JSGE-APAGE Joint Conference

THE 7TH ASIAN-PACIFIC TOPIC CONFERENCE

Advanced Imaging in Gastroenterology

April 19th, Tuesday, 2016
April 20th, Wednesday, 2016
Keio Plaza Hotel Tokyo

Organizers :
Japanese Society of Gastroenterology (JSGE)
Asian Pacific Association of Gastroenterology (APAGE)

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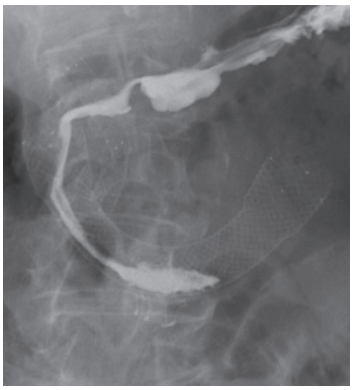

Image courtesy of Douglas A. Howell, MD, FASGE
Portland Gastroenterology Associates, Portland, Maine.

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Contents

Welcome Message from Chairman

Kazuichi Okazaki,
Director in Charge, JSGE Asian Liaison Committee,
Japanese Society of Gastroenterology

It is my great pleasure to welcome you to the seventh Asian Pacific Topic Conference (APTC) held in Tokyo on the 19th and 20th April, 2016, followed by the 102nd annual meeting of the Japanese Society of Gastroenterology (JSGE). Since 2010 the APTC has been organized jointly by JSGE and the Asian Pacific Association of Gastroenterology (APAGE). APTC is a monothematic scientific conference focusing on a single topic of urgent importance related to digestive diseases.

This year, we focus on advanced imaging and digestive diseases, which are recent topics in the field of gastroenterology and hepatology. Recent advances in imaging, use of diagnostic and therapeutic indices, have the potential to improve disease characterization and outcomes in GI disorders. We will be considering a variety of aspects, not only topics relating to digestive diseases, but also those to basic sciences. This conference aims to promote education, research and medical care through mutual exchange of opinions for digestive diseases in the Asia-Pacific region.

This topic is now emerging in Asia-Pacific region, and I believe the distinguished delegates of the Societies and their recommended young investigators are invited and can join extensive discussions on this theme. I hope this meeting will be very fruitful, not only providing an opportunity to strengthen friendship among young scientists, but also greatly contributing to promote scientific and educational programs of both Societies.

I wish to express my sincere appreciation to Prof. Kentaro Sugano, the president of APAGE and Prof. Tooru Shimosegawa, the president of JSGE for their generous supports to this meeting.
I hope all of the delegates will have fruitful time and enjoy staying in Tokyo.

Welcome Message from JSGE President

Tooru Shimosegawa, MD
President,
Japanese Society of Gastroenterology

On behalf of all members of the Japanese Society of Gastroenterology (JSGE) and as an organizer of the Asian-Pacific Topic Conference (APTC), I express my sincere thanks to and give a warm welcome to all attendees of the 7th APTC in Tokyo. Especially, I thank the guest speakers and participants from various countries for your great support to this meeting. This time the APTC will be held immediately before the 102nd JSGE annual spring meeting, making the week a really big academic event for gastroenterology in Japan. I hope all attendees at APTC will participate in the 102nd JSGE meeting as well and enjoy it. The APTC started as an academic meeting of APAGE in 2010 aiming at not only an exchange of the latest information on the most important topics we need to discuss, but to raise young investigators who are the future for the development of gastroenterology in the Asia-Pacific region. The topic of this APTC, "Advanced Imaging in Gastroenterology", is really timely and may introduce us the cutting-edge technologies in this field and their usefulness and applications to the clinical practice. I congratulate Prof. Kazuichi Okazaki, chairman of this conference, for the widely covered and extensive contents for this meeting. I also express my sincere appreciation to Prof. Kentaro Sugano, the president of the APAGE, for his generous supports to this meeting.

Internationalization of the JSGE, especially cooperation with neighboring countries in the Asia-Pacific region for the development of gastroenterology, is an important subject, which Prof. Sugano had pursued during his term of the JSGE president for a long time. I intend to follow in his footsteps and do my best to strengthen the ties between the JSGE and the APAGE. I hope the 7th APTC will be successful, fruitful and helpful in deepening friendships among JSGE and APAGE members. April in Japan is a good season for sightseeing with cherry blossoms everywhere and you can enjoy plenty of delicious spring flavors and foods. I hope you all will be satisfied with the conference and enjoy your stay in Tokyo.

Welcome Messages for the 7th APAGE-JSGE Single Topic Conference

Kentaro Sugano MD,
President, Asian Pacific
Association of Gastroenterology

Dear Colleagues,

On behalf of APAGE, I thank JSGE organizers led by Professor Kazuichi Okazaki for hosting the 7th APAGE-JSGE Single Topic Conference in conjunction with the 102nd general assembly of JSGE. The APAGE-JSGE single topic conference was started under agreement between APAGE and JSGE to highlight various issues that are keen to be discussed in this region. The first meeting focusing on functional gastrointestinal disorders was held in Tokyo in 2010. Since then, this topic conference has been held in Japan and APAGE countries in alternative manner. The last meeting featuring inflammatory bowel diseases was held in Islamabad, Pakistan under Professor Aamir Ghafoor Khan's outstanding leadership. Throughout the past 6 meetings, our understandings on the topics were deepened, giving us a momentum to step forward. More importantly, mutual friendship between APAGE gastroenterologists and Japanese colleagues has been greatly nurtured.

The topic in this meeting is advanced imaging in gastroenterology. I think this is the first time to have "imaging" as a topic in this conference series. As imaging such as radiography, ultrasound, magnetic resonance imaging, and endoscopy has been heavily utilized in the field of gastroenterology, gastroenterologists are very much familiar with routine diagnostic imaging. However, marked progress has been made in recent years, which certainly increases our capability of managing patients. Also at the cutting edge, newer imaging modalities have been introduced to help our understanding on the pathogenesis of gastrointestinal diseases, which may be utilized in clinical diagnosis in the near future.
As mentioned earlier, this topic conference is held one day before JSGE general assembly organized by Professor Mamoru Watanabe. Those who wish to attend the JSGE meeting are welcome to the JSGE meeting, where many international sessions with distinguished speakers are planned. Thus attending this topic conference does have the opportunity to attend two meetings consecutively.

I hope you enjoy exciting intellectual inputs from the state-of-the-art lectures and presentations at the topic conference and be convinced of our bright future of imaging in the field of gastroenterology.

Conference Information

Date:
April 19th, Tuesday April 20th, Wednesday, 2016

Venue:
Keio Plaza Hotel Tokyo
2-2-1 Nishi-Shinjuku, Shinjuku-Ku, Tokyo
160-8330 Japan

Main Theme:
Advanced Imaging in Gastroenterology

Topics:
I .Advanced Imaging in Endoscopy
II .Advanced Imaging in Surgery
III. Molecular Imaging
IV. Functional Imaging
V .Advanced Imaging of the Liver

Official Language:
English

Smoking:
Smoking is forbidden anywhere except from smoking areas.

Mobile Phones
During the lectures, you are prohibited from using a cellular phone or PHS. Please turn it off or put it on silent mode.

Filming and Photographing of Conference Rooms:
Taking pictures, filming and recording are prohibited. Please do not bring cameras, video recorders or other filming equipment into the presentation venues.

Committee

Chairman Kazuichi Okazaki (Kansai Medical University, JSGE Asian Liaison Committee Chairman, JSGE)

JSGE President Tooru Shimosegawa (Tohoku University Graduate School of Medicine)

APAGE President Kentaro Sugano (Jichi Medical University)

JSGE Asian Liaison Committee

Program Director Yoshinori Igarashi (Toho University Omori Medical Center)
Hiroyuki Imaeda (Saitama Medical University)

Members Keiichi Kubota (Dokkyo Medical University)
Soji Ozawa (Tokai University School of Medicine)
Hiroshi Kashida (Kindai University Faculty of Medicine)
Takuji Gotoda (Nihon University School of Medicine)
Sumiko Nagoshi (Saitama Medical Center, Saitama Medical University)
Hironori Yamamoto (Jichi Medical University)
Takao Itoi (Tokyo Medical University)

Organizers Japanese Society of Gastroenterology (JSGE)
Asian Pacific Association of Gastroenterology (APAGE)

Faculty Members of APTC2016

JSGE

Hata, Jiro
Iijima, Hiroko
Inoue, Haruhiro
Irisawa, Atsushi
Kitano, Masayuki
Kinoshita, Yoshikazu
Mori, Toshiyuki
Moriyasu, Fuminori
Nishimura, Satoshi
Ogawa, Masahiro
Ohtsuka, Kazuo
Sugimoto, Maki
Sumiyama, Kazuki
Taniai, Makiko
Tsuji, Yoshihisa
Urano, Yasuteru
Yoshida, Masashi

APAGE

Ho, Khek Yu
Zeng, Fang
Goh, Khean-Lee
Khan, Aamir Ghafoor
Tang, Chengwei
Chiu, Philip Wai Yan
Tandan, Manu
Kim, Tae Il
Ho, Shiaw-Hooi
Lau, Gabriel
De Lusong, Mark Anthony A.
Soetikno, Roy M.
Lu, Ching-Liang
Pittayanon, Rapat
Singh, Rajvinder
Abdullah, Murdani

Sponsoring Companies

FUJIFILM Medical Co., Ltd.
Olympus Corporation

Time Table

Apr. 19th (DAY 1)		
	Harmony Room (Main Tower 44F)	
18:00-	Evening Seminar	
19:00- -21:00	Invited Welcome Dinner	
Apr. 20th (DAY 2)		
	OHGI Room (South Tower 4F)	
7:15-	Registration	Poster Mounting
8:00-	Opening Remarks	
8:10-	Topic I Advanced imaging in endoscopy-1	
9:10-	Topic I Advanced imaging in endoscopy-2	
10:10-	Coffee Break	
10:25-	Topic I Advanced imaging in endoscopy-3	
11:50-	Luncheon Seminar	
12:35-	Photo Session	
13:05-	Topic II Advanced imaging in surgery	Poster Exhibition
13:50-	Topic III Molecular imaging	
14:30-	Topic IV Functional imaging	
15:30-	Coffee Break	
15:45-	Topic V Advanced imaging of the liver-1	
16:15-	Topic V Advanced imaging of the liver-2	
16:45-	Announcement of best poster Award	
16:55-	Closing Remarks	
17:05-		Poster Removal
17:20-	Farewell Party (Venue: NISHIKI Room (Keio Plaza Hotel, South Tower 4F))	

Registration

Registration Desk:
Apr. 19th In front of Room "Harmony", Main Tower 44F Keio Plaza Hotel Tokyo
Apr. 20th In front of Room "OHGI", South Tower 4F Keio Plaza Hotel Tokyo

Opening Hours:

April 19th, Tuesday	17:30-19:00
April 20th, Wednesday	07:15-16:30

Registration Fee:
Free of charge

Entitlements:
Participation Registration Includes;
- Admission to the Conference
- Admission to the Farewell Party
- Syllabus handout
- Lunch box

Social Programs

Welcome Dinner (Invitation only)
Date and Time: April 19th, Tuesday 19:00-21:00
Venue: "Harmony Room", Main Tower 44F Keio Plaza Hotel Tokyo
Style: Course

Farewell Party
Date and Time: April 20th, Wednesday 17:20-19:00
Venue: "NISHIKI Room", South Tower 4F Keio Plaza Hotel Tokyo
*Please feel free to attend the Farewell Party taking place after the closing remarks.

Presentation Instructions

1) Preview Corner

- Location: In front of "OHGI Room", South Tower 4F
- Opening hours:
- April 20th, Wednesday 7:15 - 16:50
- Please check your presentation data 1 hour prior to your presentation time to verify that the outcome is correct when using the equipment provided. If you are using your own laptop for your presentation, you can bring your laptop to the preview corner when checking your data.

2) At Your Presentation

- Files should be formatted for Windows or Mac (for MS Office, version 2003 or later)
- PowerPoint slides should be set to the 4:3 aspect ratio, resolution XGA(1024 x 768 pixel)
- Please note that PowerPoint animation may not work properly under certain circumstances
- If you are using video in your presentation, please let us know in advance. (Windows Media Player, DVD-Video, Real Player, QuickTime, FLV (YouTube, Ustream, Keynote))
- Make sure you bring the original video with you even if it is inserted in the PowerPoint file
- If you would like to use your Mac laptop, please bring your own VGA adapter cable for your presentation.
- Projection will only be on one single screen.

Poster Exhibition

Poster Exhibition will be held from 8:00 to 17:05 on Apr. 20th in OHGI Room, South Tower 4F at Keio Plaza Hotel. There is no oral presentation.

1) Schedule

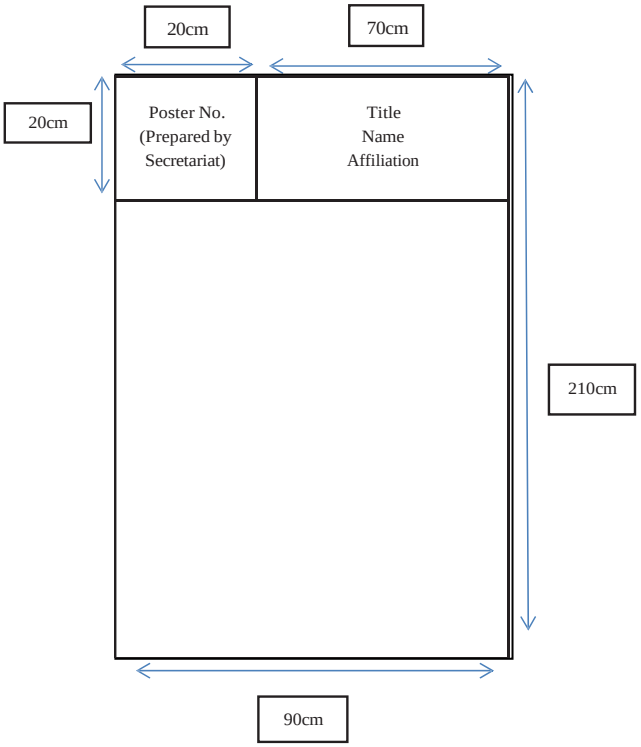
Mounting Time: April 20th, Wednesday 7:15-7:50
Poster Exhibition: April 20th, Wednesday 8:00-17:05
Removal: April 20th, Wednesday 17:05-17:15

Notice: Best Poster Award will be held from 16:45 -16:55 at OHGI Room, 4F.

2) Space Available

Each Poster Presenter is allocated the following space: 210cm high x 90cm wide.

IMPORTANT NOTICE DO NOT EXCEED THE SPACE ALLOCATION

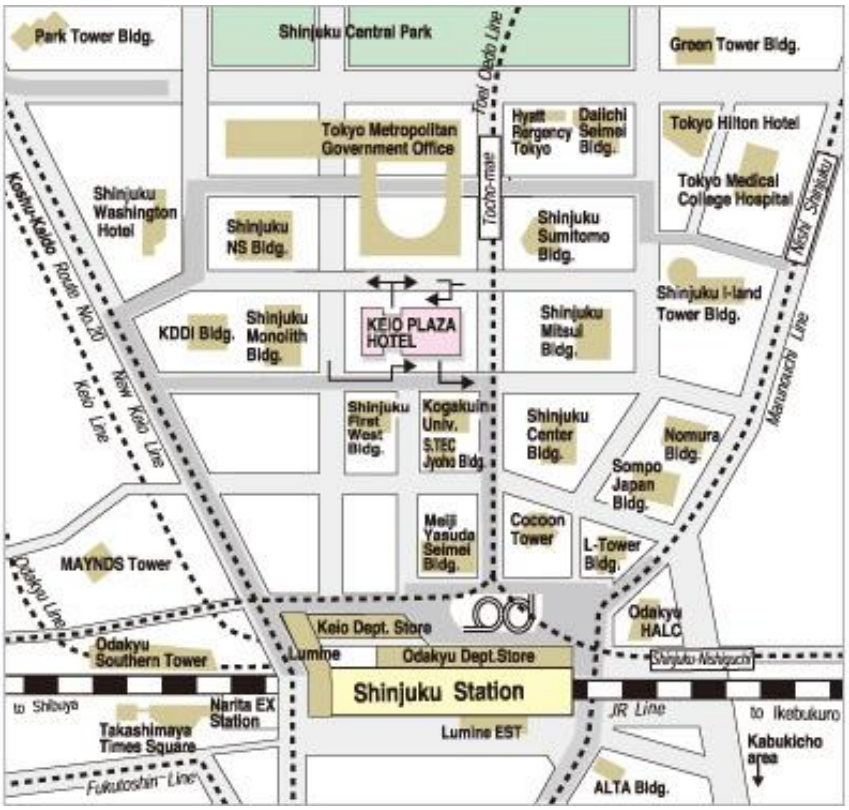


*All posters may be displayed on the assigned panels throughout the exhibition period (from 8:00 to 17:05 on Apr. 20th).

*Posters will be exhibited for the duration of the conference.

Access Information

Venue: Keio Plaza Hotel Tokyo
2-2-1 Nishi-Shinjuku, Shinjuku-Ku, Tokyo
160-8330 Japan



Airport Access

From/To Narita International Airport

■**By Airport Limousine Bus**
Duration: approx. 120 minutes.
Fare: Adult JPY 3,100　Child JPY 1,550

■**By Narita Express NEX**
Duration: approx. 81 minutes.
Fare: Adult JPY 3,190　Child JPY 1,590

From/To Haneda Airport

■**By Airport Limousine Bus**
Duration: approx. 70 minutes.
Fare: Adult JPY 1,230　Child JPY 620

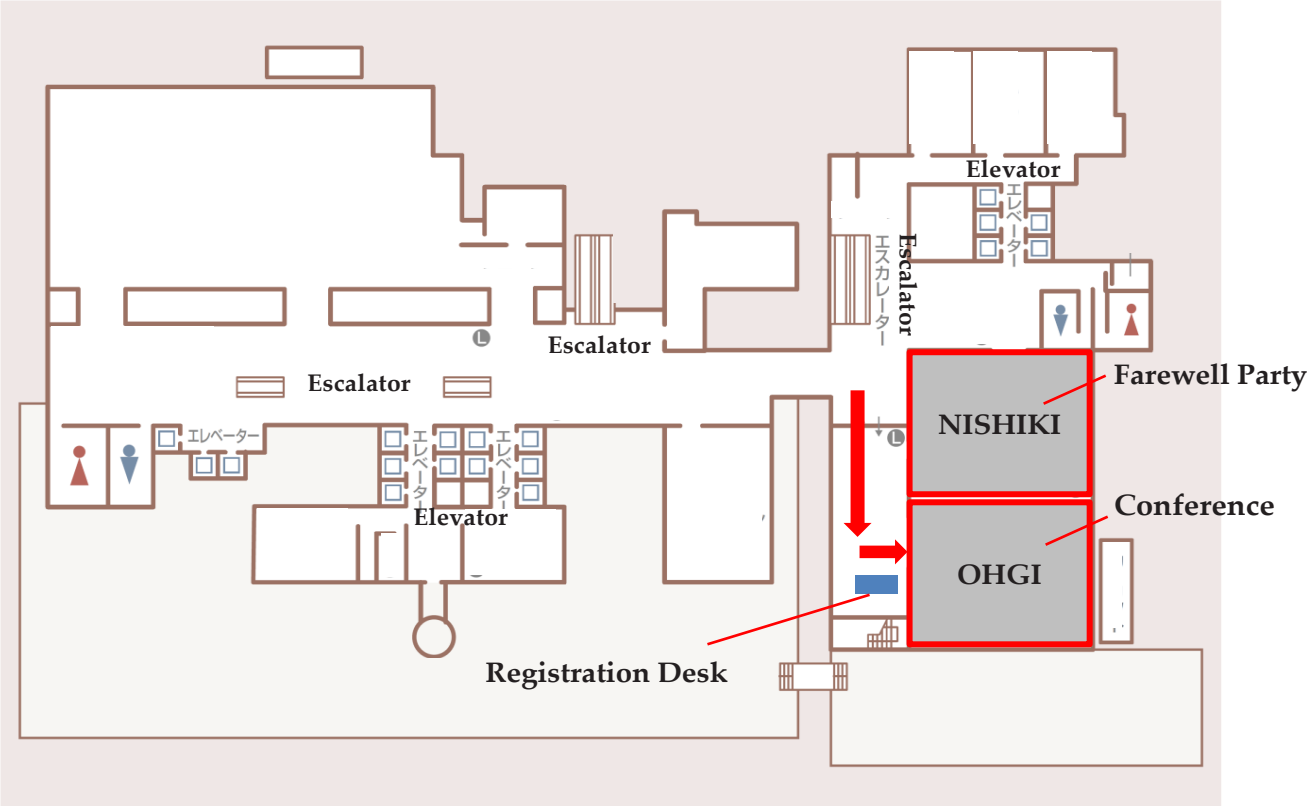
■**By Keikyu Line/JR Yamanote Line**
From Haneda Airport, take the Keikyu Line to Shinagawa Station and change trains to the JR Yamanote Line that goes in the direction of Shibuya. Get off at Shinjuku Station. It takes about a 5 minute walk from the west exit of Shinjuku Station to the hotel.

■**By taxi**
Time required is approximately 45-60 minutes. Fare to be around JPY 8,000～12,000. *The fare and travel time may differ depending on the traffic.

Floor Guide

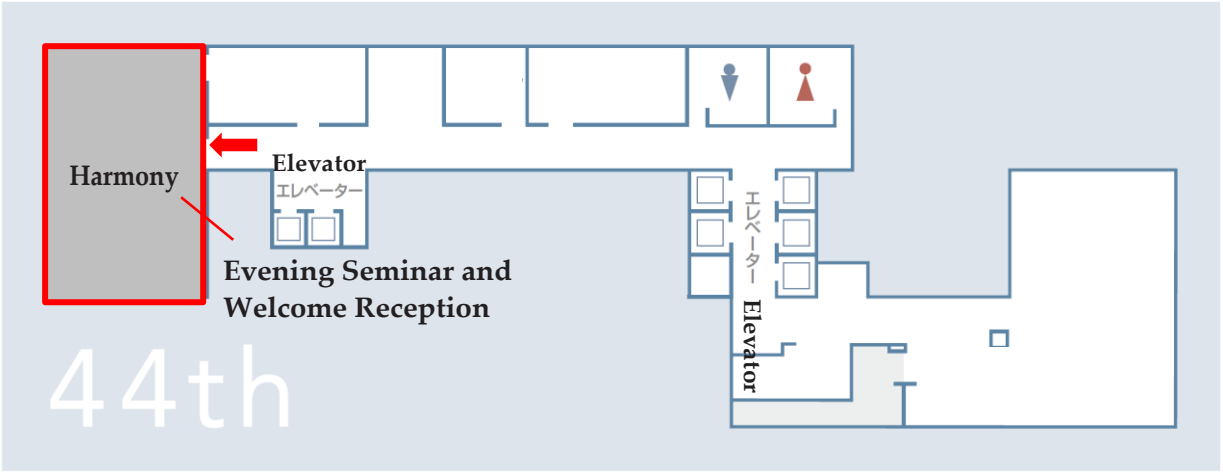
Keio Plaza Hotel, South Tower 4F

OHGI Room April 20th, Wednesday 8:00-17:05
NISHIKI Room April 20th, Wednesday 17:20-19:00



Keio Plaza Hotel, Main Tower 44F

April 19th, Tuesday 18:00-21:00



Contacts

Conference Secretariat:
c/o: Oscar Japan Co., Ltd.
Address: Neocity Mitaka, 3-35-1 Shimorenjaku, Mitaka-shi, Tokyo 181-0013
Email: aptc-secretariat@oscar-japan.com
TEL: +81-422-24-6814 FAX: +81-422-24-6812

Conference Website:
URL: http://www.jigyou.com/APTC7/

Program

April 19th (DAY 1) Harmony Room (44F)

18:00-19:00/

Evening Seminar

Supported by: FUJIFILM Medical Co., Ltd.

Moderator: Yoshikazu Kinoshita

Shimane University School of Medicine, Japan

Latest advances in endoscopic imaging

Hironori Yamamoto

Jichi Medical University, Japan

Irreversible electroporation therapy for unresectable local advanced pancreatic cancer (LAPC)

Fuminori Moriyasu

Tokyo Medical University, Japan

19:00-21:00/

Welcome Dinner (Invitation only)

Moderator: Soji Ozawa *Tokai University School of Medicine, Japan*

April 20th (DAY 2) OHGI Room (4F)

8:00-8:10/

Opening Remarks

Tooru Shimosegawa *President, Japanese Society of Gastroenterology*

8:10-9:10/

Topic I: Advanced imaging in endoscopy-1

Chairpersons: Roy M. Soetikno
Singapore General Hospital, Singapore
Haruhiro Inoue
Showa University Koto-Toyosu Hospital, Japan

8:10-8:25 **Lecture-1 Time Trend in the Development of Advance Endoscopy Imaging of the Gastro-Intestinal Tract**
Shiaw-Hooi Ho
University of Malaya Medical Center and University of Malaya Specialist Centre, Malaysia

8:25-8:40 **Lecture-2 Advances in image enhanced endoscopy for upper gastrointestinal cancers**
Philip Wai Yan, CHIU
The Chinese University of Hong Kong, Hong Kong

8:40-8:55 **Lecture-3 Advanced Imaging in Gastroenterology**
Rapat Pittayanon
King Chulalongkorn Memorial Hosptial, Thailand

8:55-9:10 **Lecture-4 VISUALIZATION OF THE BILIARY SYSTEM – A REVIEW**
Manu Tandan
Asian Institute of Gastroenterology, India

9:10-10:10/

Topic I: Advanced imaging in endoscopy-2

Chairpersons: Khean-Lee Goh
University Malaya Medical Centre, Malaysia
Hiroshi Kashida
Kindai University Faculty of Medicine, Japan

9:10-9:25 **Lecture-1 The Role of Advanced Endoscopy Imaging for Detecting Sessile Serrated Adenomas**

Murdani Abdullah

Universitas Indonesia, Indonesia

9:25-9:40 **Lecture-2 Magnifying endoscopy in the esophagus**

Haruhiro Inoue

Showa University Koto-Toyosu Hospital, Japan

9:40-9:55 **Lecture-3 Clinical applications of confocal laser endomicroscopy in intestinal diseases**

Tae Il Kim

Yonsei University College of Medicine, Korea

9:55-10:10 **Lecture-4 Confocal laser endomicroscopy**

Kazuki Sumiyama

Jikei University School of Medicine, Japan

10:10-10:25 **Coffee Break**

10:25-11:40/

Topic I: Advanced imaging in endoscopy-3

Chairpersons: Rajvinder Singh

Lyell McEwin Hospital and the University of Adelaide, Australia

Takuji Gotoda

Nihon University School of Medicine, Japan

Commentator: Hiroyuki Imaeda

Saitama Medical University, japan

10:25-10:40 **Lecture-1 Realtime Diagnosis of GI Neoplasia**

Khek Yu Ho

National University of Singapore, Singapore

10:40-10:55 **Lecture-2 Advanced imaging in endoscopy Deep into the Small Intestine**

Kazuo Ohtsuka

Tokyo Medical and Dental University, Japan

10:55-11:10 **Lecture-3 Advanced Endoscopic Imaging, Therapeutic Endoscopy, ERCP, EUS, ESD/ EMR**

Roy M. Soetikno

Singapore General Hospital, Singapore

11:10-11:25 **Lecture-4 Sessile Serrated Adenomas: Misconceptions, Detection, Characterisation and Resection**

Rajvinder Singh

Lyell McEwin Hospital and the University of Adelaide, Australia

11:25-11:40 **Lecture-5 Endoscopic Ultrasound Imaging in Caustic Esophageal Injuries**

Mark Anthony A. De Lusong

University of the Philippines, Philippine

11:50-12:35/

Luncheon Seminar

Supported by: Olympus Corporation

Moderator: Yoshinori Igarashi

Toho University Omori Medical Center, Japan

11:55-12:15 **Lecture-1 EUS Imaging Diagnosis**

Masayuki Kitano

Kindai University, Japan

12:15-12:35 **Lecture-2 Advanced imaging in endoscopy Deep into the Small Intestine**

Atsushi Irisawa

Fukushima Medical University Aizu Medical Center, Japan

12:35-12:50 **Photo Session (place to be announced)**

13:05-13:50/

Topic Ⅱ: Advanced imaging in surgery

Chairpersons: Philip Wai Yan, Chiu

The Chinese University of Hong Kong, Hong Kong

Soji Ozawa

Tokai University School of Medicine, Japan

Commentator: Keiichi Kubota

Dokkyo Medical University, Japan

13:05-13:20 **Lecture-1 Augmented reality and 3D printing for surgical navigation**

Maki Sugimoto

Kobe University Graduate School of Medicine, Japan

13:20-13:35 **Lecture-2 Indocyanine green fluorescence guided surgery – Development and clinical appreciation of the brightfield full-color fluorescence camera and the brightfield full-color fluorescence laparoscopes**

Masashi Yoshida

International University of Health and Welfare Hospital, Japan

13:35-13:50 Lecture-3 High Resolution Imaging in Endoscopic Surgery

Toshiyuki Mori

Kyorin University, Japan

13:50-14:30/

Topic Ⅲ: Molecular imaging

Chairpersons: Tae Il Kim

Yonsei University College of Medicine, Korea

Kazuki Sumiyama

Jikei University School of Medicine, Japan

13:50-14:10 Lecture-1 Intraoperative, rapid and sensitive imaging of tiny tumors by novel fluorogenic probes for aminopeptidases

Yasuteru Urano

The University of Tokyo, Japan

14:10-14:30 Lecture-2 Multi-scale in vivo observation by two photon microscope

Satoshi Nishimura

Jichi Medical University, Japan

14:30-15:30/

Topic Ⅳ: Functional imaging

Chairpersons: Ching-Liang Lu

Taipei Veterans General Hospital/ National Yang-Ming University, Taiwan

Hironori Yamamoto

Jichi Medical University, Japan

Commentator: Yoshikazu Kinoshita

Shimane University School of Medicine, Japan

14:30-14:45 Lecture-1 Clinical Application of Gastrointestinal Ultrasound

Jiro Hata

Kawasaki Medical School, Japan

14:45-15:00 Lecture-2 Current topics of functional Image for digestive disease

Yoshihisa Tsuji

Shiga University of Medical Science/ Kurashiki Central Hospital, Japan

15:00-15:15 **Lecture-3 The cerebral function and structure changes in functional dyspepsia patients and the influence of acupuncture treatment**

Fang Zeng

Chengdu University of Traditional Chinese Medicine, China

15:15-15:30 **Lecture-4 Application of Functional Brain Imaging in Gastroenterology/Hepatology**

Ching-Liang Lu

Taipei Veterans General Hospital/ National Yang-Ming University, Taiwan

15:30-15:45 **Coffee Break**

15:45-16:15/

Topic Ⅴ: Advanced imaging of the liver-1

Chairpersons: Aamir Ghafoor Khan

Lady Reading Hospital, Pakistan

Makiko Taniai

Tokyo Women's Medical University, Japan

15:45-16:00 **Lecture-1 Micro blood flow imaging in liver tumors using contrast enhanced ultrasonography**

Masahiro Ogawa

Nihon University Hospital, Japan

16:00-16:15 **Lecture-2 Advanced Visualization of Liver Fibrosis**

Chengwei Tang

West China Hospital, Sichuan University, China

16:15-16:45/

Topic Ⅴ: Advanced imaging of the liver-2

Chairpersons: Chengwei Tang

West China Hospital, Sichuan University, China

Sumiko Nagoshi

Saitama Medical University, Japan

16:15-16:30 **Lecture-1 The Latest Trends in the Noninvasive Diagnosis of Liver Diseases**

Hiroko Iijima

Hyogo College of Medicine, Japan

16:30-16:45 **Lecture-2 Imaging of Diffuse Fatty Infiltration of the Liver**

Gabriel Lau

Dunedin Hospital, New Zealand

16:45-16:55/

Best Poster Award Ceremony

Moderator:	Hiroshi Kashida	*Kindai University Faculty of Medicine, Japan*
Presenter:	Kazuichi Okazaki	*Chairman, The 7th Asian-Pacific Topic Conference*

16:55-17:05/

Closing Remarks

	Kentaro Sugano	*President, Asian Pacific Association of Gastroenterology*

17:20-19:00/

Farewell Party

Moderator:	Hiroshi Kashida	*Kindai University Faculty of Medicine, Japan*

Poster Exhibition List

1. **Enteroscopic and MR findings of small intestine in Crohn's disease**
   Kento Takenaka
   Tokyo Medical and Dental University, Japan

2. **Pilot study of endoscopic retrograde 3-dimensional - computed tomography enteroclysis for the assessment of Crohn's disease**
   Hiroki Tanabe
   International University of Heralth and Welfare Hospital, Japan

3. **New endoscopic Imaging System For Evaluation of Colonic Mucosal Inflammation in Ulcerative Colitis**
   Yusuke Honzawa
   Kyoto University, Japan

4. **Prospective Cohort Study of the Impact of Endoscopic Submucosal Dissection on Gastric Motility and Upper Abdominal Symptoms**
   Shin Kono
   Tokyo Medical University, Japan

5. **Usefulness of Perfusion Parametric Imaging for follow up of patients with alcoholic hepatitis**
   Yasushi Matsukiyo
   Toho University Omori Medical Center, Japan

6. **Confocal Raman Spectroscopy for Endoscopic Diagnosis of Eosinophilic Esophagitis - Is Eosinophile Detection Possible?**
   Naoki Oshima
   Shimane University School of Medicine, Japan

7. **Evaluation of intestinal patency using a patency capsule: Current status**
   Teppei Omori
   Tokyo Women's Medical University, Japan

8. **Intravoxel incoherent motion diffusion-weighted imaging is a better indicator of high grade hepatocellular carcinoma than conventional apparent diffusion coefficient**
   Shintaro Ichikawa
   University of Yamanashi, Japan

9. **Linked color imaging, a novel endoscopic enhancement system is useful for the assessment of mucosal inflammation in ulcerative colitis.**
   Kazuhiko Uchiyama
   Kyoto Prefectural University of Medicine, Japan

10. Assessment of small bowel motility in patients with bloating using Cine-MRI

Akiko Fuyuki

Yokohama City University, Japan

11. Linked color imaging facilitates detection for early gastric cancers missed by white light imaging endoscopy

Yoshimasa Miura

Jichi Medical University, Japan

12. Visualization of pancreatic inflammation in mouse model

Shin Hamada

Tohoku University Graduate School of Medicine, Japan

13. Effectiveness of auto-fluorescence imaging systems for differential diagnosis of colorectal lesions

Naoto Tamai

The Jikei University School of Medicine, Japan

14. Imaging Colon of Rhesus Macaques with Colonoscopy

Zhiyin Huang

Sichuan University, China

15. An activatable photosensitizer targeted to γ-glutamyltranspeptidase for tumor selective photodynamic therapy

Mako Kamiya

Graduate School of Medicine, The University of Tokyo, Japan

16. Indocyanine green fluorescence during gastrointestinal surgery for preventig anastomotic leakage

Hironori Ohdaira

International University of Health and Welfare Hospital, Japan

17. Role of Narrow band imaging in diagnosing Tc-99m scintigraphy negative Meckel's Diverticulum in Adult Patients with Obscure GI Bleeding using single balloon enteroscope.

