Cellvizio®

probe-based Confocal Laser Endomicroscopy (pCLE) & needle-based Confocal Laser Endomicroscopy (nCLE)

See clearly, act faster





Physician Speaker Presentation - INT - V1.03 - Dec 2015



What is Confocal Laser Endomicroscopy ?



Transverse view Ex-vivo Microscopic Invasive Delayed imaging



The Confocal Laser Endomicroscopy technology





- **Probe**-based and **needle**-based microscope used during endoscopic procedures
- **Compatible** with existing **endoscopes** and endoscopic accessories
- Minimally invasive **microscopic images** of tissue, available in **real-time**
- Access the Gastro-Intestinal, Respiratory and Urinary systems
- Different probes for different indications

The Cellvizio® Systems are regulated Medical Device, CE marked (Class IIa - NB : LNE/G-MED) and FDA cleared; Cellvizio systems are intended to allow confocal laser imaging of the internal microstructure of tissues in anatomical tracts, i.e. gastrointestinal, respiratory or urinary, accessed through an endoscope or endoscopic accessories. These statements and the associated references to specific clinical studies, are not intended to represent claims of safety or effectiveness for detecting or treating any specific condition or disease state. Rather this information is intended to provide useful reference to selected published literature describing physician experiences with the associated clinical uses. These statements have not been reviewed, cleared, or approved by the U.S. FDA. Please note that the interpretation criteria are suggested descriptive features and do not represent definitive diagnostic landmarks and are a result of input from trained and well qualified person. Any diagnostic assessment should always be made by the attending physician, based on the evaluation of all sources of clinical, endoscopic and other relevant information. Please consult labels and instructions for use.



Real time microscopic imaging

3

⇒Probe appears on endoscopic image ➡Probe positioned in contact with mucosa





A wealth of applications



5 **Images obtained during research and clinical studies - these indications have not been cleared by regulatory authorities*

Main targeted indications in the Gastrointestinal Tract



- Barrett's Esophagus
- •Gastric Diseases
- Bilio-Pancreatic Strictures
- Pancreatic Cysts
- Colorectal Lesions
- Inflammatory Bowel Disease

Barrett's Esophagus



Objectives

To evaluate the sensitivity and specificity of pCLE added to white light endoscopy (WLE) for the detection of high grade dysplasia (HGD) and early cancer (EC)

Study Design

- Prospective multi-center randomized controlled study
- 5 centers (tandem design: 2 endoscopists at each center)
- Centralized pathology
- Evaluated 101 patients undergoing Barrett's Esophagus surveillance or treatment evaluation

Sharma P. et al., Real-time Increased Detection of Neoplastic Tissue in Barrett's Esophagus with probe-based Confocal Laser Endomicroscopy: Final Results of a Multi-center Prospective International Randomized Controlled Trial, GIE, 2011.



Non dysplastic BE

Dysplastic BE

Cellvizio DONT BIOPCE study 2/2

Results

Location based

ALL Locations (n=874) Prevalence = 7%	Sensitivity		Specificity	PPV	NPV	10	
WLE		34 %		93 %	43 %	90 %	٤
WLE or NBI	p=0.01	45 % —		88 %	38 %	91 %	e
WLE or pCLE		68 %	0.01	88 %	47 %	95 %	2
WLE or NBI or pCLE		76 %	p=0.01	84 %	43 %	96 %	

Patient based

ALL Patients (n=101)	Sensitivity	Specificity	PPV	NPV	Areas with HGD/EC missed	• A as
WLE	87 %	71 %	57 %	93 %	4 (13%)	as
WLE or NBI	97 %	56 %	49 %	98 %	1(3%)	• L AL
WLE or pCLE	94 %	67 %	56 %	96 %	2 (6%)	• [
WLE or NBI or pCLE	100 %	56 %	50 %	100 %	0 (0%)	39 [°]

Sharma P. et al., Real-time Increased Detection of Neoplastic Tissue in Barrett's Esophagus with probe-based Confocal Laser Endomicroscopy: Final Results of a Multi-center Prospective International Randomized Controlled Trial. GIE, 2011.





