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 Advanced Endoscopic Mucosal Imaging and resection techniques which are not commonly used in general practice but is rapidly evolving and increasingly being adopted

 Type of specimens Pathologists can come to expect mucosal, submucosal, full thickness



Stomach

Colon



Stomach

Colon

• SCC

- Where we are at
- Pushing the boundaries

• BE

- Where we are at
- Pushing the boundaries

• SCC

- Where we are at
- Pushing the boundaries
- BE
- Where we are at
- Pushing the boundaries

SCC

• Detection

• Characterization

• Rx

SCC

• Detection

• Characterization

• Rx

SCC: Detection



Lugol chromoendoscopy



'Pink colour' sign





Detection

• Characterization (Depth)

• Rx

Magnifying Endoscopy Classification for SCC

Туре	Magnified endoscopic findings of microvessels			Invasion depth
Α	<i>Without</i> severe irregularity		Normal <i>IPCL</i> or with mild irregularity	Normal or LGIN
В	<i>With</i> severe irregularity (i.e. Abnormal vessels)	1	With a loop-like formation	EP / LPM
		2	<i>Without</i> a loop-like formation	MM / SM1
		3	Highly dilated abnormal vessels	>SM2

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Japanese Esophageal Society. Esophagus 2011

Japanese Esophageal Society Classification

Туре	A1	A2	B1	B2	B3
Vascular finding	ĥ	Ņ	Loop vessel	Non-loop vessel	Thick green vessel
Epithelial finding			AVA-small (<0.5 mm)	AVA- medium (0.5-3mm)	AVA-large (>3mm)
Most likely	Non-neoplasm		Neoplasm		
pathology	Normal	Inflam	m1-2	m3-sm1	>sm2
ER	NO		YES	+/-	NO

















Treatment: Endoscopic Submucosal Dissection

Any lesion >1cm (most lesions)













What Gastroenterologists need

• Differentiation between dysplasia and inflammation

 Depth of invasion into mucosa/submucosa (um) after Endoscopic Resection ...may help with treatment decisions

• SCC

- Where we are at
- Pushing the boundaries

• BE

- Where we are at
- Pushing the boundaries

What we know

1. Endoscopic Mucosal Resection: An essential staging procedure



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Moss et al AJG 2010

When to perform EMR?



- Evidence of any focal abnormality
- Any lesion < 15 mm that requires an en-bloc resection
- Larger lesions, however, can be resected piecemeal

What we know 2. long term follow up

Long Term EMR F/u

Gastroenterology 2014;146:652-660

CLINICAL—ALIMENTARY TRACT

Long-term Efficacy and Safety of Endoscopic Resection for Patients With Mucosal Adenocarcinoma of the Esophagus

Oliver Pech,¹ Andrea May,² Hendrik Manner,² Angelika Behrens,² Jürgen Pohl,² Maren Weferling,² Urs Hartmann,² Nicola Manner,² Josephus Huijsmans,² Liebwin Gossner,³ Thomas Rabenstein,⁴ Michael Vieth,⁵ Manfred Stolte,⁶ and Christian Ell²

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ERs (n)	2687
ERs per patient; median (interquartile range)	1 (1–3)
Major complications, n (%)	15 (1.5%)
Major bleeding	14
Perforation	1
Complete local remission, n (%)	963/1000 (96.3)
Time until complete local remission (mo),	1 (1–3)
median (interguartile range)	
Follow-up (mo), mean ± SD	56.6 ± 33.4
Metachronous lesions, n (%)	140/963 (14.5)
Long-term complete local remission after	938/1000 (93.8)
repeat ER, n (%)	

Table 2. Acute and Long-term Results

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What we know 3. Factors associated with recurrence

Variable	Relative risk
Long-segment Barrett's oesophagus	1.9 (1.06 to 3.3)
Time until CLR achieved >10 months	0.3 (0.12 to 0.75)
Piecemeal resection	2.44 (1.13 to 4.89)
Multifocal neoplasia	2.1 (1.16 to 3.99)
No ablative therapy of Barrett's oesophagus after CLR	2.5 (1.52 to 3.85)
CI, confidence interval: CLR, complete local remis	ssion.

