

## Enhanced Endoscopic Imaging

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*Dr. Sharma is a member of the National Cancer Institute (NCI's) Barrett's esophagus working group. He has been actively involved in the major national and international gastroenterology organizations and is the Chair of American Gastroenterological Association Institute Education and Training Committee, Chair of the American College of Gastroenterology Public Relations Committee, Chair of the OMGE (World Organization of Gastroenterology) Outreach Committee and a member of the American Society Gastrointestinal Endoscopy Research Committee.*

Good morning. This is the session on Enhanced Endoscopic Imaging. I have selected the abstracts for presentation which I thought were either novel or have clinical application either immediately or in the near future. I have one abstract which I will discuss at the end on NOTES which is transluminal endoscopic surgery. The rest of the abstracts I will discuss are more clinically based.

Let's start off first with colonoscopy and colonoscopic imaging.

***Abstract 218737: "Screening colonoscopy with confocal laser endomicroscopy (CLE) for in vivo diagnosis of colorectal neoplasias"***

This is from a group in Mainz, Germany. Confocal laser endomicroscopy allows imaging of the different layers of the epithelium-subsurface microscopic imaging. In most of the current endoscopes, the light gets reflected from the superficial layer, and that is the image that we see. There are many different types of endoscopic imaging - magnification, chromoendoscopy and narrow band imaging. These are surface imaging, so it only gives you information about the surface tissue. What CLE does is to use multiple images which instead of just seeing the surface, you are able to see below the surface. This group performed colonoscopy in 280 patients using CLE. The goal of their study, in this case, was to determine if CLE can predict histology. Are we able to differentiate adenomas from hyperplastic polyps and cancers? The study design is simple; if you see a polyp, you take a biopsy and correlate it with histology. It is a simple sensitivity, specificity analysis, and that is how they presented their data. They found that CLE was very sensitive and very specific (94.1%) in making the diagnosis of neoplastic polyps. The only

side effect was transient skin discoloration. There are three major issues in colon cancer screening and surveillance that these imaging techniques can address: The first issue is polyp detection. Can we improve the miss rate? The second issue to address is distinguishing hyperplastic versus tubular adenomas. If we could accurately recognize a hyperplastic polyp, we can just leave it alone. We will reduce needless biopsies. The third issue is related to the tools. Can we get a simpler instrument and can we differentiate adenoma versus cancer? Confocal laser endomicroscopy is commercially available. Do all of us go out, buy and start using it? I think, at this time, it needs to be evaluated further.

**Abstract 221701: “The Aer-O-Scope™ OmniVision System, A 360° panoramic view of the colon”**

The Aer-O-Scope™ is a disposable, self-propelling, self-navigating endoscope. The same group of investigators published an article in which they studied this device in 12 humans and it was successful in reaching the cecum in 10. They have made some changes so that the scope provides a 360° view. The scope consists of an introducer with a balloon and on the top of the balloon is a camera. There is a cable connected to a foot pedal. In this system, you pass the introducer into the rectum and inflate the balloon. The balloon stays in the rectum and it is fixed at the anus to prevent any air leakage from the colon. The balloon is filled with CO<sub>2</sub> and as the balloon propels upwards it will carry this cable along with it. The camera provides a 360° view. The 360° view allows viewing behind the folds addressing one of the miss rate issues that we discussed. This is an animal (pig) model study to see if you can get adequate images. The hope would be in the future that a nurse practitioner or physician assistant or somebody else can do the procedure as this self propels to the cecum, taking pictures along the way. The cable is connected to a workstation with a laptop so you can look at the images. In the feasibility trial they were able to reach the cecum in 10 out of the 12 patients; most without sedation. They followed this procedure with a standard colonoscopy and found some red marks along the way probably caused by pulling the cable and by some friction. They did not see any tears, bleeding or perforation. It appears at least these preliminary data are very promising. If some device like this becomes available in the future you can see how it may impact your practice.

**Abstract 225454: “Detection and classification of adenomas using high-resolution endoscopy, video autofluorescence imaging and narrow band imaging incorporated in one colonoscope”**

This study addresses two issues: can we detect more polyps and if we detect more polyps, can we identify the histology? This is a prototype endoscope not commercially available. It includes white light endoscopy for high resolution endoscopy (HRE), autofluorescence imaging (AFI), and narrow band imaging (NBI) in one endoscope. AFI is based on the light tissue interaction. On AFI, in the colon and the esophagus you see “normal tissue” in green. The problem with AFI is the false positive rates; some of the “normal areas” may also appear blue. You may be able to avoid this if you combine AFI with narrow band imaging. NBI uses a filter which allows only narrow wavelengths of light to pass through, specifically the blue light. It has a predominance of blue light, but there is also a band of the green light. There have been studies with NBI showing that it can predict histology. The principle for multimodality imaging technique is that you do AFI, look at all the “abnormal areas” get close to these areas and then examine it with NBI. If NBI shows the mucosal pattern of a neoplastic polyp, then you can remove it. Forty-one patients have been studied. The main point of the study was that it is feasible/possible to combine HRE, AFI and NBI in the same scope. This is one of those techniques or combination techniques we need to be thinking about in the future.

