Jurgensen C et a. EUS-guided alcohol ablation of an insulinoma. Gastrointest Endosc. 2006;63:1059-62.

TOWARDS THE FUTURE

Carrara S et al. Endoscopic ultrasound-guided application of a new hybrid cryotherm probe in porcine pancreas: a preliminary study. Endoscopy 2008;40:321-6.

Diagnostic imaging of pancreatic NETs: "take home message" 1

- To date the predominants imaging modalities for pancreatic endocrine tumors are CE spiral CT, EUS and SRS (Octreoscan). They provide the most cost-effective and accurate means for detecting/diagnosing and staging most cases of pancreatic NETs

- **in case of a suspected pancreatic lesion CE MDR-CT remains the first staging method of choice. It has replaced DSA and has achieved similar or only slightly lower accuracy than EUS in detecting pancreatic tumors**

- EUS had the highest accuracy in assessing tumor size and lymph node involvement and remains the first choice in diagnosis of small tumors

Diagnostic imaging of pancreatic NETs: "take home message" 2

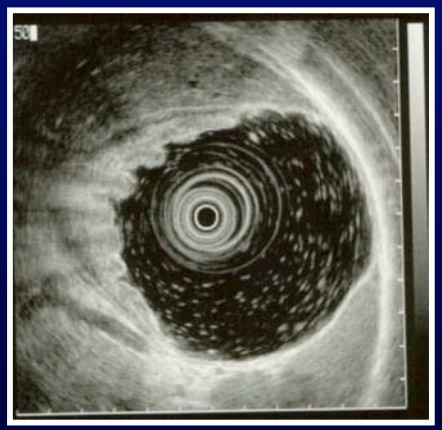
- EUS is highly accurate in the localization of pancreatic NETs and is cost effective when used early in the preoperative localization strategy. EUS decreases the need for additional invasive tests and avoid unnecessary morbidity and resource consumption.

- the choice of staging modalities clearly varies among different centers depending on the availability of the high-end imaging modalities and the local expertise.

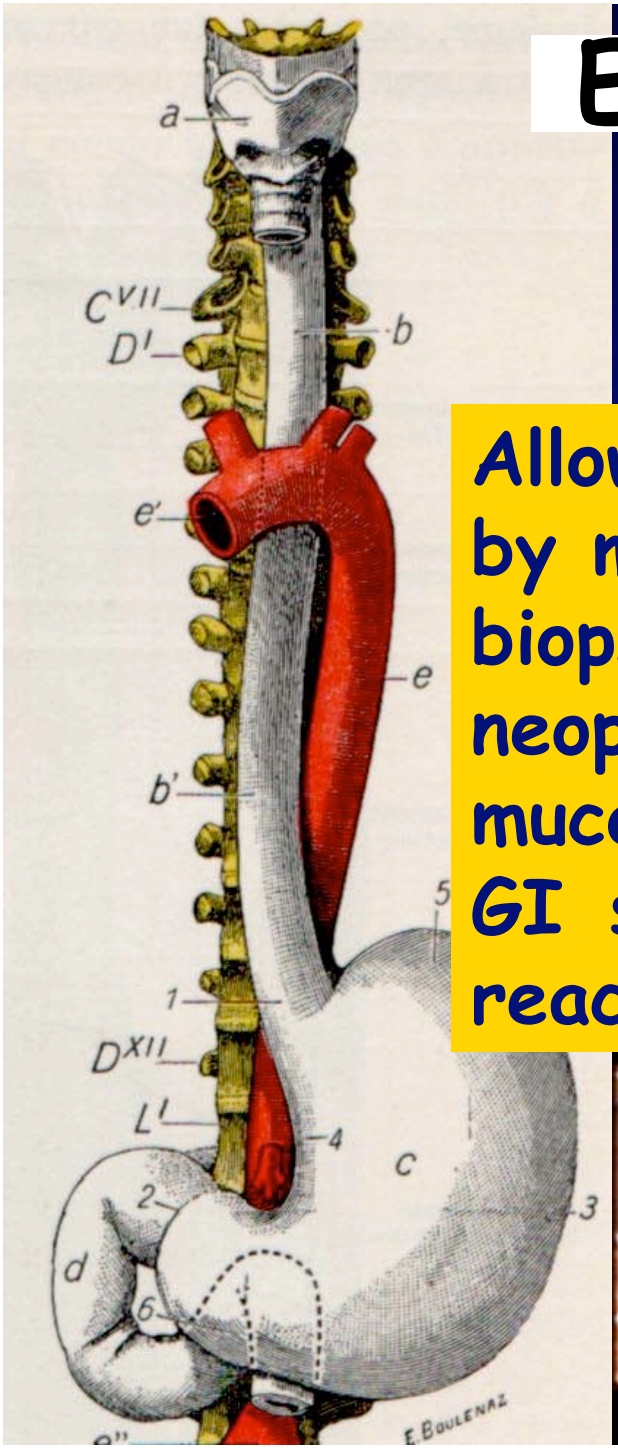
- Cyto- or Histological confirmation is warranted only **when the results can alter patient management** or prior to palliative CR-Therapies in pts not eligible for surgery or in DD of pancreatic masses

ENDOSCOPY AND EUS FOR THE DIAGNOSTIC MANAGEMENT OF GI WALL NETs (so-called CARCINOIDs)

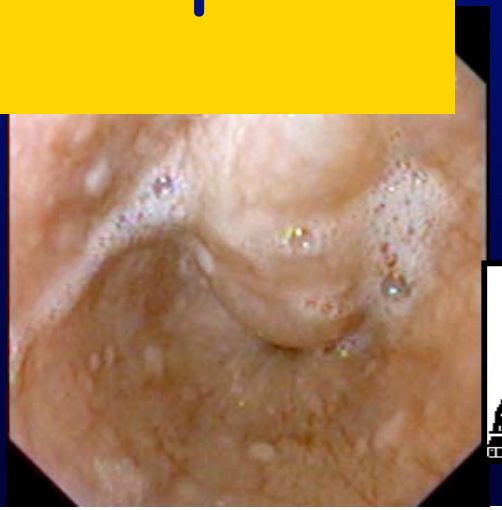
- Accurate diagnosis, localization and pre-operative staging are MANDATORY in order to offer the patient the best treatment (the best cost-benefit ratio in the single case)



ENDOSCOPY



Allow us to detect and diagnose, by means of targeted endoscopic biopsies, neuro-endocrine neoplasias localized in the mucosa and submucosa of all the GI sites that an endoscope can reach



We can see up to .....

- gastroscopy

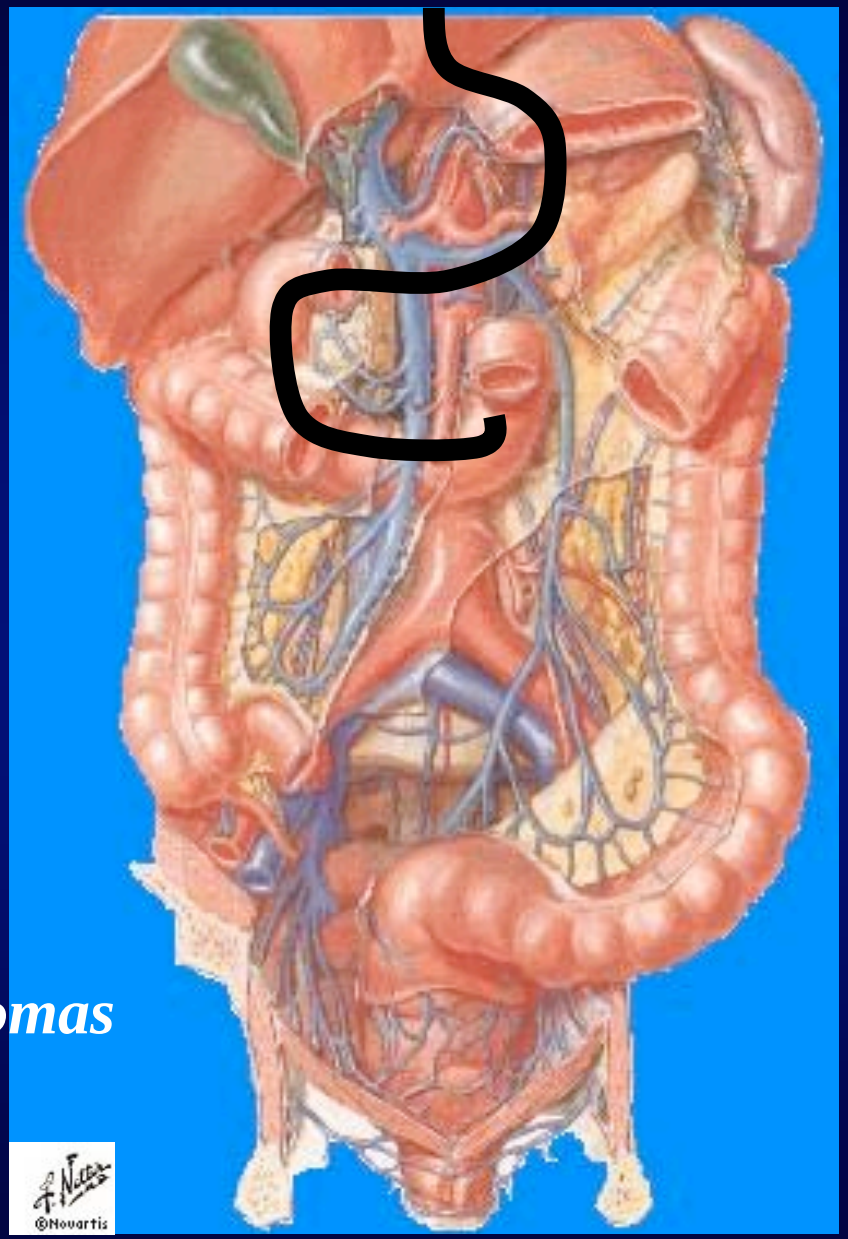
Carcinoids

Gastrinomas

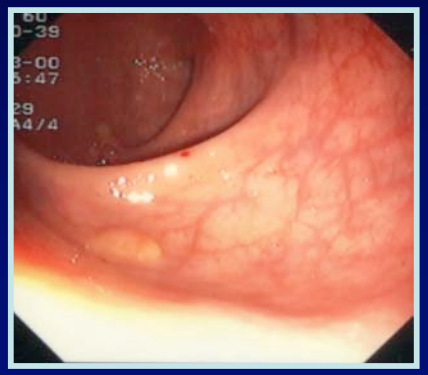
Somatostatinomas

Insulinomas

Vipomas,GRFomas, Glucagonomas, PPomas, Non functioning Tumors



We can see up to.....