Addition of pCLE is twice as sensitive WLE alone, and 1.7 times as sensitive WLE & NBI to detect dysplasia

Use of pCLE resulted in detection of L HGD/EC patients (100% Sensitivity)

Jsing pCLE in addition to WLE & NBI, % of patients could be spared opsies completely (NPV = 100%)

Canto et al. Study 1/2

Objectives

To compare **HDWLE with random biopsy** (standard approach of Seattle protocol) with HDWLE + eCLE and targeted biopsy

Study Design

- Prospective multi-center randomized controlled study
- 5 centers
- Centralized pathology
- Evaluated 192 patients undergoing Barrett's Esophagus surveillance or referred for early neoplasia, randomized to Arm 1 (HDWLE + random biopsy) or Arm 2 (HDWLE + eCLE + targeted biopsy)



Canto M. et al., In vivo endomicroscopy improves detection of Barrett's esophagus-related neoplasia: a multicenter international randomized controlled trial. GIE, 2013

Results

• **Tripled diagnostic yield** of physical biopsies for neoplasia, with 22% of biopsies showing dysplasia for targeted sampling, compared to 6% for random sampling, while **decreasing the number of physical biopsies by 80%**

• Changed the treatment plan in 36% of patients

Location based

Per-biopsy analysis (n=978)	Sensitivity	Specificity	PPV	NPV	Accuracy
HDWLE	10 %	99 %	67 %	94 %	93 %
HDWLE with CLE	86 % ^{p<0}	.000193 %	65 %	p:=0.006 98 %	92 %

Patient based

11

Per-patient analysis (n=192)	Sensitivity	Specificity	PPV	NPV	Accuracy
HDWLE	40 %	98 %	75 %	90 %	89 %
HDWLE with CLE	95 % p<0.00	⁰⁰¹ 92 %	77 %	p:=0.005 98 %	93 %

S

Sensitivity for the detection of neoplasia in BE patients



Study results show that HDWLE + CLE targeted biopsies surpasses the PIVI threshold, supporting its use as an approach to BE surveillance:

Increased the Sensitivity for neoplasia detection from 40% to 95% Increased the NPV from 90% to 98%

Objectives

To evaluate the dysplasia detection rate in BE patients under surveillance for WLE with standard random biopsy (standard approach of Seattle protocol) and WLE + pCLE and standard random biopsy

Study Design

- Prospective single-center randomized controlled study
- Blinded gastrointestinal pathologist for the diagnosis of dysplasia
- Evaluated 100 patients undergoing Barrett's Esophagus surveillance, randomized to Arm 1 (HDWLE) + random biopsy) or Arm 2 (HDWLE + pCLE + random biopsy)



Results

The dysplasia detection rate was significantly higher in the pCLE **group** (28%) than in the HD-WLE group (10%) (p=0.04) • Biopsies could have been avoided in 58% of patients with a targeted biopsy approach, based on the **100% NPV of pCLE**

Per-patient analysis (n=100)	Sensitivity	Specificity	PPV	NPV	Diagnostic yield of biopsies	30
HDWLE		Not publis	10 %	20		
HDWLE + pCLE	100 %	83 %	67 %	100 %	28 % p=0.04	10

Dysplasia detection rate (diagnostic yield of biopsies)



HDWLE HDWLE + pCLE

Gastric Diseases

Objectives

To assess the **diagnostic yield** of magnifying Flexible Spectral Imaging Color Enhancement (ME-FICE) + pCLE for Gastric Intestinal Metaplasia (GIM) detection

Study Design

- Prospective, blind comparison of pCLE with ME-FICE (using light blue crest, large long crest and villous pattern as criteria) on gastric lesions
- Single center
- Evaluated 60 patients with previous histology confirmed as GIM undergoing a surveillance EGD
- Standard and 100x ME-FICE used for screening of lesions, and pCLE used to confirm the presence of GIM. ME-FICE and pCLE results then compared with final histopathology of biopsies

Pittayanon R. et al. Flexible Spectral Imaging Color Enhancement plus probe-based Confocal Laser Endomicroscopy for Gastric Intestinal Metaplasia Detection. Journal of Gastroenterology and Hepatology, 2013.