Hrushikesh Chaudhari

Asian Institute of Gastroenterology, India

18. Evaluation of Tumor-associated Stroma and its Relationship with Tumor Hypoxia using Dynamic Contrast-enhanced CT and 18F-Misonidazole PET in Murine Tumor Models

Sho Koyasu

Graduate School of Medicine, Kyoto University, Japan

19. Clinical implications of advanced endoscopy

Toshiharu Sakurai

Kindai University Faculty of Medicine, Japan

20. Usefulness of three-dimension biliary simulation using CT with Drip-infusion Cholecystocholangiography (DIC-CT)

Takayuki Shiraki
Dokkyo Medical University, Japan

21. New endoscopic finding of lower esophageal sphincter in esophageal achalasia : "Corona appearance"

Hironari Shiwaku
Fukuoka University, Japan

22. Usefulness of contrast enhanced ultrasonography in diagnosis of hepatic focal nodular hyperplasia

Yukinobu Watanabe
Nihon University Hospital, Japan

23. A possibility of cordless camera for laparoscopic surgery ~ Can LED light be used as a portable light source? ~

Hisae Aoki
Sanraku Hospital, Japan

24. Preoperative imaging of thoracic duct for thoracic esophagectomy

Junya Oguma
Tokai University School of Medicine, Japan

25. Advanced Endoscopy Imaging in Surveillance Oesophago-Duodenoscopy (OGDS) Post Radiofrequency Ablation for Barrett's Esophagus – Preliminary Experience and Pilot Series in Malaysia

Zhi-Qin WONG
University Malaya Medical Centre, Malaysia

26. Probe based multiphoton microscopy and colon neoplasm

Eun Sun Kim
Korea University College of Medicine, Korea

27. Radiological Diagnosis and Staging of Hepatocellular Carcinoma Using Multiphasic CT Scanning

Ruveena Bhavani
University Malaya Medical Centre, Malaysia

28. Management of Gallbladder Rupture In A Pediatric Patient

Danny Joseph Tuazon
University of the Philippines, Philippine

29. Early video capsule endoscopy in patients with obscure gastrointestinal bleeding- a single hospital experience

Yen-Po Wang
Taipei Veterans General Hospital, Taiwan

30. A prospective multicentre study assessing the utility of Narrow Band Imaging with dual focus magnification in differentiating colorectal neoplasia using the NICE and Modified Sano's classification

Kuan Loong Cheong
The Lyell McEwin Hospital, Australia

31. Usefulness of non-invasive assessment of liver fibrosis using six different ultrasound elastography devices in patients with chronic hepatitis and the difference of liver stiffness between HBV-related chronic hepatitis and non-HBV-related chronic hepatitis

Takashi Nishimura
Hyogo College of Medicine, Japan

32. Endoscopic Appearance of Serrated Adenoma Using White Light Endoscopy, Narrow Band Imaging, and Blue Laser Imaging

Hasan Maulahela
University of Indonesia, Indonesia

33. The use of endocystoscopy for the early detection of esophageal neoplasm: a case series

Shannon Chan
The Chinese University of Hong Kong, Hong Kong

34. Effects of ambient temperature on ablation zone size: An experimental study with Microwave ablation in ex vivo bovine livers

Andre Poon
Dunedin Hospital, New Zealand

35. Reevaluation of diagnostic ability of fluorescence cytology using 5-aminolevulinic acid during endoscopic ultrasound-guided fine needle aspiration for pancreatic lesions

Tsukasa Ikeura
Kansai Medical University, Japan

Evening Seminar

DAY1 April 19th 18:00-19:00　Harmony Room (44F)

Supported by:　FUJIFILM Medical Co., Ltd.

Moderator: Yoshikazu Kinoshita

Shimane University School of Medicine, Japan

Latest advances in endoscopic imaging

Hironori Yamamoto

Jichi Medical University, Japan

Irreversible electroporation therapy for unresectable local advanced pancreatic cancer (LAPC)

Fuminori Moriyasu

Tokyo Medical University, Japan

Latest advances in endoscopic imaging

Hironori Yamamoto

NAME: Hironori Yamamoto, M.D., Ph.D.

EDUCATION:

1978-1984 Jichi Medical School, Tochigi, Japan

INTERNATIONAL TRAINING:

1990-1991 Mayo Clinic, Rochester, MN

1991-1993 University of Texas Southwestern Medical Center, Dallas, TX

APPOINTMENT:

2007 Professor of Medicine, Jichi Medical University
Head of the Department of Endoscopic Research and International Education (Funded by Fujifilm)

2009 Visiting Professor of Surgery, Surgical Endoscopy, Department of Surgery, National University of Singapore

2014 Professor and Chairman, Department of Medicine, Division of Gastroenterology, Jichi Medical University

HOSPITAL APPOINTMENTS:

2008- Director, Endoscopy Center, Jichi Medical University Hospital

2012- Director, Gastroenterology Center, Jichi Medical University Hospital

2015- Vice President of Hospital, Jichi Medical University Hospital

AWARDS AND HONORS:

1998 The 55th Congress of Japan Gastroenterological Endoscopy Society Award

1999 Runner-up, 1999 Audio Visual Award of the American Society for Gastrointestinal Endoscopy (ASGE)

2000 The 59th Congress of Japan Gastroenterological Endoscopy Society Award

2006 American Society for Gastrointestinal Endoscopy (ASGE) Audiovisual Award
"Double-balloon endoscopy for diagnosis and treatment of small intestinal diseases"

2006 The 31st Harushige Inoue Award "Double balloon endoscopy"

2009 The 19th Nikkei Business Publications, Inc. Award

2015 American Society for Gastrointestinal Endoscopy (ASGE) 2015 Crystal Awards
"International Service Award"

2015 German Society of Gastroenterology 2015 (Leipzig, Germany) "Endoscopy Award"
(Gastroenterologie Viszeralchirurgie Viszeralmedizin)
(State of the Art Lecture: Small bowel endoscopy -a challenge for more than 10 years)

Latest advances in endoscopic imaging

Hironori Yamamoto
Professor of Medicine, Jichi Medical University

One of the ultimate goals of gastrointestinal (GI) endoscopy is a reduction in GI cancer-related deaths. GI cancers result in a large proportion of cancer-related deaths in many countries. The incidence and mortality rates from GI cancers are increasing worldwide. Although non-operative management, such as chemotherapy, has undergone major advances, early detection and resection are still the main strategy for the treatment of GI cancers. Endoscopy plays an important role in the management of GI cancers.

For the detection of early stage GI cancers, recognition of subtle changes in color and morphology is important. Recent advances in endoscopic imaging technology have made early detection easier. Image-Enhanced Endoscopy (IEE) is an endoscopic technique to enhance the contrast of the image. Conventionally, the dye spray method using indigo carmine, has been used to enhance the contrast to facilitate the recognition of early GI cancers. Recently, equipment-based techniques have been developed to make the recognition of abnormal tissue easier. In general, equipment-based IEE methods are designed to enhance visualization of the microvessels of the mucosa, which are altered in abnormal tissues. Equipment-based IEE includes narrow-band imaging (NBI), flexible spectral imaging color enhancement (FICE), blue-laser imaging (BLI) and linked-color imaging (LCI), etc. Of these various techniques, LCI is unique and has great potential to increase the detection rate of early GI cancers.

LCI images are acquired by simultaneously using narrow-band short wavelength light and white light in an appropriate balance. The information for several colors is simultaneously expanded so that the reddish and whitish colors become redder and whiter respectively. As a result, a good contrast image of bright and similar color tone to a white light image is obtained. LCI can be used in screening endoscopy from the beginning to the end because the color tone is similar to natural white light images. However, with color enhancement of even mild redness, caused by altered microvessels of the mucosa, the recognition of early neoplastic lesions become much easier. Therefore, LCI is a promising IEE method to improve the detection rates of early GI cancers.

Another important factor in improving the early detection of GI cancers is to make the endoscopy procedure more tolerable for patients. In order to widely dissseminate screening endoscopy, it should be easy to undergo. Transnasal endoscopy is a good way to make the endoscopy easier for patients. Fujifilm has a transnasal endoscope, the EG-L580NW, as part of the LASEREO system. Using transnasal endoscopy with LCI, the early detection of gastric cancer is expected. For the characterization of early gastric cancers, magnifying endoscopy with BLI, using the EG-L600ZW endoscope, is useful. The EC-L600ZP is a new colonoscope which is part of the LASEREO system, suitable for both detection and characterization. This colonoscope has a slim and flexible shaft with curve-tracking capabilities. Therefore, it is suitable for screening colonoscopy with easy insertion. At the same time, it has a high-definition CMOS sensor and optical zoom function, up to 135 times. Easy insertion and high image quality with LCI and BLI are available.

New double-balloon endoscopes (DBE) have also improved the image quality compared to previous models. The EN-580T is a new therapeutic DBE with a 3.2mm accessory channel. Despite the larger accessory channel in the same outer diameter slim scope, the image quality is significantly improved. In addition to the high quality CCD, a near focusing lens up to 2mm enables detailed observation of small intestinal villi. The EN-580XP is a new diagnostic DBE with an outer diameter of 7.5mm. Despite the very small diameter, it has the same high quality CCD as the EN-580T.

In this lecture, I will introduce the latest advances in endoscopic imaging using Fujifilm endoscopes.

Irreversible electroporation therapy for unresectable local advanced pancreatic cancer (LAPC)

Fuminori Moriyasu

Birth & Place: September 3, 1950
Hiroshima,Japan

Marital Status: Married

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Home Address: 4-14-14-3502 Akasaka, Minatoku,Tokyo,107-0052,Japan .

Education: Graduated -Ph.D.in Post-Graduate School of Medicine,
Kyoto University,1986-M.D.in Kyoto University School of Medicine,1975

Professional Experience:

-Chairman & Professor, Department of Gastroenterology and Hepatology,
Tokyo Medical University, Japan, 2000-present
-Associate Professor, Department of Gastroenterology and Hepatology,
Kyoto University Post-Graduate School of Medicine,1996
-Assistant Professor, The First Department of Internal Medicine,
Kyoto University School of Medicine,1986

Membership: Japanese Society of Internal Medicine
Japanese Society of Gastroenterology
The Japan Society of Hepatology
The Japan Society of Ultrasonics in Medicine
The Japan Society for Portal Hypertension
Japanese College of Angiology
American Institute of Ultrasound in Medicine

Publications: More than 170 publications in English on various topics in the areas of gastroenterology, hepatology and ultrasound.

Irreversible electroporation therapy for unresectable local advanced pancreatic cancer (LAPC)

Fuminori Moriyasu
Department of Gastroenterology & Hepatology, Tokyo Medical University

[Purpose] Irreversible electroporation (IRE) is a new local ablation therapy. IRE induces apoptosis of cancer cells through nano-sized irreversible electroporation of the cell membrane by high voltage DC electrical pulses. IRE has been used for local for therapy of advanced pancreatic cancer (LAPC) since 2008 in USA and EU.
[Materials and methods] We performed IRE therapy on unresectable LAPC patients. The safety and efficacy of the IRE therapy was evaluated for cytoreductive and down staging effects. This study was performed under approval by the Internal Review Board.

Equipment used was an IRE system (NanoKnifeR, AngioDynamics, N.Y., USA). Subjects were six LAPC patients (4 males and 2 female; averaged age: 62 years. Four patients were cancers of the pancreatic head, and two patients had cancer of the pancreatic body. IRE was performed under surgical laparotomy in 3 patients and using a percutaneous approach in 3 patients. Ultrasound guidance was used in both approaches.

[Results] Three IRE electrodes were used in one patients and 4 electrodes were used in 5 patients. Ablation conditions were as follows: electrical voltage, 3,000V; pulse length, 90 microseconds; and averaged pulse number, 630 pulses. The average of operating time was 2.5 hours.

The averaged observation period was 9 months. The response rate was 5/6 patients (83%) and resectability was considered in 2/6 patients (33%). Adverse events with grade >3 were severe abdominal pain in 3/6 patients (50%) for a few days after IRE, pancreatitis in 2/6 patients (33%), and gastrointestinal bleeding in 2/6 patients (33%).
[Conclusions] A down staging effect and an anti-cancer response was observed using IRE therapy in LAPC.

Topic I

Advanced imaging in endoscopy-1

DAY2 April 20th 8:10-9:10　OHGI Room (4F)

Chairpersons:

Roy M. Soetikno

Singapore General Hospital, Singapore

Haruhiro Inoue

Showa University Koto-Toyosu Hospital, Japan

Lecture-1 **Time Trend in the Development of Advance Endoscopy Imaging of the Gastro-Intestinal Tract**

Shiaw-Hooi Ho

University of Malaya Medical Centre and University of Malaya Specialist Centre, Malaysia

Lecture-2 **Advances in image enhanced endoscopy for upper gastrointestinal cancers**

Philip Wai Yan, CHIU

The Chinese University of Hong Kong , Hong Kong

Lecture-3 **Advanced Imaging in Gastroenterology**

Rapat Pittayanon

King Chulalongkorn Memorial Hosptial, Thailand

Lecture-4 **VISUALIZATION OF THE BILIARY SYSTEM – A REVIEW**

Manu Tandan

Asian Institute of Gastroenterology, India

Time Trend in the Development of Advance Endoscopy Imaging of the Gastro-Intestinal Tract

Dr. Shiaw-Hooi Ho

Dr. Shiaw-Hooi Ho is a Consultant Physician and Gastroenterologist in both University of Malaya Medical Centre and University of Malaya Specialist Centre. He is also a Senior Medical Lecturer in the Department of Medicine, University of Malaya. He received his basic medical degree in 2001 and went on to obtain his Master's Degree in Internal Medicine from University of Malaya in 2009. Dr. Ho completed his fellowship in gastroenterology from University of Malaya in 2012 and obtained his National Specialist Register in Internal Medicine and Gastroenterology in the year of 2012 & 2013 respectively. Following his attachment in Japan under the Japanese Society of Gastro-Enterology (JSGE) Research Fellowship Award, he began to promote the use of image-enhanced endoscopy (IEE) and endoscopic submucosal dissection (ESD) both in the detection and management of early gastrointestinal (GI) neoplasia.

Dr Ho also performs various other GI therapeutic endoscopy. He received many short stint training in various other renowned GI center-of-excellence (COE) worldwide eg National Center for Global Health and Medicine (Tokyo, Japan), Fukuoka University (Hakata, Japan), Kyushu University (Hakata, Japan), SoonChunHyang University Hospital (Bucheon, Korea) and Asian Institute of Gastroenterology (Hyderabad, India).

Dr Ho is also a faculty of Asian NBI Group (ANBIG), an academic interest group, which organize many local and international ANBIG workshops with the aim to promote detection and treatment of early GI neoplasia among GI healthcare practitioners. Besides that, he is also a member faculty of the 2015 Asia-Pacific consensus on the approach of difficult biliary access.

Apart from endoscopy, he is also the chairman of telemedicine working group of Malaysia Research and Education Network (MYREN). He also plays an important role (both board member and steering committee member) in the medical working group (MWG) of Asia-Pacific Advanced Network (APAN) which is active in organizing various international teleconferences among healthcare practitioners.

Time Trend in the Development of Advance Endoscopy Imaging of the Gastro-Intestinal Tract

Shiaw-Hooi Ho

Consultant Physician and Gastroenterologist in both University of Malaya Medical Centre and University of Malaya Specialist Centre

Advancement in image capturing and displaying technology have progressed by leaps and bounds over the last few decades. New innovations are being continuously introduced which changed the role of gastrointestinal (GI) endoscopy from a mere observational tool to a sophisticated real time diagnostic and therapeutic tool. From the published literatures, modern endoscopy can be largely divided into four eras based on the innovation milestones and their clinical impact in the field of GI endoscopy.

Era of modern video endoscopy and conventional chromoendoscopy (from 1983)

Conventional dyes used in endoscopy are broadly classified into non-absorptive (contrast), absorptive and reactive types. The main strength of conventional chromoendoscopy (CE) lies in its ability to increase detection of GI lesions e.g. Lugol's iodine and indigo-carmine dye.(1-4) However, it is not widely practiced as it is deemed to be time-consuming and cumbersome to use. Furthermore, certain dyes are not readily available in many countries.

Era of magnification chromoendoscopy (from 1996)

This was one of the most exciting era where many interesting observations were made using high magnification endoscopy (ME). Optical magnification of up to 150 times allows visualisation of the mucosal capillary network and offers a glimpse onto the first appearance of early luminal malignancy. Inoue et al first reported the magnification appearance of normal oesophageal mucosa and early oesophageal squamous cell carcinoma (ESCC) by demonstrating a change in the structure of intra-epithelial papillary capillary loop (IPCL) in 1996 and 1997 respectively.(5, 6) Barrett's oesophagus (BO) was also studied extensively under magnification chromoendoscopy. Using indigo-carmine dye spraying and Olympus magnification endoscope (GIF-Q160Z, 115x), Sharma et al identified 3 mucosal pattern of BO, namely ridged/villous pattern, circular pattern, and irregular/distorted pattern.(7) Ridged/ villous pattern had 97% yield for intestinal metaplasia while circular pattern 17%. Irregular or distorted pattern was strongly (100%) correlated with HGD. Yao et al were among the pioneers who first described the magnification appearance of early gastric cancer (EGC) under white light magnification endoscopy.(8) In the colon, Kudo et al first described the colonic pit pattern under magnifying chromoendoscopy using crystal violet staining.(9, 10) He divided the patterns into 5 major types which were proven later in many studies to have high predictive values of the underlying histology and depth of invasion.(11)

Era of high definition endoscopy, magnification optical-digital chromoendoscopy and endomicroscopy (from 2004)

This golden era witnessed the birth of new technologies like narrow band imaging (NBI), i-Scan, flexible spectral imaging colour enhancement (FICE) and later, blue laser imaging (BLI). In the proposed classification of advanced endoscopy imaging by Tajiri and Niwa,(12) these new technologies are grouped under optical-digital CE which is part of image enhanced endoscopy (IEE). These technologies enhance the contrast difference and highlight the subtle changes in mucosal surface and capillary pattern which are among the first few structures to change secondary to tumour proliferation and angiogenesis induced by tumour growth. Among these, NBI has the most widely published data. In the oesophagus, the use of non-magnified NBI allows detection of ESCC by demonstrating a well demarcated brownish area.(13) Together with magnification, it allows clearer visualization of the IPCL pattern. In the stomach, NBI is often used with ME to allow diagnosis of EGC by observing irregularity in either the micro-vascular or micro-surface pattern together with the presence of a demarcation line ("VS" classification system).(14) It also facilitate the detection of premalignant condition like intestinal metaplasia,(15) which is seen as light blue crest under magnification NBI.(16) More interesting development took place in the lower GI tract, assessment under NBI either under magnification (e.g. Sano classification) or non-magnification (NBI International Colorectal Endoscopic or NICE classification) were proven to be useful and highly accurate in predicting the histology.(17, 18) Occurring at the around same time was the introduction of high definition (HD) endoscope and monitor. It was shown in a meta-analysis that HD alone contributed to modest improvement in colonic adenoma detection rate (ADR) of 3.5% compared to standard definition (SD) white light endoscopy (WLE).(19) Endomicroscopy and endocytoscopy were introduced since 2004 which offered microscopic imaging at up to 1400-fold magnification. Many case series had confirmed its usage in providing accurate real-time histologic or cytologic assessment.(20) However, a decade has passed and its use is still not popular. It is in the author's opinion that the likely cause is due to lower perceived value compared to what is already a very good optical diagnostic tool provided by high definition magnification endoscope with optical-digital CE.

Era of improved optical-digital chromoendoscopy and novel wide field-of-view endoscope (from early 2010s)

Realising the limitation of darken image when optical-digital CE was used, the industries have overcome this issue by introducing second generation optical-digital CE with brighter light source and perhaps better image sensor. Though better in visibility,(21, 22) data is still not

strong to suggest its use as primary screening tool. At around the same time, a wider field-of-view endoscope was introduced. Gralnek et al reported a much lower adenoma miss rate (7% versus 41%, p<0.0001) in a novel 330-degree field-of-view endoscopy system (FUSE) when compared with conventional endoscope.(23)

In conclusion, not just the improved detection rate, clinical data have shown that the current advanced endoscopy imaging is capable of accurate differentiation of GI lesions. With this, we are said to enter an era of “optical biopsy” with many more exciting development await us.

References

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6. Inoue H HT, Nagai K, et al. Ultrahigh magnification endoscopic observation of carcinoma in situ of the esophagus. Dig Endosc. 1997;9:16-18.
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12. Hisao Tajiri HN. Recent Advances in Electronic Endoscopes: Image-enhanced endoscopy. JMAJ. 2008;51(3):199-203.
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16. Uedo N, Ishihara R, Iishi H, Yamamoto S, Yamada T, Imanaka K, et al. A new method of diagnosing gastric intestinal metaplasia: narrow-band imaging with magnifying endoscopy. Endoscopy. 2006;38(8):819-24. Epub 2006/09/27.
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18. Hayashi N, Tanaka S, Hewett DG, Kaltenbach TR, Sano Y, Ponchon T, et al. Endoscopic prediction of deep submucosal invasive carcinoma: validation of the narrow-band imaging international colorectal endoscopic (NICE) classification. Gastrointestinal endoscopy. 2013;78(4):625-32. Epub 2013/08/06.
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22. Yoshida N, Hisabe T, Hirose R, Ogiso K, Inada Y, Konishi H, et al. Improvement in the visibility of colorectal polyps by using blue laser imaging (with video). Gastrointestinal endoscopy. 2015;82(3):542-9. Epub 2015/04/09.
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Advances in image enhanced endoscopy for upper gastrointestinal cancers

Philip Wai Yan, CHIU

Name: Philip Wai Yan, CHIU

Academic qualifications:

MBChB (CUHK)	1994
FRCS (Edin)	1998
FRCS (Edin)(Gen)	2001
FHKAM (Surgery)	2001
MD (CUHK)	2009

Previous academic positions held:

Associate Professor, Department of Surgery, CUHK 2005 – 2011

Present academic position:

Professor, Department of Surgery, CUHK (since 2011)

Director, CUHK Jockey Club Minimally Invasive Surgical Skills Center (since 2011)

Director, CUHK Chow Yuk Ho Technology Center for Innovative Medicine (since 2014)

Assistant Dean (External Affairs), Faculty of Medicine, Chinese University of Hong Kong (since 2013)

Research work:

1. Pioneer in development of Endoscopic Surgery
   - First to perform Endoscopic Submucosal Dissection (ESD) for treatment of early GI cancers in Hong Kong,currently experienced more than 250 cases of ESD
   - First to perform Per Oral Endoscopic Myotomy (POEM) for treatment of Achalasia in Hong Kong
   - Pioneered performance of Per Oral Endoscopic Tunnel Resection (POET) for treatment of gastrointestinal submucosal tumors
2. Research and Development in Robotic Surgery
   - Pioneer the performance of robotic esophagectomy for treatment of squamous esophageal cancer
   - Perform world first robotic ESD for treatment of early gastric cancer in a multicenter prospective study
3. Translational research in biomedical engineering and application in surgery
   - Development of a novel laparoscopic liver retractor with Mediconcepts
   - Development of a novel ESD device for treatment of early gastrointestinal cancers

Publication records: (*as the corresponding author)

Until Feb 2016, published 177 peer reviewed articles (ISI Web of Science search) with H-index of 21.

Section A - Five most representative publications in recent five years

1. *Chiu PW, Chan FK, Lau JY. Endoscopic Suturing for Ulcer Exclusion in Patients With Massively Bleeding Large Gastric Ulcer. Gastroenterology. 2015 Jul;149(1):29-30
2. *Chiu PW. Novel endoscopic therapeutics for early gastric cancer. Clin Gastroenterol Hepatol. 2014 Jan; 12(1):120-5
3. *Chiu PW, Wu JC, Teoh AY, Chan Y, Wong SK, Liu SY, Yung MY, Lam CC, Sung JJ, Chan FK, Lau JY, Ng EK. Per

oral endoscopic myotomy for treatment of achalasia: from bench to bedside. Gastrointest Endosc. 2013 Jan;77(1):29-38.

4. Phee SJ, Reddy N, Chiu PW, Rebala P, Rao GV, Wang Z, Sun Z, Wong JY, Ho KY. Robot-assisted endoscopic submucosal dissection is effective in treating patients with early-stage gastric neoplasia. Clin Gastroenterol Hepatol. 2012 Oct 10(10):1117-21.
5. *Chiu PW, Teoh AY, To KF, Wong SK, Liu SY, Lam CC, Yung MY, Chan FK, Lau JY, Ng EK. Endoscopic submucosal dissection (ESD) compared with gastrectomy for treatment of early gastric neoplasia: a retrospective cohort study. Surgical Endoscopy 2012; Dec 26(12):3584-91.

Section B - Five representative publications beyond the recent five-year period

1. *Chiu PW, Ng EK, Cheung FK, Chan FK, Leung WK, Wu JC, Wong VW, Yung MY, Tsoi K, Lau JY, Sung JJ, Chung SS. Predicting mortality in patients with bleeding peptic ulcers after therapeutic endoscopy. Clin Gastroenterol Hepatol. 2009 Mar;7(3):311-6;
2. *Chiu PW Chan KF, Lee YT, Sung JJ, Lau JY, Ng EK. Endoscopic submucosal dissection (ESD) for treatment of early neoplasia of the foregut using combination of knives. Surgical Endoscopy 2008; 22(3):777-783
3. *Chiu PW, Hu B, Lau JY, Sun LC, Sung JJ, Chung SS. Transoral intragastric endoscopic plication of bleeding peptic ulcer: a survival study in a porcine model. Gastroint Endosc 2006; 63(4):681-5
4. Chiu PW, Chan AC, Leung SF, Leong HT, Kwong KH, Li MK, Au-Yeung AC, Chung SC, Ng EK. Multicenter prospective randomized trial comparing standard esophagectomy against definitive chemoradiotherapy for treatment of squamous esophageal cancer – early results from CURE. Journal of Gastroint Surg 2005; 9(6):794-802
5. *Chiu PW, Lam CY, Lee SW, Kwong KH, Lam SH, Lee DT, Kwok SP. The effect of scheduled second endoscopy on peptic ulcer rebleeding – a randomized controlled trial. Gut 2003; 10:1403-7

Others (Awards, Research Achievement and Services):

Achievements

1. State Scientific & Technological Progress Award, State Council of People's Republic of China (2007)
2. Research abstract awarded Best of Digestive Disease Week, United States (2011)
3. Higher Education Outstanding Scientific Research Output Award 2nd class award in Technological Advancement, Ministry of Education of the People's Republic of China (2012)
4. Champion of the World Cup of Endoscopy, American Society of Gastrointestinal Endoscopy (2012)
5. Outstanding contribution award, Chinese Society of Digestive Endoscopy (2015)

Patent

Development of a new device for performance of Endoscopic Submucosal Dissection

1. Japan: Japan Patent Office (JPO) patent application on 19th May 2009 (No. 2010-268845)
2. China: State Intellectual Property Office (SIPO) – Utility Model Application on 7th May 2013 (No. 201320240576.6)
3. Korea: Korean Intellectual Property Office (KIPO) – Korean Utility Model Application on 7th May 2013 (No. 20-2013-0003568)

Robotic system – Development of Robotic Endoscope with Suturing Ability

1. US Patent – provisional application filed (EFS ID: 20560299)
2. China: State Intellectual Property Office (SIPO) – provisional application filed

Advances in image enhanced endoscopy for upper gastrointestinal cancers

Philip WY Chiu

Professor, Department of Surgery, Institute of Digestive Disease, The Chinese University of Hong Kong

Abstract

Upper gastrointestinal (GI) cancers are common in Asia. The cases in Asia amount to more than 70% of the gastric cancers worldwide. Upper gastrointestinal cancers carries grave prognosis, with 5 year survival of around 40% for gastric cancers and 30% for squamous esophageal cancers. On the contrary, the 5 year survival for early stage upper GI cancers is generally more than 80%. Endoscopic recognition of early stage upper GI cancers is difficult. A recent research of 837 patients demonstrated that endoscopic examination of more than 7 minutes allowed higher detection rate of high risk gastric lesions [1]. Recent advances in endoscopic technologies allowed image enhancement to enable endoscopists to have better delineation of early microvascular and microstructural changes for early upper GI neoplasia. Image enhanced endoscopy (IEE) aimed to improve endoscopic recognition and characterization of early upper GI cancers. A multicenter prospective randomized comparison between high definition white light endoscopy (HD-WLE) and narrow band imaging (NBI) showed that those received NBI endoscopy demonstrated higher detection of gastric intestinal metaplasia [2]. NBI with magnification also enhanced diagnosis of early gastric cancers through delineation of microvascular (MV) and microstructural (MS) patterns [3]. Our prospective study comparing NBI against lugol chromoendoscopy demonstrated that NBI achieved a similar sensitivity but higher specificity for recognition of early esophageal cancers among high risk population.

One of the major obstacles to recognition of early upper GI neoplasia is the lack of educational program on training for recognition of the endoscopic features. In a standardized training program for diagnosis of early GI cancers conducted in Asian countries, we compared the results of pre and post test after the training. The results demonstrated a significant improvement in diagnosis of early esophageal and gastric cancers after the standardized training.

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Advanced Imaging in Gastroenterology

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Publications in "Advanced Imaging in Gastroenterology"

1. Pittayanon R, Rerknimitr R. Review Article: Role of Confocal Laser Endomicroscopy for the Detection of Early Gastrointestinal Malignancy. Thai Journal Gastro. 2011;12(1):52-6.
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Field of Interests

1. Imaged-enhance endoscopy (IEE) eg. NBI, FICE, BLI
2. Confocal laser endomicroscopy
3. Peroral endoscopic myotomy (POEM)
4. Endoscopic submucosal dissection (ESD)
5. Endoscopic mucosal resection (EMR)
6. Epidemiology
7. Upper GI disease esp. gastric and esophageal cancer
8. Upper GI bleeding

Advanced Imaging in Gastroenterology

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Currently, the technology in gastrointestinal (GI) endoscopy imaging is rapidly developed. From the evidence-based review, its role is not limited only for diagnosis but also for predicting treatment response in some GI disease.

In the past, chromoendoscopy is a well-known technique to enhance epithelial abnormality, especially malignancy change. However, chromoendoscopy is not widely adopted in many parts of the world. One of the important reasons is that this technique needs the experienced endoscopist to interpret the images during the procedure. In addition, the requirement of cumbersome spraying method is inconvenience and need time to prepare. Later, an easier technique called image-enhanced endoscopy (IEE) such as Narrow-band Imaging (NBI), Flexible spectral Imaging Color Enhancement (FICE) and i-scan have been reported as the technique to facilitate targeted biopsy. Over a decade, the highest magnification (1000X) in clinical endscopy, confocal laser endomicroscopy (CLE) has been introduced as real time evaluation of both GI cancerous and non-cancerous lesion. The roles of CLE have been utilized at different levels from research base to the real practice in the field of diagnostic endoscopy. The potential indications of CLE include 1) differentiate malignant from non-malignant lesion in suspected area which still questionable by standard technique i.e. Barrett's esophagus, indeterminate biliary stricture, pancreatic mass, 2) Targeted biopsy of suspicious malignant or premalignant lesion i.e. gastric intestinal metaplasia, early gastric cancer, 3) Real-time diagnosis for endoscopic management i.e colonic polyp, dysplastic change in IBD and 4) Predicting treatment response i.e. anti-TNF treatment in IBD. However, CLE still limited to expert centers due to suboptimal validities of the criteria and it is still not practical to be adopted for day-to-day practice.

