dysplastic changes are easier to discover. "Further studies with larger numbers of patients will show whether Hi Line actually improves diagnosis and results in an increased detection rate", says Scheppach.

Take time for the examination

The gastroenterologists at Juliusspital also carried out a colonoscopy on Michael K. using Hi Line. "Due to his positive family medical history the 43 year-old had resolved to undergo an examination", says Scheppach. Then, during the colonoscopy, the physicians discovered a polypoid, partially ulcerated rectum tumour which, following the histological examination, was classified as a moderately differentiated adenocarcinoma (T3 N2 M0). "Because no technology can replace the care of the examiner, colonoscopies should never be carried out under time pressure", according to Scheppach. "It is important to leave yourself time also when extracting the endoscope and to go forward and back again, particularly in the bends". In this case the long withdrawal period also revealed no further lesions. Michael K. was the first case to be accepted into the programme of the newly established, certified Bowel Centre at Juliusspital Würzburg. After neoadjuvant radiochemotherapy, a deep anterior rectal resection followed with subsequent adjuvant chemotherapy. To date the patient has had no relapse.

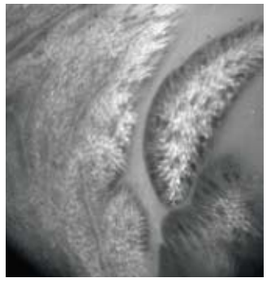
Prof Wolfgang Scheppach, lead clinician at the Medical Clinic specialising in gastroenterology/rheumatology at Juliusspital Wuerzburg during the documentation of a colonoscopy using the PENTAX Hi Line system

Good service ensures trouble-free procedures

"For a medium-sized specialist hospital such as Juliusspital, a reliable service from the endoscope supplier is essential", says Scheppach. "We therefore store replacement devices on site, so as to enable immediate replacement in the event of an equipment fault." As a result, delays in the clinical routine can be avoided. Good and reliable care of patients and close co-operation with the referring doctors are very important to Scheppach: "We are interested in steadily improving the gateways between outpatient and in-patient care". At the beginning of 2009 the NaviAid™ BGE system for enteroscopy using the "push-and-pull"-technique was established. The Wuerzburg physicians also use newly-developed products such as the paediatric colonoscope and the dual-channel endoscope early on in close consultation with PENTAX. This enables clinical aspects to be taken into account from an early stage during product testing. Even after the installation of the Hi Line systems, staff at Juliusspital are therefore interested in offering innovative examination procedures. "For future work with Hi Line I would like to see more studies showing how well lesions can be classified macroscopically", says Scheppach, "and whether you can therefore do without biopsies for a histology or carry out more targeted biopsies".

ENDOMICROSCOPY IN AUSTRIA –

REFERENCE REPORT FROM THE MEDICAL UNIVERSITY OF VIENNA



Endomicroscopic photograph of Morbus Whipple

As the second-largest Centre in Austria, the Department of Gastroenterology and Hepatology at the Medical University of Vienna has had an endomicroscopy system since September 2009. The system is currently used mainly in the upper gastrointestinal tract.

An initial study using endomicroscopy is dealing with the specific mucosal resections of high-grade intraepithelial neoplasias in Barrett's mucosa. Before the scheduled mucosal resection, the "mapping" of suspect areas is carried out and the neoplastic area then resected.

Endomicroscopy is designed to facilitate an exact assessment of the tissue to be removed and thus help overcome the drawbacks of conventional diagnostic procedures in the esophagus. The histology of the resection is used as the gold standard and is compared with the endomicroscopic in-vivo findings. The project is being carried out as part of a PhD-study in close co-operation with the Departments of Clinical Pathology and Surgery.

After participation in visiting physician programmes and hands-on training at the University Hospital of Mainz and the Benjamin Franklin Campus of Charité Berlin, the first examinations in Vienna were performed mainly in the upper gastrointestinal tract. The main focus was on Barrett's esophagus, but other questions, such as the existence of an acute graft-versus-host reaction following allogenic bone marrow transplantation, were also investigated with the aid of endomicroscopy. More exotic indications such as a case of Morbus Whipple have also since been clarified using confocal laser microscopy.

