



Mauna Kea Technologies

DDW 2009 Cellvizio Presentations Compendium



Mc Cormick Place, Chicago



Cellvizio Booth, Chicago

Through 34 presentations and posters on specific Cellvizio studies and more than 50 communications on Confocal Laser Endomicroscopy, key opinion leaders from many countries expressed the usefulness and importance of our product.

Oral Communications

Specific Cellvizio studies

Topic : ASGE Endoscopic Video Forum
Abstract # : Sp342
Title : **Digital cholangioscopy with Narrow Band Imaging and Confocal Microscopy**
Author : Ram Chuttani

Topic : New innovation on colorectal cancer screening
Abstract # : Sp455
Title : **In vivo colorectal neoplasia detection using peptide-targeted confocal endoscopy**
Author : Thomas D. Wang

Topic : Regulation of mucosal immune responses and mesenchymal cell function
Abstract # : 708
Title : **in-Vivo Detection By Confocal Endomicroscopy of Two Distinct Structural Abnormalities in Angioarchitecture and Increased Vascular Permeability in Colonic Mucosa of Patients with IBD in Remission: Mechanistic Implications**
Authors : Andrzej S. Tarnawski, Emmanuel Coron, Jean-François Mosnier, Amrita Ahluwalia, Marc Le Rhun, Jean-Paul Galmiche, Tamara Matysiak-Budnik

Topic : Image-based detection of malignancy
Abstract # : 780
Title : **Quantitative In Vivo Assessment of Vascular Permeability in Human Colonic Mucosa Using Confocal Endomicroscopy: Clinical Implications for Colonic Neoplasia**
Authors : Tamara Matysiak-Budnik, Emmanuel Coron, Jean-François Mosnier, Marc Le Rhun, Jean-Paul Galmiche, Amrita Ahluwalia, Andrzej S. Tarnawski

Topic : Imaging & Advanced Technology distinguished abstract plenary
Abstract # : 854
Title : **Probe-Based Confocal Endomicroscopy Is Equivalent to Standard Four-Quadrant-Stepwise Biopsy Technique for Diagnosis of Neoplasia Arising from Barrett'S Esophagus**
Authors : Alexander Meining, Michael Vieth, Thomas Rosch, Stephan Miehle, Valentin Becker, Mario Anders, Heiko Pohl, Ahmed Madisch, Tibor Schuster, Monther Bajbouj, Roland M. Schmid

Topic : Endoscopic optical biopsy techniques
Abstract # : Sp845
Title : **Biliary imaging**
Author : Alexander Meining

Oral Communications

Other presentations mentioning Cellvizio

Topic : Novel technologies for the diagnosis of GI disorders
Abstract # : Sp398
Title : **State-of-the-Art Lecture: Kenneth Wang**
Author : Kenneth Wang

Topic : New diagnostic modalities for the early detection of biliary cancers
Abstract # : Sp517
Title : **Endoscopic approaches**
Author : Adam Slivka

Topic : Image-based detection of malignancy
Abstract # : Sp741
Title : **State of the art Overview**
Author : Herbert C. Wolfsen

Topic : Endoscopic optical biopsy techniques
Abstract # : Sp842
Title : **Confocal endomicroscopy : The best of GI imaging ?**
Author : Sharmila Anandasabapathy

Topic : Endoscopic optical biopsy techniques
Abstract # : Sp843
Title : **Endoscope vs probe**
Author : Marcia I. Canto

Topic : Preventing death from gastrointestinal malignancy
Abstract # : Sp36
Title : **Doing Better Than Random Biopsies: Real-Time Imaging of Barrett's Esophagus**
Author : Prateek Sharma

Topic : Inflammatory Bowel Disease
Abstract # : Sp68
Title : **The Endoscopists' Corner: Who's At Risk and What Should We Do? Preventing IBD-Associated Colorectal Cancer**
Author : Bret Lashner

Topic : President Plenary Session
Title : **JACK A. VENNES, MD AND STEPHEN E. SILVIS, MD STATE-OF-THE-ART ENDOWED LECTURE: Integrating New Endoscopic Imaging and Therapeutic Approaches to Barrett's Esophagus in 2009**
Authors : Gary W. Falk