In the future, these technologies may be more advanced. We should keep the eyes on their improvement and adopt for clinical practice properly.

VISUALIZATION OF THE BILIARY SYSTEM – A REVIEW

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Awards:

Awarded the ISG J Mitra Endoscopy Award for the year 2011 for contribution in the field of GI endoscopy. This is awarded annually by the Indian Society of Gastroenterlogy to one Endoscopist for outstanding contribution to the development of Endoscopy in India.

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VISUALIZATION OF THE BILIARY SYSTEM – A REVIEW

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Indeterminate biliary strictures have often posted diagnostic and management challenges for the treating gastroenterologists. Ideal visualization of the biliary tree for a correct and early diagnosis is one of the final frontiers for the therapeutic endoscopist. In today's practice despite the best evidence from imaging and tumour markers 10-25% of all strictures which were presumed malignant turned out to be benign. For cholangiocarcinoma, on the other hand an early diagnosis offers the best chance of survival. R0 resection rates in cholangiocarcinoma have an average survival of 43 months compared to 24 months for R1 resection. It is imperative that a correct and early diagnosis be made in all indeterminate biliary strictures in the best interest of patient management. This abstract will limit itself to the newer technologies of imaging the biliary tree with respect to indeterminate strictures and highlight both efficacy and limitations.

Imaging of the biliary system: Ultrasound, CT scan, MRCP and Endosonography are established techniques for imaging the biliary system. They are safe and non invasive but have several limitations in both consistency and reliability for indeterminate biliary strictures. In indeterminate biliary strictures the diagnostic yield of brush cytology using ERCP is between 30 – 50%. When combined with intraductal biopsy a yield between 55 – 71% is achieved. ERCP has the disadvantage of being associated with complications of sphincterotomy and transpapillary access notably pancreatitis, bleeding and perforation.

Newer modalities of imaging the biliary system:

Cholangioscopy: Cholangioscopy is the direct visualization of the biliary system and was first introduced as an intraoperative procedure as early as 1941. Per oral cholangioscopy (POCS) can be a dual operator based system such as the mother baby scope or single operator based procedure – the Spy glass direct visualization system as well as direct POCS using the ultra slim endoscope. Mother baby scope requires two skilled endoscopists and has the limitation of lack of adequate deflection as well as poor vision. The Spy glass direct visualization system is a single operator system. The limitations of the Spy glass system included less than satisfactory vision and fragility of the optical probes. The digital version of Spy glass system introduced recently offers the advantages of better vision, greater maneurvibility and ease of use. Direct POCS uses an ultra slim endoscope with a diameter of 5 – 6 mm. The main advantages are better vision and large working channel. Results with POCS in indeterminate biliary strictures especially with Spy glass and ultra slim endoscopes have been very encouraging with positivity varying between 85 – 90%. Spy glass directed biopsy (Spy bite) has shown positivity between 82 – 97 %. Our own experience reveals that a visual impression of the lesion is better than directed biopsy (78% Vs 50%) for indeterminate biliary strictures. Mucosal neovascularisation and irregular dilated vessels are typical of malignancy while mucosal nodularity and luminal stenosis are highly suggestive. Methylene blue can be spread on the affected area for better localization. Advanced imaging with autofluroscense makes the abnormal mucosa appear green or black and increases sensitivity at the expense of specificity. NBI prototypes have also been used for both surface and vessel examination but the presence of blood and mucus is a distinct limitation. Further validation and experience with these advanced imaging techniques is awaited. POCS offers advantages of therapeutic application for malignant biliary strictures. Ablation therapy for inoperable strictures using photodynamic therapy (PDT) YAG laser ablation, radio frequency ablation or APC can all be performed via POCS. POCS can also be utilized for cannulating complex strictures following liver transplantation as well as evaluation of unexplained haemobilia.

Intraductal Ultrasound: (IDUS): IDUS using a thin (2.9mm) probe passed over a guide wire offers good imaging of the biliary system. A diagnostic accuracy of 62 – 89% has been reported for indeterminate biliary strictures. Hyperechoic strictures with irregular margins are established criteria for malignancy. Asymmetry of lesion, tumour size > 10 mm, presence of lymphnodes and interruption of bile ducts are some of the other features which suggest malignancy. IDUS

helps in accurate T staging of the lesion for the purpose of resection. Its limitations include the need for validation of criteria for malignant and benign strictures. Examination is also hindered by earlier bile duct manipulation. IDUS is best performed prior to placement of biliary stents.

Probe based confocal laser endomicroscopy (pCLE) : pCLE involves the use of a mini probe (1-2.5 mm diameter) passed through the working channel of ERCP or cholangioscope. Real time image at the depth of 40-70 microns is obtained Intravenous injection of fluroscein dye is given prior to visualization. Initial results in indeterminate biliary strictures are very encouraging with the working group showing sensitivity, specificity, PPV, NPV of 98%, 67%, 71% and 97% respectively. The Miami classification and the subsequent Paris modification have framed criteria for malignant strictures which include thick dark or white bands of 40 microns. Leak of fluroscein dye and dark clumps of cells are suggestive of malignancy. This relatively new technology has the limitation of requiring specialized equipment. Bleeding from friable tumours interferes with the images. Movements of either the patient or operator can also interfere with image capturing. It is a time dependent procedure after injection of the dye.

Visualization of the biliary system for a correct and early diagnosis of indeterminate biliary stricture are essential in optimizing management. Cholangioscopy as well as the newer techniques discussed earlier help provide an accurate diagnosis. Further validation and application at larger number of centers will help in the establishment of these technologies in the algorithm of management of indeterminate biliary strictures.

Topic I

Advanced imaging in endoscopy-2

DAY2 April 20th 9:10-10:10　OHGI Room (4F)

Chairpersons:

Khean-Lee Goh

University Malaya Medical Centre, Malaysia

Hiroshi Kashida

Kindai University Faculty of Medicine, Japan

Lecture-1 **The Role of Advanced Endoscopy Imaging for Detecting Sessile Serrated Adenomas**

Murdani Abdullah

Universitas Indonesia, Indonesia

Lecture-2 **Magnifying endoscopy in the esophagus**

Haruhiro Inoue

Showa University Koto-Toyosu Hospital, Japan

Lecture-3 **Clinical applications of confocal laser endomicroscopy in intestinal diseases**

Tae Il Kim

Yonsei University College of Medicine, Korea

Lecture-4 **Confocal laser endomicroscopy**

Kazuki Sumiyama

Jikei University School of Medicine, Japan

The Role of Advanced Endoscopy Imaging for Detecting Sessile Serrated Adenomas

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The Role of Advanced Endoscopy Imaging for Detecting Sessile Serrated Adenomas

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Sessile serrated adenoma now is considered as a precursor of microsatellite unstable colorectal carcinoma. Serrated pathway has recently emerged as the second pathway leading to colorectal cancer. The serrated pathway characterized by aberrant methylation of promoter region of specific gene.

Sessile serrated adenoma morphologically similar to hyperplastic polyp when using conventional endoscopy imaging. Current advancement of endoscopy imaging such as HD white light endoscopy, chromoendoscopy, Narrow Band Imaging, and Blue Laser Imaging allow us to discriminate sessile serrated adenomas from hyperplastic polyp. Endoscopic appearance of SSA is typically a pale, large, sessile lesion that rests on the crest of the mucosal folds.
A SSA is predominantly found in the proximal colon of middle-aged women and grows to larger sizes than other serrated adenomas. It is strongly associated with the BRAF mutation that is MSI-H and CIMP-H, and considered to be a precursor to dysplastic serrated adenomas and serrated adenocarcinoma. Some studies try to identify the characteristics of sessile serrated adenoma because previous classification using NICE classification cannot discriminate between hyperplastic polyp and serrated adenoma.

Hezewinkel et al study show the characteristics of sessile serrated adenoma are cloud-like surface (OR, 4.91; 95% CI, 2.42-9.97), indistinct borders (OR, 2.38; 95% CI, 1.14-4.96), irregular shape (OR, 3.17; 95% CI, 1.59-6.29), and dark spots inside the crypts (OR, 2.05; 95% CI, 1.02-4.11). The sensitivity, specificity, and accuracy of NBI for differentiating serrated polyps containing either none or all 4 endoscopic SSA/P features were, respectively, 89%, 96%, and 93%. Study by Yamada et al found that dilated and branching vessels in NBI with magnification is a potential unique feature for sessile serrated adenoma.

Magnifying endoscopy in the esophagus

Haruhiro Inoue

He is a surgeon and an endoscopist. He is a professor of Showa University, School of Medicine, and currently directs Digestive Diseases Center, Showa University Koto-Toyosu Hospital in Tokyo. He was graduated from Yamaguchi University, school of medicine in 1983. Right after graduation from medical school, he took his residency at 1st department of surgery, Tokyo Medical and Dental University. He spent there and its affiliated hospitals more than 13 years. During this period he got a Japanese board of Surgery, Gastrointestinal surgery and Endoscopic surgery. In 2006 he was honored of crystal award from ASGE and nominated to honorary member of the society. In 2008 he became a Fellow of ASGE (FASGE). In 2009 he promoted a Professor of Showa University and also organize Showa University International training center for Endoscopy (SUITES). In 2010, he became an honorary member of Russian Society of Endoscopy (No.007). In 2011 he received a Pioneer in Endoscopy award from SAGES (Society of American Gastrointestinal Endoscopic Surgeons). In 2012 he became an honorary member of German Society of Radiology and Digestive Endoscopy. In 2013 he received Crystal award (ASGE: International service award), which was his second-time honor from ASGE.

He develop a cap-EMR technique in 1993, which made EMR easier.
In 2000 he reported world first EMR for Barrett intramucosal cancer.
In 2003 he reported circumferential EMR for Barrett esophagus with
HGD. This is also the first clinical case of ARMS (antireflux
mucosectomy). In 2008 he performed world-first clinical case of POEM (per-oral endoscopic myotomy). Until now he treated more than 1000 achalasia patients by POEM surgery. In 2014 he reported ARMS (anti-reflux mucosectomy) procedure for PPI-resistant GERD. He has more than 500 impact factors.

Magnifying endoscopy in the esophagus

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In 1996 we reported IPCL (intra-papillary capillary loop) can be observed using magnifying endosocope in the squamous epithelium [1]. IPCL is located at intra-epithelial papilla and runs perpendicularly in the epithelium as a most peripheral vessel of esophagus with a diameter of 7 to 10 μ, which allows single RBC (red blood cell) passes through it. This vessel demonstrates characteristic morphological change according to epithelial atypia from low grade dysplasia to high grade [2]. Definite carcinoma in situ of the esophagus shows characteristic morphological changes; dilatation, tortuous running, caliber irregularity and shape variety (so-called 4 features of microangiographic changes in esophageal malignancy) [3]. Observation of IPCL morphological changes with magnifying endoscopy is essential to make tissue characterization.

IPCL changes also reflect cancer invasion depth. In intra-mucosal cancer IPCL generally keeps “loop” figure. But in submucosal invasive cancer “loop” figure of IPCL was often lost and new large tumor vessels appear particularly in exposed cancer tissue, which has more than 9 times larger caliber than normal IPCL [4]. Comprehensive analysis of IPCL findings were summarized [5, 6]. Abnormal vessels which still keep original IPCL pattern is characteristic to Intra-mucosal cancer. Extra-large enlarged abnormal vessels are typically observed in deep invasive submucosal cancer. Japanese esophageal society classification [7] including AVA [8] is now arranged and waiting for publication.

After this achievement we endeavored to observe microcellular structure using ultra-high magnifying endoscopy. Endocytoscopy is an ultrahigh magnifying endoscopy which enables to visualize nucleus [9, 10]. According to cytological atypia endocytosocpic findings are classified into 5 categories [10]. CM (crystal violet and methylene blue) double staining creates excellent contrast of nucleus from cytoplasm similar to hematoxylin-eosin staining [11]. A new endocytoscope has extremely wide range of magnifying function. It enables regular endoscopic observation (8X) to endocytoscopic observation (400X). Both magnifying observation and endocytoscopic observation are now involved in a part of regular endoscopic observation. In other words, when we perform endoscopic check-up of upper GI endoscopy, a suspected area can be at first detected by non-magnifying endoscopy. Magnifying endoscopy is used to characterize suspected area with observation of IPCL pattern. Finally cytological atypia can be evaluated by ultrahigh magnification. Endocytoscopic evaluation seems to be relevant to histological image. Endocytoscopy may replace conventional biopsy diagnosis at least in the case of receiving anti-coagulant. In the near future endocytoscopic diagnosis can be done under computer basis.

Recent advancement of endoscopic imaging offers us seamless observation from non-magnifying view to cellular-level imaging.

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Clinical applications of confocal laser endomicroscopy in intestinal diseases

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Scientific Publication (Selected)

1. High-risk metachronous polyps are more frequent in patients with traditional serrated adenomas than in patients with conventional adenomas: a multicenter prospective study. Yoon JY, Kim HT, Hong SP, et al. Gastrointestinal Endoscopy 2015;82:1087-93.
2. The effect of prediagnostic aspirin use on the prognosis of stage III colorectal cancer. Kim B, Park SJ, Hong SP, et al. International Journal of Clinical and Experimental Medicine 2015;8:13435-45.
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4. The Role of Barrier Dysfunction and Change of Claudin Expression in Inflammatory Bowel Disease. Kim TI. Gut and Liver 2015;9:699-700.
5. Nonsteroidal anti-inflammatory drugs suppress cancer stem cells via inhibiting PTGS2 (cyclooxygenase 2) and NOTCH/HES1, and activating PPARG in colorectal cancer. Moon CM, Kwon J-H, Kim JS, Oh S-H, et al. International Journal of Cancer 2014;134:519-529.
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8. Chemopreventive drugs: Mechanisms via inhibition of cancer stem cells in colorectal cancer. Kim TI. World J Gastroenterol 2014;20:3835-46.
9. Colorectal stenting: An advanced approach to malignant colorectal obstruction. Hong SP, Kim TI. World J Gastroenterol 2014;20:16020-8.
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Clinical applications of confocal laser endomicroscopy in intestinal diseases

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Confocal laser endomicroscopy (CLE), an adaption of confocal laser scanning microscopy, uses laser light for excitation and captures laser-induced fluorescence from a defined imaging plane depth, provides high resolution microscopic images at subcellular resolution, and enables deep as well as superficial tissue imaging. However, submucosal infil¬tration cannot be detected by current wavelengths. Usually, intravenous fluorescein has been used to improve the optical contrast in cellular, subcellular, connective tissue and vessel architecture at high resolution, but does not stain nuclei. The CLE must be performed in direct contact with the mucosa. CLE images represent optical sections parallel to the horizontal tissue surface, which is in 90° to conventional histopathologic section. For the interpretation of microscopic images, adequate training is needed in the endoscopic technique and knowledge of mucosal histopathology. Because CLE provides high magnification within a small field of view, CLE can be combined with chromoendoscopy or HD-WLE (high definition white light endoscopy) to identify suspicious areas.

Many studies on CLE have demonstrated the ability of gastroenterologists to obtain and interpret microscopic images of the gastrointestinal tract during endoscopy. The information from CLE has been successfully used to minimize sampling error by microscopically targeted biopsies and to guide endoscopic interventions. In addition, CLE also can visualize cellular changes in their natural microenvironment free of artefacts, enabling fundamental insights into mechanisms of intestinal diseases in clinical and translational science.

CLE not only enable prediction of histology, but actual visualization of microscopic tissue details in real time during endoscopy. Therefore, it has resulted in the use of intravital microscopy to actually plan and guide endoscopic interaction. Initial studies demonstrated the utility of CLE in the evaluation of colonic polyps. On the basis of a simple-to-use classification, colonic neoplasia could be differenti¬ated from regenerative and normal mucosa with high accuracy. However, due to difficulties in obtaining good microscopic quality of CLE images, increasing quality and experience with new HD WLE, and interobserver variability, there have been some controversial data on the comparison of CLE with HD WLE and virtual or real chromoendoscopy.

Intra¬vital visualization has been utilized for microscopically guided ‘smart’ biopsies in diseases affecting large mucosal areas, because conventional random biopsies are subject to substantial sampling error. CLE could be also used to characterize suspicious lesions noted during pancolonic chromoendoscopy during surveillance colonoscopy for ulcerative colitis, suggesting usefulness of chromoendoscopy-guided CLE to abrogate the need for random biopsies and improve the clinical management of UC. In addition, on the relevance of achieving mucosal healing in inflammatory bowel disease (IBD), CLE will have a role as an excel¬lent tool for microscopic surveillance of inflammation under therapy. In subcellular level of IBD, CLE could provide additional information, such as epithelial gaps found more frequently in patients with IBD, supporting previous findings of impairments in the epithelial barrier even in the absence of gross or microscopic changes on conventional endos¬copy or biopsy.

In further advanced step, CLE could be used for translational studies of epithelial function and molecular imaging due to its unique ability to visualize details at subcellular level in their natural microenvironment, free of the artifacts induced by biopsy sampling. Therefore, in the future, CLE might contribute to our understanding of disease pathogenesis by in vivo imaging.

In conclusion, CLE could be an adjunct to get ‘smart’ fewer biopsies instead of obtaining a larger number of untargeted random biopsy samples. In addition, CLE is not just a real time evaluation of histopathology, but also offers a unique microscopic view into changes of epithelial physiology and pathophysiology in the natural microenvironment. Furthermore, CLE might become more interesting as the ideal tool for on-site diagnosis, when resect-and-discard or diagnose-and-leave-in-place strategies are to be applied to clinical practice. However, there have been some issues to be solved, such as substantial amount of time to be added to the endoscopy procedure, limited field of view, cost-effectiveness, and low feasibility in acquisition of good-quality CLE videos and images. Additional studies in various diverse clinical settings are needed before it can be applied in routine clinical practice, extending the role of the endoscopist.

Confocal laser endomicroscopy

Kazuki Sumiyama

Dr Sumiyama graduated from the Jikei University School of Medicine in 1998. He completed a two year-residency at Jikei University Hospital in 2000. He received a PhD degree from Jikei University Graduate School of Medicine in 2003. He has been promoting a series of both basic and clinical research projects in the gastrointestinal endoscopy field as a principle investigator. He has been the director and the professor of department of Endoscopy at Jikei University since 2015. He was also a former post-doctoral fellow at the Mayo Clinic College of Medicine (2005-7)and achieved alot of internationally recognized developmental researches for novel endoscopic therapies including Confocal Endomicroscopy, Submucosal Endoscopy, NOTES and Full Thickness Resection. He was awarded many academic honors in his career as an GI endoscopist. He has published 158 papers (71 of them in English) and 243 abstracts and also invited by academic societies 83 times for lectures or live demonstrations so far.

Confocal laser endomicroscopy

Kazuki Sumiyama
Department of Endoscopy
Jikei University School of Medicine

Confocal laser endomicroscopy (CLE) is a technology which make fluorescence microscope compatible with flexible endoscopy. The technique greatly increases image contrast and resolution especially in the depth direction by eliminating out-of-focus light through a pinhole. CLE has been shown to have diagnostic value equal to that of histopathological examination. A series of studies in GI field has demonstrated that CLE systems could help reduce the requirement for biopsies and identify tumor differentiation and stages regardless of target organ. Although, there are two clinically available CLE systems, namely embedded CLE and pCLE, only pCLE is commercially available in Japan. pCLE imaging is horizontal subsurface imaging, which differs from traditional histopathological assessment. Therefore, discrepancies in the interpretation of CLE may exist between endoscopists and pathologists. We conducted an international multicenter study involved German and Japanese institutions and aimed to evaluate the influence of reviewers' clinical backgrounds on interpreting probe-based confocal laser endomicroscopy (pCLE) findings for diagnosis of superficial gastric lesions. In our study, the accuracy of diagnosis using WLE+pCLE was higher for gastroenterologists than for pathologists. Although we also evaluated the influence of pathology training on pCLE interpretation by gastroenterologists, such training had no effect on pCLE interpretation. Also, accuracy for pCLE was significantly higher for Japanese reviewers than German reviewers in diagnosis of superficial gastric lesions. We surmise that expertise in WLE is essential to achieving accurate diagnosis by pCLE because a histopathology-based diagnosis is established using a fixed sample, whereas a CLE-based diagnosis uses moving images similar to endoscopic diagnosis. In addition, we have been exploring the methodology to morphologically analyze enteric nervous system (ENS) within deeper layers of the gut wall using pCLE. So far, we have demonstrated the technical feasibility of real-time pCLE imaging of the myenteric nerve plexus by topically applying neurological fluorescent stains and utilizing pCLE via transmural or serosal approach in both animal experiments and a human pilot study. We believe that the technological advantages of CLE would not be restricted in superficial tissue imaging, and would be useful for physiological analysis of the entire gut.
gut wall.

Topic I

Advanced imaging in endoscopy-3

DAY2 April 20th 10:25-11:40　OHGI Room (4F)

Chairpersons:

Rajvinder Singh

Lyell McEwin Hospital and the University of Adelaide, Australia

Takuji Gotoda

Nihon University School of Medicine, Japan

Commentator:

Hiroyuki Imaeda

Saitama Medical University, japan

Lecture-1 **Realtime Diagnosis of GI Neoplasia**

Khek Yu Ho

National University of Singapore, Singapore

Lecture-2 **Advanced imaging in endoscopy Deep into the Small Intestine**

Kazuo Ohtsuka

Tokyo Medical and Dental University, Japan

Lecture-3 **Advanced Endoscopic Imaging, Therapeutic Endoscopy, ERCP, EUS, ESD/ EMR**

Roy M. Soetikno

Singapore General Hospital, Singapore

Lecture-4 **Sessile Serrated Adenomas: Misconceptions, Detection,Characterisation and Resection**

Rajvinder Singh

Lyell McEwin Hospital and the University of Adelaide, Australia

Lecture-5 **Endoscopic Ultrasound Imaging in Caustic Esophageal Injuries**

Mark Anthony A. De Lusong

University of the Philippines, Philippine

Realtime Diagnosis of GI Neoplasia

KHEK-YU, HO

NAME: KHEK-YU, HO

PRESENT POSITIONS:

Vice Dean (Research), Yong Loo Lin School of Medicine, National University of Singapore
Group Director (Research), National University Health System, Singapore
Professor of Medicine, Yong Loo Lin School of Medicine, National University of Singapore
Senior Consultant, Department of Medicine, National University Hospital, Singapore
Director, National Referral Laboratories, Pte Ltd (NRL)

UNDERGRADUATE AND POSTGRADUATE QUALIFICATIONS:

2007 Fellow qua Physician of Royal College of Physicians (Glasgow)
1998 Doctor of Medicine, National University of Singapore, Singapore
1997 Fellow of Academy of Medicine Singapore (Gastroenterology)
1994 Fellow of Royal Australasian College of Physicians (Internal Medicine)
1986 MBBS (1st class honours), University of Sydney, Australia

AWARDS AND HONOURS:

2013 Orator, Macau Society of Digestive Endoscopy Lecture, Macau
Guest Professor, Xiamen University, China
Orator, Francisco Roman Memorial Lecture (Joint Annual Convention of the Philippine Society of Gastroenterology and Philippine Society of Digestive Endoscopy)

2012 President's Technology Award (the highest honour bestowed on exceptional research scientists and engineers in Singapore for their excellent achievements in science and technology)
Advisory Professor, Digestive Disease Center, Konkuk University Medical Center, Korea
Member, International Advisory Committee, SSR Medical College, University of Mauritius
Guest Professor, Hebei Medical University Cangzhou School of Clinical Medicine, China
Orator, Nihal Marcus Memorial Oration (Gastroenterological, Digestive and Endoscopy Society of Sri Lanka)
Orator, Seah Cheng Siang Memorial Oration (Gastroenterological Society of Singapore)
Honorary Professor, GEM Hospital & Research Centre, Coimbatore, India

2011 Inaugural NUHS Leadership Award - Clinical Innovator (Individual) Award
Honorary International Life Membership of the Society of Gastrointestinal Endoscopy of India for contribution to endoscopic training in India

2010 Journal of Gastroenterology and Hepatology Foundation Emerging Leadership Lecturer

2005 Winner of "Oral Presentation Award", Asia-Pacific Digestive Week, Korea.

2003 Orator, Francisco Roman Memorial Lecture (Joint Annual Convention of the Philippine Society of Gastroenterology and Philippine Society of Digestive Endoscopy)

2003 Faculty Teaching Excellence Award, National University of Singapore

2000 Faculty Teaching Excellence Award, National University of Singapore

Realtime Diagnosis of GI Neoplasia

(Lawrence) Khek-Yu Ho
Vice Dean, Yong Loo Lin School of Medicine, National University of Singapore
Senior Consultant, Department of Medicine, National University Hospital, Singapore

The standard diagnosis of GI neoplasia and pre-neoplasia is dependent on endoscopic visualization of the lesion and subsequent confirmation by histopathological examination. With advanced endoscopic imaging technologies allowing negative predictive values ≥90%, it might soon be possible to achieve optical “diagnose and leave” strategy. Learning curve to achieve accurate optical diagnosis remains a challenge for most endoscopists; thus a realtime objective diagnostic tool is much needed.

We have developed the world’s one-of-a-kind In-Vivo Molecular Diagnostic System, which is capable of providing real-time and operator-independent diagnosis of tissues during endoscopic examination. It is based on Raman spectroscopy – a vibrational technique that enables molecular information to be captured when tissue molecules are agitated by a laser beam. The fibre-optic probe delivers a laser beam and captures the molecular ‘fingerprint’ of any tissue it comes into contact with – and the information is analyzed in real-time. Cancerous and precancerous tissues have different molecular ‘fingerprint’ from healthy tissue – so a diagnosis is provided in < 1 second. Proof of effectiveness has been demonstrated in close to 1,000 patients with a diagnostic accuracy of > 90% for stomach, esophageal and colon cancerous tissues. Its significance lies in the ability of the technology to allow clinical decision on the spot, enabling strategies such as “diagnose & discard”, “diagnose and target”, “diagnose & resect”, “diagnose & mark”, and “resect & discard”, thus saving time, cost, and minimizing complications by obviating unnecessary biopsy, and limiting resection margin.

Advanced imaging in endoscopy Deep into the Small Intestine

Kazuo Ohtsuka

Academic Background

1982 - 1988	M.D.	Niigata University, School of Medicine, Niigata, Japan
1991 - 1995	Ph.D.	Niigata University, Faculty of Medicine, Niigata, Japan

Positions

1988-1989	Resident of Niigata University Hospital
1989-1991	Resident of Akita Red Cross Hospital
1995	Niigata University Hospital
1995-1998	Research Scholar of University of Southern California
1998-2001	Niigata University Hospital
2001-2012	Showa University, Northern Yokohama Hospital
2012-	Tokyo Medical and Dental University

Certification

1988	Medical license in Japan
1999	Fellow of the Japanese Society of Internal Medicine
2000	Board Certified Member of Japanese Society of Gastroenterology
2003	Board Certified Member of Japan Gastroenterological Endoscopy Society

Research Fields

Diagnosis and therapy of inflammatory bowel disease
Developing and innovating the small bowel endoscopy

Publications

1. Comparison of magnetic resonance and balloon enteroscopic examination of deep small intestine in patients with Crohn's disease. Gastroenterology. 2014; 147:334-342.
2. Blinded nonrandomized comparative study of gastric examination with a magnetically guided capsule endoscope and standard videoendoscope. Gastrointest Endosc. 2012;75:373-381.
3. Diagnosis and treatment of small bowel diseases with a newly developed single balloon endoscope. Digestive Endoscopy. 2008;20:134–137.

Advanced imaging in endoscopy Deep into the Small Intestine

Kazuo Ohtsuka
Endoscopy, University Hospital of Medicine
Tokyo Medical and Dental University, Tokyo, JAPAN

In the last century, the small intestine was called “the dark continent of the gastrointestinal tract.” It is a large and important organ and plays a central role in the digestion and absorption of nutrients. In addition, it has been established that the intestine is a principal organ in the immune and endocrine systems. However, direct access to the deep small intestine has presented considerable difficulty. The small intestine is only fixed at the ligament of Treitz and the ileocecal valve and meanders in the abdominal cavity. Therefore, inserting a conventional endoscope into the gut only stretches the gut without advancing the endoscope.

The development of double balloon endoscopy (DBE) in 2001 addressed this problem. In DBE, the endoscope is inserted into the deeper regions of the small intestine by holding the gut with the scope and overtube balloon. It enabled direct visualization of the entire small intestine for diagnosis and treatment. In 2007, single balloon endoscopy (SBE) was developed, comprising an endoscope, overtube with a balloon, and air pump controller. DBE and SBE are categorized as types of balloon-assisted endoscopy (BAE). In contrast to DBE, SBE does not have a scope balloon; hence, this angulation can be used for grasping the intestinal tract while advancing the overtube.

Despite the availability of BAE, achieving total enteroscopy still poses some challenges. Retained air inhibits deep insertion by sharply bending the gut and preventing the shortening of the gut. Carbon dioxide (CO2) is rapidly absorbed from the mucosa and is not retained in the lumen. Hence, CO2 insufflation improves intubation depth and total enteroscopy rate. SBE can be performed by a single operator, and the advantage of the single operator method is that the endoscopist has full control of the scope and overtube. It also improves the likelihood of a better outcome. Both antegrade and retrograde insertion are generally needed to visualize the entire small intestine. Pancreatitis and aspiration pneumonia are important complications of BAE and mostly occur during antegrade insertion. To decrease the rate of such complications, it is recommended that retrograde insertion is made to the maximum depth followed by antegrade insertion for the remaining gut. At our institute, 10% of SBEs achieved total enteroscopy through only retrograde insertion.

Image-enhanced endoscopy is an important diagnostic method in upper gastrointestinal endoscopy and colonoscopy. Narrow band imaging (NBI), which is excellent for improving blood vessel visibility, is widely used for diagnosing neoplasia. Carcinoma in the small intestine is rare, and intestinal bleeding is clinically important. Angioectasia is a major cause of intestinal bleeding. It is sometimes difficult to distinguish angioectasia from mucosal injuries that may occur during insertion procedures. NBI clearly depicts angioectasias in a dark green and artifacts in a brown color. This is called the “dark green sign” and is useful for deciding whether the lesion needs treatment or not.

Enteroscopy is also important in diagnosing Crohn’s disease (CD). Most patients with CD have small bowel lesions with some having lesions only in the deep small intestine which cannot be accessed using ordinary ileocolonoscopy. Magnetic resonance enterography (MRE) is a recommended modality for the assessment of CD. It clearly reveals inflammatory lesions. It can also depict extra-luminal lesions such as abscesses. CD has two pathological aspects; they are inflammatory activity and intestinal damage accumulation. We directly compared MRE and BAE findings of 100 CD cases. MRE detected ulcerative lesions with 82.4% sensitivity [95% confidence interval (CI), 75.4%–87.7%]. In addition, MRE accessed major stenoses of 9.2 mm diameter, which could not be accessed using BAE, with 58.8% sensitivity [95% CI, 37.6%–77.2%] and 90.0% specificity [95% CI, 88.4%–91.5%]. MRE is less sensitive at detecting intestinal damage, such as stenoses; BAE is preferred for identifying intestinal damage. Suitable imaging approaches should be selected to assess CD lesions in the small intestine.

BAE is also important in endoscopic therapies. Stenosis causes obstruction and plays a role in the exacerbation of CD. Recent advances in BAE have enabled endoscopic dilation; however, restenoses sometimes occur when the lesion is in the active phase. To avoid surgical intervention, annual endoscopic dilation has been proposed. Capsule endoscopy (CE) is a non-invasive and useful modality for the detection of mucosal lesions of CD, especially in the early stage. However, CE sometimes retains the proximal side of the stenosis. Although the development of the patency capsule may decrease capsule retention, there have been reports of retention. Dilatation of stenosis and removal of retained CE are performed as therapeutic enteroscopy.

The small intestine has become a new frontier that needs further investigation, and BAE is one of the important modalities to achieve that end.

Advanced Endoscopic Imaging, Therapeutic Endoscopy, ERCP, EUS, ESD/ EMR

Roy M. Soetikno

Advanced Endoscopic Imaging, Therapeutic Endoscopy, ERCP, EUS, ESD/ EMR

Roy M. Soetikno

Dept. of Gastroenterology and Hepatology, Singapore General Hospital

Sessile Serrated Adenomas: Misconceptions, Detection, Characterisation and Resection

Rajvinder Singh

A/Prof. Rajvinder Singh MBBS MPhil FRACP AM FRCP is the Director of Gastroenterology at the Lyell McEwin and Modbury Hospitals, South Australia and a Clinical Associate Professor of Medicine at the University of Adelaide, South Australia, Australia.