The method of endomicroscopy had first to be learned, before it could be applied in clinical practice. The presence of a pathologist who facilitated the evaluation of the images was very helpful during the initial examinations. For this reason, two workstations designed for the expert assessment of the endoscopic and endomicroscopic images have now also been set up in the Department of Pathology. The pathologists have thus the opportunity to access the material directly. For gastroenterologists, the advantage lies in being able to discuss unclear changes and becoming more competent in assessing the images.

Further studies are planned, in addition to this initial one. Here, a co-operative agreement with other centres working in the area of endomicroscopy is indispensable and offers hope for some interesting studies in the future.

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FAMILIARISE YOURSELF WITH HI LINE DURING AN INTERESTING TRAINING COURSE AT OUR MEDICAL EDUCATION CENTRE IN MAINZ

At our Medical Education Centre in Mainz we offer doctors interested in the Hi Line endoscopy system a personalised training course.

During the course you will get to know Hi Line in detail and gain a thorough insight into the use of the system in everyday clinical practice. Important functionalities of the processor, the high-resolution endoscopes and application possibilities of the i-scan technology in particular will be explained in detail during lectures. In addition, you can watch the practical application of Hi Line during various live-examinations covering different diseases.

The limited number of participants at Hi Line training courses guarantees that all the questions and needs of those attending can be discussed in detail on a one-to-one basis. The training course takes place on one day, so that attendance can be scheduled to suit you.

Register at medical@pentax.de and take advantage of the opportunity to attend a valuable training course and to familiarise yourself with Hi Line and the i-scan technology in clinical practice.

Hi Line training course (1-day seminar):

17 May 2010
18 May 2010
4 October 2010
5 October 2010

Costs:
EUR 250 (plus VAT)

DISCOVER INTERESTING CASE STUDIES ON THE NEW HI LINE DVD

In order to show the functionalities of the Hi Line endoscopy system clearly, PENTAX has produced a DVD. On this DVD, two international experts demonstrate the advantages of the Hi Line system in clinical practice.

By means of various clinical case studies and examples, the entire Hi Line system is demonstrated clearly in detail on the DVD.

Interesting video sequences show how the Hi Line HD+ image quality facilitates the orientation and detection of small and flat lesions and how the i-scan modes further supports detection and characterisation of lesions in the entire GI tract.

Order a free copy of the DVD today at www.pentax.de/hilineDVD or get in touch with your local representative

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Publisher:
PENTAX Europe GmbH
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22527 Hamburg

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Editorial management:
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Design and editorial support:
RosenbauerSolbach Werbeagentur

Printed by:
Dräger + Wullenwever print + media GmbH & Co. KG

Image sources:
PENTAX LIFE CARE

PENTAX HI LINE DISCUSSED

"Thanks to virtual chromoendoscopy a window of opportunity is opening up for us. We can discover dysplasias at an early stage – and treat them more effectively as a result. Basically this offers us a new opportunity for prevention."

Prof Raf Bisschops, Head of the Gastroenterology Department at the University Hospital of Gasthuisberg in Leuven and Associate Professor of the Gastroenterology Clinic of the Catholic University of Leuven, Belgium

"Better image resolution due to high-resolution endoscopy allows details and contrasts of the intestinal mucosa to stand out much more clearly. Initial clinical studies indicate that high-resolution endoscopy is the decisive factor in the improved diagnosis of early forms of cancer."

Dr Arthur Hoffman, Deputy Head of Interdisciplinary Endoscopy at the University Hospital of Mainz

"Thanks to Hi Line with HD+ and i-scan, tissue and vessel structures can be detected better than with standard endoscopy. To what extent this will really lead to the clinically relevant, improved detection of flat lesions remains to be shown in studies involving larger patient numbers."

Prof Wolfgang Scheppach, Senior Consultant at the Medical Clinic specialising in gastroenterology/rheumatology at Juliusspital in Würzburg

"Newly developed image-enhanced endoscopy techniques not only enabled us to unravel new facets of colorectal carcinogenesis, but also provided essential grounds for quality colonoscopy and more refined clinical decision-making."

Dr Silvia Sanduleanu, Dept. of Gastroenterology and Hepatology, University Hospital of Maastricht, The Netherlands

"With the development of the Hi Line series, the PENTAX Research and Development Department has met the needs of our customers: an efficient, future-proof endoscopy system that both helps improve medical outcomes and meets the need for good value for money."

Ralph Loehner, International Sales Manager, PENTAX LIFE CARE

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Closing date is 31.07.2010.

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