Topic : Esophageal Potpourri
Abstract # : Sp634
Title : **State-of-the-Art Lecture: New Horizons in Endoscopic Therapy**
Authors : Ram Chuttani

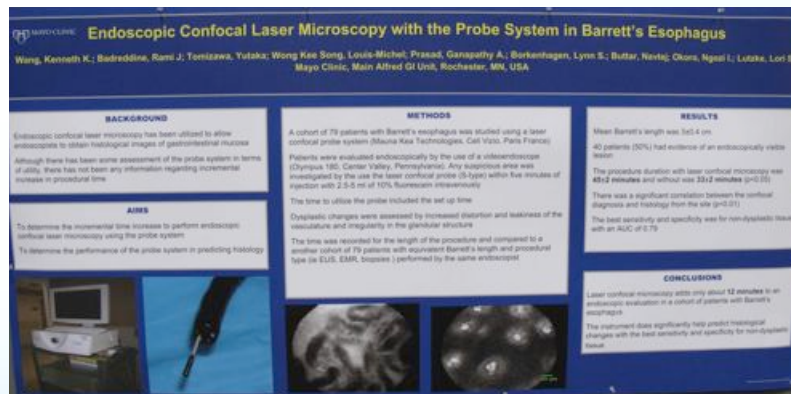
Poster presentations

Esophagus

Abstract # : W1351

Title : **Endoscopic Confocal Laser Microscopy with the Probe System in Barretts Esophagus**

Author : Kenneth K. Wang, Rami J. Badreddine, Yutaka Tomizawa, Louis-Michel Wong Kee Song, Ganapathy A. Prasad, Lynn S. Borkenhagen, Navtej Buttar, Ngozi I. Okoro, Lori S. Lutzke



Abstract # : W1362

Title : **Accuracy and Inter-Observer Agreement of Experts for Probe-Based Confocal Laser Endomicroscopy Detection of Dysplasia in Barrett'S Esophagus**

Authors : Michael B. Wallace, Julian A. Abrams, Monther Bajbouj, Ajay Bansal, Anna M. Buchner, Charles J. Lightdale, Prateek Sharma, Herbert C. Wolfsen, Alexander Meining

Colon

Abstract # : T1165

Title : **Generation of a New Classification Scheme for Probe-Based Confocal Laser Endomicroscopy By International Experts Including Their Interobserver Agreement and Accuracy**

Authors : Frank J. van den Broek, Alexander Meining, Michael B. Wallace, Anna M. Buchner, Susanne van Eeden, Jessica A. van Es, Paul Fockens, Evelien Dekker

Abstract # : T1166

Title : **Interobserver Agreement and Accuracy Among International Experts of Probe-Based Confocal Laser Microscopy (pCLE) in Predicting Colorectal Neoplasia**

Authors : Victoria Gomez, Anna M. Buchner, Evelien Dekker, Frank J. van den Broek, Alexander Meining, Muhammad W. Shahid, Marwan Ghabril, Paul Fockens, Michael B. Wallace

Poster presentations

Abstract # : T1170
Title : **Colonic Biopsy Specimens Obtained During Confocal Endomicroscopy Are In Vivo Prestained with Fluorescein and Exceptionally Suited for Cellular and Molecular Imaging**

Authors : Emmanuel Coron, Jean-François Mosnier, Amrita Ahluwalia, Marc Le Rhun, Andrzej S. Tarnawski, Tamara Matysiak-Budnik, Jean-Paul Galmiche

Abstract # : W1416
Title : **The Learning Curve for In Vivo Probe Based Confocal Laser Endomicroscopy (pCLE) for Prediction of Colorectal Neoplasia**

Authors : Anna M. Buchner, Victoria Gomez, Kanwar R. Gill, Marwan Ghabril, Daniela Scimeca, Muhammad W. Shahid, Sami R. Achem, Michael F. Picco, Douglas Riegert-Johnson, Massimo Raimondo, Herbert C. Wolfsen, Timothy A. Woodward, Muhammad K. Hasan, Michael B. Wallace

Abstract # : W1427
Title : **Probe Based Confocal Laser Endomicroscopy (pCLE) in Predicting Recurrence of Neoplasia After Endoscopic Mucosal Resection of Colorectal Lesions**

