Incontro del GIC
Tumori rari G.I.S.T. e N.E.T.
Torino, 15 novembre 2011

Il ruolo del Gastroenterologo per la diagnosi ed il trattamento dei NET.

Claudio G. De Angelis

Centro Tumori Neroendocrini e malattie del pancreas

Servizio di Endoscopia Digestiva

SCDU Gastroepatologia

Tumors arising from gut endocrine cells (the diffuse endocrine system,DES, of the gut) has been classified by experts of the WHO as endocrine tumors of the GI tract

As many as 15 highly specialized types

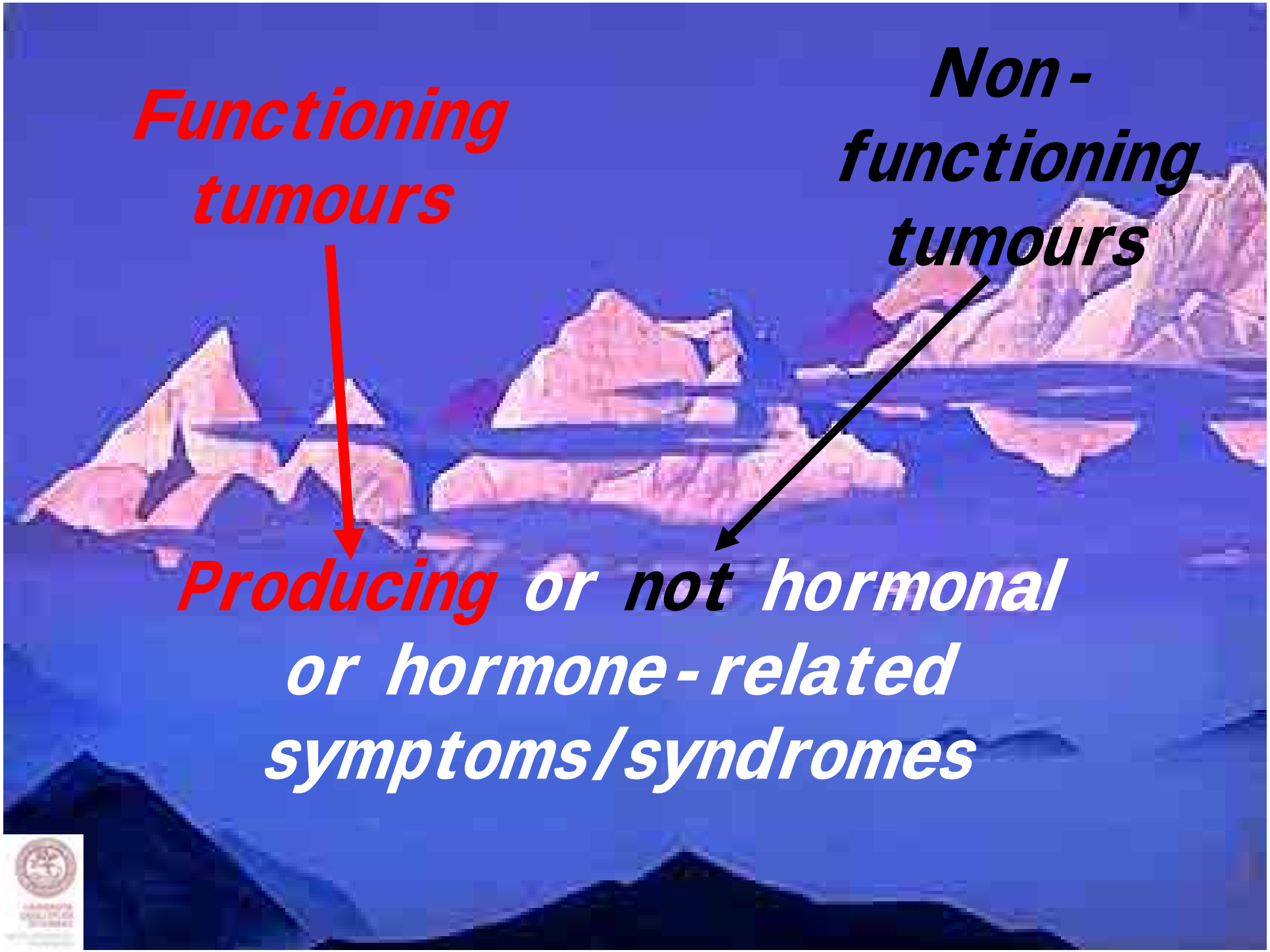
Endodermal origin

From local multipotent GI stem cells

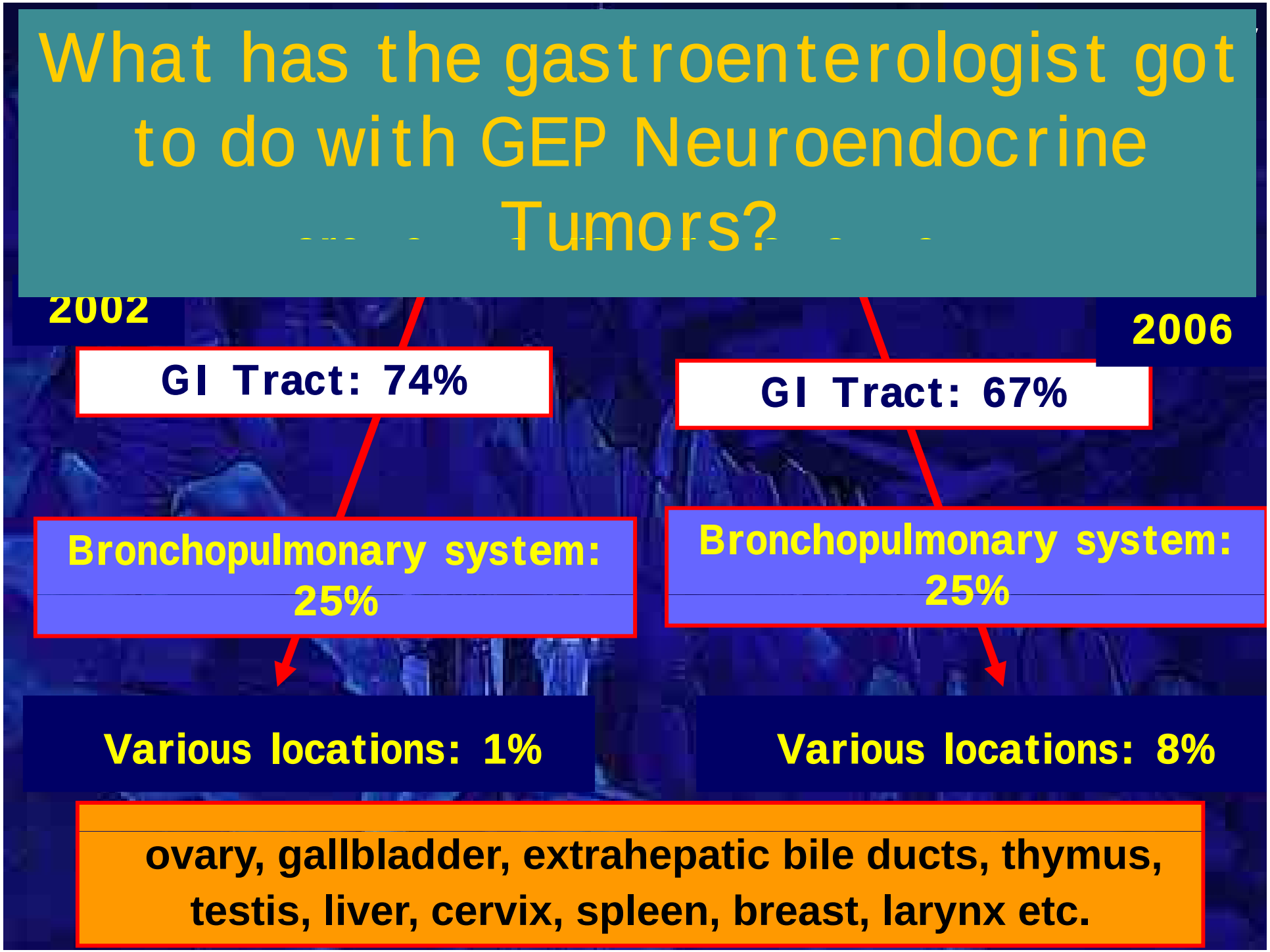
Usually divided in:

GI carcinoids

Pancreatic endocrine tumors


Functioning tumours
Non-functioning tumours
Producing or not hormonal or hormone-related symptoms/syndromes

What has the gastroenterologist got to do with GEP Neuroendocrine Tumors?



GEP (NEURO)-ENDOCRINE TUMORS:

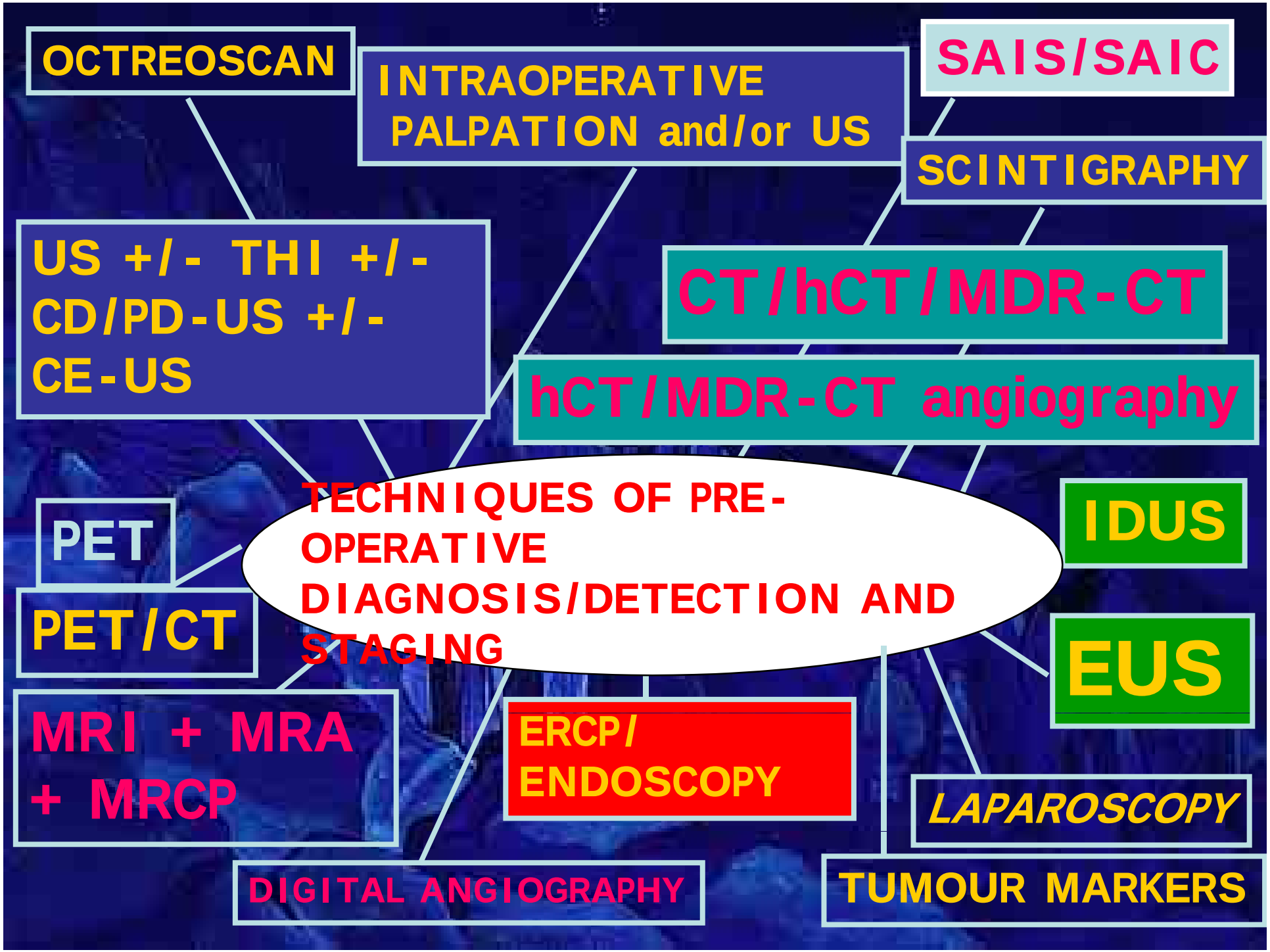
" A COMPLEX DILEMMA FOR DIAGNOSTIC IMAGING"