16

Pittayanon et al. Gastric Intestinal Metaplasia Study 2/2

Results

Adding pCLE to ME-FICE increases accuracy for the detection of Gastric Intestinal Metaplasia (GIM) to 92,5%

All locations (n=60)	Sensitivity	Specificity	PPV	NPV	Accuracy
ME-FICE	95.6 %	79.2 %	74.5 %	96.7 %	85.8 %
ME-FICE + pCLE	96.5 %	90.5 %	86.2 %	97.1 %	92.5 %

Gastric Intestinal Metaplasia, evidenced by the presence of goblet cells (arrows)



Accuracy of detection of GIM



Pittayanon R. et al. Flexible Spectral Imaging Color Enhancement plus probe-based Confocal Laser Endomicroscopy for Gastric Intestinal Metaplasia Detection. Journal of Gastroenterology and Hepatology, 2013.

Bok et al. Early Gastric Cancer Study 1/2

Objectives

To compare the accuracy of conventional endoscopic forceps biopsy and pCLE for the diagnosis of superficial gastric **neoplasia** before endoscopic resection

Study Design

- Prospective, blind comparison of pCLE imaging with forceps biopsy using endoscopic resection as reference standard
- Single center
- Evaluated 46 patients undergoing endoscopic resection of gastric lesions (54 lesions in total) post diagnostic evaluation with pCLE and biopsies of suspicious areas. Biopsy and pCLE results were then compared with final histopathology of specimens

Bok G.H. et al. The Accuracy of probe-based Confocal Endomicroscopy versus Conventional Endoscopic Biopsies for the Diagnosis of Superficial Neoplasia (with videos). Gastro-Intestinal Endoscopy, 2013.



Differentiated Gastric dysplasia adenocarcinoma

Undifferentiated adenocarcinoma

Bok et al. Early Gastric Cancer Study 2/2

Results

 Forceps biopsy misses cancerous lesions, with a sensitivity at 75% only

 Adding pCLE increases sensitivity and NPV of neoplasia detection in the stomach to >95%

• The **overall accuracy of forceps biopsy + pCLE reaches 98,1%**, compared to 85,2% for forceps biopsy alone

All locations (n=54)	Sensitivity	Specificity	PPV	NPV	Accuracy
Forceps Biopsy	75.0 %	100.0 %	100.0 %	73.3 %	85.2 %
pCLE	90.6 %	90.9 %	93.5 %	87.0 %	90.7 %
Forceps Biopsy + pCLE	96.9 %	100.0 %	100.0 %	95.7 %	98.1 %

Bok G.H. et al. The Accuracy of probe-based Confocal Endomicroscopy versus Conventional Endoscopic Biopsies for the Diagnosis of Superficial Neoplasia (with videos). Gastro-Intestinal Endoscopy, 2013.

20 %

100 %

80 %

60 %

40 %

Detection of gastric neoplasia



Forceps biopsyForceps biopsy with pCLE

Li et al. New pCLE Classification Study 1/2

Objectives

To propose a new probe-based confocal laser endomicroscopy (pCLE) classification of gastric pit patterns and vessel architecture, and to assess the accuracy and inter-observer agreement

Study Design

- Prospective, single center, blind evaluation of pCLE using biopsy as reference standard
- Two phase design:
 - Phase 1: establishment of a new pCLE classification based on 291 videos from 32 patients
 - Phase 2: Evaluation of 240 patients (1878 locations) using HDWLE and pCLE at 7 standardized locations + endoscopic suspected lesions. pCLE results were then compared with final histopathology of specimens
- Live pCLE evaluation by 1 endoscopist and blinded offline pCLE evaluation by 3 other endoscopists for Inter-Observer Agreement (IOA) calculation

Li et al. New pCLE Classification Study 2/2

Results

 New pCLE classification of pit patterns and vessel architecture in the stomach correlates well with histopathology, with specificities over 99% and sensitivities ranging from 89% to 92% for the diagnosis of Atrophic Gastritis, GIM and Gastric Neoplasia

 IOA "substantial" for the differentiation of neoplasia vs. nonneoplasia (K=0.70)