Upon completion of his GI training, he received the Lancet International Fellowship, which enabled him to undertake a higher research degree on Narrow Band Imaging in Barrett's Oesophagus at the University of Nottingham, UK. He has a keen interest in Endoscopic research focusing mainly on Advanced Endoscopic Imaging Techniques and Endoscopic Treatment of premalignant and malignant lesions in the gastrointestinal tract. He has been successful in obtaining various grants nationally to further investigate the utility of novel endoscopic imaging techniques in the detection of dysplasia and early cancer.

A/Prof Singh has made substantial contributions to research with over 100 high quality scientific journal publications. Amongst these are senior authorship of national and international consensus guidelines in both Australia and the Asia Pacific Region. Present ongoing research includes multicentre national and international collaborative studies on the detection, characterisation and endoscopic treatment of Colon Polyps, Early Gastric Cancer and Barrett's Oesophagus.
He is an Editorial Board member of Endoscopy, a Co-Editor of Endoscopy International Open, the Contributing Associate Editor in Chief of the World Journal of Gastroenterology and an Editorial Board member of the World Journal of Gastrointestinal Endoscopy. He is the current chair of the Australian Gastroenterology Endoscopic Association and a committee member of the American Society of Gastrointestinal Endoscopy's International Initiative.

His global reputation has led to speaking engagements and live endoscopy demonstrations around the world including in the USA, UK, Japan, Korea, India, Singapore, New Zealand, Indonesia, Taiwan, Hong Kong, Thailand, Malaysia, Myanmar among other countries.

Sessile Serrated Adenomas: Misconceptions, Detection, Characterisation and Resection

Rajvinder Singh

Director of Gastroenterology at the Lyell McEwin and Modbury Hospitals, South Australia and a Clinical Associate Professor of Medicine at the University of Adelaide, South Australia, Australia.

It is currently postulated that colorectal cancer (CRC) arises from 3 different pathways: the well-known adenoma to carcinoma route (50-70%); `Lynch syndrome' (3-5%); and more recently the serrated pathway (30-35%). According to the World Health Organization (WHO), there are 3 types of serrated lesions present in the colon: Hyperplastic Polyps (HP), Sessile Serrated Adenomas/Polyps (SSA/P) and Traditional Serrated Adenomas (TSA), the latter two strongly associated with development of CRC. HP and SSA/P appear to be endoscopically similar, even with Image Enhancing Endoscopy techniques. Careful evaluation of gross morphological features and focal interrogation of the surface on closer views may enable optimal characterization and successful endoscopic resection. This presentation will look at the present available data on misconceptions, detection, characterization and endoscopic resection of SSA/P.

Endoscopic Ultrasound Imaging in Caustic Esophageal Injuries

Mark Anthony A. De Lusong

Prof. Mark Anthony A. De Lusong, MD FPCP, FPSG, FPSDE

Received his diploma in Medicine at the University of the Philippines College of Medicine.

Internal Medicine Residency and Gastroenterology Fellowship at the Philippine General Hospital.

Advanced Endoscopy Fellowship at California Pacific Medical Center in San Francisco, USA.

Exchange scholarship program for ESD at Kyushu University Hospital in Fukuoka, Japan.

He is currently an Associate Clinical Professor of the University of the Philippines.

He serves as the Training Program Director of the University of the Philippines, Philippine General Hospital, Section of Gastroenterology and incumbent Treasurer of the Philippine Society of Digestive Endoscopy.

He has authored and co authored numerous papers and researches presented and published locally and internationally.

He is also a member of the editorial board and peer reviewer of various medical journals.

Endoscopic Ultrasound Imaging in Caustic Esophageal Injuries

Mark Anthony A. De Lusong
Associate Clinical Professor of the University of the Philippines

Esophageal caustic injury in the pediatric population is largely accidentally and potentially preventable. In adults, however, it is mostly due to the goal of ending one's life. Household bleach or 5% sodium hypochlorite is the most frequently reported ingested caustic substance in the Philippines, but rarely injures the esophagus or stomach. Most common agents involved with significant gastrointestinal injury ingested intentionally and accidentally in the Philippines include strong alkaline liquids such as sodium hydroxide (NaOH) and highly acidic substances, such as hydrochloric acid.

Although the standard diagnostic tool for caustic injuries is still upper gastrointestinal endoscopy, other imaging modalities like MRI, CT scans and endoscopic ultrasonography are slowly emerging as supportive tools, especially in addressing the need for emergency surgery, whose morbidity and mortality remains high even in the best hands, and in predicting the prognosis of the patient. Endoscopic ultrasonography in combination with standard video endoscopy may offer a better diagnostic modality for this subset of patients particularly in the evaluation of the damaged esophageal mucosa.

Local Philippine data has shown a gradual decrease of cases, but numbers are significant enough to cause substancial medical burden. Even in this day and age, robust data about caustic injuries are still lacking.

Therefore, in this lecture, my main objectives are:

1. To present local and international data on caustic injury
2. To discuss current evidence of using EUS in the evaluation of esophageal caustic injuries
3. To propose an EUS classification for the management of esophageal caustic injuries.

Luncheon Seminar

DAY2 April 20th 11:50-12:35　OHGI Room (4F)

Supported by: Olympus Corporation

Moderator: Yoshinori Igarashi

Toho University Omori Medical Center, Japan

EUS Imaging Diagnosis

Masayuki Kitano

Kindai University, Japan

Advanced imaging in endoscopy Deep into the Small Intestine

Atsushi Irisawa

Fukushima Medical University Aizu Medical Center, Japan

EUS Imaging Diagnosis

Masayuki Kitano

FACILITY: Department of Gastroenterology and Hepatology
Kinki University, School of Medicine, Osaka-Sayama, Japan

EDUCATION:

Medical Education:

1984-1990 Tottori University, Yonago, Japan
1990 M.D., (Medical License), Tottori University School of Medicine
1994 Ph.D. (Dr. of Medical Science), Tottori University

APPOINTMENTS:

1994-1996 Medical Staff in 2nd Department of Internal Medicine, Tottori University Hospital
1996-1998 Visiting Scientist in Department of Pharmacology, University of Lund
1998-2000 Research Associate in Department of Clinical Pharmacology, Faculty of Medicine, Tottori University
2000-2001 Research Associate in Department of Gastroenterology and Hepatology, Kinki University, School of Medicine
2001-2007 Assistant Professor in Department of Gastroenterology and Hepatology, Kinki University, School of Medicine
2007-present Associate Professor in Department of Gastroenterology and Hepatology, Kinki University, School of Medicine

SOCIETY

Japan Gastroenterological Endoscopy Society (Councilor)
Japanese Society of Clinical Pharmacology and Therapeutics (Councilor)
The Japan Society of Gastroenterology (Councilor)
Japan Pancreas Society (Councilor)
The Japan Society of Internal Medicine
The Japan Society of Ultrasonics in Medicine
The Japan Society of Hepatology
Japan Society of Clinical Oncology
Japan Biliary Association
Japanese Society of Medical Oncology
Japan Society for Medical Education
American Society of Clinical Oncology
American Society of Gastrointestinal Endoscopy

AWARDS

1996 The Uehara Memorial Foundation, Postdoctoral Fellowship
2008 Japan Research Foundation for Clinical Pharmacology, Research Award
2009 Japan Society Ultrasound in Medicine, Ito Award

EDITORIAL BOARD

2014 World Journal of Gastroenterology
2014 Pancreatology
2014 Journal of Medical Ultrasonics
2016 Digestive Endoscopy (Associate Editor)

PEER REVIEWING SCIENTIFIC ARTICLE PUBLICATION:

118 peer reviewing articles (English)

EUS Imaging Diagnosis

Masayuki KITANO
Department of Gastroenterology and Hepatology,
Kinki University Faculty of Medicine

Recent developments that aim to overcome this limitation of conventional EUS have led to the evolution of several upcoming EUS imaging techniques, including contrast-enhancement and tissue elastography techniques. These techniques provide detailed information on the structure of the tissue and thus greatly improve the diagnostic capabilities of conventional EUS.

I. Contrast-enhanced EUS

a. Principle

Intravenous ultrasound contrast agents are microbubbles consisting of a gas core that is stabilized by a shell. Contrast-enhanced EUS selectively depicts the signals produced by microbubble oscillation or breakage.

b. Diagnosis of solid mass in the pancreas

On contrast-enhanced EUS, solid pancreatic lesions can be characterized on the basis of their enhancement patterns relative to their surrounding tissue. There are three main enhancement patterns, namely, hypo-, iso- or hyper-enhancement. Contrast-enhanced EUS depicts pancreatic ductal carcinomas as nodules with hypo-enhancement that mostly have irregular vessels. A recently published meta-analysis showed that hypo-enhancement in contrast-enhanced harmonic EUS diagnoses pancreatic adenocarcinomas with a pooled diagnostic sensitivity and specificity of 94% and 89%, respectively. Contrast-enhanced harmonic EUS (91% sensitivity and 94% specificity) is superior to contrast-enhanced CT (71% sensitivity and 92% specificity) in diagnosing small (≤2 cm) ductal carcinomas. In particular, contrast-enhanced harmonic EUS is useful for characterizing small neoplasms that contrast-enhanced CT cannot identify.

c. Diagnosis of cysts in the pancreas

Contrast-enhanced EUS also aids the diagnosis of pancreatic cysts by depicting the vascularity of structures such as the cyst wall, septa, or mural nodules. It also discriminates contrast-enhancing mural nodules from non-enhancing mucus clots. This is particularly important in the case of intraductal papillary mucinous neoplasm.

d. Diagnosis of gastrointestinal subepithelial tumors

Contrast-enhanced harmonic EUS visualizes the vessels flowing from the periphery to the center of gastrointestinal stromal tumors (GISTs). By contrast, contrast-enhanced CT cannot identify most of these vessels. All high-grade malignant GISTs possess these contrast-enhanced harmonic EUS-depicted irregular vessels. When contrast-enhanced harmonic EUS is used to diagnose high-grade malignancy GISTs on the basis of higher echo intensity and the presence of irregular vessels, it is more sensitive than when conventional EUS variables (i.e., large size, lobular border, and heterogeneous structure) are employed.

e. Differentiation of malignant from benign lymph nodes

When malignant lymph nodes are defined as heterogenesou enhancement, contrast-enhanced EUS is more accurate than standard and color Doppler EUS. Thus, contrast-enhanced EUS may be helpful in terms of identification of suspicious lymph nodes for which pathological diagnosis with EUS-FNA is required. In addition, patients with EUS-FNA failure can be correctly N-staged by contrast-enhanced EUS.

f. Relation to EUS-FNA

Contrast-enhanced EUS can complement EUS-FNA in terms of identifying pancreatic ductal carcinomas that have false-negative EUS-FNA findings. When ductal carcinomas were defined as tumors with hypo-enhancement on contrast-enhanced harmonic EUS and/or a positive EUS-FNA, the ductal carcinomas were detected with a sensitivity

and specificity of 100% and 92.6%, respectively: adding contrast-enhanced EUS to EUS-FNA increased the sensitivity of EUS-FNA from 92.2% to 100%.

Since contrast-enhanced EUS clearly depict some subtle lesions that conventional EUS cannot identify, they can also be used to identify the target of EUS-FNA. Moreover, they can be employed to find specific sites within a lesion that would be more suitable for EUS-FNA than other sites. In particular, contrast-enhanced EUS can identify the avascular sites in a lesion; this would also help to prevent EUS-FNA sampling of necrotic areas and improve the sensitivity with which EUS-FNA diagnoses pancreatic tumors.

II. EUS elastography

a. Principle

The main principle of tissue elastography is that the compressive force on the tissue causes axial tissue deformation (strain), which is then calculated by comparing the echo sets before and after the compression. The degree of deformation serves as an indicator of the stiffness of the tissue: the deformation is smaller in hard tissue than in soft tissue.

b. Diagnosis of solid mass in the pancreas

EUS elastography is increasingly being used to improve the characterization of the benign or malignant nature of a lesion because more elastic (soft) tumors are more likely to be benign while less elastic (hard) tumors are more likely to be malignant. EUS elastography discriminated between benign and malignant masses with a pooled sensitivity of 95% and a pooled specificity of 67%.

c. Differentiation of malignant from benign lymph nodes

On EUS elastography, the predominant red-green and predominant blue patterns diagnose benign and malignant lymph nodes, respectively, with high sensitivity (88%) and specificity (85%).

III. Conclusion

Contrast-enhanced EUS and EUS elastography that have enabled EUS to detect, characterize, and stage tumors in the upper gastrointestinal tract and pancreatobiliary system. Moreover, they complement EUS-FNA by correctly diagnosing lesions with EUS-FNA false-negative findings and by identifying the most appropriate target site of EUS-FNA.

Advanced imaging in endoscopy Deep into the Small Intestine

Atsushi Irisawa

Name: Atsushi Irisawa
Gender: Male
Birth Date: November 24, 1962
Title: Professor
Institution and its address:
Department of Gastroenterology.
Fukushima Medical University, Aizu Medical Center.
21-2, Maeda, Tanisawa, Kawahigashi. Aizuwakamatsu, 969-3492, Japan
Tel: +81-242-75-2100 Fax: +81-242-75-2568
E-mail:irisawa@fmu.ac.jp

Education:

1996 Ph.D. Dr. of Medical Science, Fukushima Medical University
(Title: The selection and evaluation of the manipulation for endoscopic injection sclerotherapy against esophageal varices with extra esophageal shunt using by endoscopic varicealography and EUS.)

1989 M.D. Cum laude, Dokkyo Medical College

Professional Training and Employment:

2010.4-present Professor, Director. Department of Gastroenterology. Fukushima Medical University Aizu Medical Center.
2007.5-2010.3 Associate Professor, Department of Internal Medicine 2, Fukushima Medical University School of Medicine.
2002-2007.4 Assistant Professor/Lecturer, Department of Internal Medicine 2, Fukushima Medical University School of Medicine.
2000-2001 Visiting Faculty, Center for EUS, Division of Gastroenterology, University of Florida (USA).
1997-2000 Assistant Professor, Department of Internal Medicine 2, Fukushima Medical University School of Medicine
1994-1997 Postdoctoral Clinical Fellow, Department of Internal Medicine 2, Fukushima Medical University School of Medicine
1989-1994 Resident in Internal Medicine, Fukushima Medical University School of Medicine

Societies:

Japanese Gastroenterological Association (councilor)
Japan Gastroenterological Endoscopy Society (councilor)
Japanese Society of Gastroenterology (councilor)
Japan Pancreas Society (councilor)
Japanese Society of Portal Hypertension (councilor)
Japanese Society of Internal Medicine (Tohoku regional counsilor)
American Society for Gastrointestinal Endoscopy (international member)

Advanced imaging in endoscopy Deep into the Small Intestine

Atsushi Irisawa
Professor, Director. Department of Gastroenterology
Fukushima Medical University Aizu Medical Center

Recent advances in Interventional EUS
Atsushi Irisawa, M.D., Ph.D.
Department of Gastroenterology.
Aizu Medical Center, Fukushima Medical University.

Now a day, interventional EUS is the most challenging and exciting filed in digestive endoscopy. EUS-guided drainage is widely accepted and performed for pancreatobiliary disorders, walled-off necrosis post severe acute pancreatitis, pancreatic pseudocyst and obstructive jaundice. These techniques are currently recognized as the standard treatment. On the other hand, EUS-guided anti-cancer therapy and vascular therapy, moreover EUS-guided gastrojejunostomy, are exactly innovative technique and have opened new and exciting clinical applications in the management of various digestive diseases. Anti-tumoral EUS-guided injection therapy, with its minimally invasive access for anti-tumoral agent delivery, is divisible into three categories: physicochemical, molecular biological, and immunological. Anti-tumoral physicochemical therapy includes ablation (ethanol injection for cystic tumor), chemotherapy (using gelled paclitaxel), and brachytherapy. Molecular biological and immunological therapies were performed as clinical trial. Recently, EUS-guided coiling therapy for gastric varices (GV) was developed. Several report showed the EUS-guided deployment of coils in the perforating feeding vein is more effective and safe than cyanoacrylate injection. We invent the new technique combined coiling and sclerosant injection using interventional EUS for isolated GV. This technique is expected as new treatment for GV. Finally, the newly developed technique is EUS-guided gastrojejunostomy. This therapeutic approach has blazed a new trail in the filed of palliative care. Thus, the interventional EUS will probably continue to progress.

Topic Ⅱ

Advanced imaging in surgery

DAY2 April 20th 13:05-13:50　OHGI Room (4F)

Chairpersons:

Philip Wai Yan, CHIU

The Chinese University of Hong Kong, Hong Kong

Soji Ozawa

Tokai University School of Medicine, Japan

Commentator:

Keiichi Kubota

Dokkyo Medical University, Japan

Lecture-1 **Augmented reality and 3D printing for surgical navigation**

Maki Sugimoto

Kobe University Graduate School of Medicine, Japan

Lecture-2 **Indocyanine green fluorescence guided surgery – Development and clinical appreciation of the brightfield full-color fluorescence camera and the brightfield full-color fluorescence laparoscopes**

Masashi Yoshida

International University of Health and Welfare Hospital, Japan

Lecture-3 **High Resolution Imaging in Endoscopic Surgery**

Toshiyuki Mori

Kyorin University, Japan

Augmented reality and 3D printing for surgical navigation

Maki Sugimoto

Maki Sugimoto MD, PhD
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Professional Society

International Society of Surgery (Active member, 2005-)
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Augmented reality and 3D printing for surgical navigation

Maki Sugimoto
Associate Professor of gastroenterology
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We developed a new surgical spatial navigation system using mixed realistic augmented tangibility by interactive superimposing 3-D hologram and Bio-Texture Modeling. Interactive stereo display was used for the existence of an interaction between the surgeon and stereo images of the patient’s anatomy depicted on the display in the form of tracking the surgeon's head and hand/arm position. Sensing the surgeon's head position created motion parallax information, an immersive depth cue that can be added to the binocular parallax already present in the display. Sensing the surgeon's hand or arm position using motion sensor attached the patient’s life size 3-D printed organ model, allowed the surgeon to manipulate the spatial attributes of the virtual and real printed organs, which can enhance spatial reasoning and augmented tangibility. Permitting the surgeon to manipulate virtual organs also allowed for the creation of a sense of spatial relations among elements in the display via proprioception. The congruence among binocular parallax, motion parallax, and proprioception increased the sense of depth and viewing comfort, enhanced the ability of our intuitive reasoning system to make reasoned sense out of the incoming perceptual information. Mixed realistic augmented tangibility should be particularly important for surgical simulation, navigation and education.

Indocyanine green fluorescence guided surgery – Development and clinical appreciation of the brightfield full-color fluorescence camera and the brightfield full-color fluorescence laparoscopes

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Japanese Study Group for Ulcer Research (JGUR), Organizer prize, 2004
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The Ulcer Research Prize 2002 (November 30, 2002):
The Histamine Receptor Prize '95 (July 28, 1995)

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International Gastric Cancer Association, The Japanese Society for Wound Healing (Director),
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Indocyanine green fluorescence guided surgery – Development and clinical appreciation of the brightfield full-color fluorescence camera and the brightfield full-color fluorescence laparoscopes

Masashi Yoshida[1], Hironori Ohdaira[1], Nobuhiro Nitori[2], Nobuhiro Tsutsui[1], Motomu Tanaka[1], Tomohisa Kadomura[2], Yoshifumi Ikeda[2], Masaki Kitajima[1], [2], Yutaka Suzuki[1]

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Conventional near infrared fluorescence cameras require dark room and their images are in monochrome because indocyanine green (ICG) fluorescence is faint. The brightfield full-color fluorescence camera (laparoscopes) and observation under room light may add new possibilities to the ICG fluorescence guided surgery.

In cooperation with Prof Sato's (Kochi University) development of HyperEye Medical System (HEMS: Mizuho Co.), we have applied it to GI tract surgery. Charge-coupled device (CCD) of HEMS has 4 sensors with 4 filters of red, green, blue and infrared, and create one bright-field full-color fluorescence image. Using prototype laparoscopy equipped with HEMS CCD (HEMS-LAP), animal experiments were performed. The other bright-field full-color fluorescence laparoscopy, PINPOINT (NOVADAQ, Canada) was privately imported and approved by ethics committee in July, 2014. Image of PINPOINT is a composition of two images, the full color and the infrared. Using these fluorescence camera systems, ICG fluorescence guided surgery was performed.

Using HEMS-LAP, small intestinal blood flow was observed after declamping of 4 or 7 hours ischemia in swine. In emergency operations of non-occlusive mesenteric ischemia and incarcerated hernias, ICG was injected i.v. and intestinal blood flow was assessed by fluorescence cameras. It was helpful to decide whether resection of the intestine is necessary or not and an extent of intestinal resection, if necessary. Blood flow of the anastomosis could be assessed by the ICG fluorescence.

Acceptable results of multicenter study on sentinel node mapping of the stomach was reported using dual tracer method. ICG fluorescence method require no radioactive tracer, however, too many ICG fluorescence positive lymph nodes tend to exist. The acceptable method of choosing sentinel nodes among ICG fluorescence positive lymph nodes is expected. After endoscopic injection of 50 micro-g/ml of ICG on the day before operation, the number of ICG positive lymph nodes was 4.67 + 2.40 using HEMS. It was similar to the results of radio-active tracer method. We speculate that this is settled by the balance of the sensitivity of the camera, intensity of ICG fluorescence and intensity of the room light. It is under examination whether non-sentinel ICG fluorescence can be cut off by room light under adequate timing and concentration of ICG injection. The pilot study using PINPOINT for examine adequate administration of ICG will be presented.

The brightfield full-color fluorescence camera and the brightfield full-color fluorescence laparoscopes allow us to observe ICG fluorescence and perform operation simultaneously without interruption by darkness. Moreover, observation under room light may allow us to cut off non-sentinel ICG fluorescence under adequate administration of ICG.

High Resolution Imaging in Endoscopic Surgery

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Education

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Recent publiications in English

Toshiyuki Mori Concept of Reduced Port Laparoscpic Surgery in Eds Mori T, Dapri G,
Reduced Port Laparoscopic Surgery, pp11-22, Springer 2014

High Resolution Imaging in Endoscopic Surgery

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Introduction

In the early development of video-endoscopic surgery in the late 80', the images displayed on the monitor were insufficient in many ways; resolution, brightness, and color reproducibility. Surgery is a typical perceptual motor skill, in which a circle of perception, judge (appreciation of anatomy and decision of what to do) and motor execution (surgical maneuver) is repeated. Perceptual information acquired during laparoscopic surgery is almost exclusively visual and compromised quality of the image has resulted in a longer operating time and increased rate of complications.

Evolution of the imaging system in laparoscopic surgery

In the beginning, resolution of a standard laparoscopic system was 640x480 pixels (VGA) with an insufficient illumination. The hue depth was decisively lacking. Precise appreciation of the surgical anatomy of the organs on which surgeons working is one of the most important steps in surgery. A very important component this step is to reconstruct the relative position of the organs in the brain (3D reconstruction). The standard video-system in laparoscopic surgery displays a 2D image. Nevertheless surgeons can reconstruct 3D images in their brain utilizing so-called visual cues. The visual cues seen on a monitor include the brightness and color, shadowing, obstruction, and motion parallax. In short, defective display of the visual cues made it difficult to precise comprehension of the surgical anatomy. For the progression of the video-system, engineers have been focusing not only the resolution of the image, but on improvement of the color space and image gradation and processing. The original VGA has evolved SVGA 800 600 to XGA (1024x768). The current standard video system is HD 1080 (1920x1080) collectively called 2K(2048x 1080). The number 2K (2,000) represents the horizontal resolution (pixels). It may be interesting what happened in laparoscopic surgery during this evolution. First understanding of anatomy is advanced. An example includes the Waldeyer's fascia lining between the mesorectum and os sacrum. It was thought one layer fascia in the era of open and early laparoscopic age. It is currently thought to have three distinct layers, namely A, B and C. A laparoscopic surgeon who observes this area with the high definition video system first proposed this distinction. Surgical anatomists later confirmed this distinction. Currently dissection of different layer is employed depending upon the extent of mesorectal resection. Another example includes distinction of the fat tissue of the transverse mesocolon from the peri-vascular fat tissue of the infra-pyloric nodes. These fat tissues are different in colors and the dissection plane can be clearly observed with the high definition video system. Although the long-term result is yet to be fully discussed, these progressions have resulted in more accurate cancer surgery with virtually no blood loss, extending indications of the laparoscopic approach in cancer surgery.

Future imaging system in endoscopic surgery

Three-dimension laparoscope is available in the market. The technology used in the 3D system is relatively simple. Parallaxed images for the right and left eyes are displayed on the monitor alternately. Only the right eye with an aid of the polarized lens observes the right eye image. The basic drawback of the current system is the fixed lens that result in a small space to be seen with real 3D. A conjugation mechanism is needed for an improvement. Also researchers found merit of 3D system only in novice surgeons demanded complex tasks. 3D video-systems have failed to show the better outcome in clinical settings. Other factor needed investigation is physiologic comparisons of 2D and 3D systems. Our preliminary physiologic study using 128ch EEG suggests that the area of excitation of the brain is different in 2D and 3D systems. Visual fatigue during laparoscopic surgery is another important factor in developing next generation video system. We recently reported the preliminary use of an 8K video system (7680x4320) in a clinical setting. Although the camera used in this feasibility study weighted 2.2 kg and sensitivity of 8K CMOS is insufficient, the image acquired with this system was astonishing. We can virtually observe wrinkles of the gallbladder serosa. We have noticed multiple tissue planes around the gallbladder by seeing different directions of capillary. No one knows, at this stage, what the 8K-system brings to endoscopic surgery. In addition to detailed observation of the surgical field, a part of the wide area of 8K image sensor can be assign to infrared or NBI (narrow band imaging), so that the mixed image can be displayed on the monitor. With evolution of an optical system and appropriate tools, laparoscopic microsurgery may be possible. By using this laparoscopic microscope, direct observation of the intra-abdominal cancer cells may become possible. The camera head would shortly become smaller and handy. The real benefit that the 8K-system brings depends on our ideas. To verify advantages of the ultra high-resolution system, physiological studies are mandatory.

Topic Ⅲ

Molecular imaging

DAY2 April 20th 13:50-14:30　OHGI Room (4F)

Chairpersons:

Tae Il Kim

Yonsei University College of Medicine, Korea

Kazuki Sumiyama

Jikei University School of Medicine, Japan

Lecture-1 **Intraoperative, rapid and sensitive imaging of tiny tumors by novel fluorogenic probes for aminopeptidases**

Yasuteru Urano

The University of Tokyo, Japan

Lecture-2 **Multi-scale in vivo observation by two photon microscope**

Satoshi Nishimura

Jichi Medical University, Japan

Intraoperative, rapid and sensitive imaging of tiny tumors by novel fluorogenic probes for aminopeptidases

Yasuteru URANO

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MAJOR PUBLICATIONS:

1. Asanuma D, et al., Nat. Commun., 2015, 6: 6463. “Cancer imaging with new activatable probes”
2. Ueo H, et al., Sci. Rep., 2015, 5: 12080. “Rapid cancer imaging of human clinical specimens”
3. Uno S, et al., Nat. Chem., 2014, 6: 681-689. “Self-blinking probes for super-resolution imaging”
4. Sakabe M, et al., J. Am. Chem. Soc., 2013, 135: 409-414. “Novel probe design strategies”
5. Urano Y, et al., Sci. Transl. Med., 2011, 3: 110ra119. “Intraoperative rapid cancer imaging”
6. Kamiya M, et al., J. Am. Chem. Soc., 2011, 133: 12960-12963. “Novel probes for lacZ”
7. Urano Y, et al., Nat. Med., 2009, 15: 104-109. “Activatable cancer imaging with antibody”

Intraoperative, rapid and sensitive imaging of tiny tumors by novel fluorogenic probes for aminopeptidases

Yasuteru Urano[1,2,3]

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Fluorescence imaging is one of the most powerful techniques currently available for continuous observation of dynamic intracellular processes in living cells. Suitable fluorescence probes are naturally of critical importance for fluorescence imaging, and we have succeeded to construct several versatile rational design strategies for novel fluorescence probes based on the concept of photoinduced electron transfer [1,2] and intramolecular spirocyclization [3,4].

As for the latter design strategy, we have synthesized and evaluated a series of hydroxymethyl rhodamine derivatives and found an intriguing difference of intramolecular spirocyclization behavior: the acetylated derivative of hydroxymethyl rhodamine green (Ac-HMRG) exists as a closed spirocyclic structure in aqueous solution at physiological pH, whereas HMRG itself takes an open non-spirocyclic structure: Ac-HMRG is colorless and non-fluorescent, whereas HMRG is strongly fluorescent. Based on these findings, we have established a general design strategy to develop highly sensitive fluorescence probes for proteases and glycosidases, by replacing the acetyl group of Ac-HMRG with a substrate moiety of the target enzyme. Specific cleavage of the substrate moiety in the non-fluorescent probe by the target enzyme generates a strong fluorescence signal. In order to confirm the validity and flexibility of our strategy, we designed and synthesized fluorescence probes for γ-glutamyl transpeptidase (GGT), leucine aminopeptidase, fibroblast activation protein, cathepsin B/L, β-galactosidase, and so on. All these probes were almost non-fluorescent due to the formation of spirocyclic structure, but were converted efficiently to highly fluorescent HMRG by the target enzymes. We confirmed that the probes can be used in living cells. These probes offer great practical advantages, including high sensitivity and rapid response (owing to regulation of fluorescence at a single reactive site), as well as resistance to photobleaching.

Very recently, we have succeeded to develop various novel protease probes which were applicable for living cell system [4]. For example, gGlu-HMRG, a novel spirocyclized rhodamine-based fluorescence probe for γ-glutamyltranspeptidase (GGT), which is well-known to be upregulated in various cancer cells, was successfully developed. By applying gGlu-HMRG to various cancerous cell lines whose GGT activity is upregulated, fast enzymatic reaction of gGlu-HMRG with GGT occurs on the plasma membrane to yield highly fluorescent product HMRG, which led us to establish a novel and highly activatable strategy for sensitive and fast-responding fluorescence imaging of tiny tumors in vivo. In mouse models of disseminated human peritoneal ovarian cancer, activation of gGlu-HMRG occurred within 1 min of topically spraying onto tissue surfaces that are suspected of harboring tumors, creating high signal contrast between the tumor and the background [5].

Encouraged by the promising results described above, we next examined the feasibility of clinical application of gGlu-HMRG during surgical procedures. We topically applied gGlu-HMRG to freshly excised human breast specimens containing various lesions together with normal tissues. We found that tumorous lesions exhibited a time-dependent increase of green fluorescence, derived from cleavage of gGlu-HMRG, that clearly distinguished them from surrounding mammary gland and fat. Breast tumors, even those smaller than 1 mm in size, could be easily discriminated from normal mammary gland tissues with 92% sensitivity and 94% specificity, within 5-15 min after probe application [6]. These findings confirmed the availability of gGlu-HMRG to detect cancerous lesions in clinical samples, which should be a breakthrough in intraoperative margin assessment during breast-conserving surgery.

Furthermore, we recently succeeded in preparing a library of activatable fluorescence probes composed of more than 250 probes for various aminopeptidases based on our molecular design strategy of intramolecular spirocyclization. We applied these probes on biopsy samples or resected specimens from esophageal cancer patients, and tried to find out tumor-specific aminopeptidase activities. As a result, we could find out the enzymatic activity of dipeptidyl peptidase-4 (DPPIV) were upregulated in tumor-positive biopsy samples, but not with tumor-negative biopsy samples. Further, we could

also detect cancer region in the resected human fresh specimens by topically spraying DPPIV-activatable fluorescence probes within 10 min. The existence of tumor was confirmed by pathology and H&E staining, and immunohistochemical results indicated the elevated expression of DPPIV in the tumor site but not in the unaffected tissue. These results clearly demonstrate that probes for DPPIV are practical for clinical application to detect human esophageal cancer during endoscopic or surgical procedures, because of its rapid and strong activation upon reaction with DPPIV on the surface of cancer cells.

Based on above achievements, we believe this rapid, low-cost, and easy method of spraying activatable fluorescence probes represents a breakthrough in intraoperative margin assessment and alternative image guidance during treatment.

References

[1] T. Miura et al., JACS, 125, 8666-8671 (2003).
[2] Y. Urano et al., JACS, 127, 4888-4894 (2005).
[3] M. Kamiya et al., JACS, 133, 12960-12963 (2011).
[4] M. Sakabe et al., JACS, 135, 409-414 (2013).
[5] Y. Urano et al., Sci. Transl. Med., 3, 110ra119 (2011).
[6] H. Ueo, Y. Shinden et al., Sci. Rep., 5, 12080 (2015).

Multi-scale in vivo observation by two photon microscope

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Multi-scale in vivo observation by two photon microscope

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We made minimum invasive fluorescence imaging system to cover from micro to macro scale for space and time space in mice, and we revealed thrombotic and inflammatory processes in diseased conditions.

First one is high resolution imaging system based on non-linear optics. Real-time, multi-color XYZT multi-photon imaging enabled us to visualize single platelet behavior, and elucidate thrombus formation in cardiovascular events. Second, macro imaging system for awake mice was developed, and free behavior monitoring revealed the tight association between metabolism and vascular reactions for daily stress. Third, wearable and implantable devices for long-time recording were developed using lens-less and on-chip technologies. We also utilized light-manipulation technique, to induce thrombus or inflammation vascular reactions, and we induced thrombus formation by photo-chemical reactions.