RFA + ER: Systematic review

	Focal RFA + EMR	Radical EMR
Number of patients	774	751
Recurrence EAC Dysplasia IM	1.5% 2.6% 16%	0.7% 3.3% 12%
Strictures	10%	33%



Desai M et al. GIE 2017

RFA= no specimen !



Careful mucosal imaging is essential

- SCC
- Where we are at
- Pushing the boundaries
- BE
- Where we are at
- Pushing the boundaries
Squamous tissue overgrowth

• LGD

HGD vs intramucosal/superficial submucosal cancer

• Squamous tissue overgrowth - margins



• HGD vs intramucosal/superficial submucosal cancer

Squamous tissue overgrowth

• LGD – margins?

• HGD vs intramucosal/superficial submucosal cancer





Squamous tissue overgrowth



 HGD vs intramucosal/superficial submucosal cancer : margins and depth





Pushing the boundaries: ESD in BE

- Lesions >1.5cm
- Nodular, depressed
- Lesion which are difficult to lift

 Lesions suspected of harboring superficial submucosal invasion

Risk of LN mets into Sm: metanalysis

	SM ₁	SM ₂	SM ₃
Lymph Nodes	8/84 (10%)	11/53 (36%)	38/80 (49%)
LV invasion	2/23 (9%)	4/15 (27%)	19/25 (76%)
Vascular invasion	1/7 (14%)	0/2 (0%)	0/12 (0%)

Adapted from G Sgourakis et al. WJG 2013

ESD – advantages and challenges

ADVANTAGES

- Straight lumen (less problems with folds)
- Repetitive once familiar
- Gravity, friendly if lesion is between 1-6 o'clock

CHALLENGES

- Narrow lumen of the oesophagus (scope maneuverability)
- Resected specimen retracts distally
- Vascular GOJ
- Thin wall of oesophagus (thicker mucosa, but thin MP..beware thinking it is thick ..POEM's)
- Gravity, unfriendly if lesion is between 7-12 o' clock









ESD in BE

Author	Year	# Patients	En bloc	Ro	Perf	Recurrence
Yang, Draganov GIE 2017	2010-2015	46	96%	76%	2%	
Subramaniam, Bhandari GIE 2017	2008-2016	143	91%	79%	0%	
Terhaggen, Neuhaus GUT 2017	2017	20 (EMR) vs 20 (ESD)		58%	10%	0% vs 5%
Bhatt DDW 2019	2019	155 (EMR) vs 74 (ESD)	41% vs 95%			39% vs 3%

BE: Pushing the boundaries

2. Complete BE excision - single session

BE: What Gastroenterologists need

• Further clarity: LGD and indefinite for dysplasia, atypia?

 Depth of invasion into mucosa/submucosa (um) and risk of LN mets

• "Volume" of cancer and risk of LN mets



Oesophagus

Stomach

Colon

Characterization

With NBI (BLI/I Scan) +/- magnification

• What is normal ?

Anatomy (gland structure and vasculature) of the corpus







Anatomy : Antrum



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Whtiehead R. Gastrointestinal and Oesophageal Pathology





Premalignant gastric lesions

- Gastric IM is considered premalignant
- Annual incidence of gastric cancer
 - Atrophic gastritis 0.1%
 - Intestinal metaplasia 0.25%
 - Mild to mod dysplasia
 0.6%
 - Severe dysplasia 6%



Figure 5. Progression rate of premalignant gastric lesions to gastric cancer in 92,250 patients with premalignant gastric lesions (90,780 censored patients).