All locations (n=1878)	Sensi	tivity	Specificity		
pCLE diagnosis for:	Real-time	Offline	Real-time	Offline	
Atrophic Gastritis type 2b pit pattern	88.51 %	89.86 %	99.19 %	99.25 %	
GIM type 2C pit pattern	92.34 %	93.69 %	99.34 %	99.40 %	
Gastric Neoplasia type 3 pit pattern & vessel architecture	89.89 %	92.13 %	99.44 %	99.50 %	



Atrophic Gastritis







pCLE diagnosis of gastric lesions

Bilio-Pancreatic Strictures



Objectives

To evaluate the efficacy of pCLE for differentiating malignant from benign bilio-pancreatic stricture

Study Design

- Prospective observational multi-center registry (5 centers)
- Enrolled 102 patients, evaluated 89
- Probe introduced via cholangiopancreatoscope (CP) or catheter
- Clinical, ERCP, tissue sampling and pCLE data collected prospectively
- FU > 30 days until confirmation of malignancy, 1 year FU otherwise



A: Cholangioscopical image of pCLE probe attached onto the mucosa of the common bile duct

B: pCLE image of malignant mucosa, showing epithelial structures with thick dark bands

C: pCLE image of benign mucosa, showing a reticular pattern with thin dark bands

ERCP Registry Study 2/2

Results

- Out of **40** malignant patients in the cohort:
 - pCLE detected **39** malignant patients in real time
 - Index pathology detected **18** malignant patients
- In terms of overall accuracy of the ERCP examination, the added value of pCLE was superior to that of tissue sampling

All patients (n=89) Prevalence= 45%	Sensitivity	Specificity	PPV	NPV	Accuracy
Tissue sampling	45 %	100 %	100 %	69 %	75 %
pCLE	98 % p<0.001	67 %	71 %	97 % p<0.001	81 %
ERCP & Tissue sampling	40 %	100 %	100 %	67 %	73 %
ERCP & pCLE	85 %	94 %	92 %	89 %	90 %

Meining A, et al., Direct visualization of indeterminate pancreaticobiliary strictures using probe based Confocal Laser Endomicroscopy - A multi-center experience. Gastrointestinal Endoscopy. GIE 2011

Sensitivity of detection of biliopancreatic malignancy



Objectives

The Paris Classification is a refinement of the existing Miami Classification to **improve the** specificity of pCLE for diagnosing benign inflammatory strictures.

Study Design

- Retrospective review of prospective registry cases
- •60 cases (27 malignant, 33 benign)
- Each case's clinical history, ERCP impression, and corresponding pCLE sequences were used to score image quality, propose presumptive diagnoses, and rate level of diagnostic confidence.
- 3 investigators

Paris Classification 2/2

Results

- Identified 4 descriptive criteria specific to benign inflammatory conditions (illustrations below)
- Improved specificity using the Paris classification for the characterization of inflammatory strictures



Specificity of pCLE for the detection of biliopancreatic malignancy



Initial Miami classification **Refined Paris classification**



Increased space between scales

Slivka, A. et al. Validation of the diagnostic accuracy of pCLE for the characterization of indeterminate biliary strictures: results of a prospective multi-center international study, GI Endoscopy, 2015

FOCUS Study 1/2

Objectives

To prospectively validate the diagnostic performance of pCLE, including inflammatory Paris criteria, in the detection of biliary cancer and compare it with the performance of alternative diagnostic strategies

Study Design

- Prospective observational multi-center study (6 centers)
- Enrolled 136 patients, evaluated 112 patients (71 malignant, 41 benign)
- Clinical, ERCP, tissue sampling and pCLE data collected prospectively
- 6months to 1 year FU for all patients



FOCUS Study 1/2

Results

• Tissue sampling detected **40** patients with cancer, and was **inconclusive for 63%** (n=72) of patients

- In patients with indeterminate tissue sampling, ERCP and pCLE
 - detected 24 additional patients with cancer
 - ruled out cancer in 30 patients with benign strictures
 - leaving only 18 patients indeterminate in the end