Authors : Anna M. Buchner, Muhammad W. Shahid, Frank J. van den Broek, Evelien Dekker, Victoria Gomez, Marwan Ghabril, Muhammad K. Hasan, Paul Fockens, Massimo Raimondo, Timothy A. Woodward, Michael B. Wallace

ERCP

Abstract # : T1323
Title : **Real-Time Intraductal Confocal Microscopy During ERCP: Feasibility and Technical Considerations**

Authors : Peter D. Stevens 1 , Yang K. Chen 2 , Raj J. Shah 2 , Ram Chuttani 3 , Douglas K. Pleskow

**Real-time Intraductal Confocal Microscopy during ERCP:
Feasibility and Technical Considerations**

Peter D. Stevens, Tamas A. Gonda, Yang K. Chen, Raj J. Shah, Ram Chuttani, Douglas K. Pleskow, Adam Silvka
1. Columbia University Medical Center, New York, NY; 2. University of Colorado Health Sciences Center, Denver, CO; 3. Beth Israel Deaconess Medical Center, Boston, MA; 4. University of Pittsburgh Medical Center, Pittsburgh, PA

Background and Aim

Despite advancements in ERCP technology (Digital Fluoroscopy, Cholangioscopy, Intraductal ultrasound, and tissue acquisition devices), accurate diagnosis of lesions remains a fundamental problem. Confocal laser microscopy has been reported to be a useful tool for in vivo imaging of cellular structures and can be used during endoscopy using a nonprobe (Carlina, Masuda, Kasa, Rasthologes, Park, France) passed through the working channel of an endoscope. This system enables in vivo hyperspectral imaging of the digestive tract. Recently a Carlina microscope has been developed for imaging the biliary and pancreatic duct. The goal of this study is to demonstrate the feasibility of intraductal confocal imaging and to describe the optimal imaging methods.

Methods and Study Design

Patients referred for ERCP to one of 4 experienced endoscopists at one of 4 centers were eligible. Study subjects were chosen based on expected timing of either a discrete lesion to be targeted for imaging or a diffuse field change to be examined. Following standard ERCP, the confocal probe was placed in contact with the area of interest. Intraductal fluorescence was given to assist imaging. Real time images were recorded.

Results

Table 1. Distribution of cases by area of abnormality

Area of Interest	n	Lowest resolution of CA*	High resolution of CA	Successful image acquisition
Ductal CBD	25	17	8	80%
Proximal CBD	3	3	0	98%
Hepatic Duct	6	5	2	87%
Pancreatic Duct	10	9	1	90%

*Lowest resolution = less than 20 microns

Table 2. Distribution of cases by equipment used

Equipment	n	Biliary success	Pancreatic success	Successful image acquisition
H-BN	21	71%	20%	50%
SpyScope	22	86%	14%	68%
GAIS	3	56%	33%	100%

Illustration of type of catheters used

Representative Images

Normal:
Normal images consist of thin, fine dark bands, less than 20 microns with normal reticular pattern with light and grey background.

Abnormal:
Loss of reticular pattern of epithelial bands, detection of villi or gland like structures

Tortuous dilated and sclerotic vessels with inconsistent branching

Presence of brick areas (abnormal fluorescence uptake)

Conclusions

Initial experience with the Carlina confocal system shows that images from within the bile and pancreatic ducts can be obtained for real time interpretation. Contrary to initial expectations, images were more easily obtained using catheters rather than cholangioscopy. Work is continuing to determine the optimal imaging methodology.

Poster presentations

Small Bowel

Abstract # : W1433
Title : **The Role of Probe-Based Confocal Laser Endomicroscopy (pCLE) in Detection of Dysplasia in Duodenal Polyps**
Authors : Muhammad W. Shahid, Anna M. Buchner, Muhammad K. Hasan, Victoria Gomez, Michael B. Wallace

Abstract # : W1454
Title : **In Vivo Histopathology with Portable Confocal Miniprobes Endomicroscopy in the Diagnosis of Celiac Disease (CD)**
Authors : Emanuele Dabizzi, Raffaele Manta, Helga Bertani, Mauro Manno, Alessandro Mussetto, Paolo Trande, Rita Conigliaro