- **Small sizes:**

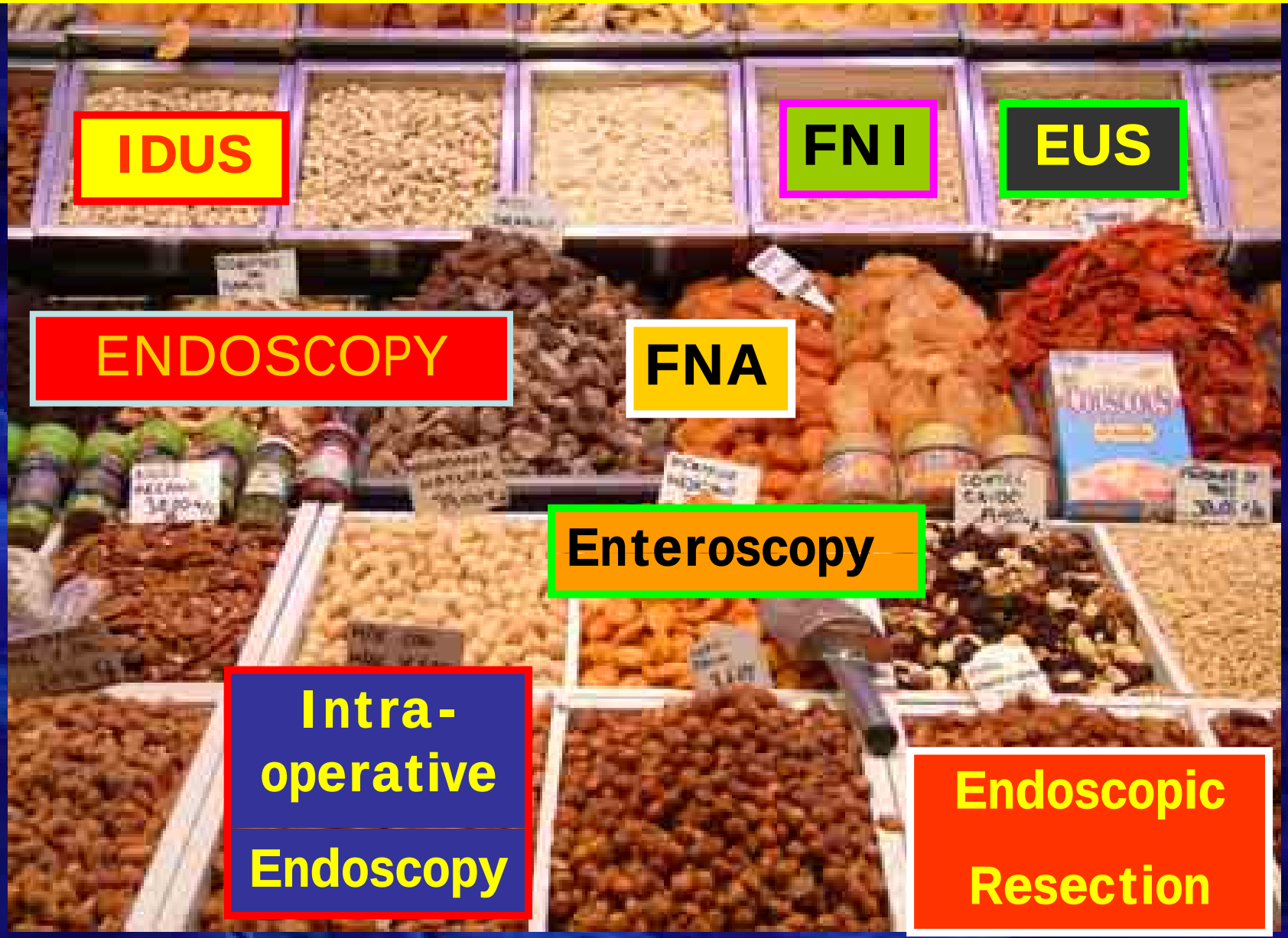
< 2 cm in 55-70% of insulinomas
< 1 cm in 38% of gastrinomas
< 1.5 cm (often) GI carcinoids
(< 1 cm: 80% of rectal carcinoids)

- **Profound site in the retroperitoneum, multiple and extrapancreatic locations**

- **Sometimes only submucosal location in the GI tract (e.g. gastrinomas)**


OCTREOSCAN
INTRAOPERATIVE PALPATION and/or US
SAIS/SAIC
SCINTIGRAPHY
US +/- THI +/- CD/PD-US +/- CE-US
CT/hCT/MDR-CT
hCT/MDR-CT angiography
TECHNIQUES OF PRE-OPERATIVE DIAGNOSIS/DETECTION AND STAGING
PET
PET/CT
IDUS
EUS
MRI + MRA + MRCP
ERCP/ ENDOSCOPY
LAPAROSCOPY
DIGITAL ANGIOGRAPHY
TUMOUR MARKERS

THE ENDOSCOPIST'S SHOP



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)

ENDOSCOPY AND ENDOSONOGRAPHY IN PRE-OPERATIVE DETECTION OF PANCREATIC NETs

- A correct pre-operative localization and staging are MANDATORY in order to select the right therapeutic options, optimize surgical treatment, reducing times and complexity of surgery:
  - IMPROVING RESULTS AND OUTCOMES

PANCREATIC NETs: THE ROLE OF ENDOSCOPIC TECHNIQUES

ERCP

Bile ducts

Carcinoids (0.3%)
Somatostatinomas (1.2%)

Ampulla

Somatostatinomas (9.3%)

Pancreas*

Insulinomas (99%)
Gastrinomas (33-79%)
Carcinoids (0.46%)
Glucagonomas (ca.100%)
Vipomas (90%)
Somatostatinomas (37.9%)
PPomas (92%)
Non-functioning (15-52%)

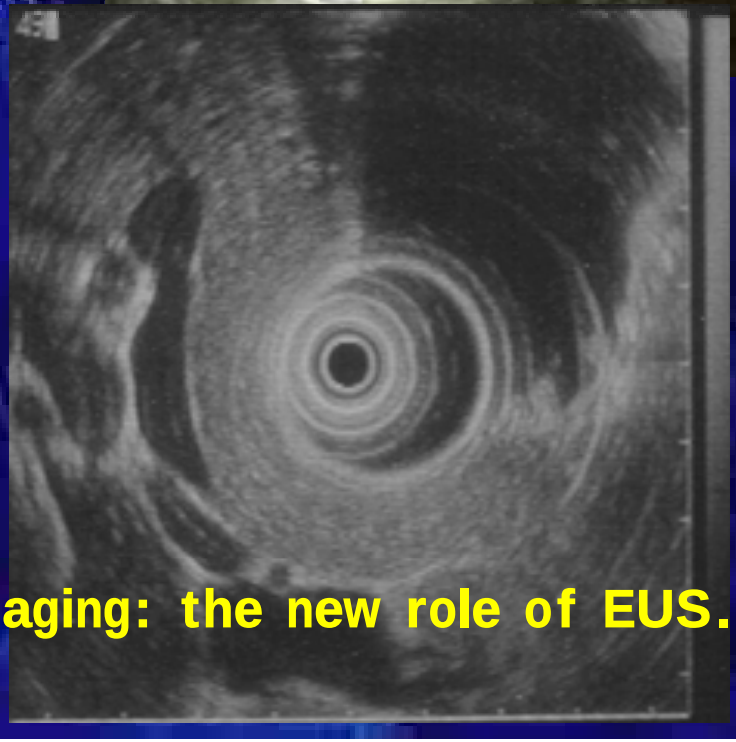
*Ogawa Y et al. Islet cell tumors of the pancreas: the diagnostic value of ERCP. Int J Pancreatol 6,1990

ENDOSCOPIC ULTRASOUND (EUS)

THE BEST CURRENTLY AVAILABLE TECNIQUE FOR IMAGING THE PANCREAS

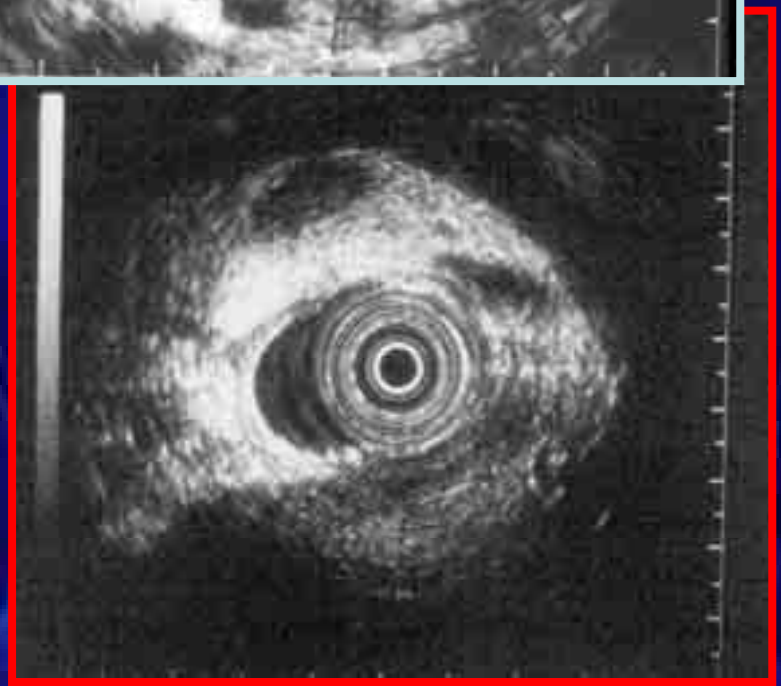
HIGH RESOLUTION IMAGES OF THE MAIN PANCREATIC DUCT AND SURROUNDING PARENCHYMA

STRUCTURES AS SMALL AS 2-3 MM CAN BE DISTINGUISHED



De Angelis C et al. Pancreatic cancer imaging: the new role of EUS. JOP J Pancreas (online) 2007;8 (1)