All patients (n=112) Prevalence= 63%	Sensitivity	Specificity	PPV	NPV	Accuracy
Tissue sampling	56 %	100 %	100 %	57 %	72 %
ERCP + Tissue sampling	85 %	69 %	83 %	73 %	79 %
ERCP + pCLE	89 %	71 %	84 %	78 %	82 %
ERCP + Tissue sampling + pCLE	89 %	88 %	93 %	82 %	88 %

Slivka, A. et al. Validation of the diagnostic accuracy of pCLE for the characterization of indeterminate biliary strictures: results of a prospective multi-center international study, GI Endoscopy, 2015



Pancreatic Cysts

INSPECT Study 1/2

Objectives

- To define **image interpretation criteria** for nCLE in pancreatic cysts and evaluate their diagnostic efficiency retrospectively
- To validate the **safety** of nCLE in pancreatic cysts

Study Design

- Prospective observational multi-center registry (8 centers)
- Enrolled 65 patients
- Probe introduced via 19G needles
- Clinical, EUSFNA and nCLE data collected prospectively
- Gold standard: surgical pathology if available, consensus final diagnosis otherwise



nCLE probe in 19G **FNA** needle



nCLE probe locked on 19G needle

INSPECT Study 2/2

Results

- First classification in pancreatic cysts defined, with one specific criteria outlined for IPMNs: papillary projection
- Potential for the differentiation of mucinous and non-mucinous cysts
- Safety demonstrated with a pancreatitis rate at 3% (lower than in previous study, thanks to safety measures such as locking device usage, and pre-loading of probe in needle)



The Papillary Projection criterion in an IPMN

Konda V.J. et al. A pilot study of in vivo identification of pancreatic cystic neoplasms with needle-based confocal laser endomicroscopy under endosonographic guidance. Endoscopy 2013

Differentiation of mucinous and non-mucinous cysts



DETECT Study 1/2

Objectives

• Determine the **feasibility and safety** of EUS-guided dual "through-the-needle" imaging and identify specific imaging features which may correlate with mucinous vs non-mucinous cysts

Study Design

- Prospective observational study in a single center
- Enrolled and evaluated 30 patients
- Cystoscopy (Spyglass through the needle imaging) and nCLE probes introduced via 19G needles
- Clinical, EUSFNA and nCLE data collected prospectively
- Gold standard: surgical pathology if available, consensus final diagnosis otherwise





Papillary projections in an IPMN

Nakai Y, et al. Diagnosis of pancreatic cysts: EUS-guided, through-the-needle confocal laser-induced endomicroscopy and cystoscopy trial: DETECT study. Gastrointestinal Endoscopy, 2015

DETECT Study 2/2

Results

 Potential for the differentiation of mucinous and non-mucinous cysts:

• The accuracy of nCLE for differentiating mucinous from nonmucinous cyst in all patients is 87%, compared to 73% for EUS morphology, and 61% for CEA

All patients (n=30)	Sensitivity	Specificity	PPV	NPV	Accuracy
EUS morphology	65 %	85 %	85 %	65 %	73 %
CEA > 192ng/mL	33 %	92 %	83 %	55 %	61 %
Cystoscopy	71 %	100 %	100 %	72 %	83 %
nCLE	77 %	100 %	100 %	77 %	87 %
nCLE + Cystoscopy	88 %	100 %	100 %	87 %	93 %

Nakai Y, et al. Diagnosis of pancreatic cysts: EUS-guided, through-the-needle confocal laser-induced endomicroscopy and cystoscopy trial: DETECT study. Gastrointestinal Endoscopy, 2015

Differentiation of mucinous and non-mucinous cysts



Objectives

• To define specific **nCLE image interpretation criteria** for in vivo characterization of **serous cystadenomas** and evaluate their diagnostic efficiency

Study Design

- Prospective observational multi-center study (4 centers)
- 31 patients enrolled and evaluated
- Probe introduced via 19G needles
- Clinical, EUSFNA and nCLE data collected prospectively
- Final diagnosis based on surgical pathology if available, consensus final diagnosis otherwise
- •2 Phases: 1. Definition of a new criteria for serous cystadenomas, 2. Offline evaluation of accuracy and interobserver agreement for previously identified criteria (6 observers)

of the nCLE probe.