De Vries et al Gastro 2008







Irregular microvasculature (V)

Irregular microstructure (S) with

Demarcation line (DL)

Yao et al Endoscopy 2009; 41:462- 67 Uedo N, Fujishiro M, Goda K, Hirasawa D, Lee JH, Morita Y, Singh R et al. Current Consensus of Experienced Endoscopists in the AP region. Digestive Endoscopy 2011





• Detection

Characterization

• Treatment (Endoscopic)

Guidelines for ER

	Histology	Size	Depth	Ulcer
		≤2/3 circumferential	M1 (intraepithelial) M2 (lamina propria)	
Esophagus	IagusSCC $\leq 2/3$ circumferentialM1 (intraepithelial) M2 (lamina propria)IagusSCC $2/3$ -circumferentialM1 (intraepithelial) M2 (lamina propria) $\leq 2/3$ circumferentialM3 (muscularis mucosae) SM $\leq 200 \ \mu m$ IACHDifferentiated $\leq 3 \ cm$ MIACHUpto SM $\leq 500 \ \mu m$			
		≤2/3 circumferential	Depth M1 (intraepithelial) M2 (lamina propria) M1 (intraepithelial) M2 (lamina propria) M3 (muscularis mucosae) SM ≤200 μm M Upto SM ≤500 μm M	
	Differentiated	Any size	М	(-)
		≤3 cm	М	(+)
STOMACH		≤3 cm	Upto SM ≤500 µm	(-)
	Undifferentiated	≤2 cm	М	(-)
Colon		≤2 cm: EMR >2 cm: ESD/WF EMR	Upto SM ≤1000 µm	

Guidelines for ER

	Histology	Size	Depth	Ulcer	
Esophagus SCC		≤2/3 circumferential	M1 (intraepithelial) M2 (lamina propria)		
	SCC	2/3>circumferential M1 (intraepithelial) M2 (lamina propria)			
		≤2/3 circumferential	Depth M1 (intraepithelial) M2 (lamina propria) M1 (intraepithelial) M2 (lamina propria) M3 (muscularis mucosae) SM ≤200 μm M Upto SM ≤500 μm M		
	Differentiated	Any size	М	(-)	
STOMACH		≤3 cm	М	(+)	
		≤3 cm	Upto SM ≤500 µm	(-)	
	Undifferentiated	≤2 cm	М	(-)	
Colon		≤2 cm: EMR >2 cm: ESD/WF EMR	Upto SM ≤1000 µm		

Guidelines for ER

	Histology	Size	Depth	Ulcer
Esophagus STOMACH		≤2/3 circumferential	M1 (intraepithelial) M2 (lamina propria)	
	SCC	2/3>circumferential	M1 (intraepithelial) M2 (lamina propria)	
		≤2/3 circumferential	M3 (muscularis mucosae) SM ≤200 μm	
		Any size	М	(-)
	Differentiated	≤3 cm	Μ	(+)
STOMACH		≤3 cm	Upto SM ≤500 µm	(-)
	Undifferentiated	≤2 cm	Depth M1 (intraepithelial) M2 (lamina propria) M1 (intraepithelial) M2 (lamina propria) M3 (muscularis mucosae) SM ≤200 μm M Upto SM ≤500 μm M	(-)
Colon		≤2 cm: EMR >2 cm: ESD/WF EMR	Upto SM ≤1000 µm	












Stomach: Microcarcinoid

Microcarcinoid tumor diagnosed with highresolution magnification endoscopy and narrow band imaging



Carcinoid misdiagnosed as gastric cancer...









Histopath





• Oesophagus

• Stomach

Colon



Endoscopic Mucosal Resection (EMR)

Full Thickness Resection (FTR)

Endoscopic Submucosal Dissection (ESD)





• FTR

• ESD

EMR-Nuances

- 1) Imaging: pre resection
- 2) Hot snare EMR
- 3) Cold snare EMR
- 4) Evaluate base : post resection
- 5) Preventing recurrence
- 6) Seeing recurrence on follow up

EMR-Nuances

- 1) Imaging: pre resection characterisation
- 2) Hot snare EMR
- 3) Cold snare EMR
- 4) Evaluate base : post resection
- 5) Preventing recurrence
- 6) Seeing recurrence on follow up