**Abstract 226219: “Accuracy of wireless capsule endoscopy for the detection of Barrett’s esophagus”**

One of the key questions for the esophageal capsule endoscopy is whether or not you can screen for esophageal diseases. Specifically, this means screening patients with GERD (Barrett’s) and patients with

liver disease for esophageal varices. I am going to present some results on Barrett's esophagus. Our group examined 84 patients with GERD symptoms or with Barrett's esophagus. Three of them were unable to swallow the capsule, and in three patients, the images were not interpretable. The sensitivity and specificity of PillCam™ for short segment were 70% and 86%. For long segment Barrett's (greater than 3 cm), the accuracy was much higher, closer to 90%. For short segments (less than 3 cm), the sensitivity and specificity were 67% and 86% respectively. As you know most of the patients that we see in our practice are patients with short segment Barrett's. In short segment, it did not perform as well as it did in long segment Barrett's.

It appears that for capsule endoscopy of the esophagus, the results are not as great as initially suggested. I think having a diagnostic tool with 70% sensitivity and 86% specificity is still quite good. If you have a patient who does not want to take a day off from work or insists on an unsedated procedure, this may be appropriate. This gives you more information. You can better inform the patient regarding the accuracy of the procedure. The technology may need to be refined further. This takes about 14 frames a second; maybe that is not good enough. In some of these photographs we were unable to look at the GE junction carefully because there was a lot of saliva (bubbles). Maybe we need to prep the patient in a different way. These data inform us that yes, we have made a new tool but we need to keep working on improving it.

***Abstract 226090: "Clinical utility of narrow band imaging (NBI) endoscopy in patients with gastroesophageal reflux disease (GERD)"***

I discussed narrow band imaging earlier. At the GE junction, using standard endoscopy, the transition between the squamous and the columnar mucosa is from white to red. When you switch to narrow band, the columnar or stomach mucosa appears more brown whereas the white squamous mucosa appears a little bit more pale. Standard upper endoscopy is insensitive for making a diagnosis of reflux disease because the majority of the patients will have a "normal" endoscopy. Now we know that some of these patients have reflux disease. It's just that we are unable to see erosions. Are there subtle findings that can be seen by NBI, not seen by standard endoscopy? In a pilot study, we evaluated two patients with erosive esophagitis, two controls with no reflux symptoms (this was done by two validated questionnaires) and two patients with non-erosive reflux disease and performed narrow band imaging. We found linear vessels in the distal esophagus and if you magnify, each one of those vessels will have a capillary loop, not seen by standard endoscopy. In the pilot study we found that patients with GERD had IPCLs that were much thicker, more dilated and increased in number. We also found small erosions and increased vascularity at the squamocolumnar junction within the mucosa not seen by standard endoscopy. As the next step, we compared NBI to standard endoscopy in 48 GERD patients and 24 controls. The table in the abstract highlights the findings. For example, tortuosity of the IPCL was found in 84% of patients with GERD and in 38% of the controls. Microerosions were found in half of the patients with GERD but in none of the controls. Perhaps soon, we will be able to enhance our diagnostic skills and look with standard endoscopy, then switch to narrow band imaging and look for any of these criteria if the patient does not have erosive esophagitis.

***Abstract 225209: "High-resolution endoscopy and the additional value of chromoendoscopy in the evaluation of duodenal polyposis in FAP patients"***

This group of investigators from the Netherlands studied patients with familial adenomatous polyposis (FAP) and evaluated the duodenum with high-resolution endoscopy (HRE) followed by chromoendoscopy to assess the number of polyps and graded them using the Spiegelman score. Chromoendoscopy did not add much to high-resolution endoscopy. It appears that in FAP patients a good examination using high-resolution endoscopy is the key.

***Abstract 224819: “Natural orifice transluminal endoscopic surgery (NOTES) cholecystectomy: A transcolonic survival study in a porcine model”***

Natural orifice transluminal endoscopic study (NOTES) is an evolving field. Transgastric cholecystectomy has been studied, but is technically difficult using current technology. The authors performed transcolonic cholecystectomy in pigs. They prepped the animals by giving them enemas and antibiotics, Betadine, etc., passed the endoscope into the colon, made an incision with a needle knife, entered the peritoneum, removed the gallbladder, closed with clips and followed the animals for two weeks. Four of five pigs survived two weeks. In the animal that died, they were unable to close the needle knife incision completely and the animal developed peritonitis. The reason I am reviewing this abstract is not because any of us will be doing this in the near future but I think we will need to keep an eye on this topic. All of us will be hearing more and more about this in the years to come.

Thank you.