In sum, we developed multi-scale imaging system which can evaluate the therapeutic strategies against thrombotic and inflammatory processes in adult-common disease.

Topic Ⅳ

Functional imaging

DAY2 April 20th 14:30-15:30　OHGI Room (4F)

Chairpersons:

Ching-Liang Lu

Taipei Veterans General Hospital/ National Yang-Ming University, Taiwan

Hironori Yamamoto

Jichi Medical University, Japan

Commentator:

Yoshikazu Kinoshita

Shimane University School of Medicine, Japan

Lecture-1 **Clinical Application of Gastrointestinal Ultrasound**

Jiro Hata

Kawasaki Medical School, Japan

Lecture-2 **Current topics of functional Image for digestive disease**

Yoshihisa Tsuji

Shiga University of Medical Science/ Kurashiki Central Hospital, Japan

Lecture-3 **The cerebral function and structure changes in functional dyspepsia patients and the influence of acupuncture treatment**

Fang Zeng

Chengdu University of Traditional Chinese Medicine, China

Lecture-4 **Application of Functional Brain Imaging in Gastroenterology/Hepatology**

Ching-Liang Lu

Taipei Veterans General Hospital/ National Yang-Ming University, Taiwan

Clinical Application of Gastrointestinal Ultrasound

Jiro Hata

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WORK EXPERIENCE :

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Apr 1989- Mar 1991: Sakugi village clinic
Apr 1991- Mar 1993: Jinseki-Sanwa Prefectural Hospital
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Apr 1995- Mar 2003: Miyoshi Central Hospital
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Japanese Society of Gastroenterology (Boardman)
Japan Gastroenterological Endoscopy Society (Boardman)
Japanese Society for Abdominal Emergency Medicine (Boardman)
Japanese Gastroenterological Association
Japanese Society of Gastroenterological Cancer Screeing
Japanese Society of Internal Medicine
Japan Society of Smooth Muscle Research
American Institute of Ultrasound in Medicine

SPECIALIZED AREA :

Ultrasonographic diagnosis, especially of gastrointestinal tract
Gastrointestinal motility
Abdominal emergency

Clinical Application of Gastrointestinal Ultrasound

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(Introduction)

Barium contrast studies and endoscopy have been the traditional methods of choice for the diagnosis of gastrointestinal diseases. On the other hand, ultrasonography has become a safe and useful diagnostic method that enables us to obtain information about the transmural changes of the gastrointestinal wall. In Japan, the gastrointestinal ultrasound is one of the major objects of concern for sonographers and to learn the method for sonographic screening of the gastrointestinal tract has become inevitable to survive as a competent abdominal sonographer. In my talk, the basic skills and clinical usefulness of sonographic diagnosis of gastrointestinal diseases will be discussed.

(Systematic screening of GI tract)

The first step of the systematic sonographic screening of GI tract is to identify the fixed segment such as the duodenum, ascending and descending colon, and rectum. Also, abdominal esophagus passes through the hiatus of the diaphragm of which the location has almost no individual variation. The second step is to trace the tube between those fixed segments. Since the small bowel is a long tube which lies between duodenum and ascending colon, it is difficult to scan it systematically.

(Image analysis)

It is not easy to obtain a correct diagnosis without an adequate interpretation of ultrasound images of the gastrointestinal tract. For this purpose, analysis of images by completing the checklist below is recommended.

1. Distribution:
   The distribution of the lesion is an important key for the differential diagnosis. For example, localized wall thickening for a short segment is more likely seen in neoplastic lesions whereas the diffuse wall thickening seen in a long segment of the bowel indicates the inflammatory disorders.
2. Wall thickness:
   Wall thickness often depends on the severity of disease. As for cancer, advanced cancers usually are thicker than early cancers, and almost the same can be applied to inflammatory diseases.
3. Wall stratification:
   Evaluation of the wall stratification tells us important information on the histopathological alteration of the lesion. Normal gastrointestinal wall shows the five-layer structure on ultrasound image. When the stratification is destroyed, the lesion is suspected to suffer a transmural damage either due to cancer or inflammation.
4. Echogenicity:
   Echogenicity of the lesion represents the structure of the lesion. When the lesion is composed of the homogenous structure, as seen in most of the malignant lymphoma, it is expressed as a hypoechoic area on ultrasound images.
5. Deformity:
   Deformity usually is a reflection of severe damage of the wall. For example, wall defects are seen in ulcerative diseases and irregular serosal margin indicates the extramural invasion of cancer diseases.
6. Compressibility / Compliance:
   Compressibility can be estimated by compressing the lesion with the probe and compliance can be evaluated by the observation of luminal distention after the ingestion of water. Reduced compressibility / compliance indicates that the lesion is hard, as often seen in cancers or severe fibrosis.
7. Peristalsis:
   Although the frequency of gastrointestinal peristalsis depends on the phase of the digestive state (inter-digestive

or post prandial), small bowel peristalsis can usually be observed in daily examination. Reduced peristalsis is a very sensitive indicator for bowel ischemia and peritonitis.

8. Luminal stenosis / dilatation:

   Luminal dilatation suggests the presence of luminal stenosis at the anal side of the intestine or gastrointestinal paralysis.

9. Extramural changes:

   Extramural changes often help us to understand the nature of the lesion. For example, gastrointestinal perforation is strongly suspected when free air is observed, and extramural invasion of tumor or extension of inflammation causes the thickening of surrounding fatty tissue, which we call the “isolation sign” since this phenomenon makes the lesion easier to detect.

10. Blood flow:

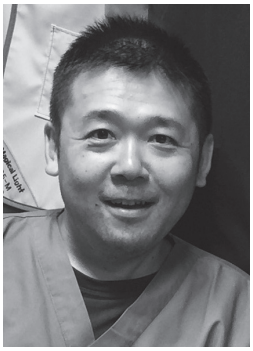
    Color Doppler provides information about the vascular structure of the lesion, although there is a limitation of demonstrable vessels since this method is dependent on the frequency shift produced by the velocity of the target. Recently, Superb Microvascular Imaging which clearly delineates vessels with low velocity has been introduced. Furthermore, contrast ultrasound can demonstrate the minute vessels regardless of their flow velocities, which can be a great help of understanding gastrointestinal perfusion.

(Clinical application of GI ultrasound)

Needless to mention, it is extremely difficult to detect early cancers especially without any preparations. On the other hand, most of advanced cancers can be detected with ultrasound which enables it to be used as a non-invasive screening method for advanced cancers. In patients with acute inflammatory diseases, ultrasound should be considered as the 1st line diagnostic modality with high sensitivity and specificity. Furthermore, in IBD patients, ultrasound can not only be used for the initial diagnosis but also for the assessment of disease activity during the course of treatment.

Current topics of functional Image for digestive disease

Yoshihisa Tsuji



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College/University:

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2006 - 2010 Ph.D., Kyoto University Graduate School of Medicine, Japan

Residency:

2001 - 2002 Junior resident, Internal Medicine, Kyoto University Hospital, Kyoto, Japan

2002 - 2006 Senior resident, Gastroenterology and Hepatology, Kurashiki Central Hospital, Japan

Fellowship:

2010 - 2011 GI trainee, Gastroenterology and Hepatology, Mayo Clinic, Rochester, USA

2011 - 2013 Clinical Research Fellow, Radiology, Mayo Clinic, Rochester, USA

PROFESSIONAL POSITIONS OR ACADEMIC RANK

2010 - 2014 Attending, Gastroenterology and Hepatology, Kyoto University Hospital, Japan

2014 - 2015 Assistant professor, Gastroenterology and Hepatology, Kyoto University Hospital, Japan

2015 Instructor in Gastroenterology, JDWNR Hospital, Bhutan

2015 - 2016 Director of Severe Digestive Team, Kurashiki central Hospital, Japan

2016 - present Associate professor, Medical Education, Shiga University of Medical Science, Japan

HONORS AND AWARDS

2006 Pancreas research foundation of Japan Award

2006 Japan Digestive Disease Week Poster Award

2006, 2010 Japan Society for the Promotion of Science, Research Fellowship (DC1 and PD),

2010 Travel award, National Pancreas Foundation, Atlanta 2012, USA

2011 Japan Society for the Promotion of Science, Award for young Investigator

2012 Poster distinction, Pancreas Club 2013, Orlando, USA

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Current topics of functional Image for digestive disease

Yoshihisa Tsuji
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There are some types of functional images using computed tomography (CT) and magnetic resonance imaging (MRI). Recently, perfusion CT/MRI and cine image, one kind of functional images, capture the attention.

Analyzing dynamics of contrast material, perfusion CT/MRI can show organ blood flow, permeability of drugs into organ, and amount of stroma, as color map. Using perfusion image, development of necrosis of early acute pancreatitis or response of chemo-radiation therapy for cancer can be predicted.

Cine image, which can be obtained by reconstruction of CT/MRI, can show motion of gut clearly. Combining stroma image from perfusion analysis and cine, we can judge whether gut disorder will be caused by adhesion or fibrosis.

In my presentation, I will talk about basics of perfusion CT/MRI and cine images, including case presentation.

The cerebral function and structure changes in functional dyspepsia patients and the influence of acupuncture treatment

ZENG Fang

Dr ZENG Fang works as professor, associate dean and Ph.D. supervisor in Acupuncture-moxibustion and Tuina School, Chengdu University of Traditional Chinese Medicine, China. She is a consultant of Traditional and Complementary Medicine for World Health Organization (WHO), and the general secretary of the Specialty Committee of Evidence-based Acupuncture-Moxibustion, China Association of Acupucture-Moxibustion, and a member of the Standing Committee, Specialty Committee of functional Imaging and Acupuncture-Moxibustion, China Association of Acupucture-Moxibustion. She focused on investigating the central pathogenesis of functional gastrointestinal disorders (FGIDs) and the underlying mechanism of acupuncture treating for FGIDs , In the past 5 years, she had published 34 SCI articles, and won the National Science and Technology Progress Second Prize of China in 2012 and Sichuan Provincial Science and Technology Progress First Prize in 2014, 2011.

The cerebral function and structure changes in functional dyspepsia patients and the influence of acupuncture treatment

ZENG Fang
supervisor in Acupuncture-moxibustion and Tuina School
Chengdu University of Traditional Chinese Medicine

Objective: The abnormal processing of visceral sensation at the level of the Central Nervous System is considered as an important pathogenesis for functional dyspepsia (FD). These studies aim to map the cerebral functional and structural changes of the FD patients in comparison to the healthy subjects (HS) and to investigate the influence of acupuncture treatment on cerebral activities of FD patients.

Methods: 1) 50 meal-related FD patients and 40 healthy subjects (HS) were included and underwent a magnetic resonance imaging (MRI) scan. The MRI sequences including 3DT1, resting Bold-fMRI and diffusion tensor imaging (DTI). The voxel-based morphometry (VBM) analysis and the tract-based spatial statistics (TBSS) were employed to identify the gray matter and White matter structure alterations in FD patients respectively. The regional homogeneity (ReHo), seed correlation analysis and Independent component analysis (ICA) were performed to investigate the cerebral functional changes in FD patients. 2) 40 FD patients and 20 HS were included and underwent an 18F-FDG Positron Emission Tomography-Computed Tomography (PET-CT). Statistical Parametric Mapping software (SPM5.0) was used to analyze the changes in resting brain glycometablism of the FD patients. 3) 72 FD patients were randomly assigned to receive either acupuncture or sham acupuncture treatment for 4 weeks. 10 patients in each group were randomly selected for 18F-FDG PET-CT scans to detect the cerebral glycometabolism changes elicited by acupuncture stimulation. The Nepean Dyspepsia Index (NDI) and Symptom Index of Dyspepsia (SID) were used to evaluate the therapeutic effect.

Results: 1) The VBM analysis showed that, compared to the HS, the meal-related FD patients showed a decreased gray matter density (GMD) in the bilateral precentral gyrus, medial prefrontal cortex (MPFC), anterior cingulate cortex (ACC) and midcingulate cortex (MCC), left orbitofrontal cortex (OFC) and right insula ($p<0.05$, FWE Corrected, Cluster size<50); **The TBSS analysis** showed that the FD patients showed increased fractional anisotropy (FA) along with reduced mean diffusivity (MD) and radial diffusivity (RD) in multiple WM tracts, including the corona radiata, internal capsule, posterior thalamic radiation, corpus callosum, external capsule, sagittal stratum, and superior longitudinal fasciculus ($P<0.05$, corrected). **The ReHo analysis** showed that the altered ReHo values ($p<0.05$, FDR corrected) were discovered in multiple brain areas in FD patients, and only the ACC and thalamus exhibited significant correlation with the severity of dyspepsia; **The Seed-based correlation analysis** revealed ACC- and thalamus-related functional connectivity differences between FD patients and controls at a voxel-wise level symptoms. **The ICA results** showed that, significant spatial differences with the default mode network (DMN) in FD patients, compared with HCs, were mainly found in the dorsal MPFC, ventral MPFC, orbitofrontal cortex (OFC), pregenual ACC, thalamus, parahippocampal gyrus, precuneus, parietal cortex, and temporal pole. Meanwhile, NDI scores were positively correlated with the pACC, and was negative correlated with the OFC. **2)** Compared to the HS, the FD patients showed higher glycometabolism in the bilateral insula, ACC, MCC, cerebellum, thalamus, PFC, precentral gyrus, postcentral gyrus, middle temporal gyrus, superior temporal gyrus and putamen, right parahippocampal gyrus and claustrum, and left precuneus ($p<0.001$); The increased glycometabolism in ACC, insula, thalamus, MCC and cerebellum showed a significant correlation with SID scores and NDI scores ($p<0.01$); **3)** The clinical data showed that, after treatment, the decrease of the SID score in acupuncture group was significantly greater than that in sham acupuncture group ($p<0.05$). The increase of NDI score between the two groups showed insignificant difference ($p>0.05$), but only the improvement of NDI score in acupuncture group was clinically significant. The PET-CT data indicated that, after treatment, acupuncture group showed an extensive deactivation in cerebral

activities compared to sham acupuncture group. In acupuncture group, the deactivations of the brainstem, ACC, insula, thalamus and hypothalamus nearly all related to the decrease in SID score and the increase in NDI score respectively ($p<0.05$, corrected).In sham acupuncture group, the deactivations of the brainstem and thalamus tended to associate with the increase in NDI score ($p<0.1$, corrected).

Conclusion: 1) The cerebral function and structure of the FD patients significantly differs from those of the HS. The ACC, insula, thalamus, MCC and cerebellum might be key regions related to the symptom severity of FD. 2) Acupuncture and sham acupuncture have relatively different clinical efficacy and brain responses. Acupuncture treatment more significantly improves the symptoms and QOL of FD patients. The more remarkably modulation on the homeostatic afferent network including insula, ACC and hypothalamus, etc. might be the potentially specific mechanism of acupuncture.

Key words: Functional Dyspepsia; Resting Brain Activity; Brain structure; Neuroimaging; Acupuncture

Application of Functional Brain Imaging in Gastroenterology/Hepatology

Ching-Liang Lu

Prof. Lu obtained his medical degree from Taipei Medical University on 1988, and went on to complete postgraduate training in internal medicine and gastroenterology at Taipei Veterans General Hospital. Further postdoctoral training was completed at the University of Oklahoma Health Science Center and University of Texas Medical Branch at Galveston, USA under the supervision of Prof. Jiande Chen and Prof. Pankaj J Pasricha. His research interests mainly focus on gastroesophageal reflux disease, functional gastrointestinal disorder and transitional studies on visceral pain mechanism and hepatic encephalopathy. Over 100 papers have been published by Prof. Lu in prestigious journals including Lancet, Gastroenterology, Gut, Am J Gastroenterology, J Hepatol, Am J Psychiatry, Pain and GI Endoscopy. He has been involved in setting up the Asian consensus for irritable bowel syndrome and functional dyspepsia. Currently, he is Professor in Institue of Brain Science at National Yang-Ming University, Director of education in Department of Medicine and Director of GI Ward in Taipei Veterans General Hospital. He also serves as a governing council member of Asia Neurogastroenterology and Motility Association (ANMA), editorial board member of J Neurogastroenterology and Motility, Advances in Digestive Medicine, and Journal of Chinese Medical Association.

Application of Functional Brain Imaging in Gastroenterology/ Hepatology

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Functional brain imaging began to emerge around 1990, which development has greatly enhanced our understanding of the complex function in the brain for both health and diseases. Blood oxygen level dependent (BOLD) functional MRI (fMRI) was the main modality used in this purpose. BOLD fMRI is a noninvasive and radiation-free technique to map brain areas of abnormal neuronal activity. BOLD fMRI can be classified to task-related fMRI and resting-state fMRI according to experimental paradigms applied. In task-related fMRI design, the subject is placed in the magnet of an MRI machine, with simultaneous stimulus (such as visual or visceral stimuli) in a controlled fashion. On the other hand, in resting-state fMRI studies, no specific stimuli was applied. Resting-state fMRI constitutes a novel paradigm that examines spontaneous brain function by using BOLD contrast without task. Spatially distributed networks can be identified to characterize resting state networks.

Within the field of gastroenterology/hepatology, functional brain imaging has been widely applied to evaluate the supraspinal mechanism in the patients with functional gastrointestinal disorders (FGIDs) and hepatic encephalopathy (HE).

FGIDs are heterogeneous disorders, including non-cardiac chest pain, functional dydpepsia(non-ulcer dyspepsia) and irritable bowel syndrome IBS. They are characterized by chronic visceral discomfort or pain without any apparent biological or anatomical causes. FGIDs, no matter in Western or Estern countries, bring a significant burden to the society and patient him/herself in terms of work productivity, medical costs, and quality of life. Functional brain imaging studies in FGIDs have identified abnormalities in evoked brain responses, resting state activity/ connectivity, as well as structures changes in gray and white matter. Brain alterations of the salience, emotional arousal, and sensorimotor networks, as well as in prefrontal regions are consistently identified in the patients with FGIDs. It is found that anterior cingulate cortex (ACC), the insula, primary somatosensory cortex, prefrontal cortex, the posterior parietal cortex and thalamus are consistently activated in both healthy controls and the FGID patients. And FGID patients would have greater activations in certain areas such as the insula and ACC.

HE is a serious neuropsychiatric complication in the patients with acute or chronic liver failure (cirrhosis), which can be further classified as over or covert HE. Overt HE is characterized by a wide spectrum of clinical manifestations from alterations of mild upsets to stupor and coma. The patients with covert or minimal HE (MHE) usually have no obvious clinical manifestation and are characterized by neurocognitive impairment in attention, vigilance and integrative function, which can only be detected by specific neuropsychiatric tests. MHE increases the risk of development of overt HE and adversely affects survival. Both task-related and resting state fMRI have been used in HE or MHE patients, yielding important insights for understanding pathophysiological mechanisms and functional reorganization of HE. For example, significantly reduced functional connectivity in the right middle frontal gyrus and left posterior cingulate cortex consisting of the default mode network was found in HE patients when compared to healthy controls. For MHE patients, reduced resting-state functional connectivity within default mode network was found to be associated with neurocognitive impairments. Using seed correlation analysis, MHE patients had disrupted thalamic functional connectivity in ventral anterior nuclei and ventral posterior medial nuclei compared to healthy controls.

To date, both FGIDs and HE are lack of biological markers and bearing a significantly unmet need in their treatment. Using multimodal brain imaging studies to explore the brain structural and functional alterations in the FGID and HE patients will be helpful to clarify the pathophysiological mechanism and functional reorganization pattern during disease progression in both diseases. Through this approach, it may provide an opportunity for developing useful markers and be facilitate to identify targets for therapeutic interventions.

Topic V

Advanced imaging of the liver-1

DAY2 April 20th 15:45-16:15　OHGI Room (4F)

Chairpersons:

Aamir Ghafoor Khan

Lady Reading Hospital, Pakistan

Makiko Taniai

Tokyo Women's Medical University, Japan

Lecture-1 **Micro blood flow imaging in liver tumors using contrast enhanced ultrasonography**

Masahiro Ogawa

Nihon University Hospital, Japan

Lecture-2 **Advanced Visualization of Liver Fibrosis**

Chengwei Tang

West China Hospital, Sichuan University, China

Micro blood flow imaging in liver tumors using contrast enhanced ultrasonography.

Masahiro Ogawa

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Senior Fellow of the Japan Society of Ultrasonics in Medicine No.715
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MEMBERSHIPS:
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The Japan Society of Hepatology
The Japanese Society of Gastroenterology
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The Japanese Society of Gastroenterological Cancer Screening
The Japanese Diabetes Society

MAJOR RESEARCH INTERESTS:
Diagnostic imaging of a gastroenterology
Ultrasonic diagnosis

Micro blood flow imaging in liver tumors using contrast enhanced ultrasonography.

Masahiro Ogawa,Yukinobu Watanabe,Mariko Kumakawa,Midori Hirayama,Katsuhiko Shiozawa,Naoki Matsumoto Hiroshi Nakagawara,Takuji Gotoda,Mitsuhiko Moriyama

Nihon University Hospital Gastroenterology

Aim : Blood-flow diagnosis is important in diagnosis of a liver tumor. The contrast enhanced ultrasonography is useful to diagnosis of a liver tumor, because high temporal and spatial resolution of ultrasonography can evaluate a detailed micro blood flow. However, an ultrasonography has a weak point where the display range is narrow, as compared with CT and an MRI. This is a reason which lowers objectivity and is not utilized in many hospitals. In recent years, ultrasonic diagnostic equipment with a magnetometric sensor appears, and this equipment is spreading. The weak point of an ultrasonography has been improved by this equipment and the ultrasound test became possible by targeting. The higher frame rate was obtained by having narrowed the display range. This detailed micro blood flow imaging is not obtained by other diagnostic imaging. The objectives of this study is the usefulness of the micro blood flow imaging of a liver tumor.

Method : The equipment used is GE medical system LOGIQE9 and Toshiba Medical Systems system APLIO500. To observe CEUS images, bolus injection of 0.5ml/of Sonazoid (Daiichi-Sankyo, Tokyo, Japan) was admnistered intravenously via an antecubital vein, followed immediately by a 10mL saline flash.When other diagnostic imaging was used together, I inspected with the equipment corresponding to a magnetometric sensor. I adjusted the display range so that the whole tumor might enter, and I inspected after that. We studied, from January 2012 to August 2015. An object is the hemangioma , the focal nodular hyperplasia, the hepatocellular carcinoma, the intrahepatic cholangiocarcinoma, and metastatic liver cancer which were diagnosed clinically.

To observe CEUS images, bolus injection of 0.5ml/body of Sonazoid (Daiichi-Sankyo, Tokyo, Japan) was admnistered intravenously via an antecubital vein, followed immediately by a 10ml saline flash. According to the traditional use in Japan, we defined arterial, portal venous, and post vascular phases, as 0-30 seconds,31-120 seconds, and 600 seconds after injection, respectively This retrospective study was approved by the research ethics board of our institution.

Results: Hemangioma with typical peripheral nodular contrast enhancement and centripetal fill-in. In patients with FNH typically central arterial enhancement can be shown in comparison to the hepatic artery with wheel-spoke phenomenon and portal venous enhancement in comparison to the portal vein. HCC are usually hyperenhancing in the arterial phase, typically with a chaotic vascular pattern or basket pattern. In the portal venous and late phases, HCC usually shows hypoenhancement. Hyperenhancement in the arterial phase is showed to be homogeneous with fill from the periphery. Intrahepatic cholangiocarcinomas have a rim like enhancement in the arterial phase but all show late phase wash out. Liver metastases are usually rim enhancement in the arterial phase and can be detected and characterized reliably as hypoenhancing lesions during the portal venous and late phases. Wash out starts early, usually in the portal venous phase, and is marked.

Discussion : High temporal and spatial resolution of ultrasonography can point out a characteristic enhancement patterns certainly as compared with CT or MRI. Especially CEUS was useful to evaluation of the small tumor which can be pointed out by neither CT nor MRI. It was also possible to have guessed a tumor grade of malignancy to liver cell cancer.
Conclusion: CEUS is a very sensitive diagnostic tool in characterizing liver tumors. It is especially useful to diagnosis in the liver tumor.

Advanced Visualization of Liver Fibrosis

Chengwei Tang

Professor, Director, Dept. of Gastroenterology, West China Hospital, Sichuan University, Chengdu, China.
Vice Chairman, Chinese Society of Gastroenterology

She received her Bachelor medical degree from West China Medical University in 1983 and obtained a Master degree from Chongqing Medical University in 1986. Dr. She was awarded Ph D (supervisor: Prof. Dr. CBHW Lamers) in Leiden University Medical Center in 1996.

During 1986-1992, Dr. Tang completed a residency and worked as a physician-in-charge and specialized in Internal Medicine and Gastroenterology in The First Hospital Affiliated to Chongqing Medical University. She became a professor and director of gastroenterology department of that hospital in 1997. Since 2002, she has been assigned as a professor and director of gastroenterology department of West China Hospital, Sichuan University.

Her main academic interests include Liver fibrosis, portal hypertension, gut peptides, pancreatitis and intestinal mucosal immune. Owing to her contributions to clinical works, basic research and development of her team, she was awarded honors of Excellent Young Scientist and Young Expert with Outstanding contribution in China. As a first or corresponding author, she has more than 200 publications including in Gastroenterology, Gut, Br J Cancer, Carcinogenesis, Int J Cancer, Shock, J Gastrointestinal Surg. Neurogastroenterology and motility, Gastrointestinal Endoscopy, Current Pharmaceutical Design, Pancreas, Alcohol, Alcohol Clin Exp Res, Cancer Biology Therapy, et al.

Advanced Visualization of Liver Fibrosis

Chengwei Tang, Jinhang Gao, Shilei Wen
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Chengdu, P. R. China

Liver fibrosis represents a sustained wound healing response to chronic or repeated liver injury regardless of their etiologies. Although hepatic stellate cells (HSCs) activated by chronic inflammation have been considered as the key players in the hepatic fibrogenic process, other cell types, i.e. hepatocyte, vascular endothelial cell or liver sinusoidal endothelial cell (LSEC) could also contribute to this process. In this presentation, advanced imaging of epithelial-to-mesenchymal transition (EMT) of hepatocytes, endothelial induced angiogenesis and remodeling of LSEC in liver fibrosis will be displayed.

1. Hepatocytes underwent the process of EMT during liver fibrosis

Thioacetamide (TAA)-induced EMT of hepatocytes is demonstrated by the increased expressions of mesenchymal biomarkers (α-SMA, FSP-1, N-cadherin and collagen I), the enhanced production of excessive extracellular matrix components (MMP-2, MMP-9 and Snail1) and the decreased epithelial biomarker (E-cadherin) in the hepatocytes of TAA-treated group. These results showed that hepatocytes underwent EMT after the persistent and sustained injurious and inflammatory stimuli.

2. Intrahepatic angiogenesis and fibrosis developed in parallel during liver fibrosis

Tissue sections stained with hematoxylin-eosin and Masson trichrome revealed that hepatic vascular areas in cirrhotic liver were greatly enlarged when compared with those in control liver. Such findings were further confirmed by the three-dimensional changes of portal veins. Vascular casts showed much more irregular, tortuous portal veins in the livers of TAA group. Correspondingly, the up-expression of hepatic CD31 and vascular endothelial growth factor in TAA group were visualized by immunohistochemistry. These findings manifested that liver cirrhosis is closely associated with increased angiogenesis, and the neovasculature is mainly located in the fibrotic areas of the liver.

3. Remodeling of LSEC is the driving forces leading to liver fibrosis

The sinusoids were regular and visible in the control group, while after TAA administration, the sinusoids were disappeared. The three dimensional morphology of the sinusoids showed comprehensive remodeling of the sinusoids with a tortuous and plexus-like appearance. Consistently, sinusoidal remodeling results in dramatically reduced in sinusoidal branching and diameter. As shown by scanning electron microscope, LSEC in the control group contained numerous fenestrae grouped into sieve plates. Whereas, fenestrae and sieve plates were severely destroyed after TAA administration, consequently, microvilli on hepatocytes were exposed in the sinusoid. The residual fenestrae were capillarized which termed as formation of organized basement membrane. Destroyed fenestrae and sieve plates of LSEC induced by TAA might lead to complete exposure of hepatocytes and HSCs to the toxicant in the blood, which might worsen fibrosis by damaging hepatocyte, advancing EMT of hepatocytes and activating HSC.

Collectively, EMT of hepatocytes, intrahepatic angiogenesis and sinusoidal remodeling occur concurrently with fibrosis. The increasing knowledge on pathophysiology of liver fibrosis might provide new therapeutic targets to reverse or ameliorate liver fibrosis.

Topic V

Advanced imaging of the liver-2

DAY2 April 20th 16:15-16:45　OHGI Room (4F)

Chairpersons:

Chengwei Tang

West China Hospital, Sichuan University, China

Sumiko Nagoshi

Saitama Medical University, Japan

Lecture-1 **The Latest Trends in the Noninvasive Diagnosis of Liver Diseases**

Hiroko Iijima

Hyogo College of Medicine, Japan

Lecture-2 **Imaging of Diffuse Fatty Infiltration of the Liver**

Gabriel Lau

Dunedin Hospital, New Zealand

The Latest Trends in the Noninvasive Diagnosis of Liver Diseases

Hiroko Iijima

Professor of Department of Hepatolo-biliary-pancreatic Medicine,
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Field of Study : Hepatology

Work Experience :

1983-1985	Department of Internal Medicine Hyogo College of Medicine
1985-1986	Department of Internal Medicine Fujimoto Hospital
1986-2000	Department of Internal Medicine Hyogo College of Medicine
2000-2003	Department of Gastroenterology Tokyo Medical University
2003-2005	Vising Clinical Professor of Department of Medical Imaging University of Toronto Toronto General Hospital Visiting Professor of Department of Medical Biophysics University of Toronto Sunnybrook Health Sciences Centre
2005-present	Department of Hepatology and Ultrasound Imaging Center, Hyogo College of Medicine.
2008-	Professor of Department of Hepatolo-biliary-pancreatic Medicine, Head of the Section of Ultrasound at Ultrasound Imaging Center, Hyogo College of Medicine.

Professional Organization :

Japanese Society of Gastroenterology
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Japan Society of Ultrasonics in Medicine
The Japanese Society of Internal Medicine
Japan Gastroenterological Endoscopy Society
The Japanese Society of Gastrointestinal Cancer screening
The Japan Society for Portal Hypertension

A Board of Directors :

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The Latest Trends in the Noninvasive Diagnosis of Liver Diseases

Hiroko Iijima

Hyogo College of Medicine.

The latest trends in the diagnosis of liver disease, particularly ultrasound-based elastography and the Superb Micro-Vascular Imaging (SMI) technology will be discussed.

Diagnosis of chronic liver disease can be confirmed by a liver biopsy; however, the procedure has several drawbacks including invasiveness and sampling errors. Recently, we use ultrasound-based shear wave elastography (SWE) to diagnose liver fibrosis, and it is an imaging-based technique that allows to assess tissue stiffness quantitatively. We have been using this noninvasive technique with several elastographies by different manufacturers, and have obtained similar diagnostic performance in the diagnosis of cirrhosis regardless of manufacturers.

Grasping tumor characteristics in B-mode imaging is essential for the sonographic diagnosis of liver tumors. Evaluating arterial hypervascularity, vascular pattern and stiffness of tumors is important in differentiation of tumors. However, in some cases, conventional color Doppler imaging was not enough to able to perform differential diagnosis due to its low sensitivity to slow flow blood vessels. SMI is a new blood flow imaging technique, which is improved from conventional color Doppler imaging, clearly depicts slow blood flow in small vessels by featuring higher frame rates and motion artifacts suppression. Diagnosis of liver tumors by SMI will be summarized.

Imaging of Diffuse Fatty Infiltration of the Liver.

Gabriel Buong Hung LAU

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EDUCATION:

1993	MB ChB (University of Otago)
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PROFESSIONAL APPOINTMENTS:

April 2006-present	Radiology Consultant, Dunedin Hospital, Dunedin, New Zealand
April 2006-present	Radiology Consultant, Otago Radiology Limited, Dunedin, New Zealand
April 2006-present	Honorary Clinical Lecturer, Medical School, University of Otago, Dunedin, New Zealand
April 2010-present	Director, Otago Radiology Limited/Pacific Radiology Group, Dunedin, New Zealand
Jan 2012-present	Editor –Diagnostic and Interventional Radiology, JMIRO
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RECENT ORAL PRESENTATIONS:

Lau GBH. TACE/RFA. 20th Annual General Meeting Interventional Radiological Society of Australasia, Sept 4-6, 2012.

Lau GBH. Expert Case Panel. 20th Annual General Meeting Interventional Radiological Society of Australasia, Sept 4-6, 2012.

Lau GBH. Debate – The Interventional Radiologist Will Be Extinct in 10 Years. 20th Annual General Meeting Interventional Radiological Society of Australasia, Sept 4-6, 2012.

Lau GBH. SIRT Australia/New Zealand Experience. 22nd Singapore Radiologcial Society, March 8-9, 2013.

Lau GBH. Can the evidence unlock the TACE vs SIRT debate. 21st Annual General Meeting Interventional Radiological Society of Australasia, July 8-11, 2013.