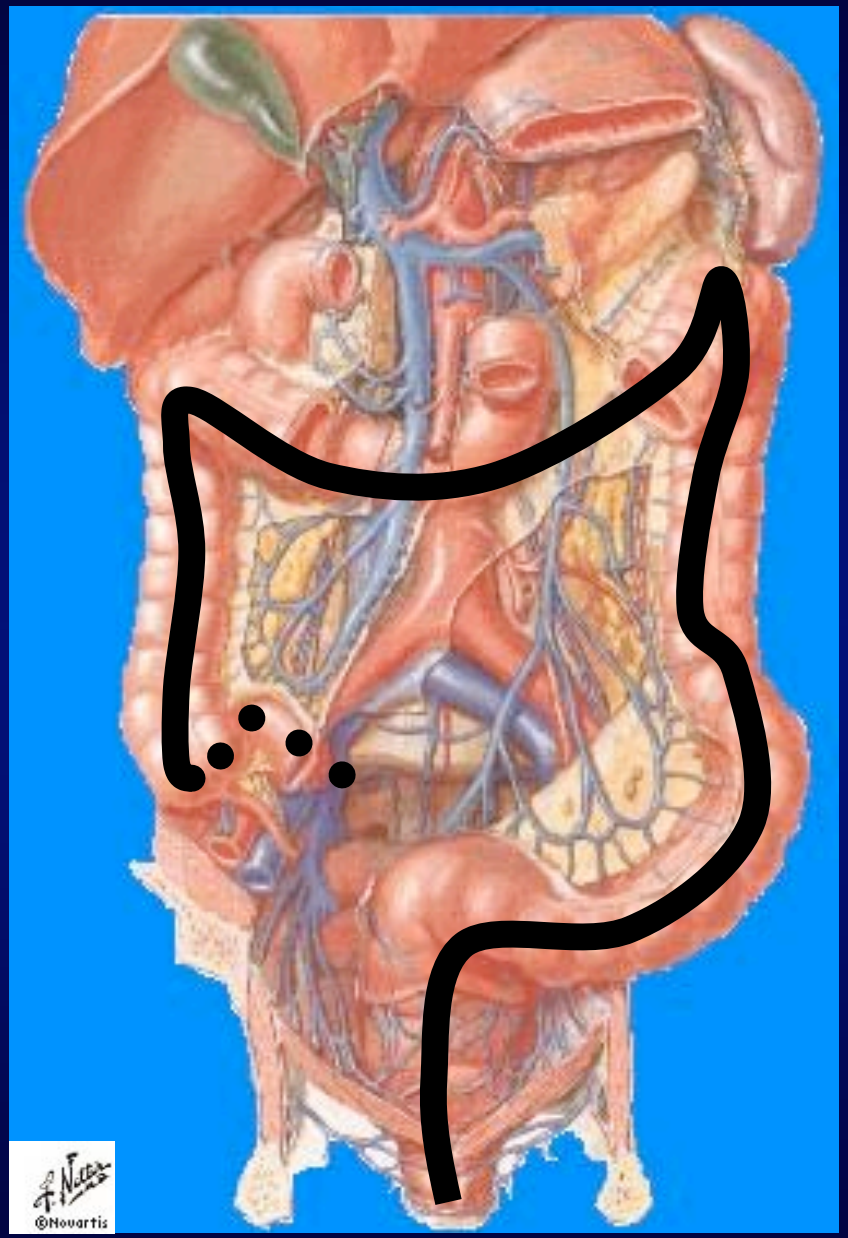


- colonscopy

Carcinoids

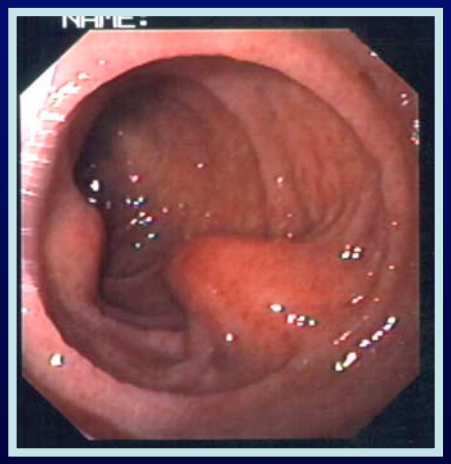
Somatostatinomas

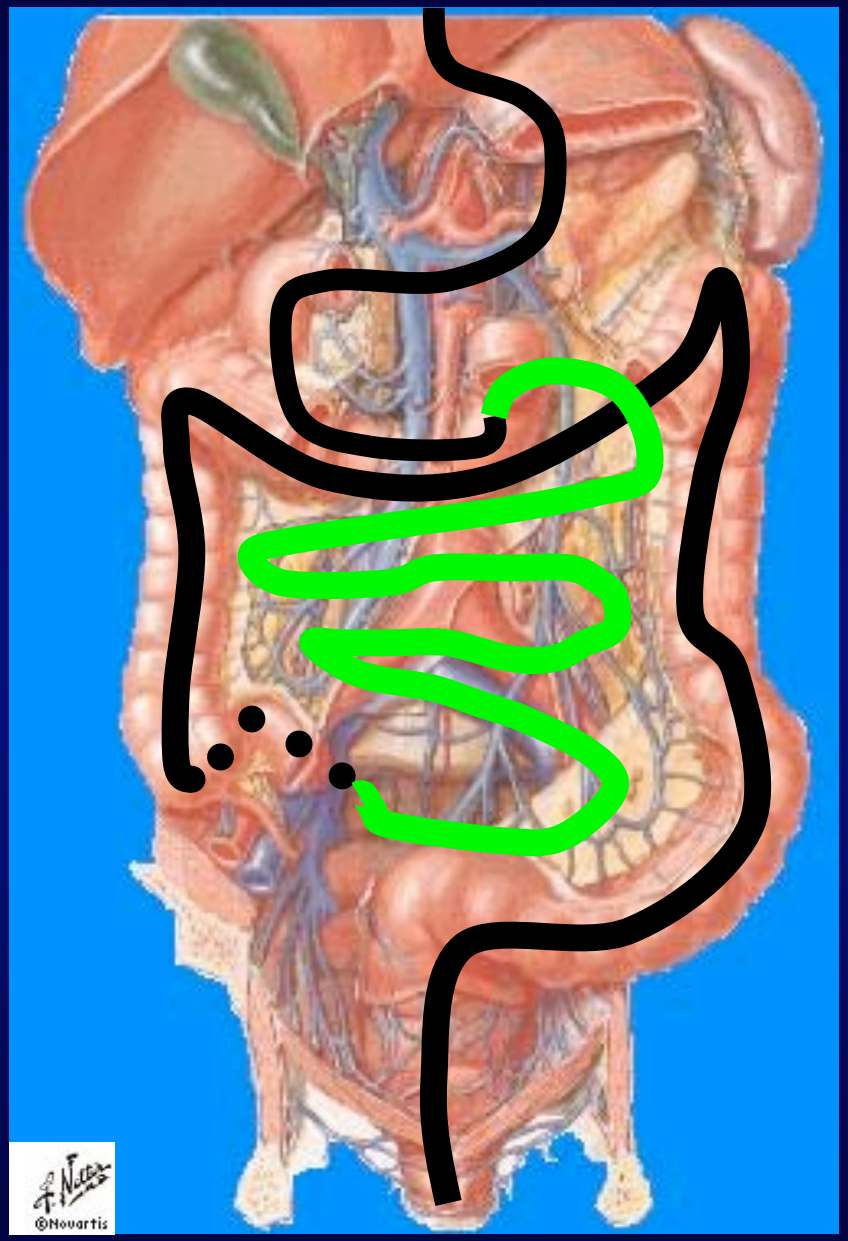
Enteroglucagonomas



We can see
up to.....

