

Endoscopia e lesione solide del pancreas



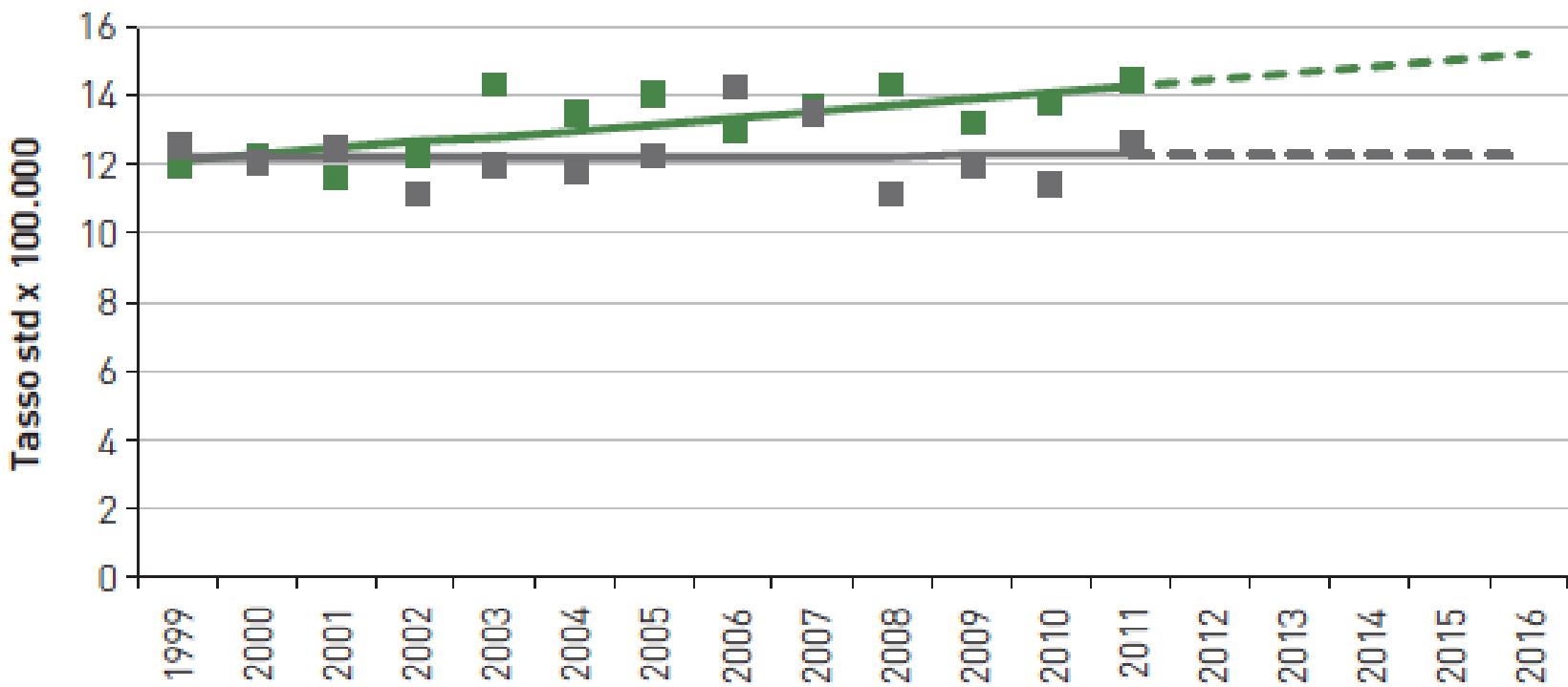
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U.O. di Gastroenterologia ed Endoscopia Digestiva
OSPEDALE BELLARIA-MAGGIORE
BOLOGNA

I NUMERI DEL CANCRO IN ITALIA 2016



Rango	Tutta la popolazione
1°	Polmone (19%)
2°	Colon-retto (11%)
3°	Mammella (7%)
4°	Stomaco (6%)
5°	Pancreas (6%)

Incidenza



Sopravvivenza a 5 anni dalla diagnosi

Pancreas	6,9 (6,8-7,0)	7,2 (6,7-7,7)
Colon	57,0 (56,8-57,3)	60,8 (60,4-61,3)
Prostata	83,4 (83,1-83,6)	88,6 (88,1-89,0)
Mammella femminile	81,8 (81,6-82,0)	85,5 (85,1-85,8)

Diagnosi precoce

Ad oggi non esistono metodi per la diagnosi precoce del carcinoma del pancreas. La malattia è di solito per lungo tempo asintomatica; solamente il 7% dei casi è diagnosticato in stadio iniziale.