a: nCLE probe protruding from a 19G needle b: EUS image of a cyst, showing the needle puncturing the cyst. Green arrow: tip of the needle. Red arrow: tip

Napoléon B, et al. A novel approach to the diagnosis of pancreatic serous cystadenoma: needle-based confocal laser endomicroscopy. Endoscopy 2015.(CONTACT)

CONTACT 1 Study 2/2

Results

- Validation of a **new criteria**, called the **superficial vascular network**
- 100% specificity and substantial interobserver agreement (kappa=0.69) for the characterization of serous cystadenomas



Characterization of Serous Cystadenoma



Objectives

• To determine new nCLE criteria for the diagnosis of pancreatic cystic lesions, to propose a comprehensive nCLE classification for the characterization of those lesions, and to carry out a first external retrospective validation

Study Design

- Retrospective observational multi-center study (4 centers, 6 observers)
- 33 patients evaluated (from CONTACT 1 prospective study)
- Clinical, EUSFNA and nCLE data collected prospectively
- Final diagnosis based on surgical pathology if available, consensus final diagnosis otherwise

Napoléon B, et al. In vivo characterization of pancreatic cystic lesions by needle-based confocal laser endomicroscopy (nCLE): proposition of a comprehensive nCLE classification confirmed by an external retrospective evaluation. Surg Endosc. 2015.

CONTACT 1 nCLE classification Study 2/2

Results

- Description and validation of new criteria for Mucinous Cystadenoma, Pseudocysts and cystic Neuroendocrine neoplasm
- High accuracies for all types of cysts: 90% for MCN, 90% for IPMN, 87% for SCA, 87% for PC, with very high specificities ranging from 90% to 100%

Mucinous cystic neoplasm (MCN), with red arrows pointing to the epithelial border criterion

Pseudocyst (PC), with arrows pointing to bright gray particles (inflammatory cells)



Napoléon B, et al. In vivo characterization of pancreatic cystic lesions by needle-based confocal laser endomicroscopy (nCLE): proposition of a comprehensive nCLE classification confirmed by an external retrospective evaluation. Surg Endosc. 2015. 36

Cystic neuroendocrine neoplasm (NEN), with arrows pointing to neoplastic cell clusters surrounded with fibrous areas



Colorectal Lesions



Objectives

To **compare** sensitivity and specificity of **pCLE to virtual** chromoendoscopy for classification of colorectal polyps using histopathology as a gold standard.

Study Design

- Prospective single-center controlled study
- 75 patients enrolled, with 119 polyps analyzed
- Surface pit pattern of all polyps was determined in vivo using virtual chromoendoscopy (VCE, either NBI or FICE)
- Recorded confocal videos were analyzed offline, blinded to endoscopic characteristics and histopathology
- pCLE images were classified as neoplastic or benign



Images of tubular adenoma A: Endoscopic image **B: FICE image** C: pCLE image D: Histopathology image

Buchner et al. Study on Characterization of polyps 2/2

Results

- pCLE demonstrated higher sensitivity compared to VCE when considering histopathology as the gold standard with similar specificity
- •pCLE may avoid the need for ex vivo histological confirmation of small polyps

All locations (n=119) Prevalence: 68%	Sensitivity	Specificity	PPV	NPV	Accuracy
VCE	p=0.01	71 % p=0.7	7	Notoub	lichad
pCLE	91 %	76 %		ΝΟΙ ΡΟΡ	IISTIEU

Buchner A. et al., Comparison of Probe-Based Confocal Laser Endomicroscopy With Virtual Chromoendoscopy for Classification of Colon Polyps. Gastroenterology 2010

Classification of colorectal polyps



Objectives

To estimate and compare the **accuracy of virtual chromoendoscopy** (VCE) and pCLE, for detection of residual neoplastic tissue at the site of prior EMR

Study Design

- Prospective, blind comparison of advanced endoscopic imaging (VCE and pCLE) using matching histology as reference standard
- Three tertiary-care referral hospitals
- 92 participants underwent follow-up colonoscopies for the evaluation of prior EMR sites within one year (129 EMR scars analyzed)