## Abstracts Discussed

### **218737: Screening colonoscopy with Confocal Laser Endomicroscopy (CLE) for in vivo Diagnosis of Colorectal Neoplasias.** *Ralf Kiesslich, Martin Goetz, Arthur Hoffman, Katharina Lammersdorf, Constantin Schneider, Michael Vieth, Manfred Stolte, Peter R Galle, Markus F Neurath*

Introduction: Confocal laser endomicroscopy (CLE) allows subsurface, microscopic imaging of living cells in colonic tissue in vivo. The aim of the present study was to assess the potential of in vivo confocal laser colonoscopy for prediction of histology during screening colonoscopy for colorectal cancer. Methods: Patients with informed consent designated for screening colonoscopy were enrolled in the study and underwent total colonoscopy with CLE (Optiscan, Australia; Pentax, Japan; excitation of 488nm argon ion laser; detection >515 nm; optical slice thickness 7µm; lateral resolution 0.7µm; frame rate 0.8 or 1.6 frames/sec with 1024x1024 or 1024x512 pixels). After reaching the cecum, a fluorescent contrast agent (fluorescein) was administered intravenously. During withdrawal of the endoscope, standardized locations (right, transverse colon, rectum) and every circumscribed lesion was examined by using the confocal microscope (fluorescence technique), afterwards biopsies were taken. Confocal images were graded according to the confocal pattern classification for the presence of neoplastic changes and compared with final histology. Results: 280 patients were included in the study. 112 colonic lesions (34 non-neoplastic, 65 adenomas, 9 adenomas with high-grade dysplasia, 4 cancers) larger than 5mm could be endoscopically diagnosed. By the use of CLE, different cellular structures, capillaries and connective tissue limited to the mucosal layer could be identified. Neoplasia could be prospectively predicted by the use of confocal pattern classification with high accuracy (Sensitivity 98.7%; Specificity; 94.1%; Accuracy: 97.3%). All patients developed a transient discoloration of the skin after fluorescein application. However, no further side effects were noted. Conclusions: In this largest prospective study on CLE carried out so far, confocal laser endomicroscopy (CLE) emerged as a safe and well tolerated additional diagnostic option for screening colonoscopy. Endoscopically identified colonic lesions can be microscopically graduated during ongoing colonoscopy and neoplasias can be predicted with high accuracy. Thus, in vivo histology can be used to target endoscopic therapy or biopsies.

### **221701: The Aer-O-Scope™ OmniVision system, A 360° Panoramic View of the Colon**

*Douglas Rex, Thomas Roesch, Bernard Levin, Jorje Pfefer, Nadir Arber*

The Aer-O-Scope™ (GI View, Ramat Gan, Israel) is a disposable, miniaturized, self-propelling, self-navigating, endoscope. In a recent human study the cecum was reached in 10 of 12 patients (Vucelic et al, Gastro 2006). The Aer-O-Scope™ includes an advanced vision system with two simultaneous scanning views that provide complete coverage of the entire surface of the colon. A standard front view system (90° forward view) is similar to a conventional endoscope, while a novel and unique imaging system provides a 360° panoramic view of the colonic surface, both in front and behind the scanner device (the OmniView) [Fig. 1]. The OmniView mechanism enables detailed inspection of the entire colon surface area, including those areas behind mucosal folds where polyps may be missed. The electro-optical capsule size is 15 mm OD x 1.5mm long containing a CMOS based digital camera. Its spatial resolution is greater than 1mm within the FOV and the depth of view is from contact up to ~100mm which is adequate for all segments of the insufflated colon. The tip is embedded within a low pressure hydrophilic coated vehicle balloon. This balloon has two functions: it is the moving part of the Aer-O-scope, propelled by gas pressure and it also serves as the imaging center of the device. The capsule is covered by a transparent dome containing the optical lenses protruding from the balloon's front end. White LED's with automatic intensity control provide illumination. The OmniVision system was tested in thirty young female pigs. In all of the Aer-O-scope examinations clear and sharp visualization of the colonic mucosa, similar to that obtained during conventional colonoscopy, was achieved. High resolution images from the digital video camera were received, processed and displayed in real time on a PC screen and digitally recorded.

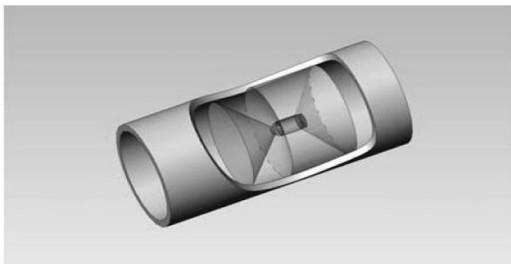


Fig. 1: Simultaneous Frontal and OmniVision Fields of View [FOV]

**225454: Detection and Classification of Adenomas Using High Resolution Endoscopy, Video Autofluorescence Imaging and Narrow Band Imaging Incorporated in One Colonoscope.** *Evelien Dekker, Mohammed A Kara, Christine C Cohen, James Hardwick, Johan Offerhaus, Bergman J Jacques, Paul Fockens*