IN VIVO HISTOPATHOLOGY WITH PORTABLE CONFOCAL MINIPROBES ENDOMICROSCOPY IN THE DIAGNOSIS OF CELIAC DISEASE (CD)

E. Dabizzi, R. Manta, H. Bertani, M. Manno, A. Mussetto, P. Trande, R. Conigliaro.
 Digestive Endoscopy Unit
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 Modena (Italy)

BACKGROUND
 Endoscopic duodenal biopsy is still critical in the diagnosis of CD, but often sampling errors and poor quality specimens may generate false-negative results. Confocal endomicroscopy (CEM) allows us to take histological information directly in vivo during routine endoscopy. So CEM could be very helpful in the management of patients with CD.

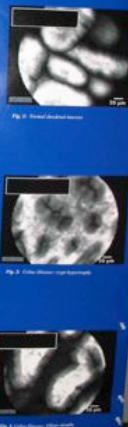
AIM OF THE STUDY
 Aim of the study is to evaluate the application of CEM and the potential benefit in the management of patients.

METHODS
 CEM (Cellvizio, Mauna Kea Technologies, Paris, France), using portable confocal mini-probes (Type 4), Type 5b) was performed in 12 patients (8 F, 4 M), mean age: 37 yrs, range 18-61 yrs underwent an upper gastrointestinal endoscopy for either suspected CD or inflammatory symptoms. Endoscopy was performed under conscious sedation (i.e. propofol) and individual with standard video gastroscopy (Fujinon EG 2970 F, Fujinon, Tokyo, Japan). We used endoscopic fluorescence (Type 5b), to enhance the diagnostic power of CEM. Real time video sequences were digitally recorded. Multiple images were taken from the same examined area. All tested sequences were put into a random order and assessed by a gastroenterologist blinded to the histopathological data. Diapores were considered as the gold standard. Values strongly (10x) greater of 3 or 4 per 1000th of the field were considered as CEM positive. Values of 1 or 2 per 1000th of the field were considered as CEM positive of CD.

RESULTS
 The patients' clinical-pathological characteristics are shown in the table. Comparing the CEM data with histology, we can assess a sensitivity of 80%, a specificity of 100%, and an accuracy of 92%.

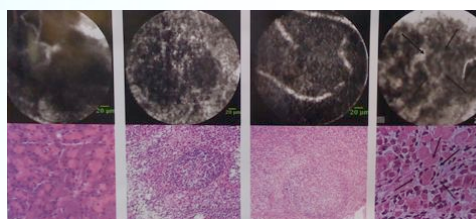
PAT	SEX	AGE	EMV/ATGA	Endoscopy	CEM	HISTOLOGY
1	F	39	-	+	10	CD
2	F	31	+	+	10	CD
3	M	35	+	+	10	CD
4	F	38	-	+	10	Normal
5	M	23	-	+	10	CD
6	F	27	-	+	10	CD
7	F	37	-	+	10	CD
8	F	32	-	+	10	CD
9	F	42	-	+	10	CD
10	M	20	-	+	10	Normal
11	F	44	-	+	10	CD
12	M	38	-	+	10	CD

CONCLUSIONS
 This is our preliminary experience with CEM applied for the diagnosis of CD. Fluorescence confocal CEM with portable mini-probes is a new helpful tool in the management of patients with CD. CEM offers the advantage of the histological examination of the mucosa during routine endoscopy, thus reducing the number of biopsy probes to be taken.



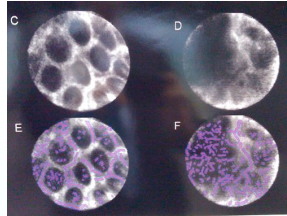
Animal studies

Topic : EUSFNA
Abstract # : S1411
Title : **Puncture-Needle Guided In Vivo Histology of Intra-Abdominal Organs Using Probe-Based Confocal Laser Endomicroscopy (pCLE) in a Porcine Model**
Authors : Valentin Becker, Stefan von Delius, Rogier P. Voermans, Paul Fockens, Timothy A. Woodward, Massimo Raimondo, Michael B. Wallace, Alexander Meining



Poster presentations

Topic : Colonic cancer
Abstract # : S2053
Title : **A new method for detection and monitoring of colonic carcinogenesis in a novel mouse model**
Authors : Valentin Becker, Florian Greten, Irina Kerle, Roland M. Schmid, Alexander Meining