- enteroscopy

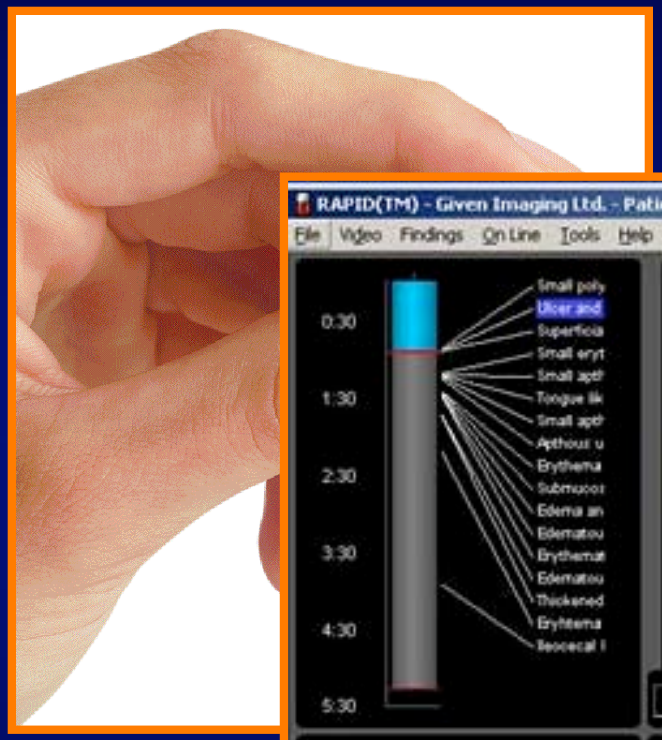


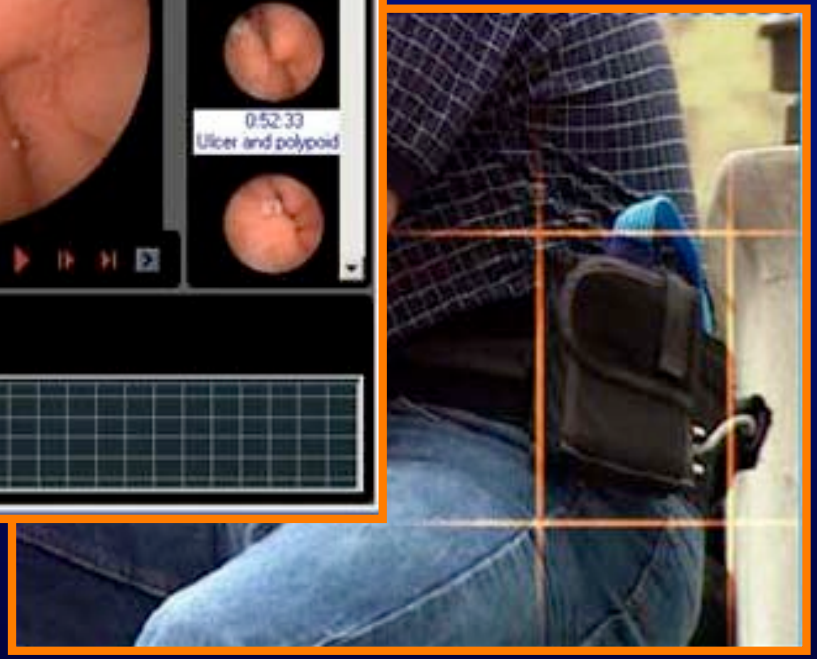


"PUSH-TYPE" ENTEROSCOPY

INTRA-OPERATIVE OR LAPAROSCOPICALLY-ASSISTED ENTEROSCOPY

VIDEO CAPSULE





EUS ITALIAN CLUB

Mouth to Cecum (or..to anum)

Teeth

Epiglottis

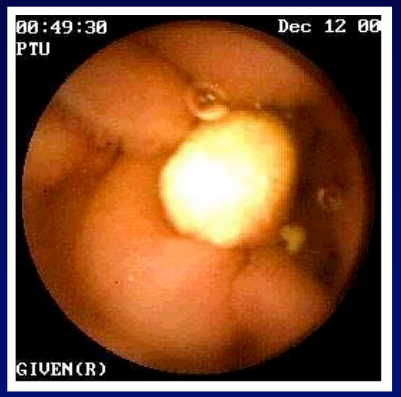
Multiple telangiectasia on a gastric fold

Small Intestine

Ileocecal valve

Wall of right colon

VIDEO CAPSULE: LIMITs



1. *Recorded images: impossible to wash the field, come back on a doubtful point, change vision angle etc.*
2. *Movements sometimes too fast: you can miss also big lesions*
3. *No operative capabilities both diagnostic and therapeutic*
4. *Contraindicated in case of stenosis*

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VIDEO CAPSULE: LIMITs

Unsuitable in case of stenoses, extensive adhesions, history of small bowel resection

or, as in the case of carcinoid tumors with retracted mesentery, should be sed with caution or preceded by the "patency capsule"

(an ingestible and dissolvable, a disintegration time-controlled capsule with an external scanner)

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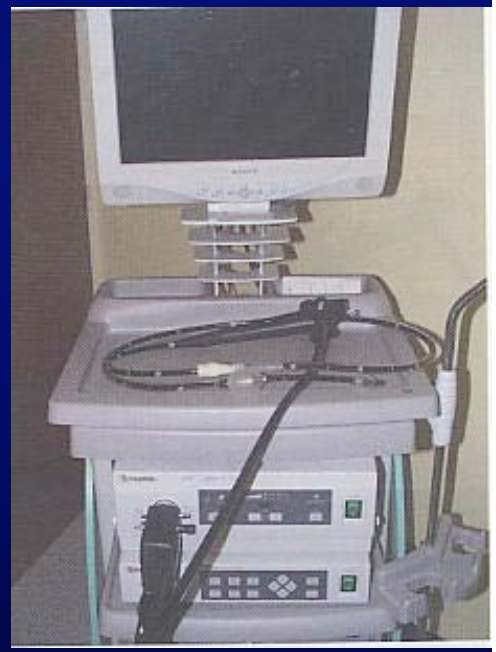
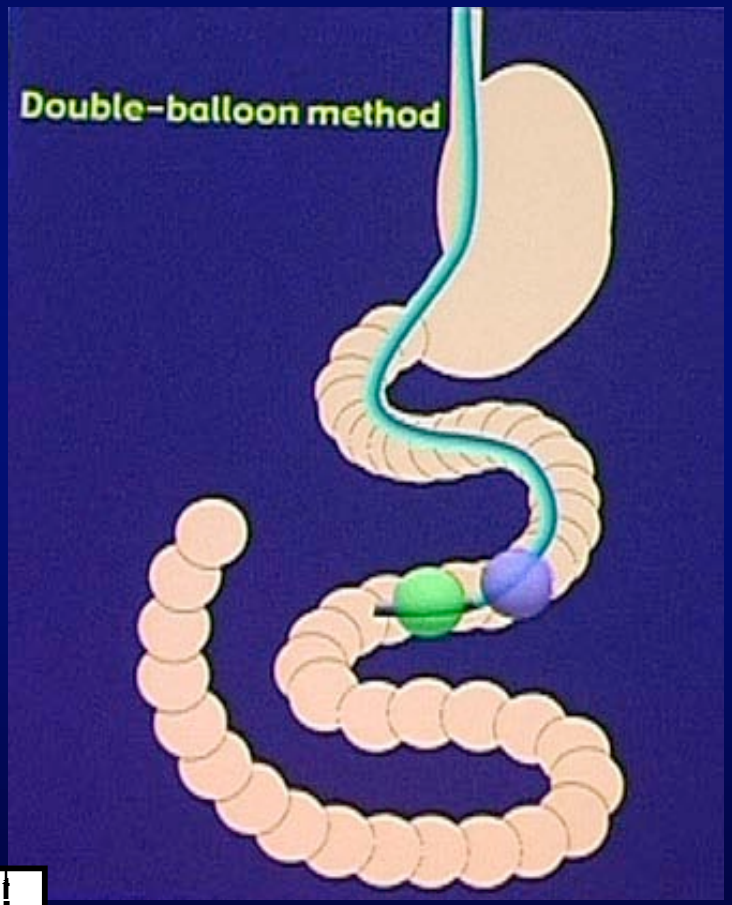
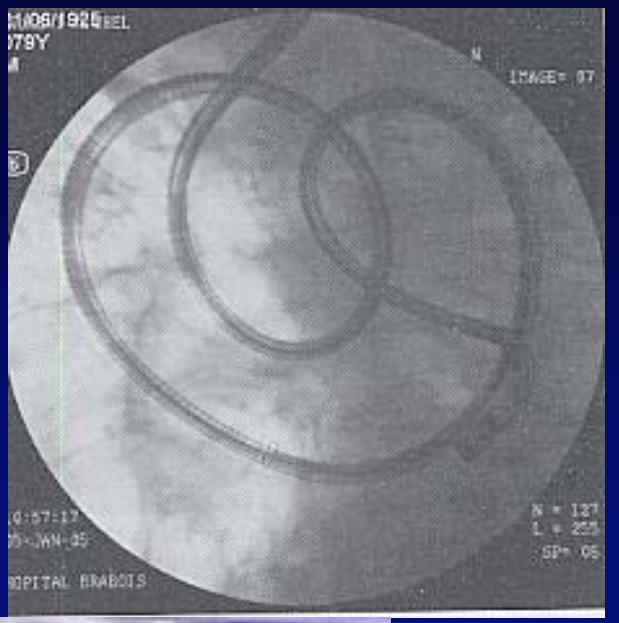
DOUBLE-BALLOON ENTEROSCOPY