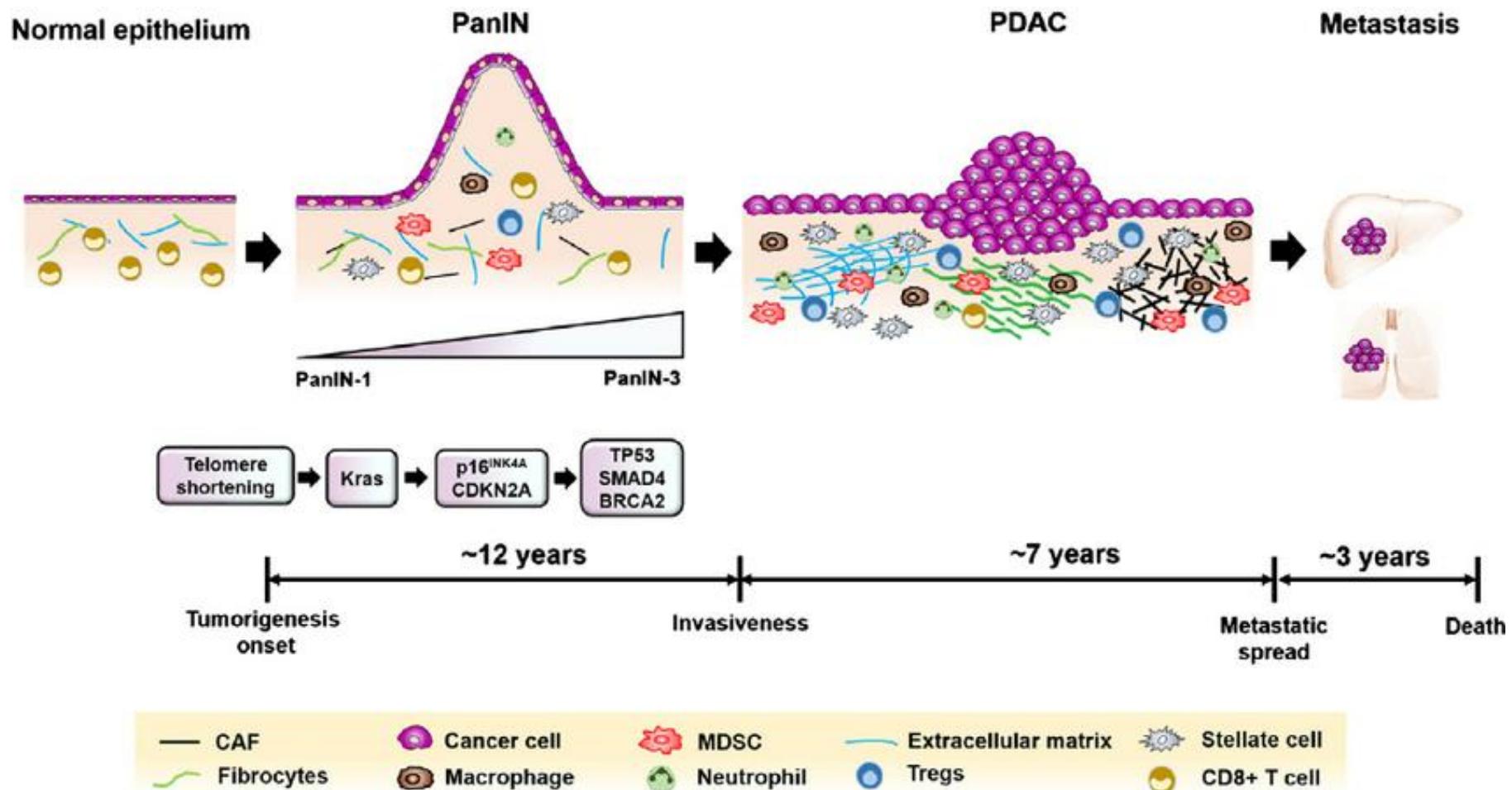
- Only 9% of patients are diagnosed when PC is localized
- 53% already have distant metastase at time of diagnosis

detection at an earlier stage and development of effective therapies “cornerstones” for cancer death reduction