GASTROENTEROLOGIA PROF. VERME - TORINO



Endoscopic UltraSound (EUS)

- In several studies EUS demonstrated high sensitivity and specificity in detecting NETs of the pancreatico-duodenal area

	n. les.	Corr. Loc.%
• Palazzo et al. 1992 (multicentric)	23	78
• Rosch et al. 1992 (multicentric)	39	82
• Thomson et al. 1994	10	70
• Zimmer et al. 1994	18	88
• Ruszniewski et al. 1995 (2 centers)	19	89
• Schumacher et al. 1996	14	57 (H83/T37)
• De Angelis et al. 1999	42	79
• Anderson et al. 2000	54 (pts)	93

EUS AND PANCREATIC NETs

Pre-operative detection of NETs in the pancreas: comparison of EUS vs Other imaging techniques

Technique	N. of pts	Detection rate	
		lesions	%
EUS	19	20/23	86.7%
US	19	4/23	17.4%
CT	19	7/23	30.4%
MRI	8	3/12	25%
Angiography	11	4/15	26.6%
SRS	9	2/13	15.4%

De Angelis C et al. 1999

CLINICAL IMPACT OF EUS ON DECISION-MAKING AND MANAGEMENT OF PATIENTS WITH PANCREATIC NETs

- All considered EUS alone gave us more information than all other imaging techniques together

- It changed treatment plans in 17/39 (44%) of pts with NETs

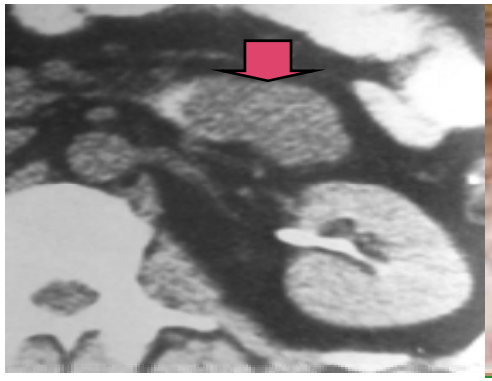
De Angelis C et al. 1999

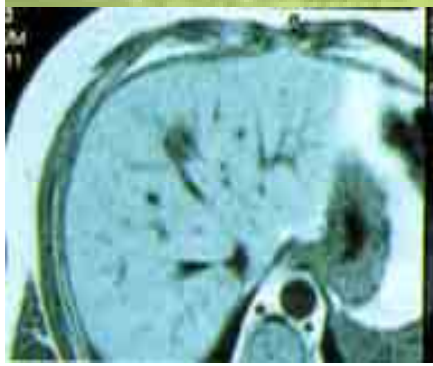
CLINICAL IMPACT OF EUS ON DECISION-MAKING AND MANAGEMENT OF PATIENTS WITH PANCREATIC NETs

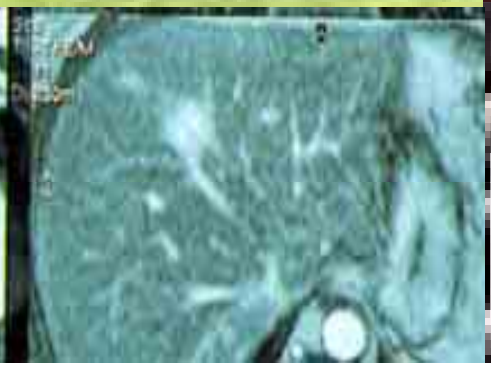
- Using EUS as first-line method for the detection of our NETs should have allowed a significant costs saving in **15/23 (65.2%) of** patients, avoiding both multiple and more invasive (like angiography in 50% of cases) and more expensive (like SRS in 45% or MRI in 32% of cases) diagnostic procedures

- Finally **6/39 patients (15.4%)** did not undergo a major surgical intervention based on the negative results of EUS examination

De Angelis C et al. 1999

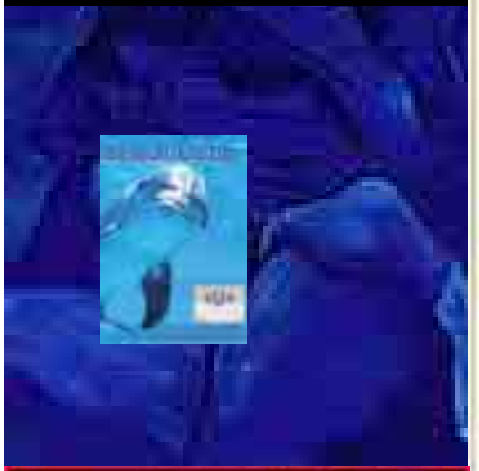


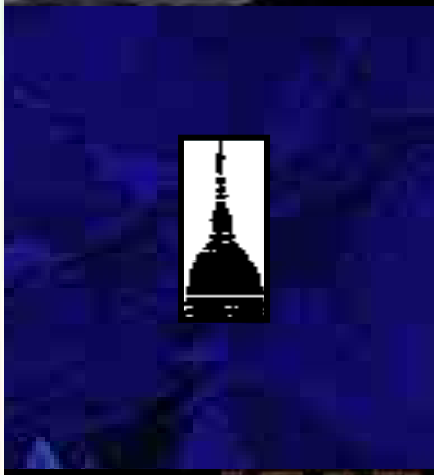


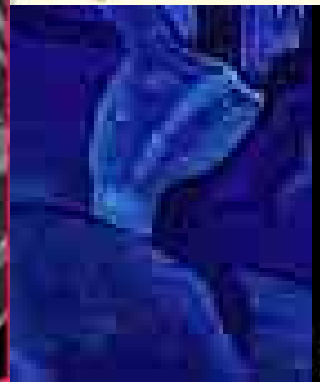


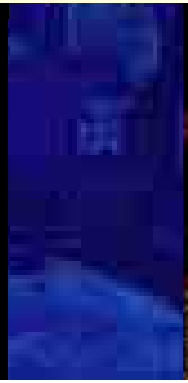

JUMP!

EGEUS
European Group
for Endoscopic
Ultrasonography

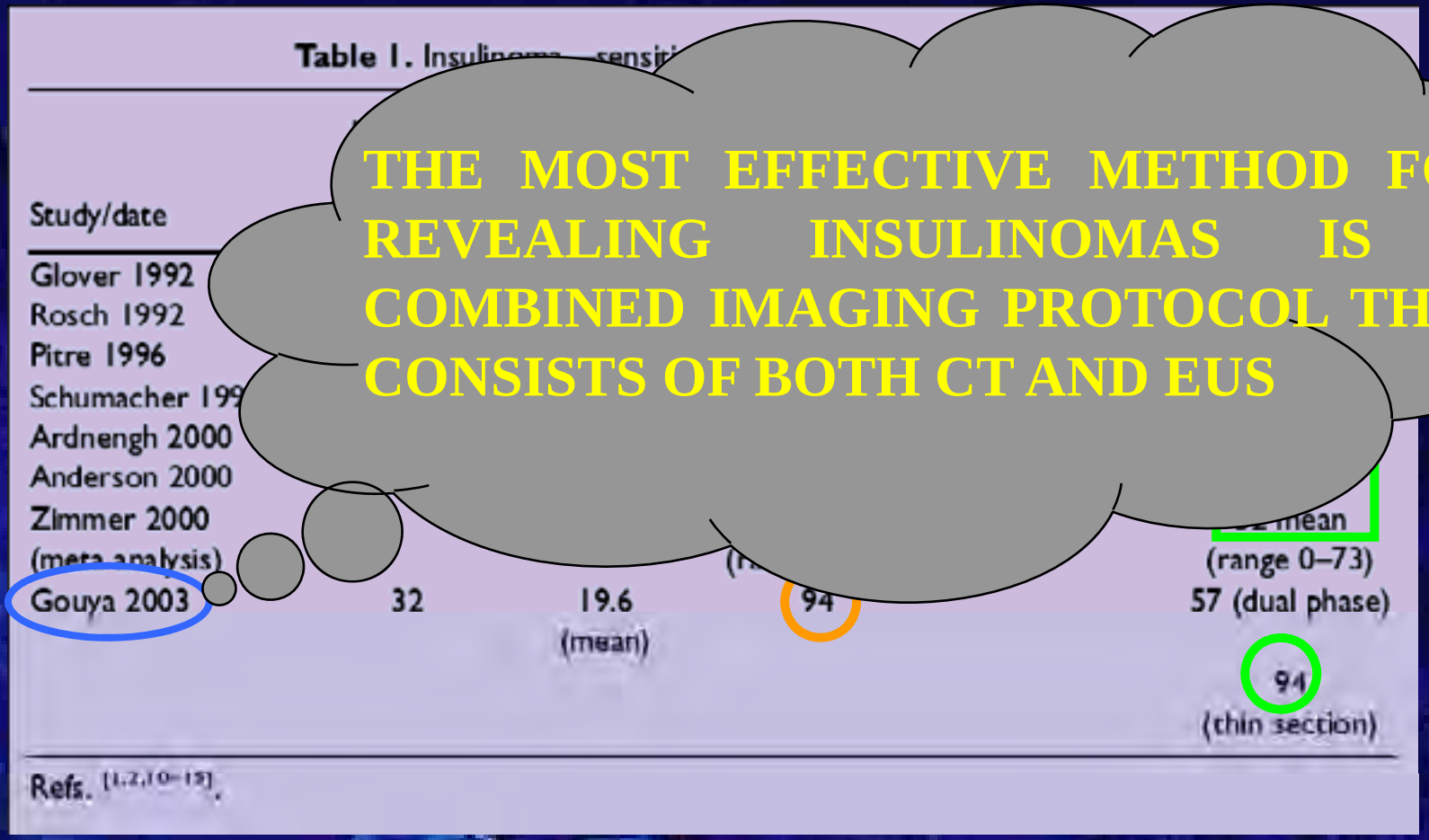






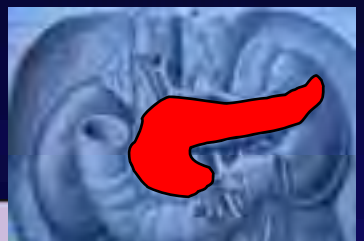


INSULINOMA



Best Practice & Research Clinical Endocrinology & Metabolism 2005; 19:177–93

INSULINOMA



Gastrointest Endosc. 2010 Nov 8. [Epub ahead of print]

EUS is still superior to multidetector computerized tomography for detection of pancreatic neuroendocrine tumors.

Khashab MA, Yong E, Lennon AM, Shin EJ, Amateau S, Hruban RH, Olino K, Giday S, Fishman EK, Wolfgang CL, Edil BH, Makary M, Cantoy MI.