Lau GBH. Management of SIRT – Toxicities and Complications. 11th APCCVIR, May 15-18, 2014.

Lau GBH. Personalisating Ablative Therapy for Oligometastatic Disease. Combined Scientific Meeting RANZCR, Sept 4-7, 2014.

Lau GBH. SIRT vs TACE HCC. 22nd Annual General Meeting Interventional Radiological Society of Australasia, Aug 26-28, 2014.

Lau GBH. Training In Interventional Radiology. 22nd Annual General Meeting Interventional Radiological Society of Australasia, Aug 26-28, 2014.

Lau GBH. Training In Interventional Radiology. Vascular Society New Zealand Meeting, Feb 20-22, 2015.

Lau GBH. Insights from the SIRTFLOX Study – What does it mean from a IR perspective. 23rd Annual General Meeting Interventional Radiological Society of Australasia, July 7-9 2015.

Lau GBH. Progress of CT Colonography. The New Zealand Society of Gastroenterology Annual Scientific Meeting, November 25-27 2015.

Lau GBH. Imaging of Fatty Liver. The New Zealand Society of Gastroenterology Annual Scientific Meeting, November 25-27 2015.

Imaging of Diffuse Fatty Infiltration of the Liver.

Gabriel B H Lau MB ChB FRANZCR EBIR[1]

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Diffuse fatty infiltration of the liver is a common imaging finding that can often lead to difficulties assessing the liver appearances. This presentation will provide an update of the imaging patterns and pifalls of diffuse fatty infiltration, and future directions.

Keywords: Diffuse fatty infiltration, Hepatic Steatosis.

Best Poster Award Ceremony

DAY2 April 20th 16:45-16:55　OHGI Room (4F)

Moderator: Hiroshi Kashida Kindai University Faculty of Medicine, Japan
Presenter: Kazuichi Okazaki Chairman, The 7th Asian-Pacific Topic Conference

<GOLD>

Naoki Oshima　Shimane University School of Medicine, Japan
P- 6 Confocal Raman Spectroscopy for Endoscopic Diagnosis of Eosinophilic Esophagitis – Is Eosinophile Detection Possible?

<SILVER>

Kento Takenaka　Tokyo Medical and Dental University, Japan
P- 1 Enteroscopic and MR findings of small intestine in Crohn's disease

Akiko Fuyuki　Yokohama City University, Japan
P-10 Assessment of small bowel motility in patients with bloating using Cine-MRI

Kuan Loong Cheong The Lyell McEwin Hospital, Australia
P-30 A prospective multicentre study assessing the utility of Narrow Band Imaging with dual focus magnification in differentiating colorectal neoplasia using the NICE and Modified Sano's classification

Takashi Nishimura　Hyogo College of Medicine, Japan
P-31 Usefulness of non-invasive assessment of liver fibrosis using six different ultrasound elastography devices in patients with chronic hepatitis and the difference of liver stiffness between HBV-related chronic hepatitis and non-HBV-related chronic hepatitis

Naoki Oshima

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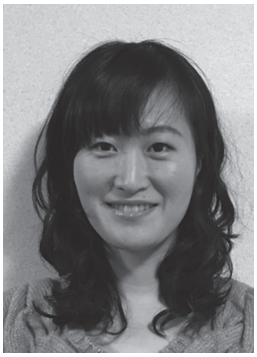

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Ohkubo H, Fuyuki A, Nakajima A, et al. Assessment of small bowel motility in patients with chronic intestinal pseudoobstruction using cine-MRI. Am J Gastroenterol. 108(7): 1130-9. 2013

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RESEARCHES

1) Demographic and Endoscopic Findings among All Medical Patients Undergoing Upper Endoscopy in Hospital Ampang from 2010 to April 2011
2) Colorectal Cancer Registry from 2009 to 2011: Ampang Hospital Experience
3) Prospective Study on Correlation of Charles Dent Questionnaire with Endoscopic Esophagitis

PUBLICATIONS

1) Narrow band imaging with magnification for the diagnosis of lesions in the upper gastrointestinal tract. World J Gastrointest Endosc. 2013 Dec 16; 5(12): 584–589
2) Detection and characterization of early malignancy in the esophagus: What is the best management algorithm? Best Pract Res Clin Gastroenterol. 2015 Aug;29(4):533-44.
3) Review Article Malignant Biliary Obstruction: Evidence for Best Practice. Gastroenterology Research and Practice Volume 2016

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Japan Gastroenterological Endoscopy Society
The Japan Society for Portal Hypertension
The Japanease Gastroenterological Association

Poster Exhibition

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Kento Takenaka Tokyo Medical and Dental University, Japan

P-2 Pilot study of endoscopic retrograde 3-dimensional - computed tomography enteroclysis for the assessment of Crohn's disease
Hiroki Tanabe International University of Health and Welfare Hospital, Japan

P-3 New endoscopic Imaging System For Evaluation of Colonic Mucosal Inflammation in Ulcerative Colitis
Yusuke Honzawa Kyoto University, Japan

P-4 Prospective Cohort Study of the Impact of Endoscopic Submucosal Dissection on Gastric Motility and Upper Abdominal Symptoms
Shin Kono Tokyo Medical University, Japan

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Yasushi Matsukiyo Toho University Omori Medical Center, Japan

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Naoki Oshima Shimane University School of Medicine, Japan

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Teppei Omori Tokyo Women's Medical University, Japan

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Shintaro Ichikawa University of Yamanashi, Japan

P-9 Linked color imaging, a novel endoscopic enhancement system is useful for the assessment of mucosal inflammation in ulcerative colitis.
Kazuhiko Uchiyama Kyoto Prefectural University of Medicine, Japan

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Akiko Fuyuki Yokohama City University, Japan

P-11 Linked color imaging facilitates detection for early gastric cancers missed by white light imaging endoscopy
Yoshimasa Miura Jichi Medical University, Japan

P-12 Visualization of pancreatic inflammation in mouse model
Shin Hamada Tohoku University Graduate School of Medicine, Japan

P-13 Effectiveness of auto-fluorescence imaging systems for differential diagnosis of colorectal lesions
Naoto Tamai The Jikei University School of Medicine, Japan

P-14 Imaging Colon of Rhesus Macaques with Colonoscopy
Zhiyin Huang Sichuan University, China

P-15 An activatable photosensitizer targeted to γ-glutamyltranspeptidase for tumor selective photodynamic therapy
Mako Kamiya Graduate School of Medicine, The University of Tokyo, Japan

P-16 Indocyanine green fluorescence during gastrointestinal surgery for preventig anastomotic leakage
Hironori Ohdaira International University of Health and Welfare Hospital, Japan

P-17 Role of Narrow band imaging in diagnosing Tc-99m scintigraphy negative Meckel's Diverticulum in Adult Patients with Obscure GI Bleeding using single balloon enteroscope.
Hrushikesh Chaudhari Asian Institute of Gastroenterology, India

P-18 Evaluation of Tumor-associated Stroma and its Relationship with Tumor Hypoxia using Dynamic Contrast-enhanced CT and 18F-Misonidazole PET in Murine Tumor Models
Sho Koyasu Graduate School of Medicine, Kyoto University, Japan

P-19 Clinical implications of advanced endoscopy
Toshiharu Sakurai Kindai University Faculty of Medicine, Japan

P-20 Usefulness of three-dimension biliary simulation using CT with Drip-infusion Cholecystocholangiography (DIC-CT)
Takayuki Shiraki Dokkyo Medical University, Japan

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P-22 Usefulness of contrast enhanced ultrasonography in diagnosis of hepatic focal nodular hyperplasia
Yukinobu Watanabe Nihon University Hospital, Japan

P-23 A possibility of cordless camera for laparoscopic surgery ~ Can LED light be used as a portable light source? ~
Hisae Aoki Sanraku Hospital, Japan

P-24 Preoperative imaging of thoracic duct for thoracic esophagectomy
Junya Oguma Tokai University School of Medicine, Japan

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Zhi-Qin WONG University Malaya Medical Centre, Malaysia

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Eun Sun Kim Korea University College of Medicine, Korea

P-27 Radiological Diagnosis and Staging of Hepatocellular Carcinoma Using Multiphasic CT Scanning
Ruveena Bhavani University Malaya Medical Centre, Malaysia

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Danny Joseph Tuazon University of the Philippines, Philippine

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Yen-Po Wang Taipei Veterans General Hospital, Taiwan

P-30★ A prospective multicentre study assessing the utility of Narrow Band Imaging with dual focus magnification in differentiating colorectal neoplasia using the NICE and Modified Sano's classification
Kuan Loong Cheong The Lyell McEwin Hospital, Australia

P-31★ Usefulness of non-invasive assessment of liver fibrosis using six different ultrasound elastography devices in patients with chronic hepatitis and the difference of liver stiffness between HBV-related chronic hepatitis and non-HBV-related chronic hepatitis
Takashi Nishimura Hyogo College of Medicine, Japan

P-32 Endoscopic Appearance of Serrated Adenoma Using White Light Endoscopy, Narrow Band Imaging, and Blue Laser Imaging
Hasan Maulahela University of Indonesia, Indonesia

P-33 The use of endocystoscopy for the early detection of esophageal neoplasm: a case series
Shannon Chan The Chinese University of Hong Kong, Hong Kong

P-34 Effects of ambient temperature on ablation zone size: An experimental study with Microwave ablation in ex vivo bovine livers
Andre Poon Dunedin Hospital, New Zealand

P-35 Reevaluation of diagnostic ability of fluorescence cytology using 5-aminolevulinic acid during endoscopic ultrasound-guided fine needle aspiration for pancreatic lesions
Tsukasa Ikeura Kansai Medical University, Japan

★Best Poster

Enteroscopic and MR findings of small intestine in Crohn's disease

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To assess both active lesions such as ulcers or aphtha and intestinal damage such as strictures is important in Crohn's disease (CD). Balloon-assisted enteroscopy (BAE) is able to assess the small intestinal lesions in detail, and also to take biopsies or to perform endoscopic balloon dilatation. Magnetic resonance (MR) enterography is a recommended imaging technique for detecting intestinal involvement in CD. However, the diagnostic accuracy of MR enterography has not been compared directly with that of BAE in the jejunum and proximal ileum. And there is no widely accepted endoscopic or MR scoring system for the entire small intestine in CD. In addition, the prognostic significance of BAE or MR enterography in the small intestine is still uncertain. Here, we evaluated the usefulness of MR enterocolonography (MREC) by comparing its findings with those from BAE. And we also evaluated the prognostic factors of the small intestinal lesions for patients' outcomes.

MREC and BAE were performed on 100 patients. The segmentation and assessment of the endoscopic findings were defined based on modified SES-CD, and those of MREC findings were defined based on modified MaRIA score as well. Physicians and radiologists were blinded to results from other studies. MREC findings were directly compared with those from BAE; the sensitivity and specificity with MREC detected CD lesions were assessed, and we evaluated the correlation between modified SES-CD and MaRIA scores. Additionally, we evaluated the prognostic factors for recurrence, hospitalization, and surgery (follow up period median 10 months).

The scope was passed in retrograde fashion and reached the proximal ileum in 98 patients (98.0%), the jejunum in 40 patients (40.0%), and the entire intestine in 11 patients (11.0%). In BAE, the CD lesions were detected in the terminal ileum (57.0%) and proximal ileum (60.2%) at same rate. In the assessment of CD active lesions, MREC detected ulcerative lesions and all mucosal lesions in the small intestine with 82.4% sensitivity and 67.5% sensitivity, respectively; specificity values were 87.6% and 94.8%, respectively. In the assessment of intestinal damage, the sensitivity and specificity of MREC for small intestinal strictures were 40.8% and 93.7%, respectively. Modified MaRIA scores correlated with modified SES-CD in the terminal ileum (R=0.725), and also did in the jejunum and proximal ileum (R=0.806). Totally, modified MaRIA scores correlated well with modified SES-CD in the small intestine (R=0.808).

For the patients' outcomes, multivariable analysis showed that endoscopic ulcerative lesions in the small intestine were independent factor for recurrence (P=0.002). Kaplan Meier method showed that endoscopic ulcerative lesions were risk factor for recurrence (P=0.001) but aphtous lesions were not (P=0.199). Active lesions detected by MREC were also independent factor for recurrence (P=0.004), and its relative risk was 2.4. Endoscopic strictures in the small intestine were independent factor for hospitalization and surgery (P=0.03, P=0.002); however, endoscopic ulcerative lesions were not independent factor (P=0.556, P=0.446). Stenotic lesions detected by MREC were independent factor for hospitalization and surgery (P=0.004, P=0.006), respectively as well; and their relative risk was 4.0 and 5.4, respectively.

Evaluation of small intestinal lesions is important in CD. MREC was useful for detecting active lesions in the deep small intestine, which lesions were the key to determine medical treatment. However, the detection of stenotic lesions by MREC was less sensitive, which lesion were associated with endoscopic or surgical treatment. BAE should be a gold standard to assess small intestinal strictures. Assessment of CD lesions in the small intestine requires the selection of a suitable imaging technique. Alternatively, it is needed to develop the new scoring system of endoscopy or MR for the entire small intestine in CD. We proposed that modified SES-CD or modified MaRIA scores could be adapted to the deep small intestine. We also showed that it was important to evaluate both active lesions and intestinal damage from the perspective of prognosis in CD. Endoscopic or MR active lesions were risk factor for recurrence, in contrast, endoscopic or MR stenotic lesions were risk factor for hospitalization and surgery; that is to say, we should distinguish active lesions and intestinal damage when we assessed CD lesions.

Title: Pilot study of endoscopic retrograde 3-dimensional - computed tomography enteroclysis for the assessment of Crohn's disease

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Abstract: Endoscopic retrograde ileography (ERIG) is applied clinically for the diagnosis and assessment of the Crohn's disease activity in many institutes. We further developed a technique named endoscopic retrograde 3-dimensional - computed tomography enteroclysis (ER 3D-CTE), in combination ERIG with 3D-CTE. Thirteen Crohn's patients were conducted in this study and the procedures were completed without any adverse events. The specific findings of Crohn's disease and length of the visualized small intestine were assessed. Various features specific to Crohn's disease were visualized using ER 3D-CTE. A cobble stone appearance or hammock-like malformation was specific and effective for diagnosing Crohn's disease and the features after the surgical operations were also well depicted. We concluded ER 3D-CTE was performed safely in Crohn's disease patients and may be useful for diagnosis and follow-up of the disease.

New endoscopic Imaging System For Evaluation of Colonic Mucosal Inflammation in Ulcerative Colitis.

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Background & Aim:
Therapeutic strategy of ulcerative colitis (UC) has drastically changed. Recently, many physicians focused on mucosal healing (MH) as therapeutic goal because achievement of MH could affect the clinical outcome of patients with UC, although endoscopic or histological scoring system is still debated. In most of clinical trial, Mayo endoscopic subscore (MES) 0 or 1 has been defined as MH in UC patients. However, MES is subjective and assessment of MES varies depending on endoscopists. Therefore, to develop the objectively quantitative scoring system of evaluating MH is required. Recent development of endoscopic imaging modalities, including both, vital and virtual chromoendoscopy and magnifying endoscopy, enabls endoscopists to visualize and interpret mucosal details of colon. Among them, i-scan is the newly developed image-enhanced endoscopic technology from HOYA/PENTAX (Tokyo, Japan). i-scan TE-c is one of digital transmission method among HOYA/PENTAX EPK-i system in conjunction with EC38-i10M. The aim of this study is to assess the significance of new endoscopic imaging system with i-scan TE-c for quantitative evaluation of colonic inflammation in UC patients.

Method:
From January 2011 to August 2015, a total of 208 examinations (39 UC patients) with MES 0 or 1 by standard white light endoscopy were reassessed by i-scan TE-c. We performed white light (WL) colonoscopy in conjunction with i-scan TE-c in UC patients with MES 0 or 1, and the difference of the tone of color between normal and inflamed colonic mucosa was given with a numeric conversion. The intensity and width of inflammatory lesion identified by modified color phase and saturation were given with a numeric conversion and visualized.

Results:
In 109 of 208 examinations, endoscopic score of Mayo was estimated as 0. In the remaining 99 examinations, that was estimated as 1. The mean i-scan TE-c score of UC patients with MES 0 and with MES 1 was 329.9±330.7 and 811.9±534.1, respectively. A significant difference of i-scan TE-c score was observed between UC patients with MES 0 and those with MES 1 ($p<0.001$). There was a considerable variation in i-scan TE-c score of UC patients with MES 1 by WL colonoscopy, suggesting that UC patients diagnosed with MES 1 had intestinal inflammation with objectively varying degrees.

Conclusion:
In UC patients with MES 0 or 1, this new imaging system with i-scan TE-c can make the inflammatory lesion visualized more clearly in comparison with WL colonoscopy, and their intensity and width digitized. Application with this new system is easy and useful for objective and quantitative evaluation of colonic inflammation in UC patients with MES 0 or 1. Further clinical trial with this new imaging system will be required for patients with quiescent UC.

Prospective Cohort Study of the Impact of Endoscopic Submucosal Dissection on Gastric Motility and Upper Abdominal Symptoms

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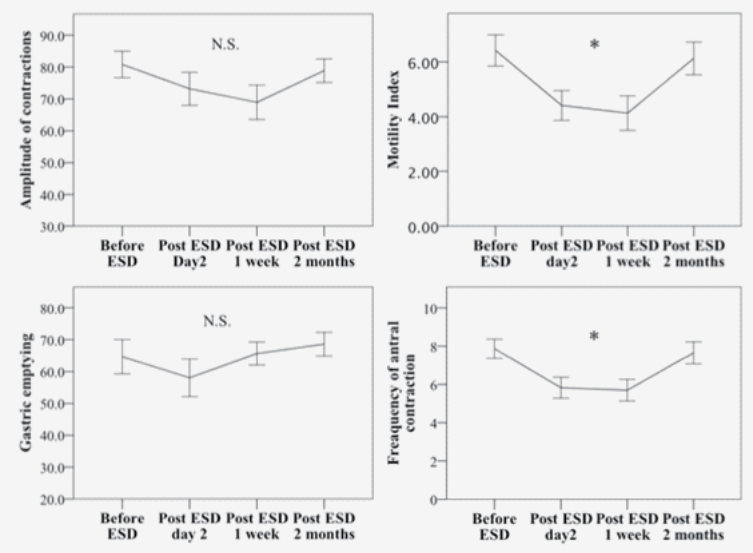
Abstract

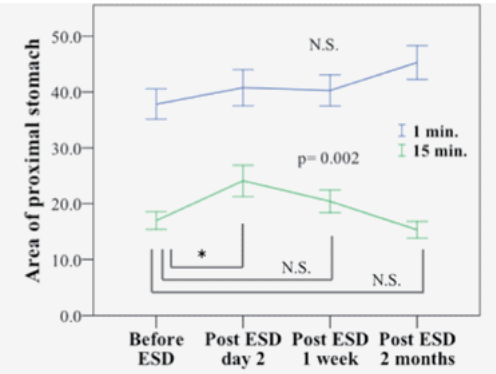
Background: Although endoscopic submucosal dissection (ESD) has become a common strategy for resection of early gastric cancer, little is known about how ESD affects gastric motility. This study prospectively analyzed gastric motility before and after ESD.

Methods: Antral motility and relaxation of the proximal stomach were assessed by extracorporeal ultrasonography on the day of ESD and after 2 days, 1 week, and 2 months. Before and 1 week and 2 months after surgery, patients completed questionnaires about their symptoms during the preceding week.

Results: Twenty-three patients (17 men, six women; mean age, 71.8 years) were enrolled. The resection sites were the gastric antrum in 14 patients and the gastric corpus/cardia in nine. ESD significantly reduced antral contraction frequency ($F=12.89$, $p<0.001$) and motility index ($F=6.955$, $p<0.001$), but did not affect gastric emptying rate ($F=1.268$, $p=0.293$) and antral contraction amplitude ($F=1.699$, $p=0.185$). Multiple comparison testing showed that antral contraction frequency and motility index were significantly reduced after 2 days and 1 week, but not after 2 months. ESD did not affect proximal stomach relaxation at 1-minute ($F=1.628$, $p=0.192$), but increased cross-sectional area at 15 minutes ($F=7.057$, $p=0.002$), with multiple comparisons showing that only measurements 2 days after ESD were significantly affected ($p=0.045$). ESD did not affect any of the six symptom subscales of the Patient Assessment of Gastrointestinal Symptom Severity Index scores.

Conclusions: Antral motility temporarily decreases without symptoms after gastric ESD but returns to preoperative levels at 2 months. Gastric ESD is an effective therapeutic strategy with superior postoperative function.





Usefulness of Perfusion Parametric Imaging for follow up of patients with alcoholic hepatitis

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Introduction

Alcoholic hepatitis is a relatively rare disease. Early diagnosis is important because alcoholic hepatitis may get worse more. Moreover, some patients show poor or prolonged disease.Therfore identifying such patients is clinically beneficial. In this study, we examined the usefulness of Perfusion Parametric Imaging (Perfusion-PI) with Sonazoid®-enhanced ultrasound in follow-up examinations of patients with alcoholic hepatitis.

Subjects and Methods

The objects are 3 patients with alcoholic hepatitis assessed at follow up the blood perfusion dynamics in the liver parenchyma with Perfusion-PI.The Toshiba Aplio XG ultrasound machine was used to acquire right intercostals images of the S5 of the right lobe of the liver with the portal vein. Imaging was started immediately after bolus injection of the recommended amount of Sonazoid® into the cubital vein and was performed for approximately 40 seconds. Acquired raw data were stored in the system hardware. Perfusion-PI was constructed from the ultrasound video images in Aplio XG data analysis software. The video was started after selecting the region of interest (ROI) within the hepatic artery. The arrival time of the contrast agent (hereinafter arrival time) was automatically calculated for each pixel in the liver parenchyma image. The time when 80% of the ROI showed arrival of the contrast agent in the hepatic artery was used as the reference time (time 0). Then automatically constructed color-coded images were displayed on the B-mode screen. Although any color can be used, the arrival times earlier or slower than that via the peripheral portal venous flow were shown in red and blue in this study. In other words, red-colored images show perfusion from hepatic artery, blue-colored images show perfusion from the portal venous to the liver. Arterialization Ratio (AR) was calculated for the purpose of quantifying arterialization. AR is calculated from made Perfusin-PI. The red percentage to the number of whole pixels is set to AR%, in other words, when AR% is a high price, it show strong arterialization.

Results

Perfusion-PI results during hospitalization were indicated arterial dominance in the blood perfusion dynamics in the liver parenchyma in all 3patients. At follow up, Perfuion-PI results came to show decreasing AR% in 2 patients as the disease condition was alleviated. However, in the remaining patient, continuing high AR% and the disease condition persisted.

Conclusion

Perfusion-PI is potentially useful during follow up of patients with alcoholic hepatitis.

Confocal Raman Spectroscopy for Endoscopic Diagnosis of Eosinophilic Esophagitis – Is Eosinophile Detection Possible?

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Background and Aims: Raman spectroscopy is based on Raman scattering from molecules. Recent studies have reported that confocal Raman spectroscopy is an effective tool for investigating digestive disease during an endoscopy procedure (Gartroenterol, 2014). Eosinophlic esophagitis (EoE) is a chronic immune-mediated esophageal disease that has received increasing attention over the past 2 decades. However, diagnosis from endoscopy findings is difficult, because endoscopic features of EoE are not pathognomonic and eosinophile infiltration is patchy throughout the esophagus. We examined the effectiveness of near infrared Raman spectroscopy for diagnosis of EoE.

Material and Methods: Using a confocal microscope, we performed Raman spectroscopy with leukocyte cells from sheep blood and analyzed them based on multivariate curve resolution for eosinophile detection. Raman spectra observed in cells from the esophagus of BALB/c mice were compared with those of cultured squamous cells. In addition, we induced experimental EoE in mice by intraperitoneal injection of interleukin-33 and evaluated Raman spectra in esophagus cells.

Results: Specific Raman marker bands based on eosinophil peroxidase were observed, which showed that eosinophiles could be clearly distinguished from other leukocyte cells. High-quality in vivo Raman spectra were observed in esophageal mucosa from the mice and that peak was similar to that of cultured squamous cells. Raman spectral shapes were significantly different between inflamed esophageal mucosa from EoE model mice and normal mucosa from wild type mice, particularly, which included signals related to eosinophil peroxidase for infiltrated eosinophile infiltration, the same as inflamed mucosa lesions shown by histological results.

Conclusion: Our findings indicate that Raman spectroscopy may be an effective non-invasive tool for correct diagnosis of EoE during endoscopy.

Evaluation of intestinal patency using a patency capsule: Current status

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[Introduction] A patency capsule (PC) is a device that can be used to evaluate the patency of the small intestinal tract. If intestinal patency is clearly demonstrated by using a PC, capsule endoscopy (CE) can be performed safely, even in patients with confirmed or suspected intestinal stenosis. We analyzed the use of PCs at our hospital and we report on the current situation and manner of operation.

[Patients and Methods] Evaluation of intestinal patency using a PC was performed in 241 patients, including 154 men and 87 women with a mean age of 45 years and BMI of 21.1 kg/m2. Among them, 66 patients had a history of intestinal tract surgery (27.4%) and 124 patients had Crohn's disease (51.4%). The time needed for judgment, the PC excretion rate, the site of PC localization in the body, and adverse events were studied. The site of PC localization was determined by tomosynthesis. If the PC showed that the intestinal tract was not patent, the result was confirmed by CT.

[Results] Patency was judged at 24 hours after swallowing the PC in all patients. Spontaneous excretion of the PC was observed in 98 patients (40.7%). The intestinal tract was judged to be patent in 218 (90.5%) patients and non-patent in 23 patients (9.5%). The known spontaneous PC excretion rate was 40.7% (98/241). Although spontaneous excretion was unknown in 143 of 241 patients, no PC was seen on plain abdominal X-ray films and it might have been excreted in 22 of these patients (15.4%). The PC reached the colon in 98 of the 143 patients (81%), with the site of localization being the cecum (n = 14), the ascending colon (n = 5), the transverse colon (n = 23), the descending colon (n = 19), the sigmoid colon (n = 23), and the rectum (n = 14). CE was performed in all 218 patients in whom patency was shown by PC evaluation, and the capsule endoscope passed through the intestinal tract successfully. CT was performed and showed a PC within the small intestine in all 23 patients with a judgment of non-patency. As adverse events, residual PC coating was seen in the small intestine in four patients and subacute ileus symptoms occurred in one patient.

[Conclusion] When a PC was localized accurately (inside or outside the large intestine), judgment of patency or non-patency was made correctly and the risk of a capsule endoscope becoming stuck was avoided. At our hospital, the patient swallows the PC on the day before capsule endoscopy. Patency is evaluated in the morning on the day of capsule endoscopy (24 hours after taking the PC). In order to locate the PC, plain X-ray and tomosynthesis are performed in patients in whom spontaneous excretion is unknown. If the PC may be localized in the small intestine, plain CT scan is also performed for further detailed investigation.

Intravoxel incoherent motion diffusion-weighted imaging is a better indicator of high grade hepatocellular carcinoma than conventional apparent diffusion coefficient

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Objective: To evaluate the utility of intravoxel incoherent motion (IVIM) derived parameters for discrimination of histological grade of hepatocellular carcinoma (HCC). Measurement reproducibility was also studied by assessing inter- and intra-reader variation.

Materials and Methods: Fifty-eight patients with 60 pathologically confirmed HCCs underwent IVIM imaging with 11 b values (0–1000 s/mm2). The diffusion parameters, i.e., apparent diffusion coefficient (ADC), slow diffusion coefficient (D), fast diffusion coefficient (D*), and perfusion fraction (f) were calculated for all HCCs. All measurements were performed by two radiologists, and one of them repeated the measurements after a 4-week interval to minimize memory bias. These parameters were compared between lesions with high and low-to-moderate histologic grade using Wilcoxon test. Further, receiver operating characteristic (ROC) analysis was performed to evaluate the discrimination ability, and inter- and intra-reader agreements were analyzed with intraclass correlation coefficients (ICC).

Results: The D and D* values (×10-3 mm2/s) were both significantly lower in high grade HCC than in low-to-moderate grade HCC for both observers ($P < 0.0183$) (D = 0.78 vs. 0.98 [reader 1-1st], 0.73 vs. 0.96 [reader 1-2nd], and 0.76 vs. 0.96 [reader 2]; and D* = 24.5 vs. 39.7 [reader 1-1st], 22.7 vs. 40.7 [reader 1-2nd], and 23.5 vs. 37.0 [reader 2]). The ADC values [×10-3 mm2/s] measured by reader 1-1st and f (%) measured by reader 1-2nd also showed a statistical difference (ADC = 0.99 vs. 1.14, and f = 27.1 vs. 21.8, $P < 0.0129$). The ROC analysis demonstrated that the D value had significantly greater Az values than the ADC for discriminating high grade HCC from low-to-moderate grade HCC (0.859 vs. 0.753 [reader 1–1st], 0.885 vs. 0.635 [reader 1–2nd], and 0.816 vs. 0.651 [reader 2], $P < 0.047$). The inter- and intra-reader ICC values were excellent for D (0.814 and 0.851) and good for other parameters (ADC, 0.786 and 0.732; D*, 0.688 and 0.724; f, 0.689 and 0.623).

Conclusion: The IVIM-derived D values showed a significantly better diagnostic performance than the ADC values in differentiating high grade HCC from low-to-moderate grade HCC. The results by the two readers and repeated measurements by one reader are reproducible, especially for the D value.

	Low-Moderate n= 47	High n = 13	P value
Reader 1, 1st			
ADC	1.14 ± 0.16	0.99 ± 0.14	0.0055
D	0.98 ± 0.12	0.78 ± 0.13	< 0.0001
D*	39.7 ± 19.1	24.5 ± 11.1	0.0066
f	24.1 ± 11.9	27.5 ± 6.0	0.0882
Reader 1, 2nd			
ADC	1.16 ± 0.17	1.08 ± 0.14	0.1386
D	0.96 ± 0.13	0.73 ± 0.13	< 0.0001
D*	40.7 ±23.9	22.7 ± 11.4	0.0069
f	21.8 ± 9.06	27.1 ± 7.04	0.0129
Reader 2			
ADC	1.16 ± 0.20	1.07 ± 0.12	0.0986
D	0.96 ± 0.17	0.76 ± 0.14	0.0005
D*	37.0 ± 19.7	23.5 ± 12.7	0.0183
f	22.5 ± 10.3	25.5 ± 7.75	0.0866

Linked color imaging, a novel endoscopic enhancement system is useful for the assessment of mucosal inflammation in ulcerative colitis.

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Background: In this study, we investigated the availability of linked color imaging (LCI), a novel endoscopic enhancement system to recognize slight differences in mucosal color, for the assessment of mucosal inflammation in UC patients. **Methods** All examinations were carried out with an EG-L590WR endoscope and a LASEREO endoscopic system (FUJIFILM Co., Tokyo, Japan). The patterns of LCI were classified as A: no redness, B: redness (with visible vessels), and C: redness (vessels are not visible). **Results:** In group A, 85.7% of the biopsy specimens were diagnosed as Matts score 2, whereas in group C, 77.8% were diagnosed as Matts score 3. The digitization of LCI strongly correlated with pathological Matts score. **Conclusion:** We can classify Mayo 1 to two subtypes by LCI relating to pathological Matts score. Besides, the digitization of LCI is considered a practical approach for evaluate intestinal mucosal inflammation in UC patients.

Assessment of small bowel motility in patients with bloating using Cine-MRI

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Background

Chronic intestinal pseudo-obstruction (CIPO) is a severe functional digestive disease characterized by recurrent clinical episodes of intestinal obstruction, in the absence of mechanical cause. CIPO may affect the entire gut from the esophagus to the rectum in the broad sense, but predominantly, the small intestine is affected.

Although no clear diagnostic criteria have been established worldwide until recently, first diagnostic criteria were proposed from Japan in 2010; which indicates that patients who have both chronic clinical symptoms and radiological intestinal dilatation without mechanical obstruction are diagnosed as CIPO.

Because of poor awareness of CIPO, only chronic abdominal symptoms are main trigger of suspicion in clinical practice. Other motility disorders characterized by chronic abdominal manifestations as well as CIPO, sometimes mislead us to improper CIPO diagnosis. Understanding of pathophysiology is very meaningful to distinguish CIPO from similar diseases.

The clinical role of cine-MRI has increased in gastrointestinal motility function, as it allows for the dynamic evaluation of small intestine. The purpose of this study was to assess the small bowel motility in patients with chronic abdominal bloating using cine-MRI, and to evaluate its usefulness in understanding pathophysiology.

Materials and Methods

Fifty patients (16 males and 34 females, mean age of 48.9 years) who were referred to our institution and underwent cine-MRI and CT scan between January 2010 and July 2015 were included. Mechanical obstruction was excluded in all cases, and all patients showed abdominal bloating ≧6 months.

Mean luminal diameter (MLD), contraction ratio (CR), and contraction cycle (CC) were calculated from cine-MRI in each subjects. MLD≧15mm and CR<60% were judged as decreased peristalsis, and MLD<15mm or CR≧60% were diagnosed as normal.

Whether or not CT images showed bowel dilatation was also considered.