Today the double-balloon enteroscopy and more recently the single balloon, allow us, with time-consuming and invasive examinations, mostly with double approach (oral and anal), to endoscopically visualize, biopsy and, in selected cases, to treat lesions all over the small intestine



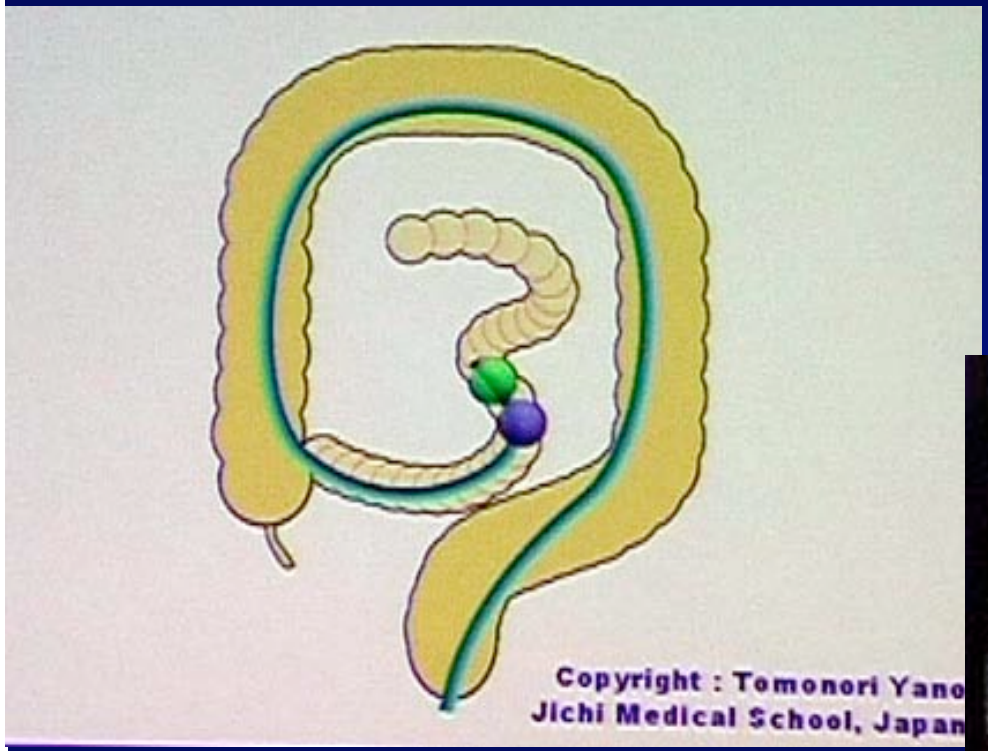
DOUBLE-BALLOON ENTEROSCOPY

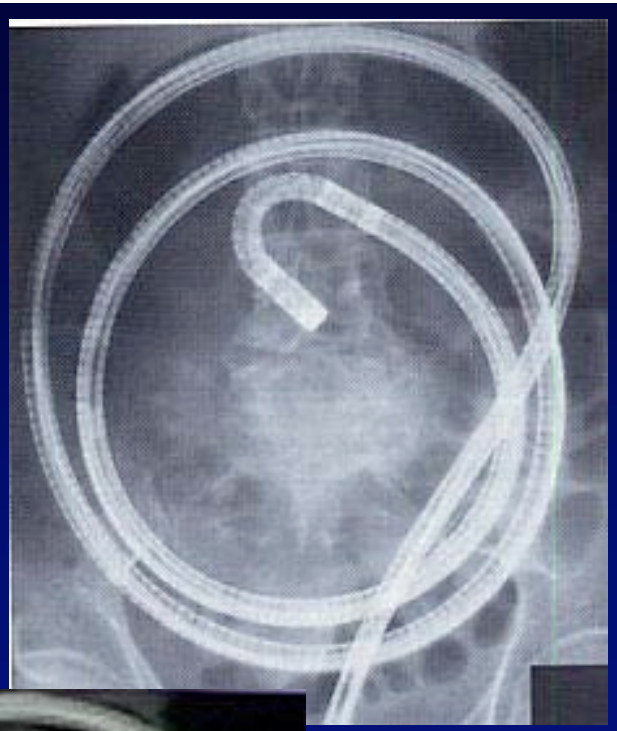




Courtesy of Prof. H. Yamamoto

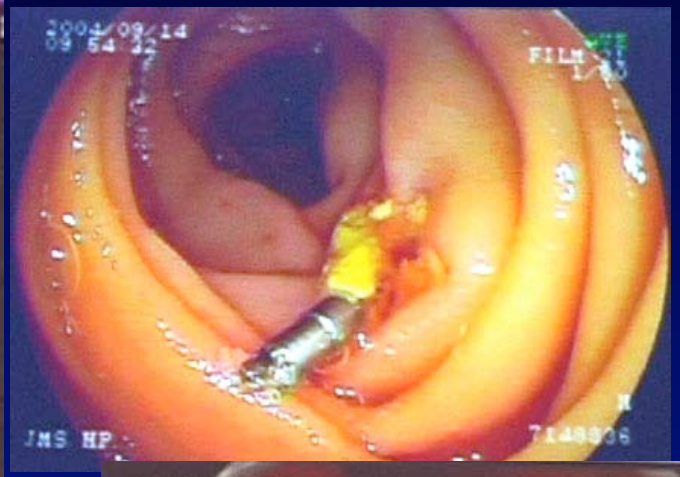
DOUBLE-BALLOON ENTEROSCOPY

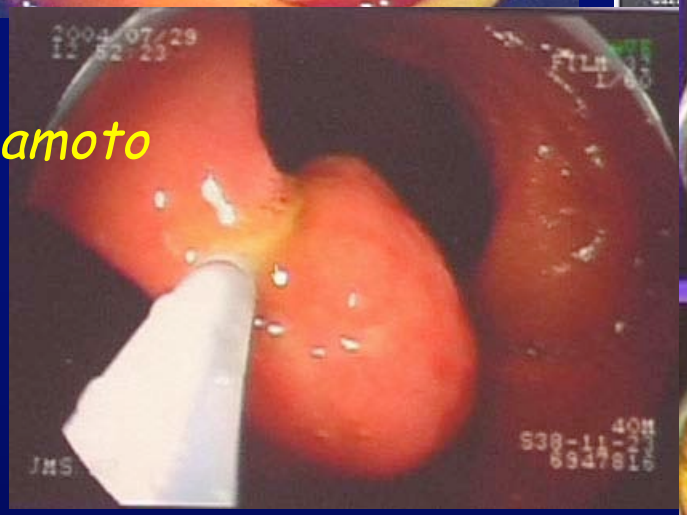


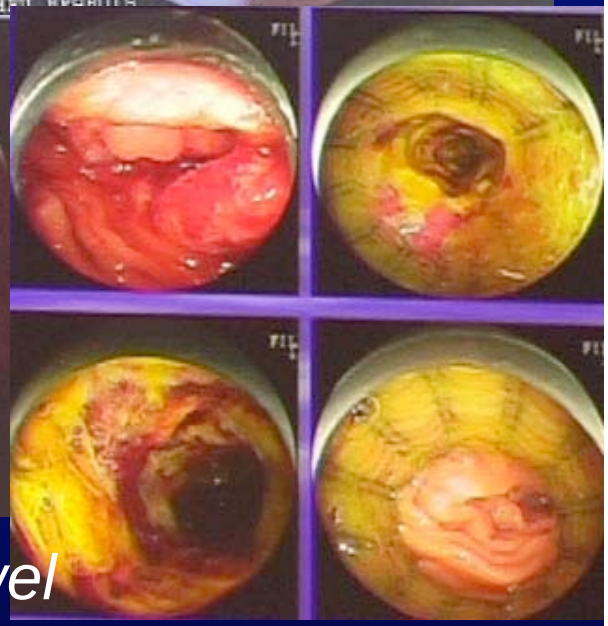


Courtesy of Prof. H. Yamamoto

DOUBLE-BALLOON ENTEROSCOPY







Courtesy of Prof. H. Yamamoto

Neuroendocrine tumors of the small bowel appear as subepithelial lesions, mostly yellowish, that can be ulcerated when they exceed 2 cm

ENTEROSCOPY (wireless and balloon endoscopy)

Preliminary studies seem to demonstrate some potential in detection and diagnosis of small bowel carcinoids.

2 papers compared video capsule endoscopy vs CT/enteroclysis:

1. One fails to demonstrate better results with video capsule.

Johanssen S et al. The yield of wireless capsule endoscopy in the detection of neuroendocrine tumors in comparison with CT enteroclysis. Gastrointest Endosc. 2006; 63(4):660-5.

2. Video capsule detected 9 small bowel NETs that were not visualized after CT and enteroclysis.

van Tuyl SA et al. Detection of small-bowel neuroendocrine tumors by video capsule endoscopy. Gastrointest Endosc. 2006; 64(1):66-72

ENTEROSCOPY (wireless and balloon endoscopy)

Preliminary studies seem to demonstrate some potential in detection and diagnosis of small bowel carcinoids.