Characterization

• Wide field view

Focal interrogation

Characterization

- Wide field view
- Paris classification
- Granularity
- Focal interrogation



Paris classification "Flat" lesions 0-II



Characterization

- Wide field view
- Paris classification
- Granularity



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Morphology & Paris Class predict Sub Mucosal Invasion (SMI)

Paris classification	n (SMI)	%	
IIa	4/132	3%	
Is	7/92	7%	
Is + IIa	5/40	13%	
IIc or IIa +c	6/13	46%	
			lla+c NC
SM	I risk	1.1.1	67%

RR = 54.0

Slide courtesy of Michael Bourke

Risk of SMI according to Gross Morphology and Location



Characterisation

- Wide field view
- Paris classification
- Granularity
- Focal interrogation
- Mesh brown capillary pattern (NBI/BLI/I scan)

Strategy based on capillary patterns







Hyperplastic Polyp

Hyperplastic Polyp




















Strategy based on capillary patterns









KL Cheong, L Zorrón Pu, R Singh (Malaysia, Brazil, Australia)





Type III_b



- 1) Imaging: pre resection
- 2) Hot snare EMR
- 3) Cold snare EMR
- 4) Evaluate base : post resection
- 5) Preventing recurrence
- 6) Seeing recurrence on follow up

- 1) Imaging: pre resection
- 2) Hot snare EMR
- 3) Cold snare EMR
- 4) Evaluate base : post resection
- 5) Preventing recurrence
- 6) Seeing recurrence on follow up

- 1) Imaging: pre resection
- 2) Hot snare EMR
- 3) Cold snare EMR
- 4) Evaluate base : post resection
- 5) Preventing recurrence
- 6) Seeing recurrence on follow up

Classification of Deep Mural Injury (DMI)

- **Type 1 :** MP visible, but no mechanical injury. May have minimal thermal injury
- **Type 2 :** Focal or generalized loss of the submucosal plane raising concern for MP injury or rendering the MP defect un-interpretable
- **Type 3 :** MP injured, target or mirror target identified
- **Type 4 :** Actual hole within a white cautery ring, no observed contamination
- **Type 5 :** Actual hole within a white cautery ring, observed contamination

Bourke et al

- 1) Imaging: pre resection
- 2) Hot snare EMR
- 3) Cold snare EMR
- 4) Evaluate base : post resection

5) Preventing recurrence

6) Seeing recurrence on follow up

A MULTI-CENTRE RANDOMIZED CONTROL TRIAL OF SNARE TIP SOFT COAGULATION FOR THE PREVENTION OF ADENOMA RECURRENCE FOLLOWING COLONIC EMR **RESULTS FROM THE "SCAR" STUDY**

Amir Klein¹, Vanoo Jayasekeran¹, Luke Hourigan³, Rajvinder Singh⁵, Gregor Brown⁴, David J Tate¹ Farzan F Bahin^{1,2}, Nicholas Burgess^{1,2}, Stephen J Williams¹, Eric Lee¹, Michael J Bourke^{1,2}

¹Department of gastroenterology and hepatology, Westmead hospital Sydney; ²University of Sydney; ³Department of gastroenterology and hepatology Princess Alexsandra Hospital Brisbane; ⁴Department of gastroenterology and hepatology Alfred Hospital Melbourne; ⁵Department of gastroenterology and hepatology Lyell McEwin Hospital Adelaide

Gastroenterology 2018

ADJUVANT THERMAL ABLATION OF THE EMR MARGIN

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Gastroenterology 2018



Endoscopic Recurrence

Histological Recurrence

Null Am Active Arm

	SC1	Null arm	Active arm	RR	NNT	р
	Endoscopic recurrence	21.6% (33/153)	5.4% (9/167)	0.25	6.17	< 0.001
Singh Austral	Histological recurrence asian Gastroir	21.7% (26/120) ntestinal Pat	<mark>4.6% (6/131)</mark> hology Society S	0.21 Scientific Confe	5.89 erence 2019	< 0.001