RESULTS: In 217 patients (with 231 PNETs) studied, CT detected 84% of tumors (54.3% of insulinomas). The sensitivity of CT for the detection of PNETs significantly increased with improvement in CT technology (P = .02; χ(2) for trend). CT was more likely to miss lesions <2 cm (P = .005) and insulinomas (P < .0001). In 56 patients who had both CT and EUS, the sensitivity of EUS was greater than CT (91.7% vs 63.3%; P = .0002), particularly for insulinomas (84.2% vs 31.6%; P = .001). EUS detected 20 of 22 CT-negative tumors (91%).

Gastrointest Endosc. 2010 May;71(6):951-9.

Usefulness of EUS combined with contrast-enhancement in the differential diagnosis of malignant versus benign and preoperative localization of pancreatic endocrine tumors.

Ishikawa T, Itoh A, Kawashima H, Ohno E, Matsubara H, Itoh Y, Nakamura Y, Nakamura M, Miyahara R, Hayashi K, Ishigami M, Katano Y, Ohmiya N, Goto H, Hirooka Y.

RESULTS: EUS showed high sensitivity (95.1%) in identifying PETs compared with MDCT (80.6%) and US (45.2%).

GASTRINOMA: problems

- the location: 50% extra-pancreatic
- lesions in the duodenal wall are smaller than the pancreatic ones (9.6 mm vs 28.7 mm)

O Kisker et al. World J Surg 1998; 22: 651-7

- EUS sensitivity for pancreatic lesions: about 93%, it falls to 50% for extra-pancreatic lesions.

T Zimmer et al. Digestion 2000; 62: 45-50

- usefulness of intraoperative endoscopic transillumination (diagnostic improvement: + 20%) and duodenotomy (+15%)

Best Practice & Research Clinical Gastroenterology 2005; 19: 753–781

MEN-I

- many tumors are small (mean 1.1 cm)

EJ Wamsteker et al. Gastrointest Endosc 2003; 58: 531-5

- very often tumors are multiple (mean 3.3 tumors/pt)

- Screening with EUS in MEN-I asymptomatic pts can be recommended

EJ Wamsteker et al. Gastrointest Endosc 2003; 58: 531-5

EGEUS European Group for Endoscopic Ultrasonography

EUS ITALIAN CLUB

MEN-I

- many tumors are small (mean 1.1 cm)

  EJ Wamsteker et al. Gastrointest Endosc 2003; 58: 531-5

- spesso [illegible] 3.3 tumori/p.te)

- [illegible] asintomatici

  [illegible]5

In 13 MEN I asymptomatic pts, an EUS follow up of 13 yrs demonstrated the appearance of pancreatic tumors in 11

Aggressive early surgical treatment may improve the prognosis for these pts.

EGEUS European Group for Endoscopic Ultrasonography

EUS ITALIAN CLUB

MEN-I

Several papers subsequently demonstrated EUS effectiveness in detecting and following small pancreatic NETs in asymptomatic patients with MEN I sindrome

Gauger PG et al. Br J Surg. 2003;90(6):748-54.
Langer P et al. World J Surg. 2004;28(12):1317-22
Hellman P et al. Br J Surg. 2005;92(12):1508-12.
Thomas-Marques L et al. Am J Gastroenterol. 2006;101(2):266-73.
Kann PH et al. Endocr Relat Cancer. 2006;13(4):1195-202

ELECTRONIC INSTRUMENTS WITH LINEAR SCANNING ALLOW:

1. EUS-GUIDED BIOPSIES (EUS-FNA)

a) ↑ SPECIFICITY FOR THE DIAGNOSIS OF PANCREATIC CANCER AND LYMPH NODES INVOLVEMENT

b) "Usefulness of EUS-guided fine needle aspiration (EUS-FNA) in the diagnosis of functioning neuroendocrine tumors"

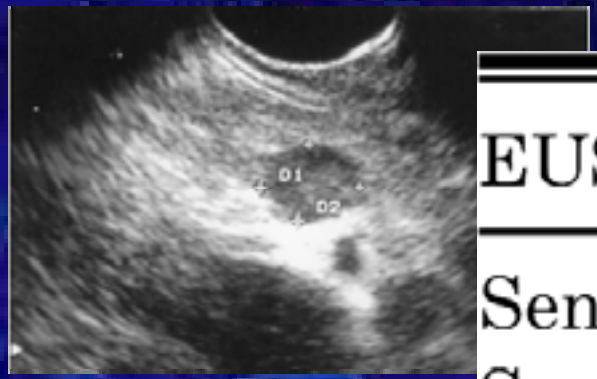
Ginès A et al. Gastrointest Endosc 2002;56:291

EUS-FNA safely provides cytologic confirmation with high accuracy in these patients.

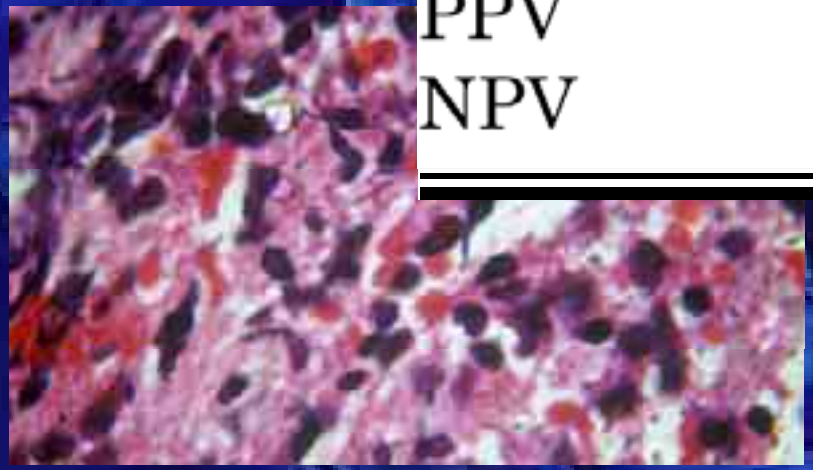
2) COLOR-DOPPLER APPLICATION

EUS-guided FNA in the diagnosis of pancreatic neuroendocrine tumors before surgery

José Celso Ardengh, MD, Gustavo Andrade de Paulo, MD, Angelo Paulo Ferrari, MD



EUS-FNA	n = 30	%	95% CI
Sensitivity	19/23	82.6	60.5, 94.3
Specificity	6/7	85.7	42.0, 99.0
Accuracy	25/30	83.3	64.5, 93.7
PPV	19/20	95.0	73.1, 99.7
NPV	6/10	60.0	27.9, 86.9



Gastrointest Endosc 2004;60: 378-84

EUS-FNA in the diagnosis of pancreatic NETs

- Other papers confirmed usefulness and effectiveness of EUS-FNA in the diagnosis of pancreatic NETs, both functioning and non-functioning.

- It is possible to reduce false positive results of only morphological EUS due to peri-and intra-pancreatic lymph nodes or splenosis nodules

Voss M et al. Gut. 2000;46(2):244-9
Gu M et al.Diagn Cytopathol. 2005;32(4):204-10.
Chang F et al. Cytopathology. 2006;17(1):10-7.
Jani N et al.Gastrointest Endosc. 2008;67(1):44-50.

EUS-FNA in the diagnosis of pancreatic NETs

- **EUS-FNA works better than CT-FNA**

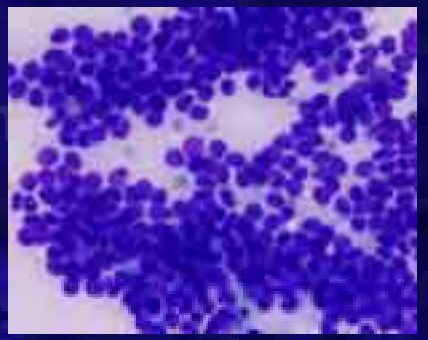
  Jhala D et al. Fine needle aspiration biopsy of the islet cell tumor of pancreas: a comparison between computerized axial tomography and endoscopic ultrasound-guided fine needle aspiration biopsy. Ann Diagn Pathol. 2002;6(2):106-12.

- **Possibility of predicting biological behaviour and outcome of the NET applying molecular biology techniques to the cell specimens obtained wth EUS-FNA .**

  Chatzipantelis P et al. The role of cytomorphology and proliferative activity in predicting biologic behavior of pancreatic neuroendoocrine tumors: a study by EUS-FNA cytology. CANCER CYTOPATHOL 2009.

AIMS

- To report our single center experience in detecting and diagnosing PETs by means of EUS-FNA on 50 pts



- and to describe the feasibility of the measurement of Ki-67 expression on cytological samples and evaluate its accuracy by comparing it with the Ki-67 expression measured on resected specimens

De Angelis C et al. **ROLE OF EUS-FNA IN THE DIAGNOSIS OF PANCREATIC NEUROENDOCRINE TUMORS AND VALUE OF KI-67 EXPRESSION MEASUREMENT ON CYTOLOGICAL SPECIMENS.** DLD 2011; 43 (suppl 1) (abs)..

CONCLUSIONS

•EUS with FNA is a valuable method in the detection and diagnosis of PETs even of very small size (< 8 mm)

•Cell blocks from needle washing: a convenient and reliable method to provide serial sections for immunocytochemistry (a large panel of antibodies can be used) and a lot of ancillary studies can be applied

•The typical cytologic findings with ICC stains allow not only the accurate identification of PETs, but also the definition of their hormone-producing capability, biological behaviour and receptor expression

•Ki-67 expression measurement on cytological samples is easy to be done on high-cellularity specimens; it shows only suboptimal accuracy assuming low cut-off values (3%), but the agreement with definitive histological measurement is very high (94,7%) when assuming high cut-off values (20%) and in the setting of PETs this seems to be the only important cut-off that can really affect clinical decision.

De Angelis C et al. Digestive and Liver Disease 2011; 43 (suppl) (abs)..

EUS: NEW PROSPECTS

- *"Contrast-enhanced EUS" could improved the already high accuracy of EUS in visualizing small pancreatic NETs and in differential diagnosis of pancreatic lesions*

EUS: NEW PROSPECTS

Endoscopy. 2010 Jul;42(7):564-70. Epub 2010 Jun 30.

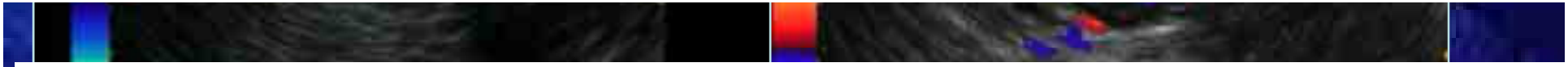
Contrast-enhanced harmonic endoscopic ultrasound in solid lesions of the pancreas: results of a pilot study.

Napoleon B, Alvarez-Sanchez MV, Gincoul R, Pujol B, Lefort C, Lepilliez V, Labadie M, Souquet JC, Queneau PE, Scoazec JY, Chayvialle JA, Ponchon T.

Gastroenterology. 2010 Oct;139(4):1172-80. Epub 2010 Jun 27.

Quantitative endoscopic ultrasound elastography: an accurate method for the differentiation of solid pancreatic masses.

Iglesias-Garcia J, Larino-Noia J, Abdulkader I, Forteza J, Dominguez-Munoz JE.