Results

Out of 50 subjects complaining of bloating, 35 cases (70%) showed bowel dilatation on CT, and met the CIPO criteria. In these cases, 23 (65.7%) also showed decreased peristalsis on cine-MRI and 12 (34.3%) did normal findings on cine-MRI. Both normal CT and normal cine-MRI findings were observed in 15 cases (30%).

Discussion

In this study, patients who met CIPO criteria had both patterns, which developed impaired small intestinal peristalsis and which did not. Especially in the former cases, decompression treatment and nutrition therapy are urgently needed because of high risk of small gut dysfunction. In this way, cine-MRI can detect differences in small bowel contractions among patients who meet criteria, and have a potential to lead to proper treatment.

Conclusion

Assessment of small bowel motility in patients with bloating using Cine-MRI is useful.

Linked color imaging facilitates detection for early gastric cancers missed by white light imaging endoscopy.

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It is difficult to identify early stage gastrointestinal cancers using white light imaging alone despite the high resolution of endoscopic images. To identify gastric tumors, several image-enhanced endoscopic systems including narrow band imaging (NBI), flexible spectral imaging color enhancement (FICE) and blue laser imaging (BLI) have been developed. These systems enhance mucosal vasculature and/or architecture without the use of dyeing. Therefore, they are useful for the diagnosis of early gastric cancers to a certain degree. However, their diagnostic efficacy of screening for early gastric cancers has not been well determined.

Recently, Linked color imaging (LCI) was developed as a new type of image enhanced endoscopy of the laser endoscopic system (FUJIFILM Co. Tokyo, Japan) with the potential to detect gastric cancer even with a distant view. This system can produce four types of imaging including white light, LCI, FICE and BLI images. LCI images are acquired by simultaneously using narrow-band short wavelength light and white light in an appropriate balance. This combination of light provides more information about the vasculature and architecture on the mucosal surface than that obtained with typical white light imaging. The acquired color information is reallocated to differentiate the colors close to the mucosal color. That is, information for several colors is simultaneously expanded so that the reddish and whitish colors become more red and more white respectively. One important issue is that LCI yields bright and high-contrast images of gastric lesions with a distant view because it provides sufficient light intensity. These characteristics suggest that LCI is suitable for screening for gastric cancers. Magnifying LCI can better demonstrate irregular or microstructure images on the mucosal surface compared with white-light images.

Most gastric cancers often accompany chronic inflammatory background mucosa. Thus, endoscopic images of the background mucosa are important to diagnose early gastric cancers. Intestinal metaplasia is a high risk marker for gastric cancer and is commonly seen surrounding a malignant lesion. However, it may be very difficult to distinguish gastric malignancy from intestinal metaplasia by conventional white-light endoscopic systems on screening examinations. LCI showed purple color mucosal changes in many cases with chronic gastritis. Thus, we attempted to examine histologically purple color lesions in the chronic inflammatory mucosa by biopsy specimens and confirmed that these lesions corresponded to intestinal metaplasia.

Ash-colored nodular changes are an endoscopic sign of gastric intestinal metaplasia using white light images, although its sensitivity is not high. LCI helps to identify intestinal metaplasia with color-contrast images by enhancing the multiple nodular changes with a clear margin. These characteristic features gave newly useful information about differential diagnosis among multiple nodular lesions. LCI showed intestinal metaplasia as purple color lesions and elevated type cancers as red or white color lesions. Moreover, an irregular surface pattern was evident in the mucosa of malignant lesion at the close-up view. The laser endoscopic system allowed more detailed examination using BLI images on simple push of button equipped on the endoscope.

Similarly, depressed type intestinal metaplasia is seen as a purple color change with a relatively regular arrangement of structure on its surface. Such characteristic appearance was useful to rule out depressed type cancers without magnification. Also, LCI images facilitate detection of depressed type early gastric cancers surrounded by intestinal metaplasia. We experienced multiple depressed type cancers missed by conventional white light images and detected by LCI images. LCI images showed depressed type cancer as reddish color lesion in many cases and surrounding intestinal metaplasia as purple color mucosa. Thus these images can demonstrate large differences in color contrast between the malignant lesion and the surrounding area, leading us to more carefully evaluate the suspicious area even at a distant view.

Current conventional endoscopy results in poor quality endoscopic images of early flat gastric cancers using xenon white light alone and therefore can miss them. These flat gastric cancers have only been diagnosed by detailed histological examination of gastrectomy specimens. The endoscopic diagnosis of subtle changes in the gastric mucosa is often difficult and may vary from benign erosive changes to a superficial malignancy. We have experienced cases of flat cancers that was not recognized using laser white light but detected by LCI images. The LCI images of flat gastric cancers can also demonstrate large differences in color contrast between the malignant reddish lesion and the surrounding purple intestinal metaplasia even at a distant view. Therefore, LCI images may have the potential to detect flat gastric lesions that are most difficult to identify using conventional endoscopy.

In conclusion, LCI yields bright and high-contrast images of gastric lesions with a distant view because it provides sufficient light intensity. Conventional endoscopy revealed a subtle mucosal change in the area of missed early gastric cancer, but LCI images showed it as a red or white lesion distinct from the surrounding non-malignant area. LCI is suitable for screening for gastric cancers.

Visualization of pancreatic inflammation in mouse model

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Background

Acute pancreatitis (AP) remains one of clinical problems in gastroenterology field, due to the high mortality and extremely high medical costs in severe cases. On the other hand, chronic pancreatitis (CP) is characterized by irreversible destruction of pancreatic parenchyma, which leads to the exocrine and endocrine pancreatic insufficiency in later stage of disease. For the establishment of novel therapy against AP or CP, various animal models have been developed. Administration of exocrine-pancreas stimulating agent, such as caerulein, ethanol or fatty acids could recapitulate histological changes compatible with acute pancreatitis, which have been subjected to the evaluation of therapeutic interventions. However, histological and biochemical evaluation of these animal models is only possible at the time of sacrifice, due to the lack of adequate monitoring marker. To conquer these problems, we employed a newly developed inflammation monitoring mouse system.

Methods

Mice bearing human IL6 BAC luciferase transgene were subjected to intraperitoneal injection of caerulein. Pancreatitis induction was performed by 7 injections of 50 μg/kg caerulein at hourly intervals. A control mouse received 7 injections of saline at hourly intervals. Detection of luciferase luminescence was performed using IVIS imaging system (Xenogen). After the IVIS analysis, mice were sacrificed and subjected to histological analysis. Expression of luciferase in pancreatic tissue was assessed by immunohistochemistry using anti-luciferase antibody (Promega).

Results

In mice received caerulein injections, luminescence of luciferase was detectable at the location of pancreas. Histological examination confirmed pancreatic edema and inflammatory cell infiltration. Immunohistochemistry for luciferase expression identified moderate staining in acinar cells. In addition, infiltrating mononuclear cells within pancreatic parenchyma, as well as mononuclear cells within blood vessels showed intense luciferase immunoreactivity.

Discussion

Caerulein-induced pancreatitis increased luminescence of luciferase from pancreas, suggesting prominent IL6 production within pancreas at an early phase of acute pancreatitis. Inflammatory cells, rather than acinar cells, were responsible for IL6 production. In addition, recruitment of inflammatory cells from blood flow was also detectable by inflammatory cell-tracing. This in vivo imaging strategy could be applied to the assessment of inflammatory response in various disease model mice.

Advanced Imaging in Endoscopy
Effectiveness of auto-fluorescence imaging systems for differential diagnosis of colorectal lesions

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Accurate, real-time endoscopic assessment of the histology of colorectal lesions facilitates prevention of unnecessary endoscopic resection and allows physicians to make adequate surveillance recommendations. We have previously reported the potential of color intensity analysis using auto-fluorescence imaging (AFI) systems to differentiate colorectal neoplastic lesions from non-neoplastic lesions.

Recently, guidelines for real-time endoscopic assessment of the histology of diminutive colorectal polyps have been proposed by The American Society for Gastrointestinal Endoscopy. These guidelines recommend that in order to not resect suspected diminutive recto-sigmoid hyperplastic polyps, there should be ≥ 90% negative predictive value (NPV) for adenomatous histology. Therefore, there is current interest in establishing a differential diagnosis modality for diminutive colorectal lesions, which will enable differentiation of colorectal neoplastic diminutive lesions with NPV ≥ 90%. In addition, because of the difficulty of classifying serrated lesions into hyperplastic polyps and sessile serrated adenoma/polyps (SSA/Ps) using endoscopic findings, a management strategy for serrated lesions is still controversial in Japan. Therefore, methods that differentiate SSA/Ps (especially SSA/Ps with cytological dysplasia) from hyperplastic polyps are demanded.

We assessed the potential of color intensity analysis using AFI systems to differentiate diminutive neoplastic lesion from non-neoplastic lesions with a NPV ≥ 90%, and SSA/Ps (especially SSA/Ps cytological dysplasia) from hyperplastic polyps.

AFI for differentiation of diminutive colorectal lesions

We retrospectively evaluated 101 diminutive colorectal lesions (≤5 mm in size) that were examined using AFI systems and then resected. The regions of interest (ROIs) on AFI images were set at the center of the diminutive lesions. Then, color intensity analysis for the ROI and calculation of the Green/Red (G/R) ratio which is obtained by dividing the green color tone intensity values by the red color tone intensity values was conducted. The mean G/R ratios for non-neoplastic and neoplastic lesions were 1.06 and 0.87, respectively, which were significantly different. The area under the receiver operating characteristic curve (ROC) for distinguishing neoplastic lesions was 0.978. A G/R ratio cut-off of <0.95 had a sensitivity, specificity, positive predictive value (PPV), and NPV of 94.2%, 91.8%, 92.5%, and 93.8%, respectively, for neoplastic lesions. The results may indicate that color intensity analysis using AFI systems enables differentiation of diminutive neoplastic lesions with NPV ≥ 90%.

AFI for differentiation of SSA/P from hyperplastic polyps

We retrospectively evaluated 87 serrated lesions that were examined using AFI systems and then resected. In each serrated lesion, the mean G/R ratio of the three ROIs was calculated. Patients with traditional serrated adenoma (TSA) were not included in this study. The mean G/R ratio of SSA/Ps was significantly lower than that of hyperplastic polyps. The area under the ROC curve (AUC) for determining SSA/P was 0.68. A mean G/R ratio cut-off of <0.97 had a sensitivity, specificity, PPV, and NPV of 62.8%, 65.9%, 64.3%, and 64.4%, respectively, for differentiating SSA/Ps from hyperplastic polyps. When SSA/Ps were divided into SSA/Ps without cytological dysplasia and SSA/Ps with cytological dysplasia, the mean G/R ratio significantly differed among hyperplastic polys, SSA/Ps without cytological dysplasia, and SSA/Ps with cytological dysplasia. SSA/Ps with cytological dysplasia had significantly lower mean G/R ratios than hyperplastic polyps and SSA/Ps without cytological dysplasia, and the AUC for determining SSA/P with cytological dysplasia was 0.97. A mean G/R ratio cut-off of <0.95 had a sensitivity, specificity, PPV, and NPV of 95.5%, 91.0%, 77.8%, and 98.3%, respectively, for differentiating SSA/P with cytological dysplasia from hyperplastic polyps and SSA/Ps without cytological dysplasia. These results may suggest that color intensity analysis using AFI systems is not effective for differentiating SSA/P from hyperplastic polyps, but is effective for differentiating SSA/Ps with cytological dysplasia from hyperplastic polyps and SSA/Ps without cytological dysplasia.

As these two studies were retrospective, we are now conducting prospective studies to confirm the effectiveness of color intensity analysis using AFI systems for real-time differentiation of diminutive colorectal lesions and serrated lesions.

Imaging Colon of Rhesus Macaques with Colonoscopy

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Rhesus macaques have been widely used in pharmacokinetics experiments due to its resemblance of macaques to humans. Also, it is a suitable animal to establish experiment model for researches of human development and diseases. However, idiopathic chronic diarrhea (ICD) is a common cause of morbidity and mortality among rhesus macaques. Detection and treatment of ICD in macaques are crucial for evaluation of pharmacokinetics experiments and animal model. Till now, no successful colonoscopy examination in macaques has been reported because imaging colon of rhesus macaques with endoscope is difficult.

Aim To clearly and safely imaging colon of rhesus macaques with endoscope.

Animals and Methods 10 adult macaques, 6~8 kg, were obtained from Kunming Institute of Zoology, the Chinese Academy of Sciences. All macaques were qualified to be maintained in the facility after quarantine and the experiments in this study were performed in accordance with guidelines of Sichuan University Institutional Animal Care and Use Committee. All animal were fasted at least 8 hours before endoscopy. As bowel preparation, each macaque was feed sulfate sodium (2.8g/kg in 100 ml water) with gavage at 3 hours and 2 hours individually before examination. About 5 minutes after ketamine (0.1ml/kg) subcutaneous injection, colonoscopy examination was performed. All procedures were performed using a conventional gastric endoscope (CV-260, Olympus, Tokyo, Japan), which was cleaned with ultrasonic cleaner (OER-A, Olympus, Tokyo, Japan) after each examination. Biopsies were taken either from normal or from lesion mucosa.

Results The basic colonoscopy skill in macaques was the same as in human. Colonoscopic procedure was generally lasting for 20-30 minutes. Colonoscope was intubated to ileocecal valve in 4 animals, but did not reach to ileocecal valve in other 6 animals due to severe strictures. There were no signs of perforation and massive bleeding during performance. All macaques woke up automatically and survived after colonoscopy examination.

Normal colonic mucosa of macaque is pale-pink in color. The submucosal vascular network is visible which was smaller than that in human beings. The rectum was 5-7 cm long beginning from the anal margin. The sigmoid varies in length. The lumen of sigmoid colon and descending colon were smaller than the transverse colon, ascending colon and cecum. The haustrations were almost invisible in sigmoid, decending and ascending colon. On the contrary, it was visible markedly in transverse colon of most macaques. The lumen of the transverse colon was triangular shape. Impressively, none of appendix orifice was observed in macaques. The ileocecal valve was apart from the cecal pole 3-5cm and located at the colonic wall, usually on the left side of the colonoscopic field of vision. It was possible to enter ileoceca orifice and examine the terminal ileum, where the intestinal villus was clearly visible. Peyer's patches were not observed in the terminal ileum lumen.

Colonic mucosal lesion of macaque included diffuse edematous, erythematosus, obscure vascular network, pinpoint ulceration scattered at the mucosa surface, circular huge ulceration and inflammatory stricture which made the endoscope could not pass through. Colon was shortened to 35cm in one macaque with a lead-pipe colon. Colonic inflammatory lesions were detected in all of 10 macaques although two animals did not manifest diarrhea.

Conclusions Colonoscopy examination is a safe and efficient way to screening colonic lesions in macaques. The performance of colonoscope in macaque is more difficult than in human being. Macaques without diarrhea may present colonic inflammatory lesions. It is necessary to perform colonoscopy when selection of macaques pre-pharmacokinetics experiments. Furthermore, colonoscopy examination and sampling would be useful in unbiased preclinical evaluation of therapeutics in this animal model.

An activatable photosensitizer targeted to γ-glutamyltranspeptidase for tumor selective photodynamic therapy

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Abstract:

Photosensitizers are chemical compounds which produce reactive oxygen species (ROS) such as singlet oxygen (1O2) by light irradiation. Photodynamic therapy (PDT) is a treatment which uses photosensitizers and light irradation to induce cell death to the targeted region such as tumors. Compared to other cancer therapies such as surgery, chemotherapy or radiotherapy, PDT has advantages of less invasiveness to the patients and precise targeting to cancer. However, it sometimes suffers from significant side effects of non-specific photodamages to skin or healthy tissue. This is because that most of the photosensitizers used for current clinical PDT are based on porphyrin, which exhibit the phototoxic effect regardless of whether distributed in tumor or in normal tissue (always-on photosensitizers).

In order to overcome this problem, we developed a novel activatable photosensitizer whose photosensitizing capabilities are turned on at tumor site. The novel photosensitizer designated as γ-glutamyl-hydroxymethyl serenorhodamine green (gGlu-HMSeR) has a serenorhodamine scaffold with γ-glutamyl group as the targeting moiety for GGT. Since gGlu-HMSeR takes a non-phototoxic spirocyclic structure, it did not show any remarkable phototoxicity to cells or normal tissue with low GGT expression. In contrast, upon reaction with GGT, gGlu-HMSeR was efficiently converted to a phototoxic HMSeR, thus showing significant phototoxicity to GGT-expressing cells. We also confirmed the drastic change in phototoxicity before/after reaction with GGT by evaluating vascular occlusion on chickchorioallantoic membrane (CAM), and gGlu-HMSeR showed PDT effect on GGT-expressing tumor inoculated on CAM. We believe that this kind of activatable photosensitizer would be one of the solutions to achieve highly selective tumor therapy.

Indocyanine green fluorescence during gastrointestinal surgery for preventig anastomotic leakage

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[Backgroun] Adequate blood supply for the reconstructed organ is important for safe gastrointestinal anastomosis. Recently, indocyanine green (ICG) has been used for visualization of the blood supply and sentinel nodes. We introduced ICG fluorescence during gastrointestinal surgery to visualize the blood supply for reconstruction. The aim of this study was to evaluate the feasibility and the usefulness of intraoperative assessment of vascular anastomotic perfusion in esophageal and colorectal surgery using ICG enhanced fluorescence.

[Methods] We have performed ICG fluorescence imaging in patients with thoracic esophageal cancer and colorectal cancer. A bolus of 5mg/ml ICG was injected intravenously through a peripheral vein. ICG fluorescence imaging was performed with the PINPOINT® (Novadaq), and the images were recorded. In esophageal cancer patients, mobilization of the thoracic esophagus and stomach were performed with thoracoscopic and laparoscopic approach. We made a 3-cm-wide astric tube were made with 5 to six 6 cm-cartridges of liner stapler device. The right gastric vessels and right gastroepiploic vessels were preserved. Before and after this preparation, we performed ICG fluorescence imaging of stomach and the gastric tube. After pulling up the gastric tube to the cervical esophagus via posterior mediastinal route, evaluation with ICG fluorescence imaging was performed in the same way. In colorectal cancer, following adequate mobilization of the sigmoid colon and TME laparoscopically, rectum was transected with liner stapler. Prior to the anastomosis, ICG fluorescence imaging for the oral side mesentery and colon and was performed outside the abdomen through a mini-laparotomy. After reconstruction with the double stapling technique, anastomosis site was evaluated with ICG fluorescence intra-corporally.

[Results] No intraoperataive or injection-related adverse effects were observed, and the blood supply was always clearly identified. In esophageal cancer patients, ICG fluorescence was easily detected in all patients 1 min after injection. Vascular networks were well visualized in the gastric wall and omentum. In colorectal cancer patients, ICG fluorescence imaging of blood supply to the mesentry and the anastomosis site were able to obtain in all cases.

[Conclusions] ICG fluorescence can be used to evaluate the blood supply of reconstructed organs and can be useful in gastroinetistinal anastomosis. In order to establish more detailed and appropriate ICG fluorescence criteria, larger study and more specific evaluations are needed.

Role of Narrow band imaging in diagnosing Tc-99m scintigraphy negative Meckel's Diverticulum in Adult Patients with Obscure GI Bleeding using single balloon enteroscope.

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BACKGROUND: Meckel's diverticulum is the most common congenital anomaly of the GI tract and it affects 2% to 3% of the population. Hemorrhage is the most common presentation of a Meckel's diverticulum, and it is considered one of the most common causes of GI bleeding especially in children. Definitive treatment is surgical resection but pre operative diagnosis is challenging considering the low sensitivity of Tc-99m scintigraphy.

PATIENTS AND METHOD: Five patients (age 11–35 yr) presenting with obscure gastrointestinal (GI) bleeding underwent multiple endoscopic and radiologic tests including Tc-99m pertechnetate scintigraphy before single balloon enteroscopy. Single-balloon enteroscopy was performed in all five patients using anal approach to evaluate the small bowel. In all cases Mackel's diverticulum was detected in distal ileum. Intubation of Mackel's diverticulum was successful in all five cases. Narrow band imaging precisely identified gastic type of mucosa in all patients. No procedure-related complications occurred. All patients underwent surgical resection of the diverticulum Histological assessment confirmed the presence of ectopic gastric mucosa. Single balloon enteroscopy along with NBI was the only nonsurgical procedure that provided a precise accurate preoperative diagnosis. On follow up no further bleeding occurred.

CONCLUSIONS: Considering the low sensitivity and limitations of Tc-99m scintigraphy, single-balloon enteroscopy with Narrow band imaging might be the modality of choice in patients with obscure GI bleed with a suspected diagnosis of Meckel's diverticulum.

Evaluation of Tumor-associated Stroma and its Relationship with Tumor Hypoxia using Dynamic Contrast-enhanced CT and 18F-Misonidazole PET in Murine Tumor Models

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Purpose: To determine the relationship between the fractional interstitial volume (Fis) as calculated on dynamic contrast-enhanced computed tomography (DCE-CT) and tumor-associated stroma, and to analyze its spatial relationship with tumor hypoxia in several xenograft tumor models.

Materials and Methods: All animal experiments were approved by the Animal Research Committee of our institution. Mice with three different xenograft tumors (U251, CFPAC-1 and BxPC-3; n = 6, 8 and 6, respectively) underwent DCE-CT then hypoxia imaging using 18F-fluoromisonidazole positron emission tomography (FMISO-PET) within 24 hours. Immunohistochemical analysis for the detection of hypoxia markers, and to quantify microvascular and stromal density, was conducted using harvested tumors. We defined two DCE-CT parameters (amount of interstitial space which is associated with the amount of stroma [Fis] and flow velocity [Fv]) and quantitatively validated them using immunohistochemistry. The FMISO uptake within the tumor was also assessed in relation to DCE-CT parameters. Imaging and immunohistochemical parameters were assessed using the Kruskal-Wallis test, Wilcoxon rank-sum test and using Pearson's correlation coefficient.

Results: Almost no α-smooth muscle actin-positive cells were found in U251 xenograft, while abundant stroma was found in the entire BxPC-3 xenograft and in the periphery of the CFPAC-1 xenograft. Quantitative analysis demonstrated a significant correlation ($R = 0.83$; $P < 0.0001$) between Fis and stromal density. FMISO uptake had a negative correlation with Fis ($R = -0.58$; $P < 0.0001$), and with Fv ($R = -0.53$; $P < 0.0001$).

Conclusion: Our data show that DCE-CT can quantify parameters associated with tumor-associated stroma. Tumor hypoxia was complementarily localized in tumor-associated stroma in the models we assessed.

Clinical implications of advanced endoscopy

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Colorectal cancer (CRC) is a major cause of cancer mortality worldwide. By the time patients are symptomatic, lesions are often advanced, with limited treatment options available. The development of effective endoscopic therapies means that neoplastic lesions can be treated with improved patient outcomes. Selecting appropriate patients for endoscopic treatment involves identifying CRCs with nul risk of lymph node spread. It has been reported that for submucosal invasive CRCs, the rate of lymph node metastasis was 0% if the submucosal depth was less than 1000 micrometers (T1a). Advanced endoscopic techniques including dye-spraying (chromoendoscopy), optical filters (narrow-band imaging, NBI) and autofluorescence of mucosal tissue (autofluorescence imaging) have been explored. The development of magnifying chromoendoscopy has facilitated the observation of mucosal pit patterns and the exact staging of early neoplasia. The noninvasive pit pattern is suggestive of intramucosal neoplasia (Tis) or submucosal invasion less than 1000 microns (T1a) which is an appropriate indication for endoscopic treatment. In lesions resected endoscopically with subsequent pathologic evaluation revealing submucosal invasion over 1000 micrometers (T1b) or in lesions demonstrating lymphatic invasion, tumor budding, vascular involvement, or poorly differentiated components, additional surgical resection would be recommended. In the WHO classification, the defining feature of CRC is invasion through the muscularis mucosae into the submucosa and carcinoma in situ (Tis) is not regarded as cancer. By contrast, in Japan some of Tis cancers are considered to have invasive potential. Based on these concepts, the Japan NBI expert team (JNET) classification was established. Type 1 tumor represents hyperplastic polyp, type 2A means adenoma or intramucosal adenocarcinoma with low grade atypia, type 2B includes intramucosal adenocarcinoma with high grade atypia or T1 cancer and type 3 means deep submucosal invasive cancer. Long-standing inflammatory bowel disease (IBD) is a risk factor for developing CRC. Neoangiogenesis and increased endothelial permeability are observed as results of chronic intestinal inflammation, whereas limited data on microvascular and crypt architecture is available. The aim of this study was to examine clinical implications of the JNET classification in colorectal neoplasia and to assess crypt and microvascular architecture in IBD by advanced endoscopy. Among 480 colorectal tumors treated by endoscopy or surgery at Kinki University between April 2010 and December 2014, 200 that were evaluated with NBI adequately were included in the study. The author selected one to four magnifying NBI images of each lesion and three experienced endoscopists diagnosed the lesions using the JNET classification. The endoscopists were not provided with any other information about the lesions. When diagnoses differed, the majority rule was applied. The diagnosis based on the JNET classification was compared with that based on conventional NBI findings (Showa classification) and pit patterns (Kudo classification). Inter-observer variability was assessed. In surface pattern, kappa value is 0.528, whilst in vessel pattern, kappa value is 0.529. In the diagnosis of T1b or beyond, sensitivity is 78% (14/18), while the specificity is 98% (178/182), suggesting that JNET classification is useful in the diagnosis of deep submucosal invasive cancer that is an indication for surgery. Type 2B lesions should be closely examined by chromoendoscopy, and endoscopic resection can be considered as total biopsy.

Probe based confocal laser endomicroscopy was performed in IBD patients. Patients with active disease showed a significant increase in crypt diameter and intercrypt distance compared to those with quiescent disease. Intramucosal changes detected by confocal endomicroscopy can predict disease relapse. Taken together, advanced endoscopy may have further clinical implications and highlight promising directions for improved diagnostic and therapeutic strategies.

Usefulness of three-dimension biliary simulation using CT with Drip-infusion Cholecystocholangiography (DIC-CT)

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Aim: Three-dimension (3D) simulation system has been making remarkable progress, and plays an important role in surgical planning for hepatectomy since the liver has complex vessel structures. However, 3D software has not been well used for evaluating biliary system, because it is difficult to describe with 3D softwere. Especially, indentification of cystic duct by preoperative imaging is very important point for laparoscopic cholecystectomy.

In this study, we compared three 3D softwares, Synapse Vincent (SV), Ziostation 2 (Zio2) and our new 3D simulation software (HSS) for 3D biliary simulation.

Method

We selected and evaluated 10 patients with cholecystolithiasis , and we performed the 3D biliary simulation using DIC-CT. We selected only one of lower part of common bile duct in each software, and evaluated whether it is possible to detect biliary systems (from lower common bile duct to cystic duct and gall bladder).

Result

There were 6 female and 4 male patients, with an average age of 59.6 years. SV detected cystic duct in three patients(30%), while Zio 2 and HSS detected it in eight patients (80%).Although SV never detected gall bladder in any patients (0%), Zio 2 and HSS detected it in eight patients (80%).

Conclusion

Zio 2 and HSS were useful for detecting biliary system from bile duct to gall bladder. However, by using SV cystic duct and gall bladder were not detected automatically.

New endoscopic finding of lower esophageal sphincter in esophageal achalasia : "Corona appearance"

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Introduction: Peroral endoscopic myotomy (POEM) is a groundbreaking method for treating esophageal achalasia. We treated 140 patients using POEM since September 2011 and achieved good outcomes. A stable treatment method is currently being established for esophageal achalasia; however, the detection of esophageal achalasia is an important issue. Therefore, here we present the therapeutic outcomes of POEM and describe the diagnostic utility of corona appearance (CA), a novel endoscopic finding for esophageal achalasia.

Subjects and methods: Subjects included 53 untreated esophageal achalasia patients who had undergone endoscopy at our hospital. CA and 5 endoscopic findings in the esophageal achalasia treatment guidelines (functional stricture of the esophagogastric junction, whitening and hypertrophy of the esophageal mucous membrane, abnormal contraction wave, expansion of the esophageal lumen, and food residue and fluid retention) were comparatively examined with respect to their sensitivity and consistency (κ-value) among multiple endoscopists. CA was positive when the following 3 criteria were met during an examination of the lower esophageal sphincter performed with the ST short hood (DH-28GR; Fujifilm, Tokyo, Japan) attached: A) ischemia along the hood, B) congestion inside the hood, and C) palisade vessel occlusion on the outside of the hood.

Results: Among the endoscopic findings, CA had the highest sensitivity (91%) with aκκ κ-value of 0.53. Other findings in descending order of sensitivity included 1) functional stricture of the esophagogastric junction (sensitivity 86%, κ-value 0.58), 2) whitening and hypertrophy of the esophageal mucous membrane (sensitivity 71%, κ-value 0.27), 3) abnormal contraction wave (sensitivity 60%, κ-value 0.32), expansion of the esophageal lumen (sensitivity 58%, κ-value 0.53), and 5) food residue and fluid retention (sensitivity 57%, κ-value 0.51). Furthermore, in 22 patients with poor (grade 1) intraluminal expansion had a CA sensitivity of 88%, indicating high sensitivity compared with other endoscopic findings, with a κ-value of 0.52.

Conclusions: Among endoscopic findings using a short hood to diagnose esophageal achalasia endoscopically, CA had the highest sensitivity, and the consistency (κ-value) between endoscopists was comparable with that of other endoscopic findings. Furthermore, similar results were obtained for cases of esophageal achalasia with poor expansion, which is difficult to diagnose with endoscopy. Results demonstrated that when diagnosing esophageal achalasia endoscopically, additional observations with an ST short hood attached can be useful in detecting esophageal achalasia.

Usefulness of contrast enhanced ultrasonography in diagnosis of hepatic focal nodular hyperplasia.

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Aim: We examined the usefulness of diagnosis to focal nodular hyperplasia by contrast enhanced ultrasonography.
Background : Also in the benign tumor of a liver, it is important to carry out early exact diagnosis. But, it is important not to give the excessive mental and economic burden to a patient.
Focal nodular hyperplasia (FNH) is a common benign solid tumor of the liver. In the past, differentiation of FNH from other hyper vascular focal lesions in liver, such as hepatocellular carcinoma (HCC) or hyper vascular metastasis posed an important diagnostic problem. At present, dynamic computed tomography (CT), dynamic magnetic resonance imaging (MRI), and contrast enhanced ultrasonography (CEUS) allow the accurate diagnosis of FNH in typical cases .Typical FNH is diagnosed by the findings of the artery called a spoke-wheel pattern, however, the detection rate of a spoke-wheel pattern is low as even the results of dynamic CT, dynamic MRI and Doppler ultrasonography. CEUS is superior to others in spatial and temporal resolution, and now becomes a standard practice in many institutions. Then, we examined the usefulness of the diagnosis to FNH by CEUS.

Methods: This retrospective study was approved by the research ethics board of our institution. We studied 18 patients with 18 hepatic tumors, including 15 male and 3 female, who is clinically diagnosed with FNH from January 2008 to August 2015. All patients received CUES, following by conventional gray-scale ultrasonography and color Doppler US. Ultrasonography was performed using a GE LOGIQ E9, S8 with a 5MHz, 4MHz convex transducer and a 9MHz linear transducer. The focus was set at bottom end of the tumors and 0.5 ml Contrast agents (Sonazoid) was injected into the antecubital vein. The cases, that central arterial enhancement can be shown in comparison to the hepatic artery with spoke wheel pattern and portal venous enhancement in comparison to the portal vein, was diagnosed as FNH. We mainly assessed the detection rates of spoke-wheel pattern by CEUS, color Doppler US, dynamic CT and dynamic MRI.

Results: The tumors, median diameter is 21.5mm (ranged, 8-93 mm). Central Color signal was observed in 17 of 18 FNHs (94.4%), but a central feeding artery with spoke-wheel pattern was observed in only 5 of 18 FNHs (27.8%) by color Doppler US. Whereas, the CEUS study showed a spoke wheel pattern in all FNHs (100%). None of the nutriment vessels extending from the center was observed by dynamic CT and dynamic MRI.

Conclusion: CEUS is a very sensitive diagnostic tool in characterizing liver tumors. It is especially useful in the diagnosis of FNH of the liver.

A possibility of cordless camera for laparoscopic surgery ~ Can LED light be used as a portable light source? ~

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Introduction

In the early development of video-endoscopic surgery in the late 80', the images displayed on the monitor were insufficient in many ways, including resolution, brightness, and color reproducibility. This compromised quality of the image made it difficult to precisely appreciate the anatomic structure, resulting in a longer operating time and increased rate of tissue injury and complication. With the progress of the CCD image sensor, the quality of image has been gradually improved. A high resolution video image of laparoscopy, however, demands more light for the limitation of sensitivity of CCD. One of the answers includes the CMOS, which has more light sensitivity. There was no report in the literature comparing CCD and CMOS in the various illumination circumstances of the laparoscopic surgery. If laparoscopic surgery is possible under low illumination, LED light can be used as a portable light source. Moreover, when the surgical field becomes dark due to bleeding, CMOS image sensor may make it possible to continue operation without increasing light intensity. In this study, we compared CCD and CMOS camera system with regard to the working efficiency under various illumination, in an intention to test the ability of the systems in the dim light.