1. ***Double or single balloon enteroscopy should be useful in detecting and biopsy tiny NEts of the small intestine, more frequently in the ileum***
2. ***but so far only few literature data ****

*Yamaguchi Tet al. Multiple carcinoid tumors of the ileum preoperatively diagnosed by enteroscopy with the double-balloon technique.
Gastrointest Endosc. 2005;62(2):315

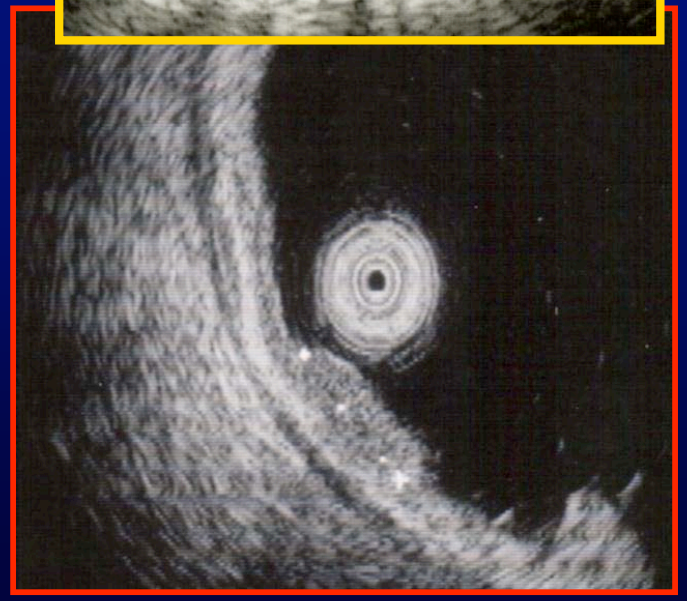
*Scherübl H et al. Double-balloon enteroscopy for the detection of midgut carcinoids. Gastrointest Endosc. 2005;62(6):994.

Hystological confirmation of a diagnosis suspected with a video capsule and/or curative endoscopic resection when facing small superficial lesions, limited to mucosa and submucosa, as in other GI sites

Yamagishi H et al. Endoscopy. 2007;39 Suppl 1:E243-4.

ENDOSONOGRAPHY (EUS)

- Can visualize the layers of the GI wall (5-9), allowing to identify also tiny lesion (2-3 mm) and to accurately stage the depth of wall invasion and/or the locoregional nodal involvement



WHAT YOU CAN ASK TO THE ENDOSCOPIST ?

- To identify/ detect the lesion (DIAGNOSIS AND LOCALIZATION)
- To stage the lesion (prognostic evaluation) (STAGING)

To treat the lesion (THERAPY)

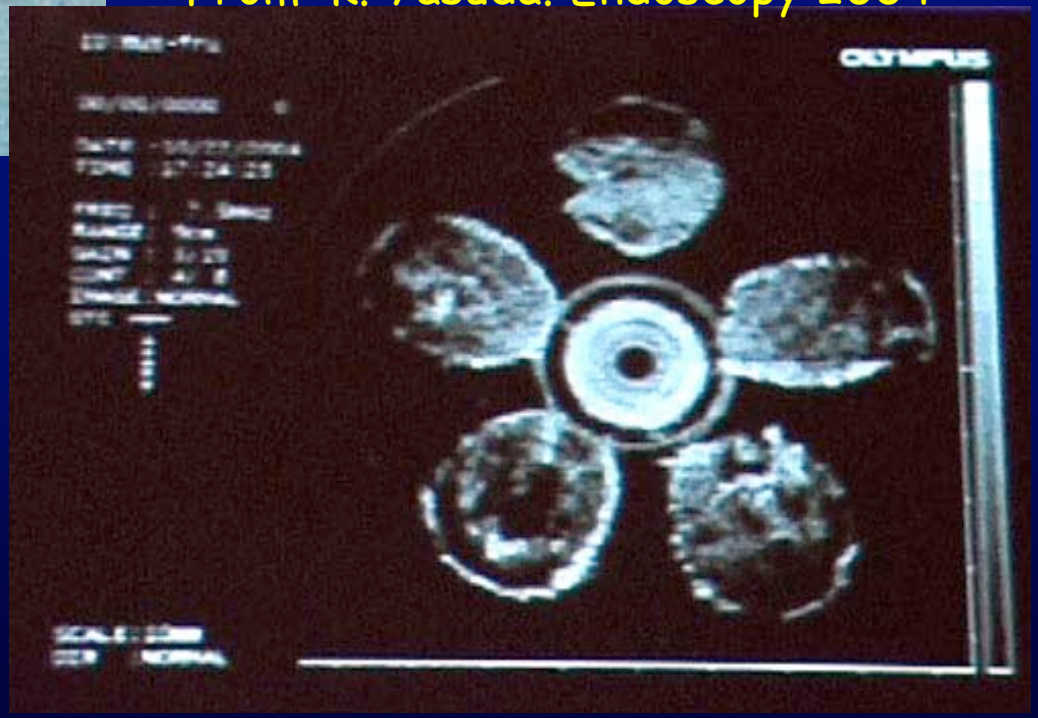
EUS IN THE ASSESSMENT OF GI TRACT NETs

- Locoregional staging of lesions localized in the wall of the esophagus, stomach, duodenum and colon-rectum, already identified and diagnosed by means of endoscopic biopsies

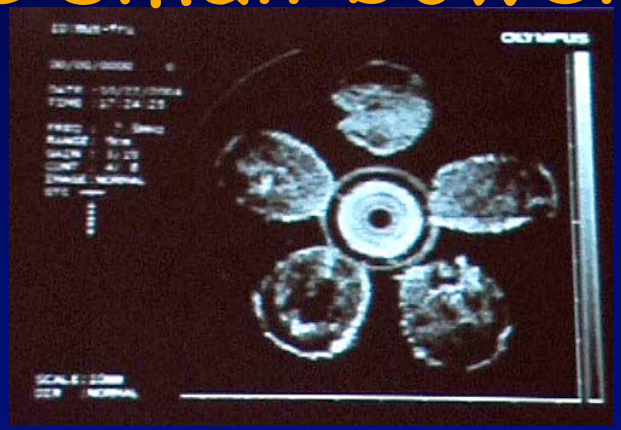
- Localization of submucosal lesions endoscopically invisible (i.e. duodenal gastrinomas), even of 2 mm in diameter

and …. what about the rest of the small bowel?

From K. Yasuda. Endoscopy 2004



and …. what about the rest of the small bowel?



From K. Yasuda. Endoscopy 2004

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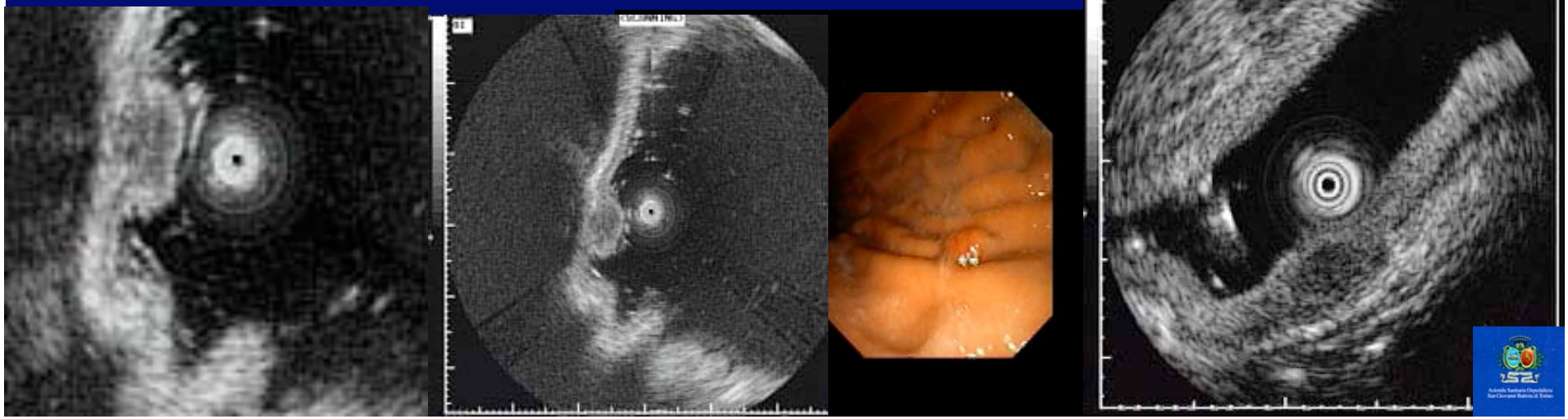
and …. what about the rest of the small bowel?

Today is also possible, with the new balloon endoscopes, to evaluate and stage, by means of miniprobes, NETs of the small bowel, so far ***beyond the grasp of*** *EUS*

Fukumoto A et al. Usefulness of EUS with double balloon enteroscopy for diagnosis of small bowel diseases. Gastrointest Endosc. 2007; 65: 412-420.