Topic : NOTES
Abstract # : W1462
Title : **Feasibility of Sentinel Lymph Node Mapping with Confocal Laserscanning Microscopy via NOTES® Peritoneoscopy**
Authors : Stefan von Delius, Valentin Becker, Johanna Sager, Dirk Wilhelm, Armin Schneider, Christoph Schlag, Hubertus Feussner, Alexander Meining

General studies

Topic : Fluorescein dose
Abstract # : W1457
Title : **Determination of the Optimal Fluorescein Dose of Probe-Based Confocal Laser Endomicroscopy in Colonic Imaging**
Authors : Michael B. Wallace 1 , Anna M. Buchner 1 , Valentin Becker 2 , Alexander Meining

Topic : Image quality
Abstract # : T1169
Title : **Contrast Improvement in Probe-Base Confocal Laser Endomicroscopy (pCLE) By Use of a Low Fluorescein Concentration**
Authors : Carsten Schmidt, Andreas Stallmach

Topic : GI-GVHD
Abstract # : T1171
Title : **Miniprobe Confocal Laser Microscopy Imaging in Gastrointestinal Graft-Versus-Host Disease**
Authors : Stephan Miehke, Daniela Aust, Renate Schmelz, Andrea Morgner, Martin Bornhäuser, Ahmed Madisch

Topic : Neoplastic mucosa identification
Abstract # : W1413
Title : **Accuracy and Inter-Observer Agreement in Identifying Neoplastic Gastrointestinal Mucosal Pathology By Probe-Based Confocal Laser Endomicroscopy (pCLE)**
Authors : Vien X. Nguyen, Cuong C. Nguyen, Jonathan A. Leighton, Shabana F. Pasha, Giovanni DePetris, Suryakanth Gurudu, Ananya Das

Poster presentations


Topic : Fluorescein safety
Abstract # : W1428
Title : **Safety of Intravenous Fluorescein for Probe-Based Confocal Laser Endomicroscopy (pCLE): a Multicenter Study**
Authors : Michael B. Wallace, Alexander Meining, Stephan Miehle, Thomas Rosch, Heiko Pohl, Charles J. Lightdale, Bernard Filoche, David L. Carr-Locke, Emmanuel Coron, Jacques Moreau, Erwan Bories, Carsten Schmidt, Matthias Löh, Paul Fockens

Topic : pCLE and MRI
Abstract # : W1438
Title : **Precision of Confocal Miniprobe Localisation Assessed By High-Field Magnetic Resonance Imaging**
Authors : Baptiste Allain, Anthony Price, Tom K. Vercauteren, Richard J. Cook, Sebastien Ourselin, Mark F. Lythgoe, David J. Hawkes

The Centre for Medical Image Computing

Precision of confocal miniprobe localisation assessed by high-field magnetic resonance imaging

Allain B.¹, Price A.¹, Vercauteren T.², Cook R.J.³, Ourselin S.¹, Lythgoe M.F.⁴, Hawkes D.J.¹
¹ The Centre for Medical Image Computing (CMIC), UCL, ² The Centre for Advanced Biomedical Imaging (CABI), UCL, ³ Mauna Kea Technologies, Paris, France, ⁴ Dental Institute, Department of Biomedical, KCL




1. Motivation

The Cellvizio® 'optical biopsy' system is a confocal fluorescence microscope that provides high resolution **real time images in vivo** (FOV: 500µm x 500µm). The microscopic images need to be localised in space if we wish to **fuse information at different scales** [1]. The **goal** of this study was to measure the precision of localisation of the miniprobe tip using high-field pre-clinical Magnetic Resonance (MR) imaging.

2. Method

Materials:

1. A 650µm diameter miniprobe in an agarose-based jelly.
2. A 9.4 Tesla MR scanner: axial scan using a gradient echo protocol (TE=4.6ms, TR=184ms, voxel resolution: 0.156mmx0.156mmx1mm).



Idea: Compute the **trajectory** of the miniprobe over the MR image slices and localise the tip with the **intensity changes** along the trajectory.