**INTRODUCTION:** Video autofluorescence imaging (AFI) and narrow band imaging (NBI) are novel techniques that may improve the detection and classification of colonic polyps. In a recent prototype, high resolution endoscopy (HRE) has been combined with AFI and NBI (Olympus, Tokyo, Japan). **AIMS & METHODS:** The aim was to evaluate the feasibility and efficacy of HRE, AFI and NBI for the detection and classification of adenomas. The prototype used in this study enables switching between HRE, AFI and NBI by using two knobs on the handle of the endoscope. During AFI, blue light is used for autofluorescence excitation and a narrow band of green light is used for reflectance. During NBI, narrowed red, green and blue light bands, with a higher intensity of blue light are used for excitation, enabling optimal visualization of the mucosal patterns without the use of stains. We enrolled patients attending for surveillance colonoscopy because of prior adenoma(s) or a family history for CRC. Segmental examination of the colon during withdrawal was performed using HRE and AFI in a randomized sequence. NBI was used to classify the pit-patterns of polyps according to the Kudo classification. Lesions were photographed using all three modalities prior to polypectomy or biopsy. Procedures were performed by 2 colonoscopists and the pathologists were blinded to the findings with AFI and NBI. **RESULTS:** Up to date, 41 patients were enrolled in this ongoing study (22 males, mean age 54 yrs SD 15). A total of 106 polyps (56 adenomas) were detected in 25 patients. In patients examined with HRE first (N=21), 43 polyps were detected with HRE (24 adenomas) and 12 additional polyps (7 adenomas) were detected with AFI; 17 of the 24 adenomas detected with HRE were also suspicious on AFI. In patients examined first with AFI, 31 polyps were detected with AFI including 15 adenomas and 20 additional polyps (10 adenomas) were detected with HRE. The table below shows the diagnostic test values for AFI, NBI and the combination of both for the detection and classification of adenomas. **CONCLUSION:** The consecutive use of high resolution endoscopy (HRE), video autofluorescence imaging (AFI) and narrow band imaging (NBI) incorporated in one colonoscope is feasible. HRE and AFI increase the detection rate of adenomas and NBI can be used to classify polyps and diagnose adenomas without the need for staining solutions. The combination of AFI and NBI may improve the diagnostic accuracy for adenomas.

Technique	Sensitivity	Specificity	Positive predictive value	Negative predictive value
AFI (detection technique)	76%	33%	47%	84%
NBI (classification technique)	80%	75%	67%	85%
AFI-NBI (detection/ classification)	76%	81%	73%	84%

**226219: Accuracy of Wireless Capsule Endoscopy for the Detection of Barrett’s Esophagus.** *Prateek Sharma, Amit Rastogi, Romeo Esquivel, Krishna Gurram, Sachin Wani, Ajay Bansal,<sup>1</sup>Srinivas R Puli, April Higbee, Lisa Camargo, Richard Sampliner*

**Introduction:** The initial step in the diagnosis of Barrett’s esophagus (BE) requires an upper endoscopy to document the presence of a columnar lined distal esophagus (suspected BE), followed by biopsies from the columnar segment. The availability of a wireless esophageal capsule (Pillcam ESO) allows the recording of images from the esophagus and can be potentially used as an office based screening tool in patients with GERD. **Aim:** To compare esophageal capsule to standard upper endoscopy for the detection of endoscopic Barrett’s esophagus. **Methods:** This study was conducted at 2 sites utilizing standardized methodology, data collection and analysis. Patients with chronic GERD and BE were prospectively evaluated; all patients initially underwent capsule endoscopy followed by standard upper endoscopy. The esophageal capsule is similar to the small bowel capsule, but acquires images from both ends (2 cameras) of the device at a rate of 7 frames/sec/camera. The quality of the images were graded from 1-5 (not scoreable-excellent). Capsule images were analyzed by investigators blinded to the upper endoscopy findings; sensitivity and specificity of these findings were then analyzed using the standard endoscopy findings as the gold standard. **Results:** Eighty-four patients were initially enrolled in the study, 3 were unable to swallow the capsule, whereas images from 3 patients could not be evaluated. Data from 78 patients were available for analysis; mean age of 56.9+12.3 years; 71 males. By standard endoscopy, BE was suspected in 41 patients; 27 with short BE (<3 cm) and 14 with long BE (>3 cm). The mean BE length was 3.17 cm. The sensitivity and specificity of esophageal capsule endoscopy for the detection of suspected BE were 73% and 86% respectively; sensitivity and specificity for the detection of short BE were 67% and 86% and for long BE were 86% and 86% respectively. The quality of the images did not contribute to the false positive/negative results. No adverse events were noted using capsule endoscopy. **Conclusions:** Esophageal capsule endoscopy can be safely performed in the majority of GERD patients undergoing screening upper endoscopy. The sensitivity and specificity of capsule endoscopy for the diagnosis of suspected BE are high especially for long BE. Future studies should test inter observer variability and the learning curve in the reading of images and steps to further improve the diagnostic accuracy capsule endoscopy.

**226090: Clinical Utility Of Narrow Band Imaging (NBI) Endoscopy In Patients With Gastroesophageal Reflux Disease (GERD).** Prateek Sharma, Amit Rastogi, Ajay Bansal, Srinivas R Puli, Sharad Mathur