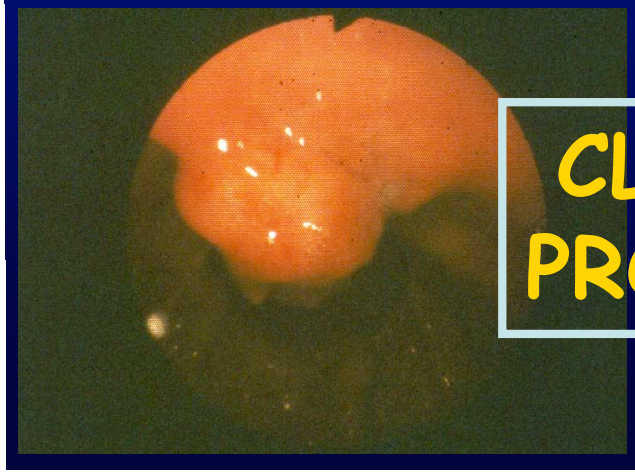
EUS IN THE ASSESSMENT OF GI TRACT NETs

- Hypo-echoic, round or oval, well demarcated lesions, mainly in the 2nd and 3rd wall layer, sometimes with transmural invasion of the GI wall

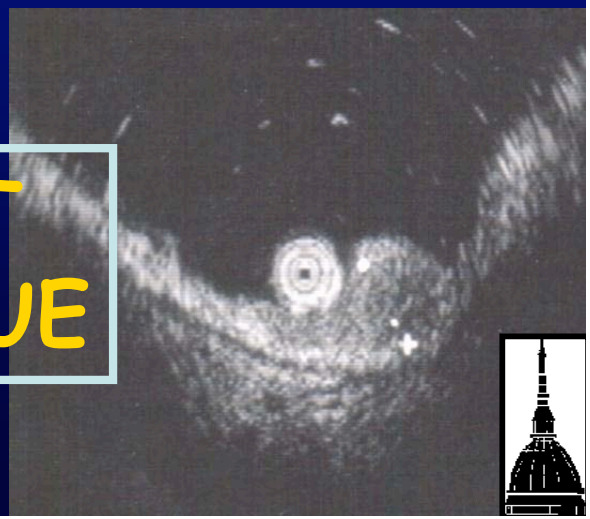


EUS IN THE ASSESSMENT OF GI TRACT NETs

- Preoperative EUS is mandatory for evaluating tumor size and depth of invasion; these features are considered to be important metastatic risk factors and the main determinants of appropriate therapy (endoscopic excision, local excision or radical resection)

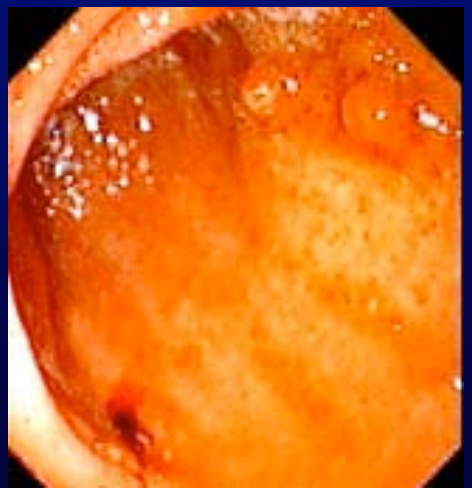


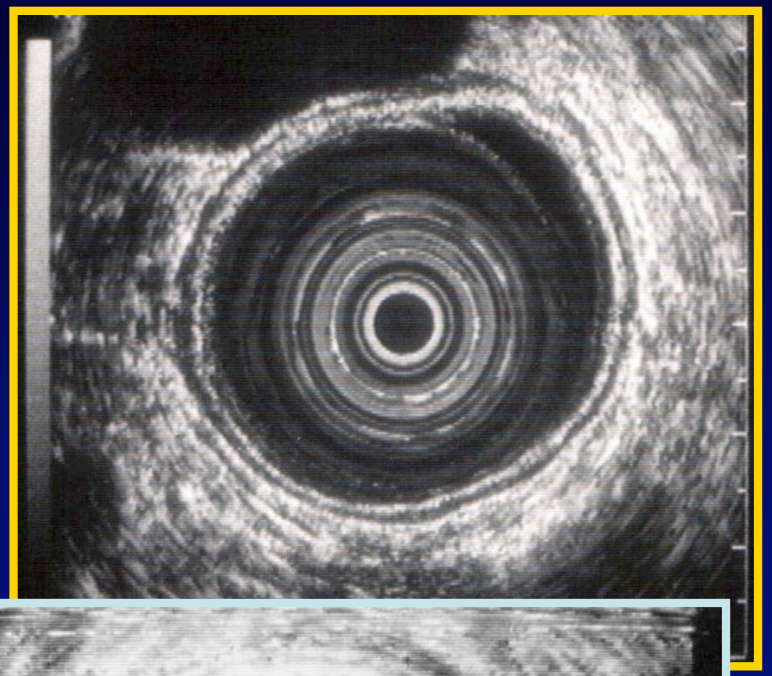
CLINICAL IMPACT
PROGNOSTIC VALUE

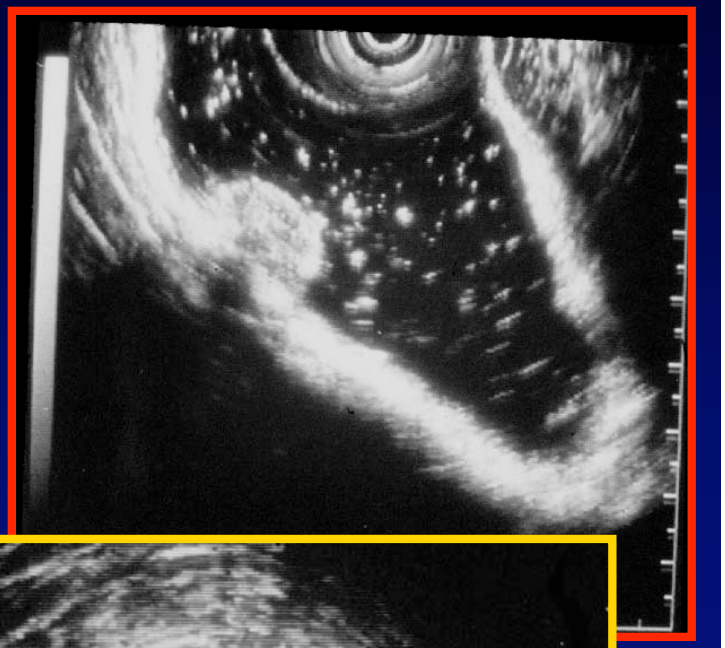


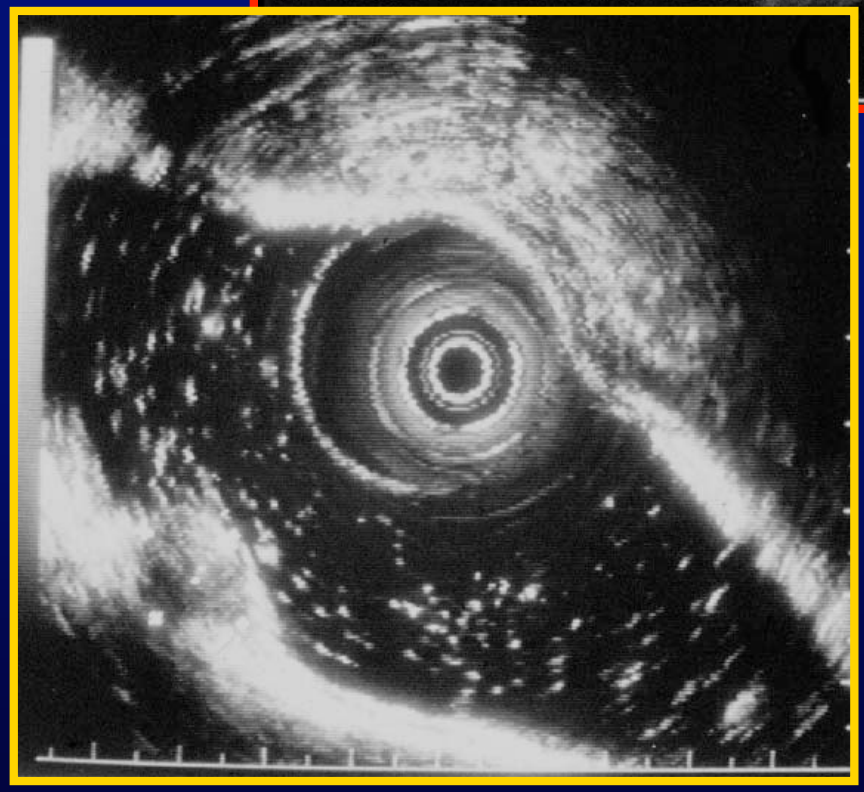
EUS IN THE ASSESSMENT OF GI TRACT NETs

1. To assess complete endoscopic resection
2. To follow-up patients









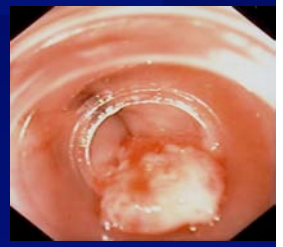
WHAT YOU CAN ASK TO THE ENDOSCOPIST ?