Tip localisation:

1. Computation of the miniprobe centroid in each slice [2].

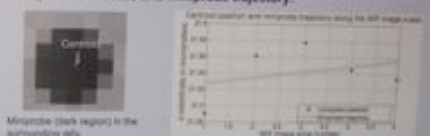
$$G = \frac{\sum_{i=1}^N (x_i - \text{max}_x) \cdot I_i}{\sum_{i=1}^N (I_i - \text{max}_x)}$$

G : pixel with the maximum intensity, max
 I_i : centroid of the miniprobe
 x_i : pixel with intensity I_i
 N : number of pixels

2. Linear regression over the computed centroids to find a straight trajectory.
3. Tip along the trajectory between 2 slices with a dramatic change in intensity.

3. Experiment

Computed centroids and miniprobe trajectory:



Precision of the computation of the miniprobe trajectory:

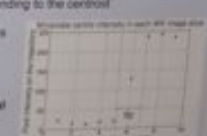
$$\text{precision} = \sqrt{\frac{1}{N} \sum_{i=1}^N (x_i - x_{\text{centroid}})^2}$$

x_{centroid} : x-coordinates of the centroid in slice i
 x_i : x-coordinates of the point on the straight line corresponding to the centroid

Result:

- Precisions along the x and y directions of the MR image, 4 experiments: **25±12.6µm** and **30±13.7µm**.

Localisation of the miniprobe tip between 2 slices correcting for partial volume: **~65µm precision** – assuming uniform contrast for tip and embedded media.



4. Conclusion

High precision of miniprobe tip localisation for microscope images with an FOV of 500µm x 500µm is approximately 30µm in plane and 65µm out of plane for the MR acquisition described.

- Assuming no significant local intensity or geometric distortion is induced by the miniprobe, MRI is a useful tool to monitor the miniprobe for **guided optical biopsies**.

References

1. Ourselin S., Image Registration and Mosaicing for Systems in Vivo Fibred Confocal Microscopy, PhD Thesis, 2005, Ecole des Mines de Paris
2. Wang W. F., Neuder E.A., Fitzpatrick J.M., 1996, An Automated Technique for Finding and Localizing Extracranial Aneurysm Arrows in CT and MR Volume Images of the Head, IEEE TMI, Vol. 15, No. 4, pp. 497-507

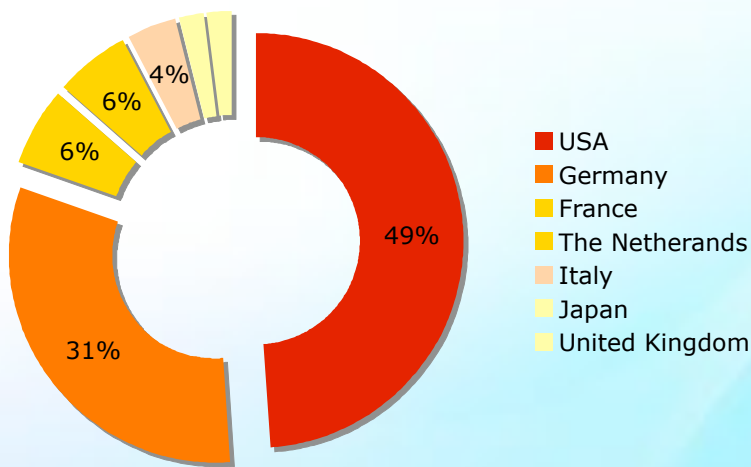
acknowledgements: Department of Health (MR) British Heart Foundation

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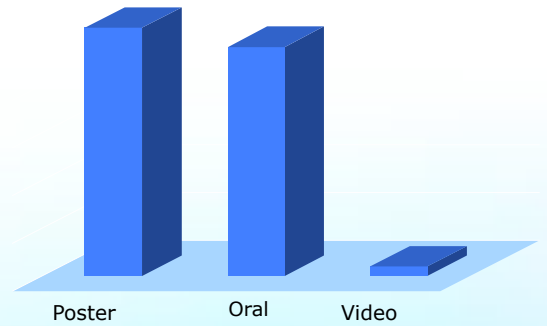
A few figures

More than 50 studies on Endomicroscopy

Endomicroscopic studies per country



Communication types



Endomicroscopic studies per application