Background : NBI is a novel imaging technique that uses narrow band filters (415, 445, 500 nm) and higher intensity blue light (smaller wavelength-less penetration) to show details of esophageal mucosal and vascular patterns. Aim: To compare findings seen only on NBI in pts with GERD and controls and to calculate sensitivity and specificity of these findings for GERD diagnosis. Methods: Reflux pts and controls without GERD symptoms filled 2 validated questionnaires (GERQ and RDQ). Then, distal esophagus was examined by white light followed by using NBI endoscope(Olympus GIFQ240Z, and 115 X) by a single investigator. Features seen only by NBI were noted:number, dilation and tortuosity of intra-papillary capillary loops (IPCL), micro erosions (ME), increased vascularity at squamocolumnar junction (SCJ), columnar islands (CI) in distal esophagus (CI) and ridge villous pattern (R/V) below squamocolumnar junction. NBI images were then evaluated by another blinded endoscopist. IPCLs were classified as increased, dilated or tortuous and other findings noted to be present or absent. Findings were compared using Fisher’s exact test; sensitivity and specificity of findings individually and in combination for GERD diagnosis were calculated. Results:72 pts were prospectively evaluated (mean age 60 yrs,67 males)- 48 GERD and 24 controls. NBI revealed a striking contrast of squamous and columnar mucosa at SCJ. Increased number, dilation and tortuosity of IPCLs, presence of micro-erosions and increased vascularity at SCJ were significantly higher in GERD pts compared to controls (Table 1). Accuracy of their combinations are shown in Table 2. Conclusion: NBI shows details of mucosa and vascularity in distal esophagus - IPCLs, micro erosions and increased vascularity at SCJ being significantly higher in GERD pts vs. controls. Also, distinctive features like increased number, dilation or tortuosity of IPCLs have a high accuracy for GERD diagnosis. These findings support an emerging role of NBI in GERD diagnosis

Table 1

	GERD	Controls	p	Sens.	Specificity
ICPL Increased	65.2 % (30/46)	15.3 % (4/26)	0.0005	65.2%	84.6%
ICPL tortuous	83.7 % (36/43)	38.4 % (10/26)	0.001	83.7%	61.5%
ICPL Dilated	81.4 % (35/43)	15.3 % (4/26)	<0.0001	81.4%	84.6%
ME	50 % (23/46)	0 % (0/26)	<0.0001	50%	100%
SCJ	43.4 % (20/46)	7.6% (2/26)	0.006	43.4%	92.3%
R/V	23.9% (11/46)	11.5% (3/26)	0.36	23.9%	88.4%
CI	39.1 % (18/46)	34.6%(9/26)	0.08	39.1%	57.7%

Table 2

	Sensitivity	Specificity
Increased or Dilated or Tortuous IPCL	88.7%	61.5%
Increased + Dilated + Tortuous IPCL	60.5%	92.3%
Increased or Dilated or Tortuous IPCL or ME	93%	61.5%
Increased + Dilated + Tortuous IPCL + ME	32.6%	100%

**225209: High-Resolution Endoscopy and the Additional Value of Chromoendoscopy In The Evaluation Of Duodenal Polyposis In FAP-Patients.** Evelien Dekker, Jan Dees, Lisbeth Mathus-Vliegen, Jan Werner Poley, Johan Offerhaus, Joep Bartelsman, Ernst Kuipers, Paul Fockens

Introduction: Duodenal polyps occur in approximately 90% of all patients with familiar adenomatous polyposis (FAP). An estimated 5% of them develop duodenal cancer, nowadays being the leading cause of death in FAP-patients. Endoscopic surveillance of the duodenum has become standard care in these patients, making use of the Spigelman classification. This classification includes number, size and histology of duodenal polyps and correlates with the risk of developing duodenal cancer. Guidelines for endoscopic surveillance have been developed in which interval is dependent on the Spigelman-classification. Since the introduction of these guidelines, the quality of endoscopic imaging has dramatically improved and chromo-endoscopy has further enhanced our ability to detect small polyps. Aim: To investigate the use of high-resolution endoscopy and the additional value of chromoendoscopy in the evaluation of duodenal polyposis in FAP-patients. Methods: All consecutive FAP-patients scheduled for a surveillance endoscopy in 2 academic centers underwent gastroduodenoscopy with high-quality forward- and sideward-viewing endoscopes. After scoring the number and size of polyps in the duodenum (bulb, D1 and DII separately), indigocarmine 0.5% was sprayed onto the mucosa and the polyps were scored again. Biopsies were

taken from the larger lesions and the papilla and were evaluated by an expert pathologist. Spigelman classifications were assessed for both procedures. Results: A total of 47 endoscopies were performed in 39 patients (19 men, mean age 48 yrs) were examined. Before the application of dye, in 37 patients (95%) duodenal polyps were seen. Spigelman-classifications were: stage 0, 2 patients (5%); stage I, 2 patients (5%); stage II, 9 patients (23%), stage III, 13 patients (33%) and stage IV, 13 patients (33%). The papilla was enlarged in 21 patients (54%); biopsies revealed dysplasia in 18 (46%). Chromoendoscopy detected more duodenal polyps in 13 procedures (mean # of polyps 27 vs 30,  $p=0.03$ ) and maximum size of the polyps increased in 5 (15 vs 16 mm, NS). The total number of points for the Spigelman-classification was increased in 7 procedures. However, this resulted in an increased Spigelman-classification in only 3 (6.4%). Discussion: Compared to historic endoscopic studies evaluating duodenal polyposis in FAP-patients, the use of high-resolution endoscopes results in increased polyp detection and subsequently a higher Spigelman-score. Although chromoendoscopy detected significantly more polyps, this resulted in a higher Spigelman stage in only 6% of endoscopies and therefore its additional value seems to be limited compared to high-resolution endoscopy.