Clin Gastroenterol Hepatol. 2010 Jul;8(7):629-34.e1-2. Epub 2010 Apr 24.

Contrast harmonic echo-endoscopic ultrasound improves accuracy in diagnosis of solid pancreatic masses.

Fusaroli P, Spada A, Mancino MG, Caletti G.

m11

aiutare il chirurgo

EUS allows identification of tiny lesions difficult to find by palpation during surgery

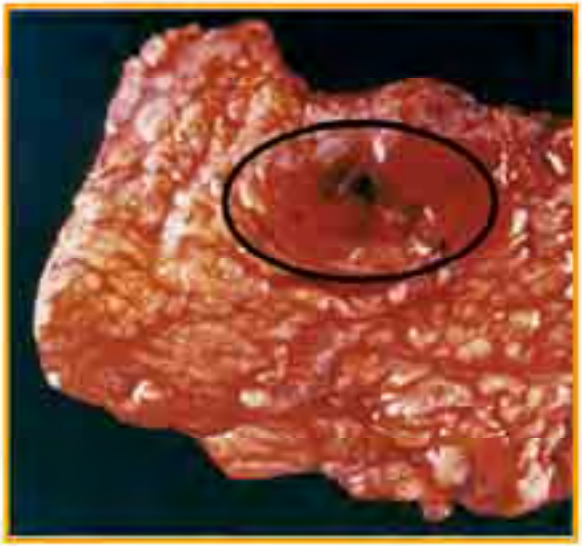
Case report

Preoperative im
guided fine neec

George N. Zograf
Karoubalis[3], Geo
Papastratis[1]

Preoperative localization of a neuro-endocrine tumor of the pancreas with EUS-guided fine needle tattooing

Frank G. Gress, MD, Mohammed Barawi, MD, Dong Kim, MD, James H. Grendell, MD



Gastromtestmal Endoscopy 2002; 55:594-7

Diapositiva 33

m11 utilizza india ink, blu dimetilene o verde di indocianina

nel primo caso tumore di 1 cm visto in EUS ma non trovato dal chirurgo neanche coneco intraoperatorio. p.te chiuso e fatto tatutaggio, poi riaperto

mauro; 11/02/2010


TOWARDS
THE FUTURE

ablare la lesione

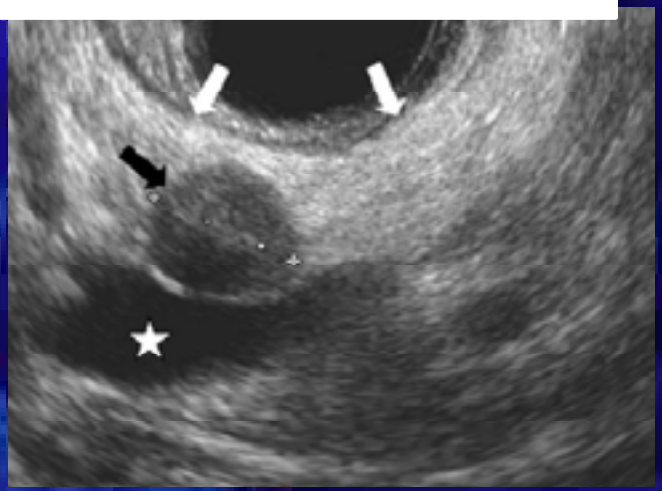
E' POSSIBILE UN TRATTAMENTO ECOENDO-GUIDATO ?

2 p.ti con insulinoma ed elevato rischio operatorio, con risposta non ottimale al diazossido.

Utilizzato etanolo 98% (3.5 e 8 cc nei due lavori). In entrambi i casi scomparsa di ipoglicemia e lesione.

Pancreatite acuta lieve in entrambi i casi.

C Jurgensen et al Gastrointest Endosc 2006; 63:1059-62
PH Deprez et al Acta Gastroenterol Belg 2008; 71:333-7



ablare la lesione

E' POSSIBILE UN TRATTAMENTO ECOENDO-GUIDATO ?

Prospettive di trattamento	Animal/ Human	Patologia
chemioterapici	A	
soluzione salina bollente	A	
TNFerade	H	adenoK
linfociti attivati	H	adenok
cellule dendritiche immature	H	adenok
virus oncolitici	H	adenok
terapia fotodinamica	A	
radiofrequenza	A	
HIFU (High Frequency Focused Ultrasound)	A	
brachiterapia	H	adenoK

R Ashida et al J Hepatobiliary Pancreat Surg 2009
J Sreenarasimhaiah Am J Med Sci 2009
MB Wallace et al. Gastrointest Endosc 2009
WR Brugge Gastrointest Endosc 2009
A Irisawa et al. Dig Endosc 2009
H Imazu et al. Endoscopy. 2009

Gastrointest Endosc. 1999 Sep;50(3):392-401.

EUS-guided radiofrequency ablation in the pancreas: results in a porcine model.

Goldberg SN, Mallery S, Gazelle GS, Brugge WR.

Department of Radiology, Massachusetts General Hospital, Harvard Medical School, Boston, USA. sgoldber@bidmc.harvard.edu

Gastrointest Endosc. 2009 Aug;70(2):372-6. Epub 2009 Jun 26.

EUS-guided radiofrequency ablation with a prototype electrode array system in an animal model (with video).

Varadarajulu S, Jhala NC, Drelichman ER.

Division of Gastroenterology-Hepatology, University of Alabama at Birmingham School of Medicine, Birmingham, Alabama 35294, USA. svaradarajulu@yahoo.com

Endoscopy. 2008 Apr;40(4):321-6.

Endoscopic ultrasound-guided application of a new hybrid cryotherm probe in porcine pancreas: a preliminary study.

Carrara S, Arcidiacono PG, Albarello L, Addis A, Enderle MD, Boemo C, Campagnol M, Ambrosi A, Doglioni C, Testoni PA.

Division of Gastroenterology and Gastrointestinal Endoscopy, Vita-Salute San Raffaele University, Scientific Institute San Raffaele, Milan, Italy.

Diagnostic imaging of pancreatic NETs: "take home message"

- 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

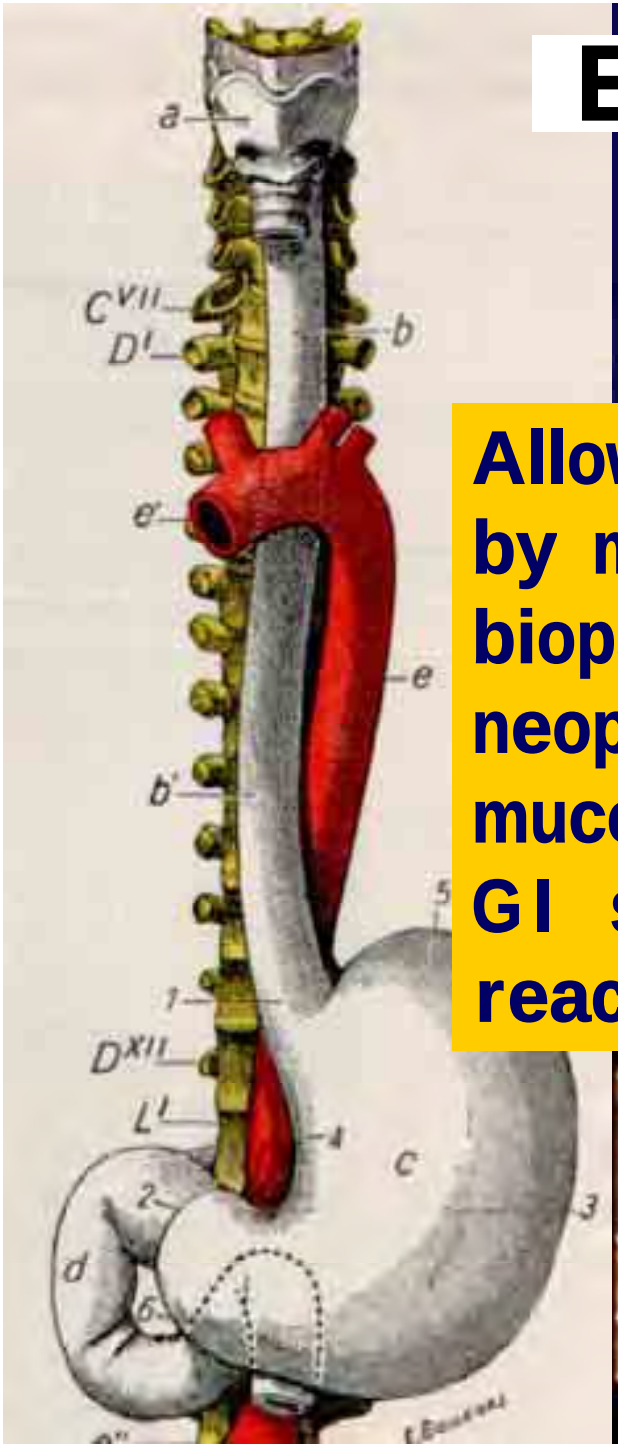
- EUS had the highest accuracy in assessing tumor size and lymph node involvement and remains the first choice in diagnosis of small tumors and for future SCREENING or FU programs

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

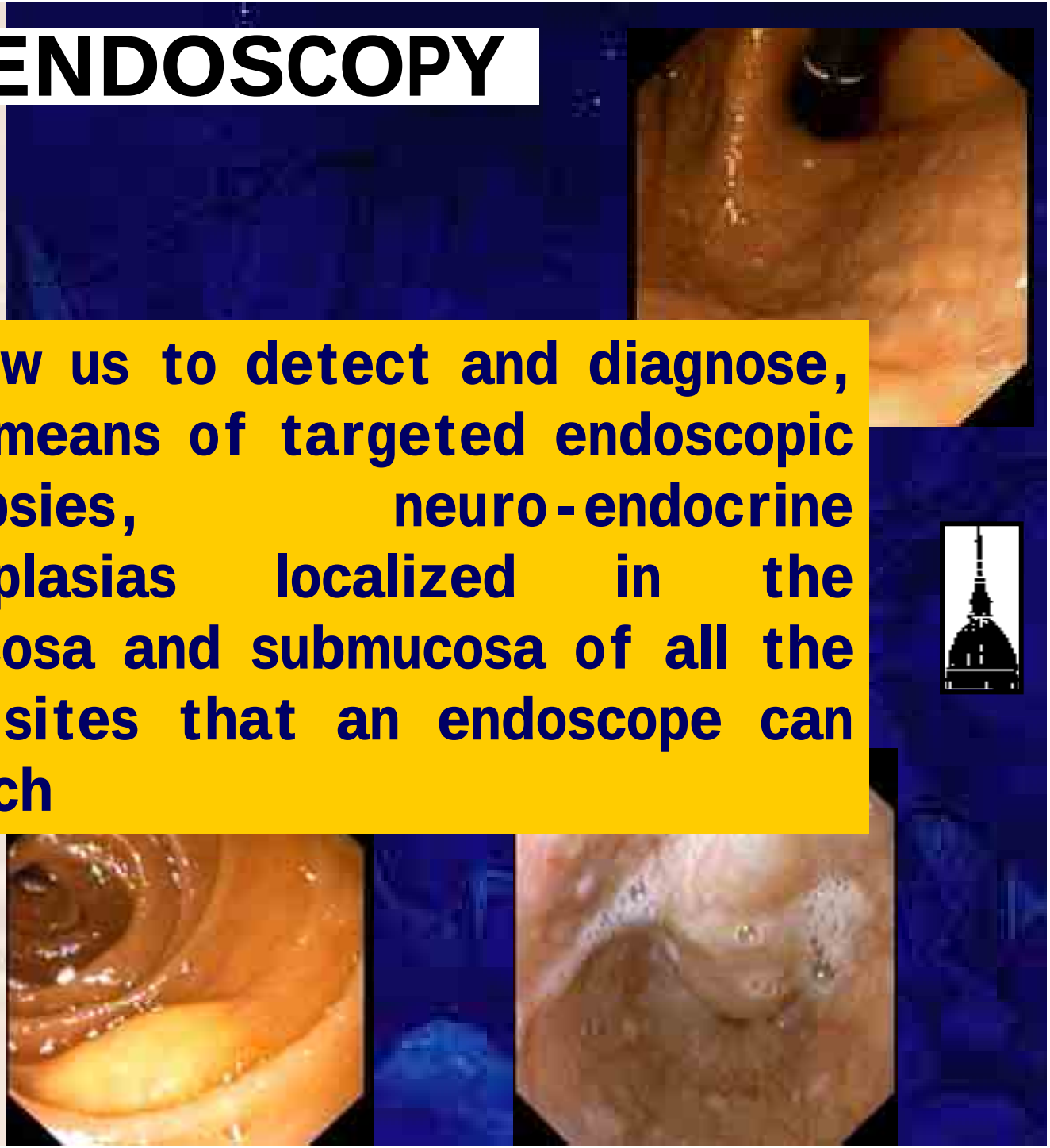
ENDOSCOPY AND EUS FOR THE DIAGNOSTIC MANAGEMENT OF GI WALL NETs (so-called CARCINOIDs)