Materials and Methods

In this study, a CMOS image sensor was used as the imaging device. This CMOS image sensor was 2/3 inches format. The resolution was 1.47 million pixels. This sensor had a wide range of spectral sensitivity characteristics. As a control, 3-CCD camera of the same resolution was used. CCD image sensor is most commonly used in laparoscopic surgery. In all experiments a 10-mm and 30-degree rigid scope was used. As a light source Xenon light source and LED light source were used.

Experiment 1

To evaluate the function of ultra-high-sensitive CMOS camera and CCD camera, the excised swine organs were set in the training box. The distances from the tip of the scope to the target (15, 10, 5, and 2 cm) were set respectively and the endoscopic images were taken using CMOS or 3CCD cameras. In this experiment a xenon light source was used. The amount of light illumination was individually adjusted to low illumination or high illumination for taking images. Low/high illumination can be adjusted on the camera control unit. In the last experiment using CMOS camera with single small cordless LED light (less than 100Lx), the target image was taken.

Experiment 2

Condition parameters were the camera, illumination and color of the sheet. CMOS and 3-CCD camera were used. 10 laparoscopic surgeons performed a ligation task using the training box. The number of the executed tasks and mistakes were counted. Tasks were repeatedly performed for 2 minutes under various conditions. To mitigate a fatigue bias, tasks in a different order (CCD first or CMOS first) were both recorded. Two different color sheets for the experiment were used. One was a red sheet and the other was standard beige color. The red sheets mimic bloody surgical field or some organs. Surgeons performed the task under 500 Lx, 1000 Lx, 2000 Lx. The results were statistically analyzed.

Result

Experiment 1

The images of the excised liver and gallbladder of the swine were taken by 3CCD and CMOS camera. Under high illumination, both 3CCD and CMOS cameras could display similar imaging quality. When the 3CCD camera was used

under low illumination, it was hard to view the target in the distance range between 15 and 5 cm. When the distance was set 2 cm away, the target could be obscurely recognized. In contrast, when the CMOS system was employed, the target could be distinctly observed regardless of the camera-target distance. Especially when the distance was set to be 2 cm away, the target could be clearly recognized like the image was taken under high illumination. It was possible to recognize the target at a distance of 15 cm with the CMOS system even when just a single LED light was used.

Experiment 2

Between 500 Lx, 1000Lx and 2000Lx, even if CMOS camera was used, there was no significant difference of the number of executed tasks. There was no significant difference of the number of executed tasks between using red and beige sheet. But there was significant difference in the number of mistakes during performing tasks in the experiment using red sheet and 3CCD camera.

Conclusion

We presented the usefulness of the CMOS camera especially in a dim condition. Safe operation may be possible under low illumination. LED light source can be used with the CMOS system. In the future, laparoscopic surgery may be performed using a cordless camera system.

Preoperative imaging of thoracic duct for thoracic esophagectomy

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Background: Confirmation of the thoracic duct (TD) during thoracic esophagectomy is very important to enable a safe lymph node dissection near the TD and to prevent chylothorax after an esophagectomy. In our hospital, the TD is three-dimensionally reconstructed from MRI results obtained before surgery as a preoperative imaging simulation. **Methods:** The usefulness of the preoperative simulation of the TD using MRI (TD-MRI) was investigated for 60 patients with thoracic esophageal cancer who underwent preoperative TD-MRI after August 2014 in our hospital. **Results:** The average patient age was 64.7 years, and 52 men and 8 women were investigated. Thoracoscopic surgery was performed for 54 cases (90%), and open surgery was performed for 6 cases. Complicated resections of the thoracic duct were performed in 33 cases (55%). The abnormal TD routes could be classified as follows: abnormal divergence, 6 cases; window formation, 3 cases; and stitch formation, 1 case. The imaging results were insufficient in 1 case, and 48 cases had a normal TD route. Cancer had invaded the TD in 1 case (3.0%), and lymph node metastases near the TD were found in 5 cases (15.2%). The volume of discharge from the thoracic drain was larger in cases with a more complicated TD resection, compared with the other cases ($P = 0.013$). In one case with an abnormal TD divergence, the divergence was confirmed to exist in the upper mediastinum based on TD-MRI, and the mediastinal lymph nodes were dissected without injuring the TD. **Discussion:** Based on the TD routes visualized using TD-MRI, the TD can be securely confirmed during surgery and the surrounding lymph nodes can be dissected carefully, resulting in a probable reduction in the risk of TD injury. The volume of discharge from the thoracic drain tended to increase in cases requiring a complicated TD resection. In our series, a few cases exhibited invasion of the TD by cancer or lymph node metastases near the TD. Therefore, complicated TD resection for the treatment of advanced esophageal cancer is expected to improve the long-term outcome of surgery.

ADVANCED ENDOSCOPY IMAGING IN SURVEILLANCE OESOPHAGO-DUODENOSCOPY (OGDS) POST RADIOFREQUENCY ABLATION FOR BARRETT'S ESOPHAGUS – PRELIMINARY EXPERIENCE AND PILOT SERIES IN MALAYSIA

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Introduction:

Barrett's oesophagus (BO) is defined as intestinal metaplasia to the distal oesophagus, which predisposes to increased risk of oesophageal adenocarcinoma. The diagnosis of BO is based on endoscopic identified columnar lined epithelium (CLE) above gastric fold and histological presence of intestinal metaplasia in the biopsied tissue. To date, there are many reported endoscopic therapeutic options available for BO which include radiofrequency ablation (RFA). It involves the careful use of thermal energy to achieve controlled ablation of the Barrett's mucosa.

Advanced endoscopy imaging such as magnification endoscopy with narrow band imaging (ME-NBI) is increasingly reported to be beneficial in detecting Barrett's associated dysplasia.(1) It is also helpful in detecting and characterizing Barrett's mucosa. We report here the use of ME-NBI in assessing treatment response following RFA treatment of BO.

Methods:

Seven patients with BO, 6 without dysplasia and 1 with low-grade dysplasia, were included in our preliminary series. RFA was performed using either a balloon-based (circumferential ablation) HALO-360 (4 patients) device or a plate-based (focal ablation) HALO-90 (3 patients) device. Long-segment (≥3cm) and circumferential-type CLE were subjected to circumferential ablation. Otherwise, plate-based catheter would be used instead. For balloon-based ablation, pre-procedure measurement of oesophageal diameter was carried out with sizing balloon. Mucosal cleaning with dedicated cap was applied in between 2 thermal applications. For plate-based catheter, mucosal cleaning was carried out once in a total of 4 thermal applications. Post procedure, all patients were given high dose proton pump inhibitor for 1 month and maintenance dose thereafter. Endoscopic evaluations using high definition white light endoscopy (HD-WLE) and ME-NBI (Using Olympus EVIS EXERA III GIF-HQ190) were carried out at 3 months post RFA. Detected CLE under HD-WLE were further analyzed using ME-NBI. The finding of any of the well-described typical appearance of Barrett's mucosa under ME-NBI such as ridge and/or villous pattern was taken as remnant Barrett's mucosa. Neo-squamous epithelium, neo-squamocolumnar junction (SCJ) and remnant CLE were carefully examined for microsurface and/or microvascular irregularity, which may suggest dysplasia.

Results:

Patients' characteristics were shown in table 1 below. Four patients with long segments BO were subjected to circumferential ablation while three patients with short segment BO were subjected to focal ablation. Upon examination by HD-WLE & ME-NBI during surveillance endoscopy, neo-SCJ was observed in all treated patients. All patients who underwent either circumferential or focal ablation achieved >50% reduction of CLE after one session of ablation however none of them achieved complete ablation at 3 months post intervention. No suspicious areas were seen under ME-NBI to suggest interval dysplastic changes.

Most patients (75%) experienced chest discomfort, chest pain and difficulty in swallowing after RFA but all resolved by 3-4 days post procedure. None of the patient reported fever post procedure. No reported strictures seen on surveillance OGDS 3 months post RFA. However, circumferential scarring was seen in all patients who underwent HALO-360 balloon ablation. Major complications like bleeding and perforation were not reported in our current series.

Conclusion:

Though single session of RFA was able to achieve >50% ablation of Barrett's mucosa, none of them achieve complete ablation. Further RFA session would be required to ablate the residual CLE. Advanced endoscopy imaging such as ME-NBI is useful in detection and characterization of Barrett's mucosa. We reported here of the use of such imaging technique to detect and characterize remnant Barrett's mucosa following novel RFA treatment.

Discussion:

BO exhibits distinctive features under ME-NBI. It was shown in various studies to conform to 5 types of microsurface patterns ie round pattern, tubular pattern, linear pattern, villous pattern and even absent of pattern.(2-5) Of which, ridge/villous pattern was known to be highly associated with Barrett's mucosa. Further analysis on the regularity of the microsurface and/or microvascular pattern can help to predict dysplastic changes that may arise from the Barrett's mucosa. In our study, as the patients were already confirmed to have intestinal metaplasia in previous analysis, remnant Barrett's mucosa was only determined endoscopically.

In view of the possibility of progression from non-dysplastic BO to dysplastic BO, ablation of all Barrett's mucosa was strongly advocated by some. There are currently few options available for endoscopic ablation namely cryotherapy, argon plasma coagulation therapy, photo-dynamic therapy and RFA.(6) Of which, RFA was shown to be highly effective in achieving complete eradication.(7-10) However, it is not known as to the number of RFA session required to achieve complete ablation. Hence, it is a common practice to repeat such procedure every 2 to 3 months until complete ablation achieved. RFA is also useful to ablate Barrett's associated dysplasia or early squamous neoplasia in those patients who are not fit for surgery. In our series, with the aid of ME-NBI, we demonstrated that single RFA was effective in ablating more than 50% of Barrett's mucosa in all our patients. Further RFA will be required to achieve complete ablation.

Probe based multiphoton microscopy and colon neoplasm

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Background and Aims: Multiphoton endomicroscopy is the recentely updated technique for endoscopy and virtual image and optical sectioning. However optimized probe has not been established for multiphoton endomicroscopic image. Therefore we developed novel probe for mitochondria and applied for colon neoplasm tissues. In cancer cell, abnormally increased mitochondrial replication is related mitochondrial dysfunction and Warburg effect.1

Methods: We used newly developed multiphoton probe for micochondria imaging which are made using benzofuran derivative (BFP, maximal multiphoton fluorescence at 570 nm, Figure 1). Fresh mucosal tissues of colonic adenoma and adenocarcinoma were obtained from endoscopic biopsy. Multiphoton probe BFP for mitochondria was stained for tissues and imaging performed using multiphoton microscopy.

Results: BFP shows high enhancement factor upon binding mitochondria, good selectivity, cell permeability, and can readily detect mitochondria in human tissues by multiphoton microscopy. Mitochondria were detected in human colon mucosa tissues. Calculated mitochondria area were increased in adenocarcinoma tissues compared to normal mucosal tissues.

Conclusions: Newly developed multiphoton probe for mitochondria are usable to image human live colon tissues.

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RADIOLOGICAL DIAGNOSIS AND STAGING OF HEPATOCELLULAR CARCINOMA USING MULTIPHASIC CT SCANNING

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INTRODUCTION:

Hepatocellular Carcinoma (HCC) is a common cancer in the Asian Pacific region. In Malaysia it is the sixth commonest malignancy and is extremely common amongst the Chinese ethnic group (1, 2).

Multiphasic CT and/or MRI scans of patients affords accurate diagnosis with it characteristicpattern of arterial enhancement of lesions with a venous phase washout without a need for a tissue diagnosis. Furthermoretogether with a careful clinical evaluation, it allows us to stage patients accurately. In the past, we have utilized the Barcelona Clinic Liver Cancer (BCLC) staging classification (1).

In the preliminary report on an ongoing study, we have analyzed the CT scans of 50 consecutive HCC patients and staged them according to the BCLC staging classification and the Japanese Integrated Staging (JIS) score.

METHODS:

This study involves 50 consecutive patients who were diagnosed to have HCC based on typical pattern of HCC on 5 phase CT scan of liver which was performed in the Radiology Department of UMMC from March till November 2015.

Scans were performed over 5 phases: non enhanced, early arterial, late arterial, portal venous and delayed phase. Patients were given 80 -100 mls of intravenous contrast in the form of Ultravist 300mg/ml, infused at the rate of 2-4 mls per second. Basic demographics, aetiology of liver disease, Child-Pugh score and Performance Score of each patient were recorded. A detailed review of CT was carried out, especially on the size, number of tumour, portal vein invasion and distant metastasis were noted.

The staging of the tumour was done based on BCLC staging classification and JIS score.

RESULTS:

Fifty patients were prospectively seen. The basic characteristicsof patients and aetiology of liver disease is as shown:

Age: Median and IQR	65.5 years (58.75,73.25)
Gender - Male: Female	44:6
Race - Malay: Chinese: Indian	18:28:4 (36/56/8%)
Etiology:	Hepatitis B: 29 (58%), Hepatitis C: 6 (12%), NASH: 8 (16%), Cryptogenic: 5 (10%), Alcohol: 2 (4%)

Tumor characteristics is stated as below:

Median size of tumor (25-75% IQR)	8.4 (6.45, 10.72)
No of tumor nodules: 1/<3/>3	28 (56%) /7 (14%) /15 (30%)
Portal invasion (%)	18 (36%)
Distant metastasis (%)	13 (50%) Location: lungs, bone

Distribution of patients based on BCLC staging classification and JIS score:

BCLC Grade	N	%	JIS Score	N	(%)
0	1	2.0	0	5	10.0
A	6	12.0	1	5	10.0
B	14	28.0	2	12	24.0
C	22	44.0	3	15	30.0
D	7	14.0	4	7	14.0
	1	2.0	6	6	12.0

DISCUSSION:

The overwhelming majority of patients presented with large tumors. Portal invasion was seen in a significant number of patients. Multiphase CT scan afforded a reliable and consistent diagnosis of HCC with the characteristic findings in all patients. The value of these CT scans included the ability to help stage patients which is important in prognostication and choice of treatment. There are however differences in stratification of patient using the 2 different classification. Follow-up data of larger cohort of patients in a HCC registry will determine which classifications give the best determination of survival and prognosis in our patients.

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Management of Gallbladder Rupture In A Pediatric Patient

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ABSTRACT

Significance: Gallbladder injury is rare occurring in 2-3% of blunt abdominal trauma. A high index of clinical suspicion is needed for its diagnosis and subsequent management.

Clinical presentation: This report describes a case of a 6-year-old male who was hit on his right torso by a vehicle while he was crossing the street. Three days after the accident, he had abdominal pain, rigidity and an abdominal ultrasound finding of hepatorenal fluid collection requiring exploratory laparotomy. Intraoperative findings were hemoperitoneum of approximately 100 mL and bile leak in the right subhepatic space. The subhepatic space was packed with omentum and JP drains were inserted. There was 250 – 300 mL bilious drainage per JP drain every day hence a CT scan was done revealing liver laceration grade 2 with minimal pericholecystic fluid. Endoscopic retrograde cholangiopancreatography (ERCP) was done which revealed contrast leakage at the gallbladder fundus hence a plastic biliary stent was inserted to bypass the cystic duct. Three weeks after ERCP, a hepatobiliary (HIDA) scan was done which showed no evidence of bile leak.

Diagnosis: Knowledge of the history and mechanism of abdominal injury from trauma with appropriate imaging tests will help arrive in the diagnosis of gallbladder rupture.

Recommendation: Gallbladder rupture though rare should be considered in the proper setting. Though cholecystectomy is the definitive management of choice in adult population some pediatric experts recommend the preservation of the gallbladder in children as was described in this case report by doing ERCP with stenting.

Keywords: Gallbladder rupture; Endoscopic retrograde cholangiopancreatography

Early video capsule endoscopy in patients with obscure gastrointestinal bleeding- a single hospital experience

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Background: Small bowel video capsule endoscopy(VCE) is suggested as the first line investigation in patients with obscure gastrointestinal bleeding(OGIB). It has high diagnostic yield and can help improve clinical management and outcome in OGIB patients. However, the ideal timing to perform VCE remained unknown. In 2015, European Society of Gastrointestinal Endoscopy suggested to perform small bowel VCE as soon as possible after the bleeding episode, optimally within 14 days. Limited data about early use of VCE is available in Asia though the etiologies of OGIB in Asia in were distinct from western countries.

Study aim: To evaluate the diagnostic yield of VCE for OGIB patients taking video capsule endoscopy within 3 days of last overt OGIB

Methods and materials: The study was performed in Taipei Veterans General Hospital, a tertiary teaching hospital. From April 2015, we started to perform VCE on all overt OGIB patients referred for VCE examination within 3 days of last overt OGIB. After signing informed consent, all patients received 2 L of polyethylene glycol at the night before the procedure followed by 8 hours of fasting. VCE (Olympus Endocapsule, Olympus, Japan) was performed at our endoscopy center or at beside. 40mg of Simethicone fluid was given to patients 20 minutes before VCE examination. We checked the site of VCE at 2 hours after ingestion of capsule and perform esophagogastroduodenoscopy to put the capsule into duodenum with roth net retriever (US endoscopy, US) if capsule retained in stomach. After 8 hours of capsule ingestion, we removed the antenna and sensors and reviewed the images within 24 hours using Olympus endocapsule software 1.0.7E on workstation. Images were reviewed at a rate of 6-15 images per second. The images review data are written.
Data are expressed as median± S.E.M. (range.)

Results: From April 2015 to Dec 2015, 9 consecutive overt OGIB received VCE at our hospital. The median age was 55±9.7(16-92) and 7 patients(78%) are male. The patients received VCE within 1±0.23 (1-3) days. 7 patients (78%) presented with melena while 2 patients(22%) presented as hematochezia. In total 9 patients, 8 patients(89%) were found with small bowel lesions related to bleeding, including 3 active oozing angiodysplasia, 1 active oozing polypoid lesion, 2 angiodysplsia, 1 Meckel's diverticulum, 1 diffuse ileal lymphoid hyperplasia and polyps, 1 multiple small bowel ulcers. Another patient was found with gastric Dieulafoy's lesion during repeat esophagogastroduodenoscopy. The small bowel cleansing quality was adequate in 6(67%) patients. According to the VCE result and their health status, 1 patient received operation, 3 patients received enteroscopy while 4 patients received medical treatment. During follow-up, only 1 patient with multiple small bowel ulcers had clinical significant re-bleeding at 40 days after VCE. His bleeding stopped spontaneously after observation and supportive treatment.

Conclusions: Early VCE examination within 3 days of last overt OGIB has high diagnostic yield. Early VCE examination is also powerful in guiding further intervention and management. Larger multi-center prospective cohort study is warranted to evaluate the long-term efficacy and cost-effectiveness in performing early VCE examination.

A prospective multicentre study assessing the utility of Narrow Band Imaging with dual focus magnification in differentiating colorectal neoplasia using the NICE and Modified Sano's classification

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Introduction
The majority of the polyps found during screening colonoscopy are small and benign but current practice still requires costly pathological interpretation. Advances in endoscopic imaging have prompted consideration of real-time diagnosis of colorectal polyps which maybe more cost-effective and reduce the number of polypectomy-associated complications. We aimed to assess the utility of the Modified Sano's versus the NICE classification in differentiating colorectal polyps.
Methods
Consecutive patients undergoing colonoscopy for any indication between June 2013 and July 2015 were invited to participate. All procedures were performed using the commercially available 190 series Exera III system (Olympus Co. Ltd, Japan) which has both Narrow Band Imaging (NBI) and Near Focus (NF) function. Based on the validated Modified Sano's capillary network pattern or the NICE classifications, real time diagnosis was made on the polyps that were detected. Each patient was randomized to have the predictions of polyps with either of these classifications but not both. All polyps were also assigned a level of confidence (high or low) to the prediction of each classification. This was followed by biopsies, endoscopic or surgical resection. The NBI-NF diagnosis was then compared to the final (blinded) histopathology analysis. The primary endpoint includes the Sensitivity (Sn), Specificity (Sp), Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of differentiating neoplastic from non-neoplastic polyps based on either classification (Sano's II, IIo, IIIa & IIIb vs. Sano's I or NICE 1 vs. NICE 2, 3). The secondary endpoints were 'endoscopic resectability' of these polyps (Sano's II, IIo, IIIa vs. Sano's I, IIIb or NICE 2 vs. NICE 1, 3), assessment of NPV for each classification for adenomatous histology in rectosigmoid polyps <5mm in size and predicted post-polypectomy surveillance intervals for each classification based on the American Society of Gastrointestinal Endoscopy (ASGE)'s Preservation and Incorporation of Valuable Endoscopic Innovation (PIVI). A total sample size of 560 high confidence polyps was calculated to achieve a 80% power to detect a difference of 7% in diagnostic accuracy for Modified Sano's over NICE classification.
Results
A total of 349 patients (175 in Modified Sano's arm and 174 in NICE's arm) were evaluated. 309 of 321 (96.3%) and 273 of 334 polyps (81.7%) were predicted with high confidence with the Modified Sano's and NICE arms respectively. The Sn, Sp, PPV and NPV in differentiating neoplastic from non-neoplastic polyps were 98.9%, 85.7%, 98.2%and 90.9% for the Modified Sano's and 99.1%, 57.7%, 95.4% and 88.2% for the NICE classification. The area under the receiver operating characteristic curve (AUC) was 0.9231 and 0.7460 for Modified Sano's and NICE classifiactions respectively (P<0.0001). The Sn, Sp, PPV and NPV in predicting endoscopic resectability were 98.9%, 86.1%, 97.8% and 92.5% for the Modified Sano's and 98.6%, 66.7%, 94.7% and 88.9% for the NICE classification. Modified Sano's classification's AUC was significantly more superior in predicting resectability than that of NICE classifiactions (0.9246 vs 0.7869, P<0.0001). The NPV for adenoma in rectosigmoid polyps <5mm in size were 96.6% and 95% with the Modified Sano's and NICE arms respectively. The calculated accuracy of post polypectomy surveillance for the Modified Sano and the NICE classifications were 98.2% and 92.1% respectively.
Conclusion
Modified Sano's classification appears to outperform the NICE classification in differentiating neoplastic polyps and predicting endoscopic resectability of a colon polyp. However, both classifications using NBI-NF meet the PIVI threshold of >90% in correctly determining post-polypectomy surveillance intervals and making real-time endoscopic assessment of the histology of diminutive colorectal polyps.

Usefulness of non-invasive assessment of liver fibrosis using six different ultrasound elastography devices in patients with chronic hepatitis and the difference of liver stiffness between HBV-related chronic hepatitis and non-HBV-related chronic hepatitis.

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Background and aims: Liver biopsy is the standard of reference for the evaluation of liver fibrosis, however, it is an invasive procedure and sampling errors can occur.

Ultrasound elastography is non-invasive methods for assessment of liver fibrosis in patients with chronic hepatitis and many studies have shown

that ultrasound elastography have good diagnostic accuracy for the assessment

of liver fibrosis in various chronic hepatitis. We evaluated liver stiffness in patients with chronic hepatitis using six different devices and compared liver stiffness in patients with different types of chronic hepatitis using Virtual Touch Quantification(VTQ, Siemens, ACUSON S2000/3000®).

Methods: 1) From February 2015 to September 2015, 126 patients with chronic liver disease who had undergone liver biopsy were enrolled. On the same day as liver biopsy, liver stiffness measurement was undergone by six different devices(ACUSON S2000 for VTQ, Aixplorer for SWE, EPIQ 7G for SWE, AplioTM500 for SwSm, LOGIQ S9 for SWE and Fibroscan for TE.) All the examinations were performed by experienced operators.

2)From October 2008 to August 2015, 1571 patients with chronic liver disease with VTQ measurements and liver biopsy were enrolled. The subjects subsequently underwent liver biopsy within 4 months before or after VTQ measurement. We evaluated to find relationship between VTQ and other parameters including the difference of etiology. These studies were approved by the hospital ethics committee in our institution.

Results: 1) 68% of patients with chronic liver disease had chronic hepatitis B and/or C and 32% had nonBnonC. The stages of liver fibrosis were 42.5%, 18.9%, 25.2%, 13.4% for F1, F2, F3 and liver cirrhosis, respectively. In all ultrasound devises, Vs value is increased with progression of liver fibrosis. Vs values were significant higher in severe fibrosis than that of significant fibrosis. The ability to diagnose liver cirrhosis by each device was determined by the area under the receiver operating characteristic curve (AUROC) analysis, and the AUROC of VTQ(ACUSON S2000)/SWE(Aixplorer)/SWE(EPIQ7G)/SwSm(AplioTM500)/SWE(LOGIQS9)/TE (Fibroscan) was 0.96/0.96/0.96/0.96/0.96/0.94 respectively and showed good ability in all devices. The correlation coefficient R of each device was very strong(0.88-0.97).

2) Multivariate analysis for the association with VTQ demonstrated that F parameter, platelet counts, serum albumin, PT-INR and were associated with VTQ($p<0.001$). Of these, F parameter had the strongest positive correlation with VTQ($P<0.001$). The progression of F parameter and the elevation of A parameter were associated with the elevation of VTQ. The diagnostic ability of F3-4 was less in HBV-chronic hepatitis than non-HBV related chronic hepatitis and cut off values of Vs values diagnosed for F3-4 were 1.22 for HBV, 1.43 for HCV, 1.37 for NBNC and Vs values for F3-4 were less in HBV-related chronic hepatitis than in non-HBV-related chronic hepatitis. In HBV cases with fibrosis stage F0-F2 or F3-4, the liver was significantly softer than that of non-HBV related chronic hepatitis ($P<0.05$). The proportion of collagen fibers per unit area was histologically smaller in patients with hepatitis B than those with non-HBV hepatitis.

Conclusion; The ability to diagnose liver fibrosis by each device was of equal significance and each device can be used as a substitute for an invasive evaluation of liver fibrosis. Non-invasive fibrosis assessment is useful in evaluating the progress of liver fibrosis. On the other hand, we found that the diagnosis accuracy of liver stiffness measurement for HBV-related chronic hepatitis was lower than that of non-HBV related chronic hepatitis. This findings show that it is necessary to pay attention to the diagnosis of fibrosis stage for HBV patients by ultrasound shear wave elastography.

Endoscopic Appearance of Serrated Adenoma Using White Light Endoscopy, Narrow Band Imaging, and Blue Laser Imaging

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Serrated adenomas now known has a higher potential for transformation to colorectal cancer compared to hyperplastic polyp. It is important for endoscopist to recognize and differentiate from hyperplastic polyps. Advancement of endoscopic imaging allow us to recognize it better. In our center we use white light endoscopy, narrow band imaging (Olympus) and blue laser imaging (Fujifilm). By using these technologies we try to study the characteristics of serrated adenomas. From Hazewinkel Y et al study show that characteristics of sessile serrated adenomas are: indistinct border, cloud like surface, and dark spot inside the crypt (NBI). We present 5 cases of serrated adenoma polyps from histopathology result with its endoscopic image characteristics. Four cases have dark spot inside the crypt by NBI or BLI and cloud like appereance. Only 1 case have indistinct border.

Examination using white light endoscopy, NBI or BLI can guide us to detect serrated adenoma polyps with certain characteristics especially dark spot inside the crypt and cloud like appearance.

The use of endocystoscopy for the early detection of esophageal neoplasm: a case series

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Department of Surgery, The Chinese University of Hong Kong

Background and aims

Early detection of esophageal cancers can significantly reduce the morbidity and improve the prognosis of these patients. A new prototype scope incorporating the endocystoscopy function into a magnifying endoscope has been designed. Previously, Inoue et al have published a pilot trial on evaluating the use of this endocystoscope in various types of benign and malignant pathology in the esophagus. An endocytoscopic atypia (ECA) classification was proposed. The sensitivity and specificity of this classification system was evaluated.

Patients and methods

All consecutive patients who had esophagogastroduodenoscopy (EGD) arranged for screening of the esophagus during the period July 2015 to December 2015 were recruited into the study. EGD with narrow band imaging and endoscocystoscopy were performed in these patients. During the procedure, the esophageal mucosa was stained with 0.5% methylene blue and then with crystal violet. The endocystoscopic findings were graded from 1 to 5 according the Inoue et al's ECA classification. The esophageal mucosa was also evaluated with narrow band imaging (NBI) and the findings were classified according to the Intrapapillary capillary loop (IPCL) pattern classification. These findings were compared against the gold standard of histopathological diagnosis which was based on the Vienna classification.

Results

From July 2015 to December 2015, twenty-three patients were included in the study. Seven of the twenty-three (30%) patients had histological confirmed cancer of the esophagus. There were six patients who had normal finding and nine patients with esophagitis. The positive predictive value for malignancy (ECA 4 and 5) was 87.5%; the negative predictive value was 100%. Sensitivity for malignancy was 100% and specificity was 93.3%. Similar findings were noted with IPCL on magnifying NBI. The positive predictive value for malignancy (IPCL 4 and 5) was 87.5%; negative predictive value was 100%. Sensitivity and specificity for malignancy were also similar at 100% and specificity 93.3% respectively. To compare the diagnostic accurary of endocystoscopy and magnifying NBI, the McNemar test was performed. The McNemar chi-squared statistic is NaN, and the McNemar chi-squared statistics with Yates correction of 0.5 is infinity, meaning that the two tests have the same diagnostic accurary.

Conclusion

Endocystoscopy had a high positive predictive value and sensitivity for esophageal malignancy. Its diagnostic accurary was comparable to magnifying NBI. It may be helpful as an adjunct for better characterization of esophageal lesions. However, further studies on interobserver variability is required.

Effects of ambient temperature on ablation zone size: An experimental study with Microwave ablation in ex vivo bovine livers.

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Introduction:

In vivo percutaneous ablation zone size of the AMICA Microwave apparatus is reported as being smaller than in ex vivo livers, with the difference attributed to 'perfusion effects'. The majority of studies in the literature of percutaneous liver ablation are performed at room temperature. We propose that ambient liver temperature may have an effect on the ablation zone size. This experiment is to determine the effect of ambient liver temperature on Microwave ablation zone sizes in ex vivo bovine livers.

Method:

A two armed experimental trial was set up with half of the bovine livers at room temperature and the other half at approximately body temperature. Three ablations at different power settings and durations were performed in each group of livers with the macroscopic ablation zone length and diameter measured and volume calculated.

Results:

No statistically significant difference in ablation zone size was detected between the two temperature cohorts for 40W ablations after both 3 and 10 minutes and the 60W ablation after 3 minutes. At an ablation power of 60W for 10 minutes there was a statistically significant increase in the ablation zone length and volume for the body temperature liver when compared with the room temperature liver, but no significant difference in the diameter.

Conclusion:

Microwave ablation zone sizes in ex vivo bovine livers at body temperature are not significantly smaller than those at room temperature, therefore the variable of higher ambient temperature of the in vivo livers cannot explain the reported smaller in vivo ablation zone sizes.

Keywords: Ablation, ex vivo, liver, microwave, temperature

Reevaluation of diagnostic ability of fluorescence cytology using 5-aminolevulinic acid during endoscopic ultrasound-guided fine needle aspiration for pancreatic lesions.

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Objective: 5-aminolevulinic acid (ALA) administered to patients having caners is metabolized into protoporphyrin IX (PpIX) in the mitochondria and is characterized by excessive intracellular accumulation in cancer cells. Since PpIX emits a typical red fluorescence when excited by irradiation with blue-violet light, cancer cells can be identified by the detection of red fluorescence. We have previously reported the utility of fluorescence cytology using ALA during endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) in 28 patients with a pancreaticobiliary mass lesion or intra-abdominal lymphadenopathy of unknown origin. The aim of this study is to reevaluate the diagnostic accuracy of this novel method using data of additionally enrolled patients with pancreatic lesions.

Materials and Methods: We prospectively enrolled 70 patients who had undergone EUS-FNA for the pathological diagnosis of a pancreatic mass lesion between December 2013 and August 2015 in the Kansai Medical University Hirakata Hospital. All of the patients were orally administered 1g of ALA 3-6 hours before EUS-FNA. The specimens obtained via EUS-FNA were mounted on a glass slide for fluorescence cytology by blue-violet light illumination and ordinary cytology. Fluorescence cytology-positive was defined as detection of strong red fluorescence clusters. In contrast, fluorescence cytology-negative was defined as vague or no red fluorescence.

Results: Fifty-four of 70 patients (77%) were finally considered as having pancreatic cancer and 16 patients (23%) as having benign lesions (autoimmune pancreatitis in 13, mass-forming chronic pancreatitis in 2, and serous cystoadenoma in 1). Fifty-one of 54 patients having pancreatic cancer were considered as fluorescence cytology-positive. On the other hand, 11 of 16 patients having benign lesions were considered as fluorescence cytology-negative. Of 5 patients having benign lesions who were considered as fluorescence cytology-positive, 3 patients were finally diagnosed as autoimmune pancreatitis and 2 as mass-forming chronic pancreatitis. Therefore, the sensitivity, specificity, and accuracy of fluorescence cytology were 94%, 69%, and 89%, respectively. In contrast, the sensitivity, specificity, and accuracy of ordinary cytology were 96%, 100%, and 97%, respectively.

Conclusions: Fluorescence cytology with ALA during EUS-FNA has an equivalent ability with ordinary cytology in detecting cancer cells. However, fluorescence cytology has the disadvantage of high false posit

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2015年11月作成
PP−JP-1279-1.0