SCREENING STRATEGIES

Timeline of Progression

PanIN-1 → Large PC



Incidental finding of solid pancreatic lesion

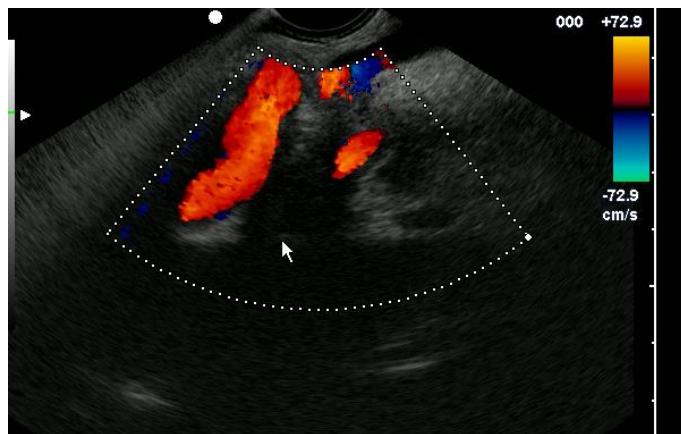
Clinical Suspicion of Pancreatic neoplasm



- MDHCT -
- MDHCT doubtful
- MDHCT +

Resectability

EUS + MDHCT PPV =



	EUS	MDHCT	EUS + MDHCT
Sens	88	90	80
Spec	67	64	93

DeWitt J et al. Ann Intern Med 2004
Shami V. et al;Pancreas 2011

	EUS	MRI
Sens	97	100

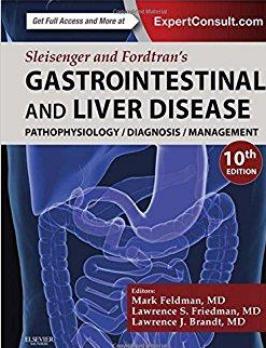
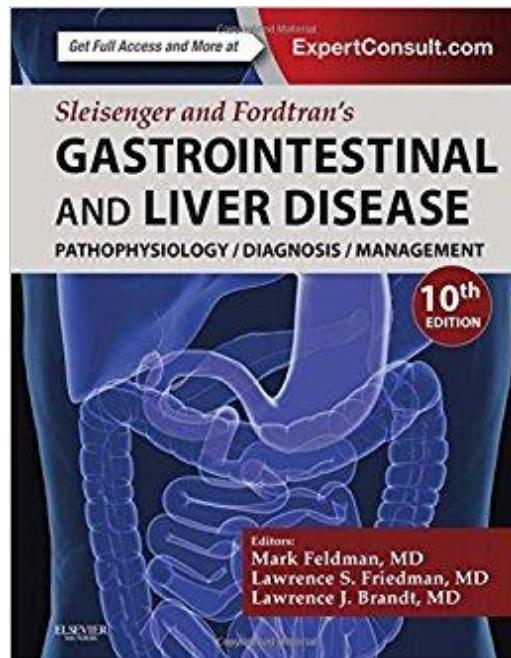


Table 20-4 Imaging Studies for the Evaluation of Jaundice

TEST	SENSITIVITY (%)	SPECIFICITY (%)	MORBIDITY (%)	MORTALITY (%)	ADVANTAGES AND DISADVANTAGES
Abdominal US	55-91	82-95	0	0	Advantages—noninvasive, portable Disadvantages—bowel gas may obscure bile duct; difficult in obese persons, operator-dependent
Abdominal CT	63-96	93-100	See disadvantages	0	Advantages—noninvasive, higher resolution than ultrasound, not operator-dependent Disadvantages—potential for contrast-induced nephrotoxicity, anaphylaxis
MRCP	82-100	94-98	See disadvantages		Advantages—noninvasive, imaging of bile ducts superior to ultrasound and CT Disadvantages—requires breath holding, may miss small-caliber bile duct disease
ERCP	89-98	89-100	3	0.2	Advantages—provides direct imaging of bile ducts; permits direct visualization of periampullary region and acquisition of tissue distal to bifurcation of hepatic ducts; permits simultaneous therapeutic intervention, especially useful for lesions distal to bifurcation of hepatic ducts Disadvantages—requires sedation, cannot be performed if altered anatomy precludes endoscopic access to ampulla (e.g., Roux-en-Y loop); has complications (e.g., pancreatitis)
Percutaneous THC	98-100	89-100	3.5	0.2	Advantages—provides direct imaging of bile ducts, permits simultaneous therapeutic intervention, especially useful for lesions proximal to common hepatic duct Disadvantages—more difficult with nondilated intrahepatic bile ducts; has complications
EUS	89-97	67-98	See disadvantages	0	Advantages—imaging of bile ducts superior to ultrasound and CT, permits needle aspiration of suspected neoplasms Disadvantages—requires sedation