- 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

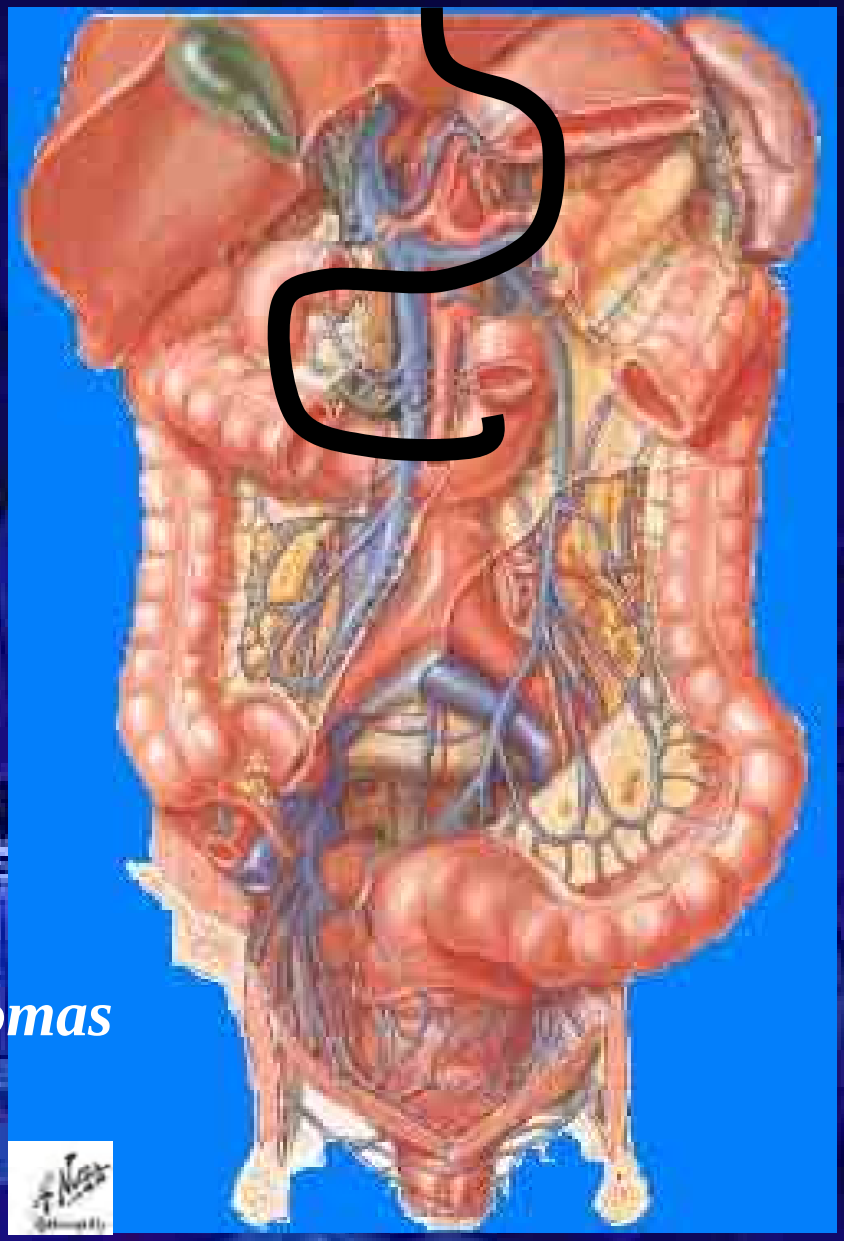
Carcinoids

Gastrinomas

Somatostatinomas

Insulinomas

Vipomas,GRFomas, Glucagonomas, PPomas, Non functioning Tumors



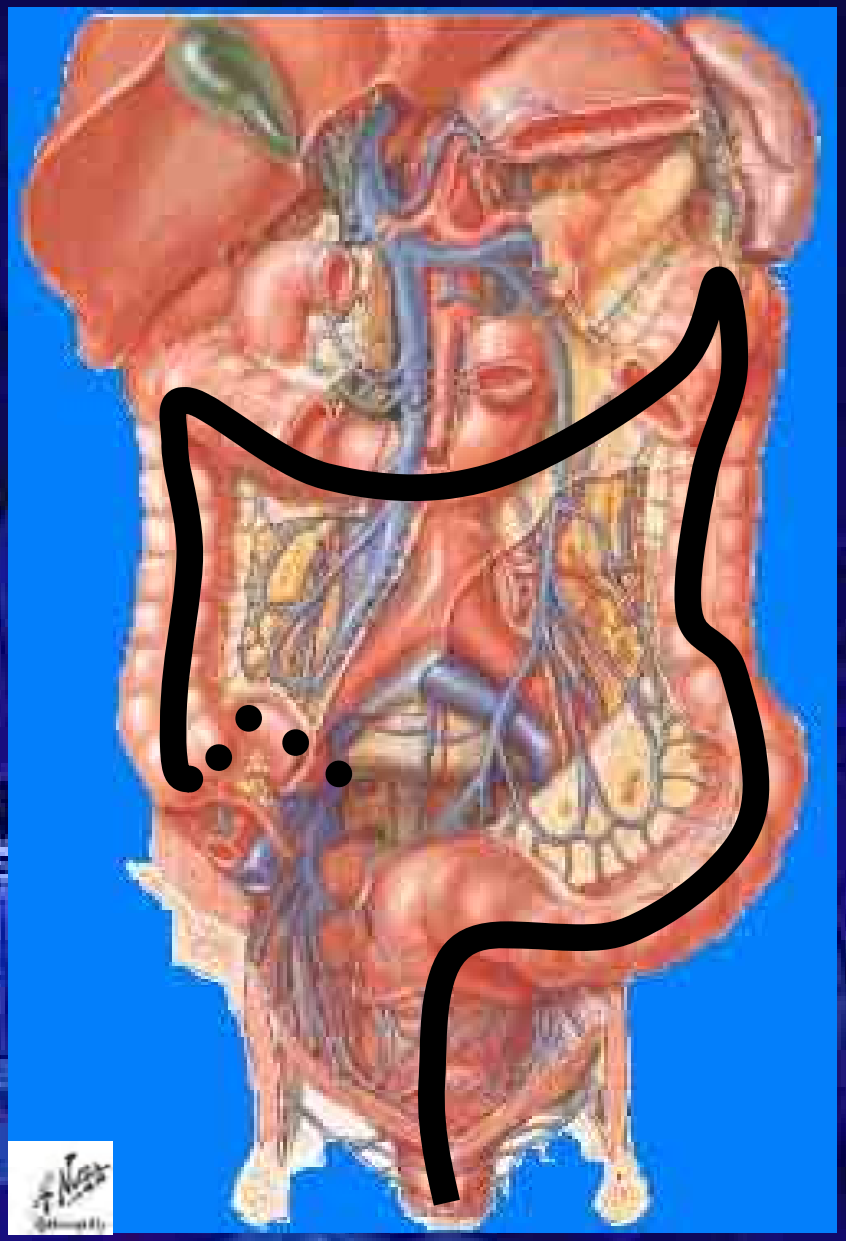
We can see
up to.....

- colonscopy

Carcinoids

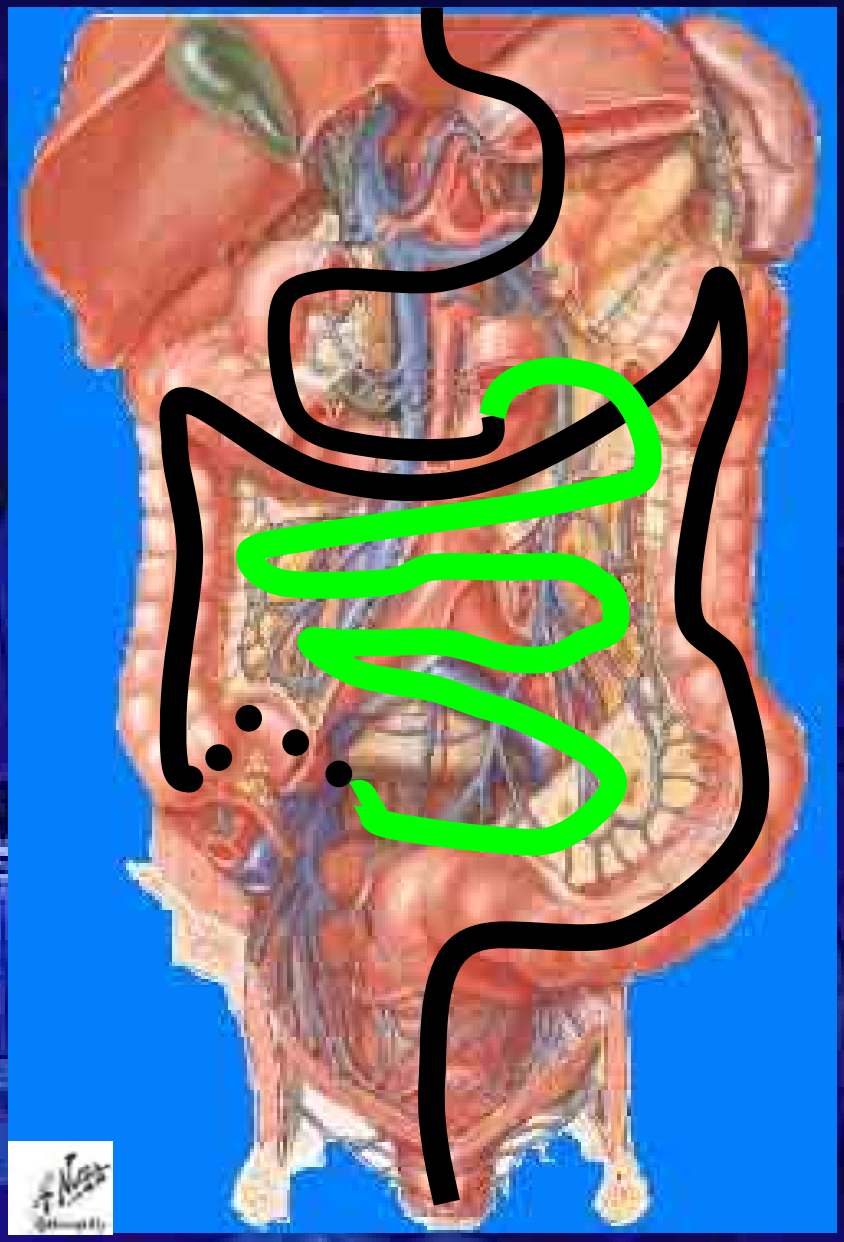
Somatostatinomas

Enteroglucagonomas



We can see up to.....