**224819: Natural Orifice Transluminal Endoscopic Surgery (NOTES) Cholecystectomy: A Transcolonic Survival Study in a Porcine Model.** *Reina D Pai, Derek G Fong, Douglas S Fishman, David W Rattner, Christopher C Thompson*

**Background and Aim:** Transgastric cholecystectomy has been reported in two non-survival studies which detail substantial technical limitations and only a 33% success rate when limited to one gastric exit site despite the use of a multiple channel locking endoscope. The aim of this study was to demonstrate feasibility and evaluate technical limitations of a transcolonic approach to cholecystectomy. **Methods:** Under general anesthesia, adult Yorkshire pigs were prepped with multiple tap water enemas, per-anal instillation of an antibiotic and betadine rinse, and external betadine scrub. A sterile dual-channel endoscope (Olympus™) was introduced through the anus and advanced through a 2 cm, anterior, trans-colonic incision created by a needle knife approximately 15 - 20 cm from the anal verge. Upon completion of intra-abdominal exploration and identification of all major upper abdominal organs, the cystic duct and artery were dissected and ligated with endoclips. Dissection of the gallbladder away from the liver was achieved using hot biopsy forceps, snare tip, prototype endoscopic scissors and an insulated-tip needle knife. The gallbladder was successfully removed with hot snare cautery. The gallbladder fossa was then lavaged with sterile water, re-examined and additional cautery or endoclips were applied for hemostasis or closing of defects. At the conclusion of each procedure, the colonic incision was closed using endoloops and/or endoclips. **Results:** The animals were survived for two weeks followed by elective termination and necropsy. Four of the five animals flourished in the post-operative period demonstrating appropriate feeding and activity patterns as well as stable weights or weight gains. The colonic incision site in all 4 animals healed completely, however external adhesions were appreciated. In the last animal complete closure of the colonic incision site was not possible and a small 4mm residual defect remained. The animal was survived for 48 hours but then sacrificed due to concerns of peritonitis. Pathology from all 5 subjects subsequently confirmed the resected organs as gallbladders. **Conclusions:** The transcolonic approach provides improved visual exposure of the gallbladder and scope stability when compared to the transgastric approach. This study demonstrates the technical feasibility of transcolonic organ resection via a single incision. The one complication appeared secondary to inadequate incision closure and not related to the organ resection. For this approach to be translated to humans, a sterile conduit, secure closure device and better instruments for triangulation are necessary.

**Additional Reading: Enhanced Endoscopic Imaging**

**221631: Chromoscopic Magnifying Colonoscopy for Colorectal Cancer Screening: Is It A Better Tool?** *Hulya Cetinkaya, Ali Tuzun,<sup>1</sup> Mehmet Bektas, Murat Toruner, Arzu Ensari, Irfan Soykan, Ali Ozden*

Background: Conventional colonoscopic examination has been reported to be one of the most commonly used techniques in colorectal cancer screening. In recent years, it has been shown that chromoscopic magnifying colonoscopy combined with chromoscopic agents permits early detection of neoplastic colorectal lesions, especially flat and depressed types which are known to be somehow difficult to detect with conventional colonoscopy. We therefore conducted a study to examine the role of chromoscopic magnifying colonoscopy in colorectal cancer screening. Subjects and Methods: 75 asymptomatic subjects over 50 years old who were admitted to Ankara University Medical School, Gastroenterology department for colorectal cancer screening were recruited into this study. Following an appropriate sedation with either propofol or midazolam, “back to back colonoscopy” was performed to each subject. Conventional pan-colonoscopy with targeted biopsy was performed initially followed by magnifying colonoscopy for chromoscopic evaluation of recto-sigmoid area. Additional biopsies were obtained as well during magnifying colonoscopy from additional suspicious lesions. Results: Thirty patients were male and forty-five subjects were female with a median age of 58 years (range: 50-60 years). Mean colonoscopy time (both first phase “conventional” and second phase “back to back” was  $35.3 \pm 13.3$  minutes. Mean volume of 0.4% Indigo Carmine was  $9.9 \pm 5.3$  milliliters. Overall, forty-one suspicious lesions were detected in 23 subjects (30.1%), following indigo carmine dye spraying and 62 additional abnormalities were detected in 48 subjects (64%). Thirteen of the additional abnormalities were serrated adenomas, while thirty lesions were flat elevated lesions, eighteen lesions were polypoid lesions and one of them was a

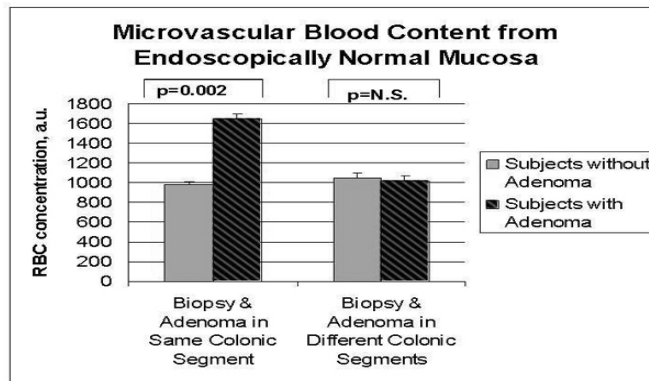
depressed lesion. Conclusion: Chromoscopic magnifying colonoscopy might be a better technique than conventional colonoscopy in detecting colorectal malignant and/or pre-malignant lesions. However, studies could be performed to evaluate cost effectiveness of this technique in colorectal cancer screening before using it in population screening.