Shahid M. et al., Diagnostic accuracy of probe-based Confocal Laser Endomicroscopy (pCLE) in detecting recurrence of colorectal neoplasia after endoscopic mucosal resection. GIE 2011



Shahid et al. Study on Colorectal EMR follow-up 2/2

Results

- Adding pCLE increases sensitivity and NPV to 100% for the detection of residual neoplasia
- Combination of VCE and pCLE could avoid repeat colonoscopy thanks to real-time re-treatment instead of empiric re-treatment

All locations (n=129) Prevalence: 22%	Sensitivity	Specificity	PPV	NPV	Accuracy
VCE	72 %	78 %	49 %	91 %	77 %
pCLE	97 %	77 %	55 %	99 %	81 %
VCE and pCLE (n=95 cases where pCLE & VCE in agreement)	100 %	91 %	80 %	100 %	94 %

Shahid M. et al., Diagnostic accuracy of probe-based Confocal Laser Endomicroscopy (pCLE) in detecting recurrence of colorectal neoplasia after endoscopic mucosal resection. GIE 2011

80 %

20 %



Detection of residual neoplasia at follow-up



Inflammatory Bowel Diseases



Kiesslich et al. Study on Local Barrier dysfunction 1/2

Objectives

• Determine whether **cell shedding and barrier loss** in humans can be detected by confocal laser endomicroscopy (CLE)

Determine if these parameters predict relapse of IBD

Study Design

- Single center prospective controlled study
- Evaluated 58 patients with IBD (47 patients with UC + 11) patients with Crohn's disease)
- eCLE was performed in IBD and control patients
- Grading system based on appearances at eCLE was devised and used to predict relapse

I. Normal

II. Functional defect

III. Structural defect

Table 1 Endomicroscopic grade (Watson grade) for in vivo identification of local barrier dysfunction

Cell shedding	Local barrier dysfunction		
Cell shedding confined to single cells per shedding site (eg, figure 1C or D)	None		
Cell shedding confined to single cells per shedding site	Fluorescein signal visible in the intestinal lumen with an intensity the same or brighter than the epithelium or fluorescein plumes out of the epithelium into the lumen (eg, figure 2D)		
Microerosions in any field. Microerosion is defined when the lamina propria is exposed to the lumen with multiple cells being shed per site (eg, figure 2E)	Fluorescein signal visible in the intestinal lumen with an intensity the same or brighter than the epithelium or fluorescein plumes out of the epithelium into the lumen (eg, figure 2E)		

Kiesslich et al. Study on Local Barrier dysfunction 1/2

Results

• Cell shedding and barrier loss detected by confocal endomicroscopy predicts relapse of IBD and has potential as a diagnostic tool for the management of the disease



Single epithelial

Local barrier dysfunction: multiple cell shedding







Atreya et al. Study on the rapeutic response in CD 1/2

Objectives

• Evaluate whether the use of CLE molecular imaging with a fluorescent antibody to Tumor Necrosis Factor (TNF) could predict therapeutic responses to biological treatment in Crohn's Disease (CD)

Study Design

- Single center, prospective observational study in 2 phases
- Quantitative measurement of ex vivo eCLE molecular imaging with fluorescent antibody to TNF
- Quantitative measurement of in vivo molecular imaging of intestinal TNF immune cells on 25 patients with active Crohn's disease and comparison with the clinical outcome

High mTN



High-resolution endoscopy



Molecular imaging in vivo

Atreya et al. Study on therapeutic response in CD 1/2

Results

 Membrane bound tumor necrosis factor (mTNF) were imaged using fluorescent antibodies to TNF

• Quantitative analysis of the eCLE images revealed that **CD patients** with high amounts of mTNF showed significantly higher short term **response rates to therapy**, compared to patients with low amounts of **m**TNF

• This method provides a **sensitivity of 84.6%** and a **specificity of** 91.7% for the prediction of response to adalimumab therapy.



Molecular imaging upon topical administration of fluorescent adalimumab to the inflamed gut of patients with Crohn's disease in vivo yielded specific signals for mTNF+ mucosal cells (arrows)