Gastroenterology 2018

- 1) Imaging: pre resection
- 2) Hot snare EMR
- 3) Cold snare EMR
- 4) Evaluate base : post resection
- 5) Preventing recurrence

6) Seeing recurrence on follow up

NBI-SCAR classification

NO RECURRENCE

- 1. Whitish/pale appearance
- 2. Round with/without slightly larger pits
- 3. Irregular sparse vessels with no change in calibre



RECURRENCE

- 1. Dark/Brown colour
- 2. Elongated or branched pit pattern
- 3. Dense capillary pattern surrounding pits



R Singh et al GIE (in press)





R Singh et al GIE (in press)

Results: Exploratory phase

	Arm	Accuracy (95% CI)	Sensitivity* (95% CI)	NPV (95% CI)
Overall	NBI- SCAR	95.0% (88.8;97.9)	100% (96.3;100)	100% (96.3;100)
	HDWLE	93.0% (86.3;96.6)	73.7% (64.3;81.3)	94.1% (87.7;97.3)
High confidence diagnoses	NBI- SCAR	100% (96.1;100)	100% (96.1;100)	100% (96.1;100)
	HDWLE	94.7% (88.3;97.7)	73.7% (64.0;81.5)	93.8% (87.1;97.2)

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R Singh et al GIE (in press)

Results: Validation

Country	Accuracy - %	Sensitivity - %	NPV - %	
(n)	(95% CI)	(95% CI)	(95% CI)	
USA (4)	88.5% (79.7;93.8)	100% (95.4;100)	100% (95.4;100)	
JAPAN (12)	95.6% (92.2;97.6)	91.7% (87.5;94.6)	99.0% (96.8;99.7)	
BRAZIL (5)	80.4% (71.6;87.0)	100% (96.3;100)	100% (96.3;100)	
SINGAPORE (5)	92.7% (85.9;96.4)	100% (96.3;100)	100% (96.3;100)	
AUSTRALIA (2)	95.0% (83.5;98.6)	100% (91.2;100)	100% (91.2;100)	

R Singh et al GIE (in press)

Inter-rater reliability : substantial (0.61)

Potential implications

- 1. Don't biopsy scar with with no features of adenoma (high confidence)
- 2. Treat scar with features suggestive of adenoma (high confidence)
- 3. Low confidence: Treat? Biopsy?



• EMR- Nuances

• FTR

• ESD

FTR: Indication

Lesions <2cm

Recalcitrant- scarred, previous attempts

Suspected of harboring superficial submucosal cancer

Consider lesions with deeper submucosal invasion? Poor surgical candidates





*

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Near Focus

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• EMR- Nuances

• FTR

• ESD

META-ANALYSIS COLORECTAL ESD VS. EMR

- En bloc resection in ESD was 92% compared to EMR (47%)
- The rate of recurrence was much lower in ESD than in EMR (1% vs 12%)
- The rate of perforation with ESD (5.7%) was significantly higher than that associated with EMR (1.4%)
- Additional surgery: ESD 9% EMR 6%

Fujiya et al. GIE 2015

ESD IN THE COLON

• When





- Pre ESD: Lesion assessment and indication
- ESD: equipment & technique
- Complications
- Training



• Pre ESD: Lesion assessment and indication

- ESD: equipment & technique
- Complications
- Training


ESD can be considered for lesions with high suspicion of limited SMI based on:

- Depressed morphology
- Irregularity
- Non Granular surface pattern, particularly if the lesions are larger than 20 mm

(strong recommendation, moderate quality evidence)

Endoscopy 2015; 829-54



An en bloc R0 resection is considered curative if:

- well-differentiated adenocarcinoma (G1/G2)
- sm1 (≤ 1 mm submucosal invasion)
- no lymphovascular invasion

(strong recommendation, moderate quality evidence) Endoscopy 2015; 829-54



• Pre ESD: Lesion assessment and indication

- ESD: (newer) equipment & technique
- Complications
- Training





What has helped

• Water jet with knifes

• Conical Caps

• Line and hook method (fishing line)