**223265: Antibody Aided Confocal Laser Endomicroscopy Allows Molecular Imaging of Colorectal Lesions In Humans.** Ralf Kiesslich,<sup>1</sup> Martin Goetz, Brigitte Bartsch, Katharina Lammersdorf, Arthur Hoffman, Constantin Schneider, Manfred Vieth, Manfred Stolte, Peter R Galle, Markus F Neurath

Introduction: Confocal laser endomicroscopy (CLE) enables in vivo histology of the mucosal layer with cellular and subcellular resolution during ongoing endoscopy. Aim of the current study was the evaluation of distinct fluorescein labeled antibodies for immediate molecular imaging and characterisation of different colonic lesions in humans. Methods: Patients with known colorectal adenomas and/or aberrant crypt foci were enrolled in the study and underwent total colonoscopy with CLE (Optiscan, Australia; Pentax, Japan; excitation of 488nm argon ion laser; detection >515 nm; optical slice thickness 7µm; lateral resolution 0.7µm; frame rate 0.8 or 1.6 frames/sec with 1024x1024 or 1024x512 pixels). After reaching the colonic lesions, a fluorescent contrast agent (fluorescein) for transient staining of vessels and crypts was administered intravenously and endomicroscopic evaluation was performed using the confocal pattern classification. Endoscopic resection was performed and the resected specimens were immediately incubated with FITC-labeled Anti-EGFR (n=4), Anti-CD44v6 (n=2) or Anti-Actin (n=1) antibodies (dilution; 1:50) for 30 minutes. Lesions were re-assessed ex vivo with CLE-endoscope after a thorough washing step. Subsequently, conventional histology and ex vivo immuno-staining on resected specimens was performed to correlate histology with the CLE findings. Results: Antibody aided confocal laser endomicroscopy specifically highlighted the corresponding epitopes on the cell surface. Cellular and subcellular detail could be seen at high resolution. Aberrant crypt foci were readily visible and highlighted by staining with Anti-CD44v6 antibodies. EGFR receptors could be quantified at the cell membrane with CLE and were confirmed histologically by ex vivo immuno-staining. Anti-Actin antibodies aimed at intracellular targets showed no contrast by CLE in the absence of cell permeability and served as a negative control. Conclusions: Confocal laser endomicroscopy enables molecular imaging in humans at high resolution. Resected colonic lesions can be immediately analysed and characterised for the presence of different receptors. Thus, antibody aided CLE may offer a rapid analysis of colorectal lesions with important implications for targeted tumour therapy.

**222410: Spectroscopic Microvascular Assessment from the Endoscopically Normal Mucosa for Colon Adenoma Identification.** Hemant Roy, Yang Liu, Young Kim, Michael Goldberg, Nahla Hasabou, Vladimir Turzhitsky, Mohammed Jameel, Eric Elton, Vadim Backman

Developing technology to decrease polyp miss rate (estimated to be 15% in expert hands) is of great importance from both a clinical and medicolegal perspective. Members of our group have been pioneered light scattering technologies for diagnosis of dysplastic lesions (Nature 2000, Nature Med 2001). We have recently developed four dimensional elastic light scattering fingerprinting (4D-ELF) (Gastro 2004), which allows unprecedented ability to quantitatively probe the mucosal micro-circulation. Using 4D-ELF, we have reported that microvascular blood content was increased in the histologically normal colonic mucosa in experimental CRC models (Gut 2005). In the present study, we assessed whether increased microvascular blood could aid in localization of colonic neoplasia. METHODS One hundred subjects undergoing colonoscopy were recruited and had two biopsies taken from the in the endoscopically-normal mucosa (at least 5 cm from any adenomas) cecum, mid-transverse colon and rectum. Fresh biopsies were subjected to 4D-ELF analysis. Microvascular (within 50 µM of tissue surface) were analyzed by an investigator blinded to colonoscopic findings. RESULTS As demonstrated in the figure, microvascular blood content was demonstrated to be markedly elevated in the endoscopically normal mucosa of patients who harbored adenomas in the respective colonic segment (right colon, transverse or left colon). The sensitivity, specificity, positive and negative predictive value of increased microvascular blood was 89%, 100%, 100% and 75%, respectively. CONCLUSIONS: We demonstrate, for the first time, that microvascular blood content in the endoscopically normal mucosa could identify patients at risk for colonic neoplasia and aid in localization. In the future, we envision that this approach (with a probe) could determine which colonic segments warrant extra endoscopic scrutiny (including possibly chromoendoscopy).