- enteroscopy



"PUSH-TYPE" ENTEROSCOPY

INTRA-OPERATIVE OR LAPAROSCOPICALLY-ASSISTED ENTEROSCOPY

VIDEO CAPSULE

VIDEO CAPSULE: LIMITs

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

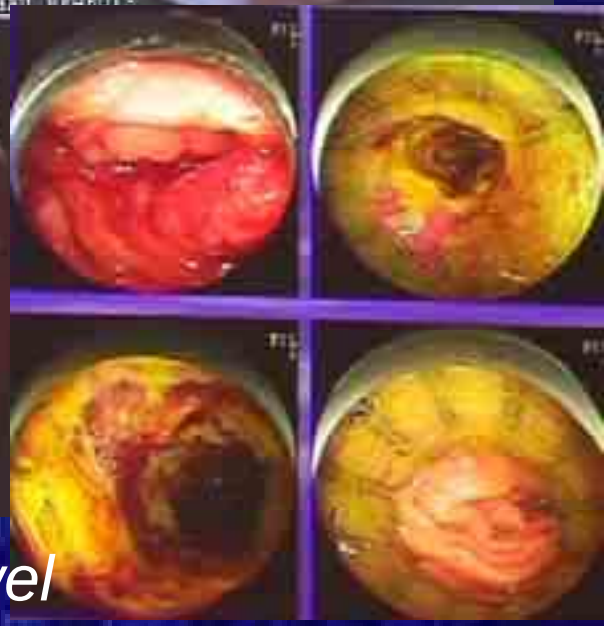
or, as in the case of carcinoid tumors with retracted mesentery, should be sed with caution or preceded by the "patency capsule"

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

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

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

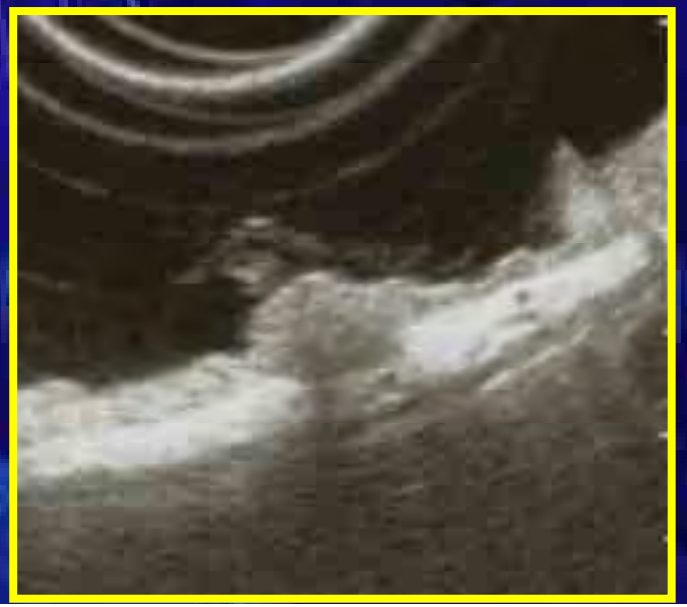
*Scherübl H et al. Double-balloon enteroscopy for the detection of midgut carcinoids. Gastrointest Endosc. 2005;62(6):994.

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.

ENDOSCOPIC ULTRASOUND (EUS)

- The close proximity of the lesion to the US probe allows us to use US frequencies so high to have a resolution power near to 0.1 mm:
- so 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

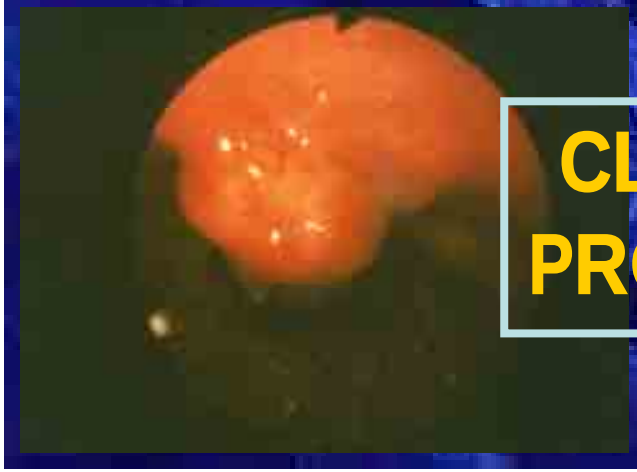
and …. what about the rest of the small bowel?

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*

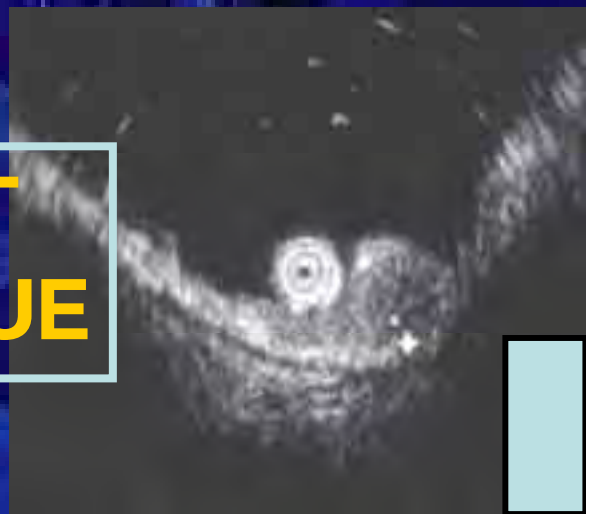
Fukumoto A et al. Usefulness of EUS with double balloon enteroscopy for diagnosis of small bowel diseases. Gastrointest Endosc. 2007; 65: 412-420.

EUS IN THE ASSESSMENT OF GI TRACT NETs

- 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)