Pocket Creation Method



• Pre ESD: Lesion assessment and indication

• ESD: equipment & technique

• Complications

• Training

Complications

Bleeding 5-6%Perforation 1-3%



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Complications

Bleeding 5-6%Perforation 1-3%



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• Pre ESD: Lesion assessment

• ESD: equipment & technique

• Complications

• Training

Proposed training for Endoscopists

- 1) Competent in therapeutic endoscopy
- 2) Observation: videos, live cases
- 3) Train on ex vivo models
- 4) Train on animal models
- 5) Supervised ESD with experts (10-30 cases)
- 6) ESD in the antrum (greater curvature)
- 7) ESD in the rest of the stomach and rectum
- 8) ESD in the oesophagus
- 9) ESD in colon ascending and transverse colon

10) ESD in the rest of the colon

Colon: What Gastroenterologists need

• SSA vs. hyperplastic polyps

• Depth of invasion (um) in submucosal cancers

• 'Area/volume' of invasion and risk of LN mets

Conclusions

Novel mucosal imaging and Endoscopic resection methods in:

- Oesophagus
- Stomach
- Colon

5th ADVANCED ENDOSCOPY IMAGING AND RESECTION MASTERCLASS

7th - 8th February 2020



5th Advanced Endoscopy Imaging and Resection Masterclass

Friday, 7th February 2020 Live cases at Lyell McEwin Hospital, Adelaide

Saturday, 8th February 2020 Lectures with live stream to Auckland, Perth and Melbourne University of Adelaide, Adelaide

COURSE DESCRIPTION

This course aims to teach Endoscopists the latest techniques on Endoscopic imaging with an emphasis on improving the diagnostic ability to detect, characterise and treat oesophageal, gastric, duodenal and colorectal lesions. A combination of cases, didactic lectures and video forums will provide a holistic overview of current diagnosis and treatment paradigms. International and national experts will grace the event and guide you in focused 'Ask the Experts' sessions.



5th ADVANCED IMAGING MASTERCLASS

FACULTY



Professor Rajvinder Singh

MBBS MRCP MPhil FRACP AM FRCP Professor of Medicine, University of Adelaide Director, Gastroenterology Department and Head of Endoscopy Interventional Endoscopist

INTERNATIONAL FACULTY



Professor Noriya Uedo

Vice-Director, Department of Gastrointestinal Oncology, Osaka International Cancer Institute, Japan

Dr. Uedo is a Vice-director of Department of Gastrointestinal Oncology, Osaka International Cancer Institute. His current research interests are application of new endoscopic imaging and therapeutic technique to management of gastrointestinal cancers and establishment of efficient training of advanced endoscopic procedures. He has published 220 articles (PubMed) and now serves as an associated editor of Endoscopy International Open, Digestive Endoscopy and Annals of Gastroenterology.



Professor Philip Wai Yan, CHIU

MD (CUHK), MBChB (CUHK), FRCSEd, FCSHK, FHKAM (Surgery) Department of Surgery, Institute of Digestive Disease, The Chinese University of Hong Kong

Philip Chiu is Professor of Division of Upper GI and Metabolic Surgery, Department of Surgery; Director of Shaw Endoscopy Center, Institute of Digestive Disease; Director of CUHK Jockey Club Minimal Invasive Surgical Skills Center; Director of CUHK Chow Yuk Ho Technology Center for Innovative Medicine and Assistant Dean (Institutional Affairs), Faculty of Medicine, Chinese University of Hong Kong. Prof. Chiu was the first to perform endoscopic submucosal dissection (ESD) for treatment of early GI cancers and in 2010, he performed the first Per-oral Endoscopic Myotomy (P.O.E.M.). His research interests include upper gastrointestinal bleeding, oesophageal cancer and minimally invasive and robotic oesophagectomy, novel endoscopic technologies for diagnosis of early GI cancers, ESD and novel endoscopic procedures as well as Natural Orifices Transluminal Endoscopic Surgery (NOTES). He has published more than 200 peer reviewed manuscripts and four book chapters.





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