- To identify/ detect the lesion (DIAGNOSIS AND LOCALIZATION)
- To stage the lesion (prognostic evaluation) (STAGING)
- To treat the lesion (THERAPY)


DIAGNOSTIC ENDOSCOPY
GEP NEUROENDOCRINE TUMORS: THE ROLE OF ENDOSCOPIC TECHNIQUES
THERAPEUTIC ENDOSCOPY

GI TRACT NETs (carcinoids): ROLE OF ENDOSCOPIC TECHNIQUES

ENDO THERAPY = CURATIVE THERAPY



Mucosal and/or submucosal Tumors

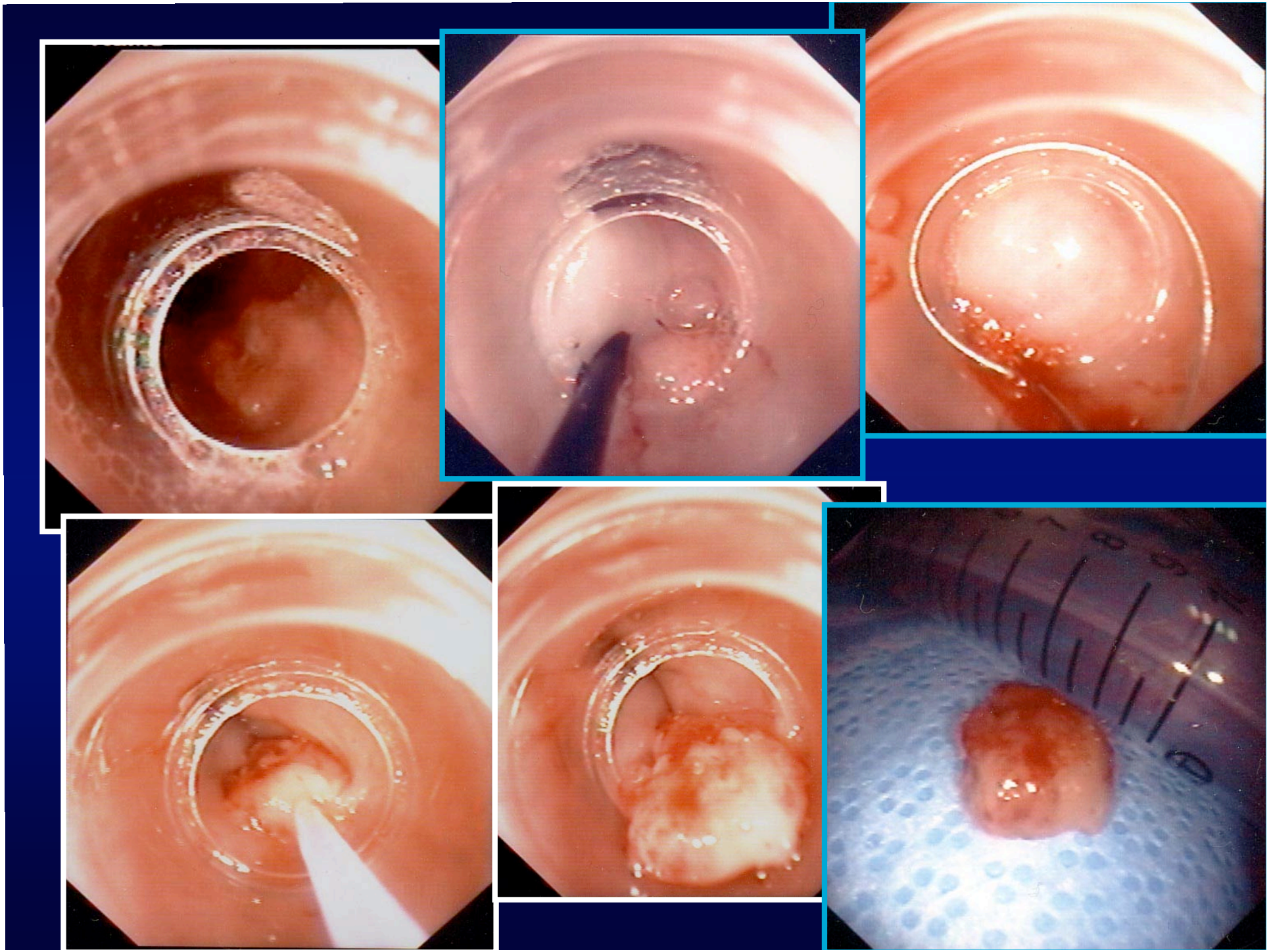
< 1 cm

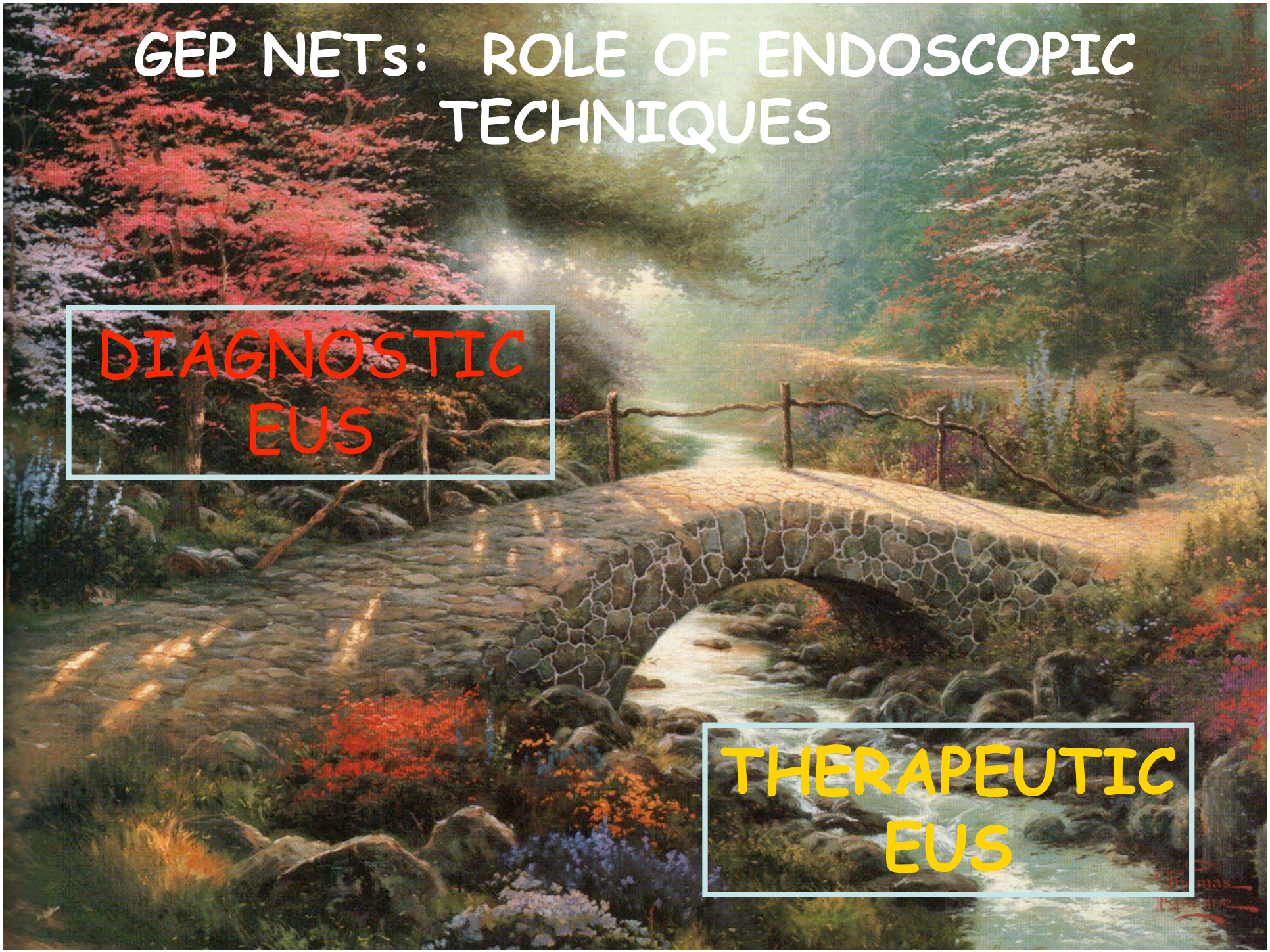
Esophagus
Stomach
Duodenum
Colon

< 1.5 cm

Rectum

Without NODAL involvement

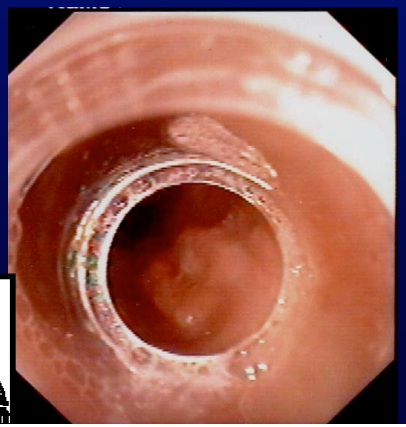
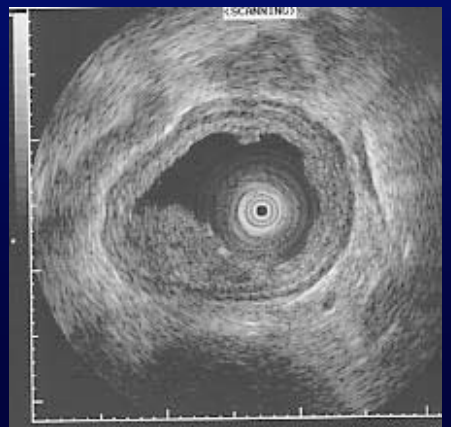
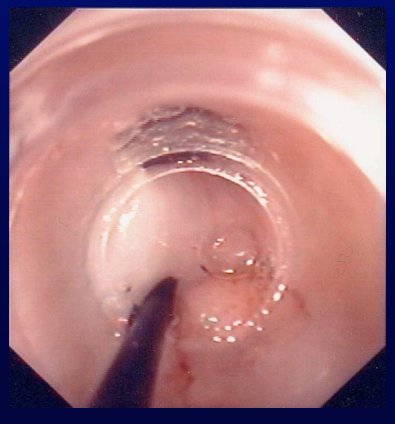
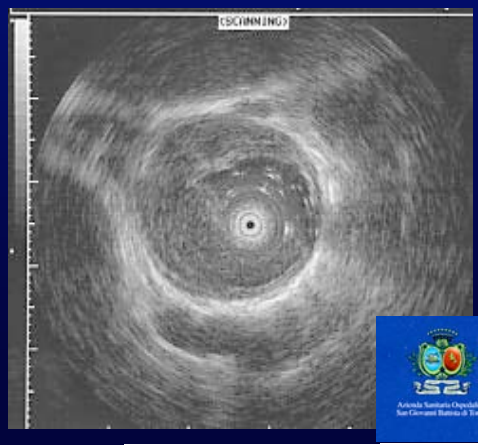



GEP NETs: ROLE OF ENDOSCOPIC TECHNIQUES
DIAGNOSTIC EUS
THERAPEUTIC EUS

High-frequency probe EUS-assisted endoscopic mucosal resection: A therapeutic strategy for submucosal tumors of the GI tract

(Waxman I et al. Gastrointest Endosc 2002)

"Carcinoid of the GI tract can be managed safely, quickly, and easily with HFPE-assisted EMR".