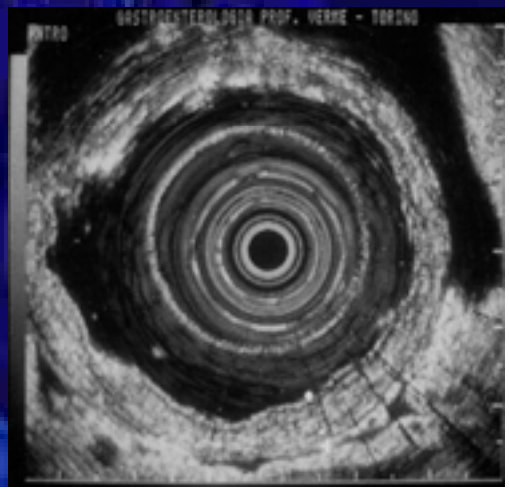


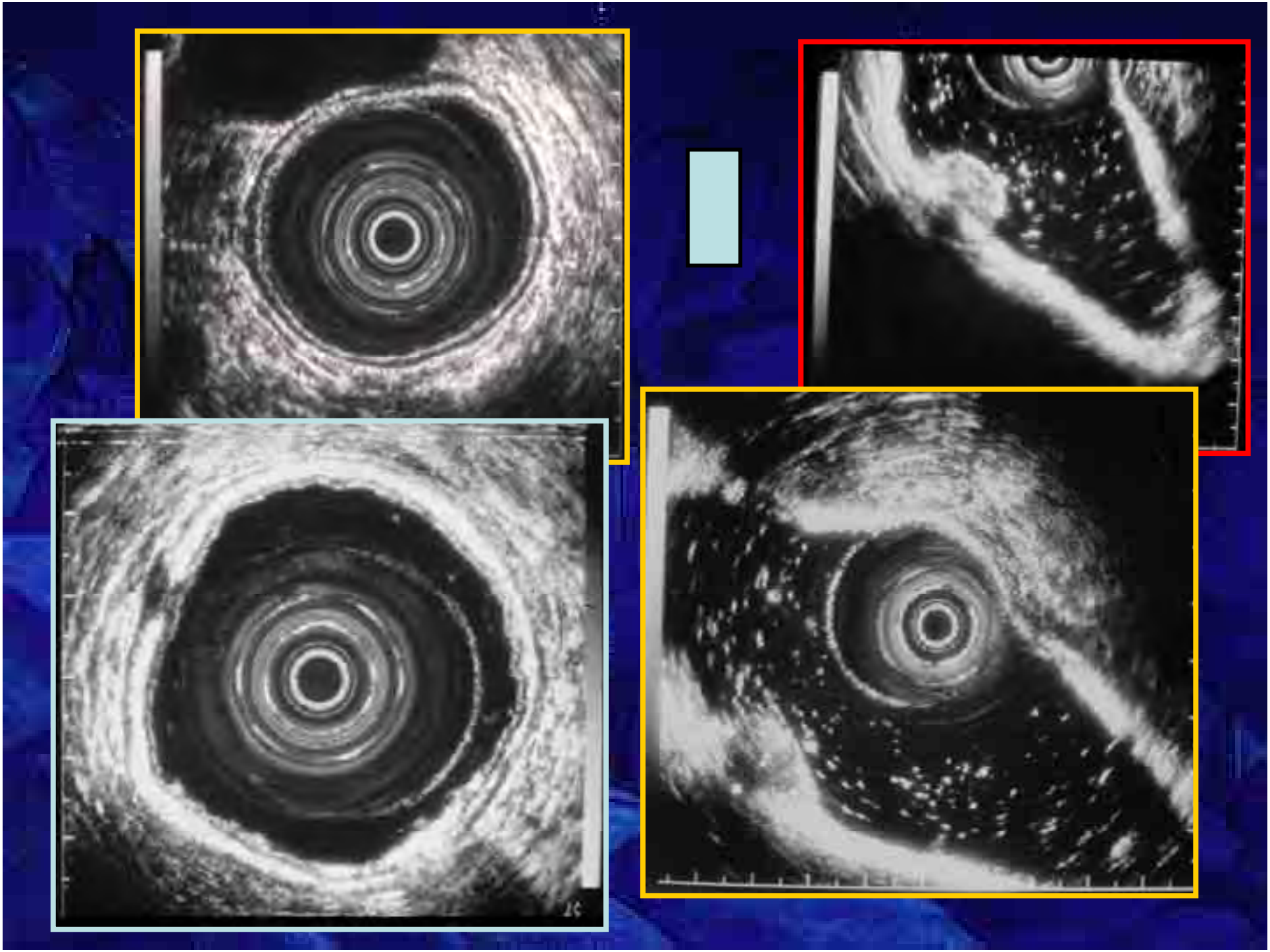
CLINICAL IMPACT
PROGNOSTIC VALUE



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

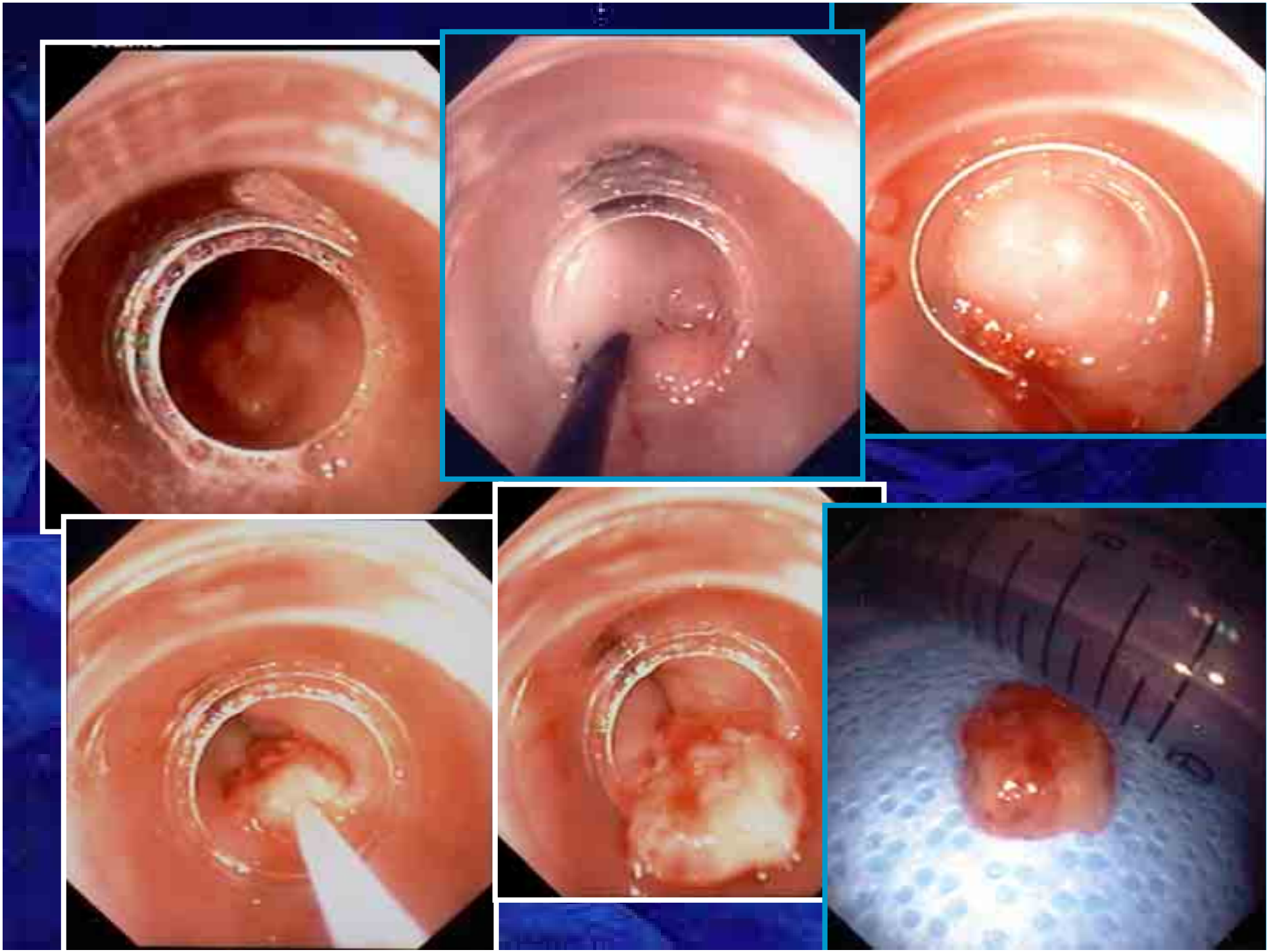
< 1 cm

Esophagus
Stomach
Duodenum
Colon

< 1.5 cm

Rectum

Without NODAL involvement

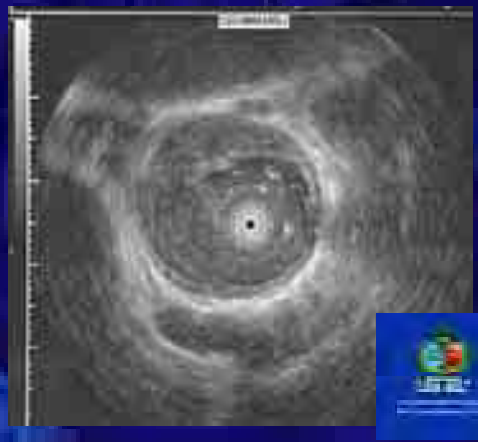


High-frequency probe EUS-assisted endoscopic mucosal resection: A therapeutic strategy for submucosal tumors of the GI tract

(Waxman I et al. Gastrointest Endosc 2002)

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



m9

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

Diapositiva 63

m9 un'altra calssificazione comprende un gruppo IV che non deriva da ECL come i primi tre ma da altre cell endocrine (serotnina gastrina ACTH et)
Il gruppo Iv si comporta come il gruppo III
mauro; 26/12/2005

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?

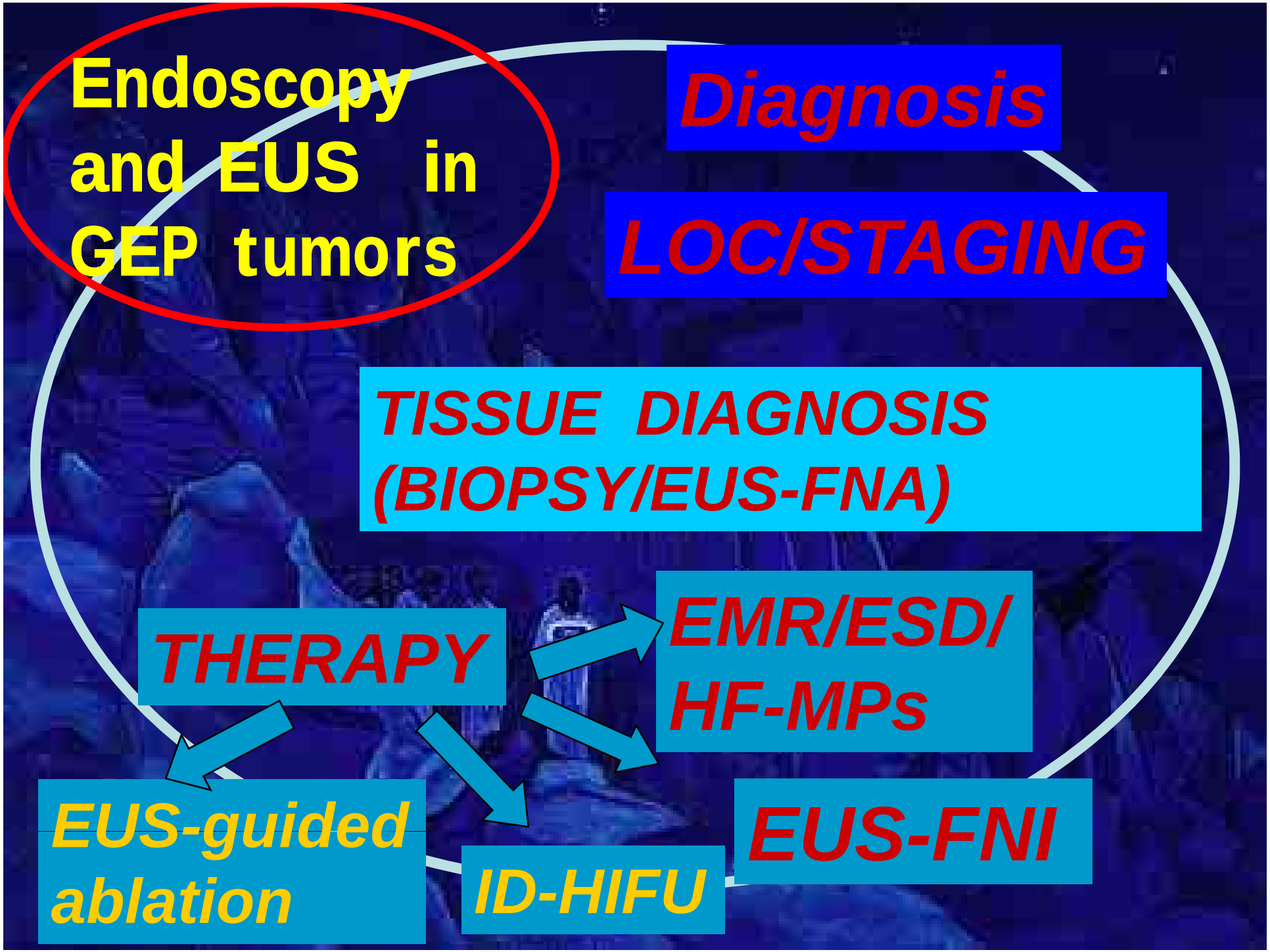
rectum

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

Successful outcomes of EMR-L with 3D-EUS for rectal carcinoids compared with historical controls.
Abe T, Kakemura T, Fujinuma S, Maetani I.
World J Gastroenterol. 2008;14(25):4054-8.

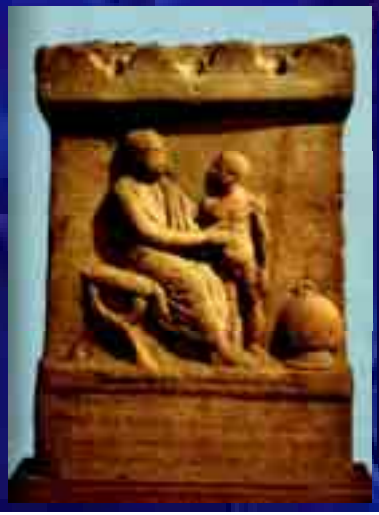
EUS


Endoscopy and EUS in GEP tumors
Diagnosis
LOC/STAGING
TISSUE DIAGNOSIS (BIOPSY/EUS-FNA)
THERAPY
EMR/ESD/ HF-MPs
EUS-guided ablation
ID-HIFU
EUS-FNI

"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