**220435: Evaluation of autofluorescence colonoscopy for the detection and diagnosis of colonic polyps.** Audrey L McCallum, John T Jenkins, Derek Gillen, Richard G Molloy

**Introduction:** Autofluorescence (AF) has been developed to enhance conventional white light (WL) endoscopy in the diagnosis of neoplastic lesions of the GI tract. It is based on the stimulation of endogenous fluorophores and produces a pseudo-colour image of tissue. Metaplastic polyps are common and do not need to be treated, whereas adenomatous polyps carry a neoplastic potential. It would therefore be helpful to be able to distinguish between adenomatous polyps and metaplastic polyps when performing colonoscopy. **Aim:** To evaluate AF for the endoscopic detection and differentiation of colorectal polyps. **Methods:** Patients were invited to attend for colonic assessment with both AF (Xillix LIFE-GI) and WL colonoscopy. The intensity of autofluorescence (AI) is quantified automatically and readings, pictures and biopsies were recorded of any visible pathology or areas of high AF. The biopsy results were analysed and an AI reading for each biopsy site obtained by subtracting the actual AI reading from the background reading for the rectum of each patient. **Results:** A total of 47 patients were assessed with AF and WL colonoscopy. A total of 33 polyps were detected (19 adenomatous and 14 metaplastic polyps). It was found that adenomatous polyps had higher AI readings (median 0.53, IQR 0.15-1.05), than metaplastic polyps (median 0.09, IQR 0.06-0.10). [Mann Whitney U-test:  $p=0.00003$ ] **Conclusion:** These early data suggest that autofluorescence colonoscopy has the potential to differentiate between metaplastic and adenomatous polyps and may have a role as a new diagnostic technique for the improved detection of colonic dysplasia and early malignancy.

**220869: Automated Virtual Microcopy Of Specimens from Gastric Biopsies Can Accurately Diagnose Gastritis and Adenocarcinoma.** Levente Ficsor, Viktor Varga, Lajos Berczi, Pal Miheller, Attila Tagscherer, Mark Li-cheng Wu, Bela Molnar, Zsolt Tulassay

**Background:** Automated virtual microscopy of specimens from gastrointestinal biopsies is based on cytometric parameters of digitized histologic sections. Diagnoses rendered by automated virtual microscopy are potentially more reproducible and more efficient than diagnoses rendered by conventional optical microscopy. To our knowledge, cytometric parameters of gastritis and of adenocarcinoma have yet to be fully characterized. Our objective was to classify gastritis and adenocarcinoma based on cytometric parameters. We hypothesized that automated virtual microscopy using this novel classification can reliably diagnose gastritis and adenocarcinoma. **Methods:** Routinely processed hematoxylin-and-eosin-stained histologic sections that showed normal mucosa (14 specimens), gastritis (25 including 6 non-atrophic, 17 atrophic, 12 intestinal metaplasia), and adenocarcinoma (30 specimens) were scanned and digitized at high resolution (0.3  $\mu\text{m}/\text{pixel}$ ) using the Zeiss Mirax Scan (Carl Zeiss Jena GmbH, Germany, Jena). Thirty-eight cytometric parameters based on density and morphometry were applied to glands, foveolae, and superficial epithelium. Twelve cytometric parameters based on cytologic detail were applied to individual cells. Statistical analysis was performed using Statistica 6.0 software (StatSoft Inc., USA). **Results:** Statistically significant differences in cytometric parameters for normal mucosa, gastritis, and adenocarcinoma were found ( $p<0.05$ ). The most discriminatory parameter was the ratio of the total number of cells to the number interstitial cells (normal mucosa  $1.43\pm 0.12$ ; gastritis  $1.23\pm 0.13$ ; adenocarcinoma  $1.1\pm 0.05$ ;  $p<0.01$ ). These differences correctly classified normal and gastritis cases versus adenocarcinoma (100%) with reasonable accuracy (86% overall). The different gastritis cases could be classified by 56% (atrophic gastritis), 86% intestinal metaplasia, 65% gastritis without atrophy and intestinal metaplasia, respectively. **Conclusions:** We describe a novel classification of gastric mucosa based on cytometric parameters. Automated virtual microscopy can be used to diagnose normal mucosa, gastritis, and adenocarcinoma with reasonable accuracy. Downstream classification of gastritis groups needs further alteration specific parameters to be included in the morphometric parameters.

**225526: Novel Technique In Understanding The Sequence of Biochemical Changes In Carcinogenesis Of Esophagus.** Geeta Shetty, Catherine Kendall, Neil Shephard, Nicholas Stone, Hugh Barr

Background: Most reports emphasise genetic changes in understanding the carcinogenesis sequence of esophageal adenocarcinoma. Biochemical changes occurring in carcinogenesis have not been evaluated to their full potential. We propose a technique, which helps to understand the biochemical events involved in the development of malignancy in Barrett's esophagus. Methods: 70,404 Raman spectra were measured on 24 snap frozen endoscopic biopsy samples. Contiguous sections were stained with H&E for analysis by a consultant gastrointestinal pathologist. Mapping studies were performed on 20µm thick sections on CaF<sub>2</sub> slides with spectra measured at 100µm steps across the samples. Analysis of spectra was done in Matlab generating principal components and pseudocolour maps. Results: Using pseudocolour maps the lines of interest were selected representing the surface changes or understanding the depth profile of tissue (Figure 1). The spectra along the selected line were analysed for the relative concentration of different biochemical constituents using mathematical least fit square method. Marked variation in the distribution of oleic acid, actin, triolein, glycogen and DNA were seen. Conclusion: Raman spectroscopy is an optical diagnostic tool, which can be used to demonstrate the biochemical changes in carcinogenesis of esophagus and identify early disease. Work is in progress to develop an in vivo endoscopic probe for real time analysis.