"Use of EUS-guided Injection in endoscopic resection of solid submucosal tumors"

Sun S et al. Endoscopy 2002

16 lesions; 9 in the muscolaris propria: no perforations; two bleedings endoscopically treated

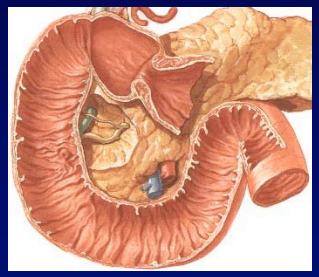
IS ENDOSCOPIC RESECTION SUFFICIENT?

stomach

Type I ACAG	• *ENDOSCOPIC RESECTION: max 5 tumors, < 10 mm* • > 5 tumors, < 10 mm: ANTRECTOMY • Diameter > 10 mm: antrectomy + surgical resection of the larger tumors • Serosal or extra-gastric involvement: total gastrectomy and lymphadenectomy
Tipo II MEN I	• ENDOSCOPIC RESECTION: TUMORS < 10 mm • SURGICAL RESECTION: TUMORS > 10 mm
Tipo III Sporadic	•ENDOSCOPIC RESECTION IS NEVER ADEQUATE

Study Group for Endocrine Abdominal Tumors Eur J Surg 1995; 161: 375

IS ENDOSCOPIC RESECTION SUFFICIENT?



duodenum

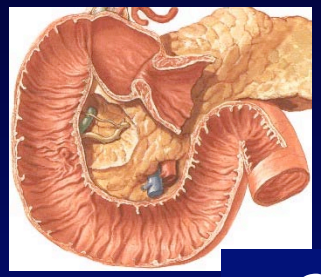
Endoscopic removal of duodenal carcinoids smaller than 1 cm that are located outside the periampullary region, with no EUS signs of invasion of the muscularis propria, is safe, patient-friendly, adequate and effective treatment.

Endoscopy 2004; 36: 651-5

EUS-assisted EMR of larger lesions has been reported

Pungpapong S et al. GIE 2006;63:703

IS ENDOSCOPIC RESECTION SUFFICIENT?



duodenum

- 99 pts with duodenal carcinoids < 10 mm:

  no one developped metastases.

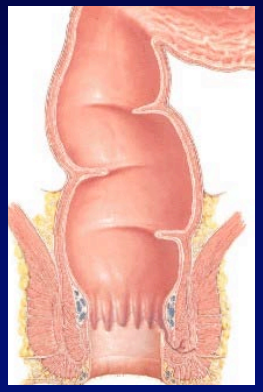
Arch Pathol Lab Med 1990; 114: 700-4

- Duodenal gastrinomas:

  77%: < 1 cm in diameter
  Nodal mts: 47%,
  Hepatic mts: 5%

Best Practice & Research Clinical Gastroenterology 2005; 19:675–697

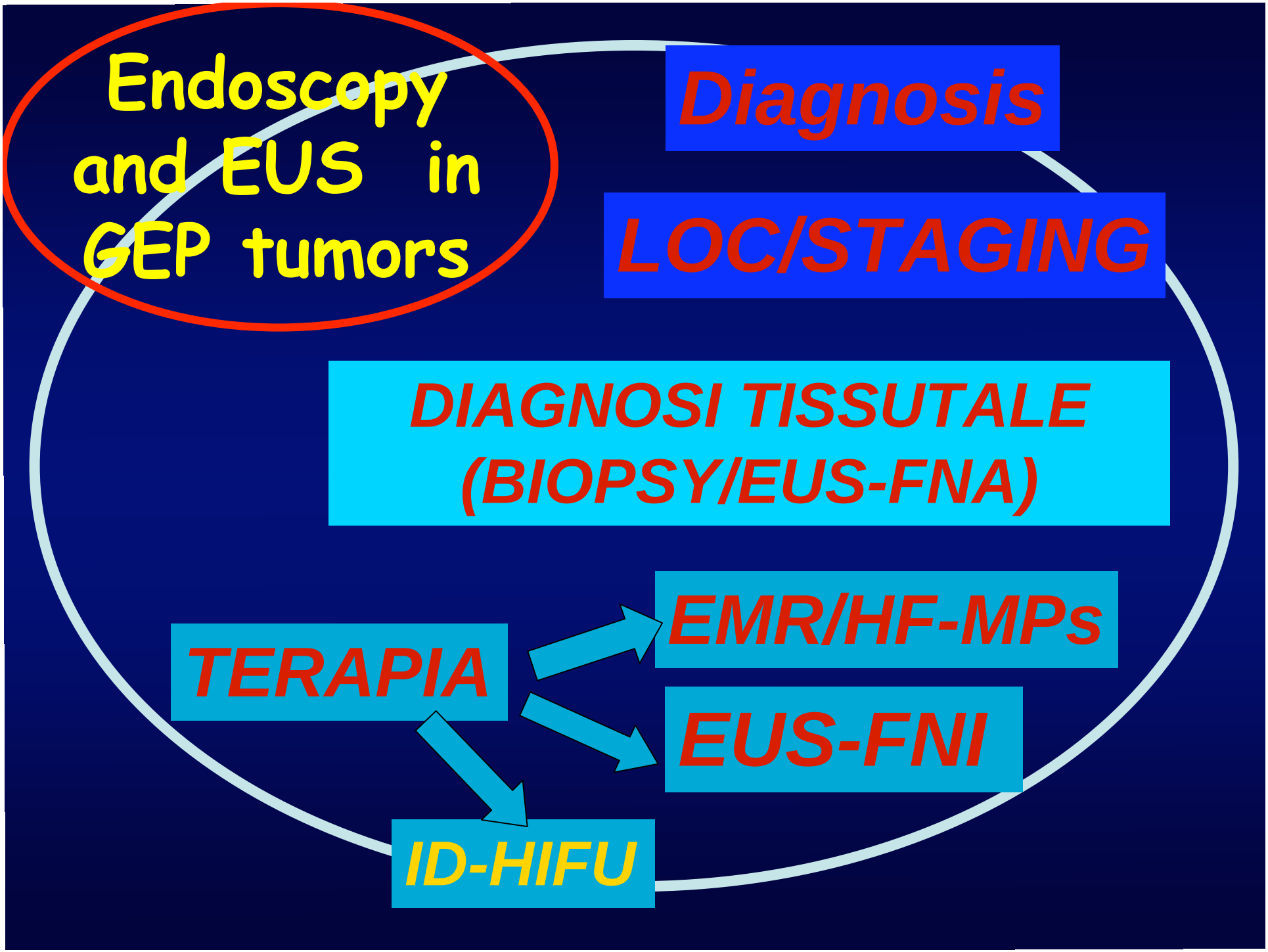
IS ENDOSCOPIC RESECTION SUFFICIENT?



rectum

Rectal carcinoid tumors that satisfy the following three conditions are indicated for local resection, including endoscopic polypectomy: a maximum diameter of 10 mm, no invasion of the muscularis propria, and no depression or ulceration in the lesion.

Dis Colon Rectum 2005; 48:285-91


Endoscopy and EUS in GEP tumors
Diagnosis
LOC/STAGING
DIAGNOSI TISSUTALE (BIOPSY/EUS-FNA)
TERAPIA
EMR/HF-MPs
EUS-FNI
ID-HIFU

"The future treatment of patients with NE tumors will be tumor-biology based and biotherapies will be tumor-targeted. With the advent of the new analogs and drugs every patients will get a "tailor-made" therapy"

adapted from: Oberg K. The Oncologist 1998;3:339

Requirements for a correct therapeutic approach:

- correct diagnosis and staging
- comprehension of the biological behaviour of the tumor
- multidisciplinary management

ASSESSMENT AND MANAGEMENT OF PATIENTS WITH SUSPECTED GEP NETs :

The ideal team (The dream team)

Expert Radiologist

EUS/endoscopy Expert

Radionuclear imaging Expert

Expert Pathologist

Dedicated surgeon

Expert Clinician

EGEUS European Group for Endoscopic Ultrasonography

EUS ITALIAN CLUB