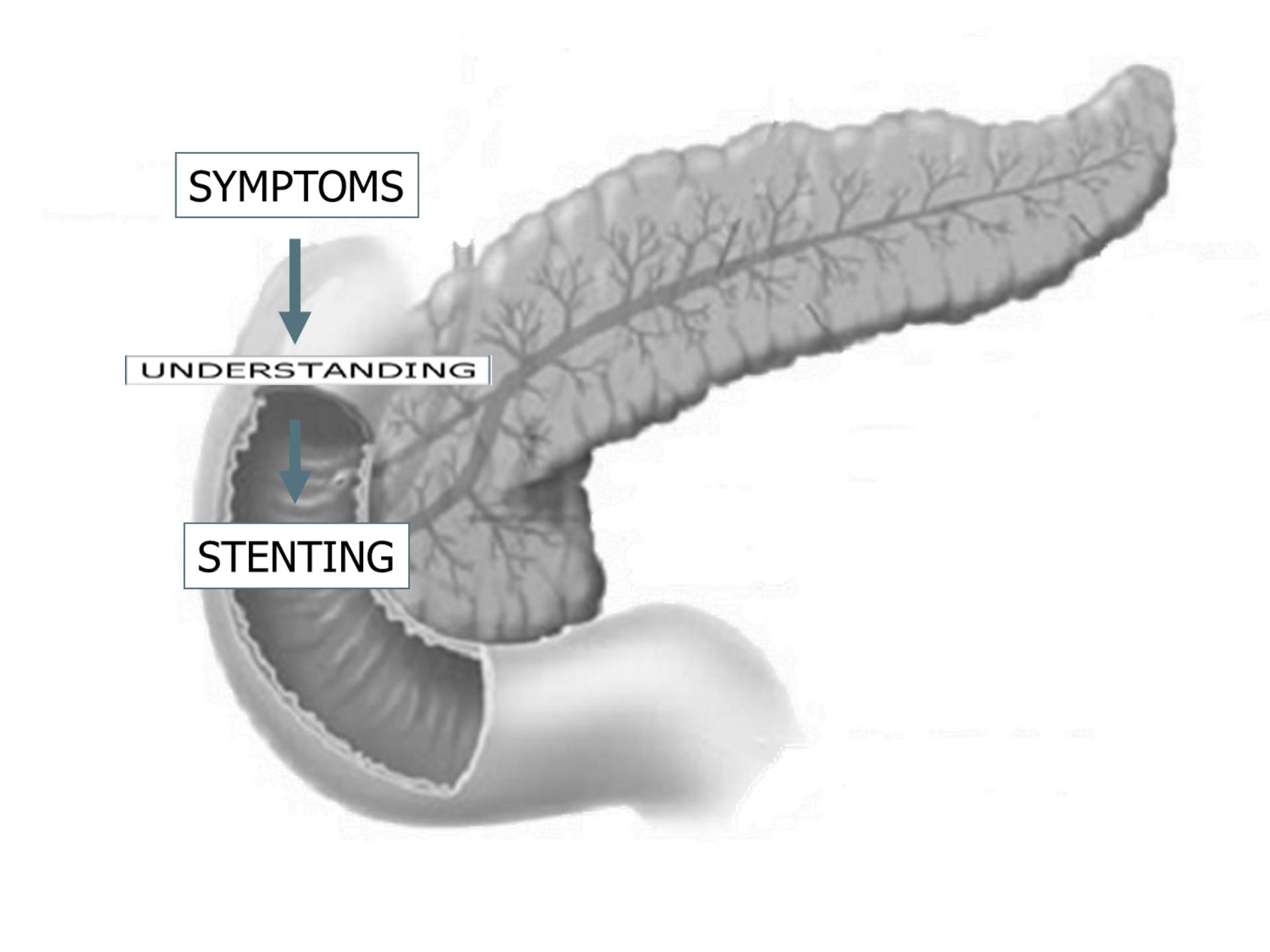
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Percutaneous THC	98-100	89-100	3.5	0.2	Advantages—provides direct imaging of bile ducts, permits simultaneous therapeutic intervention, especially useful for lesions proximal to common hepatic duct Disadvantages—more difficult with nondilated intrahepatic bile ducts; has complications
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SYMPTOMS





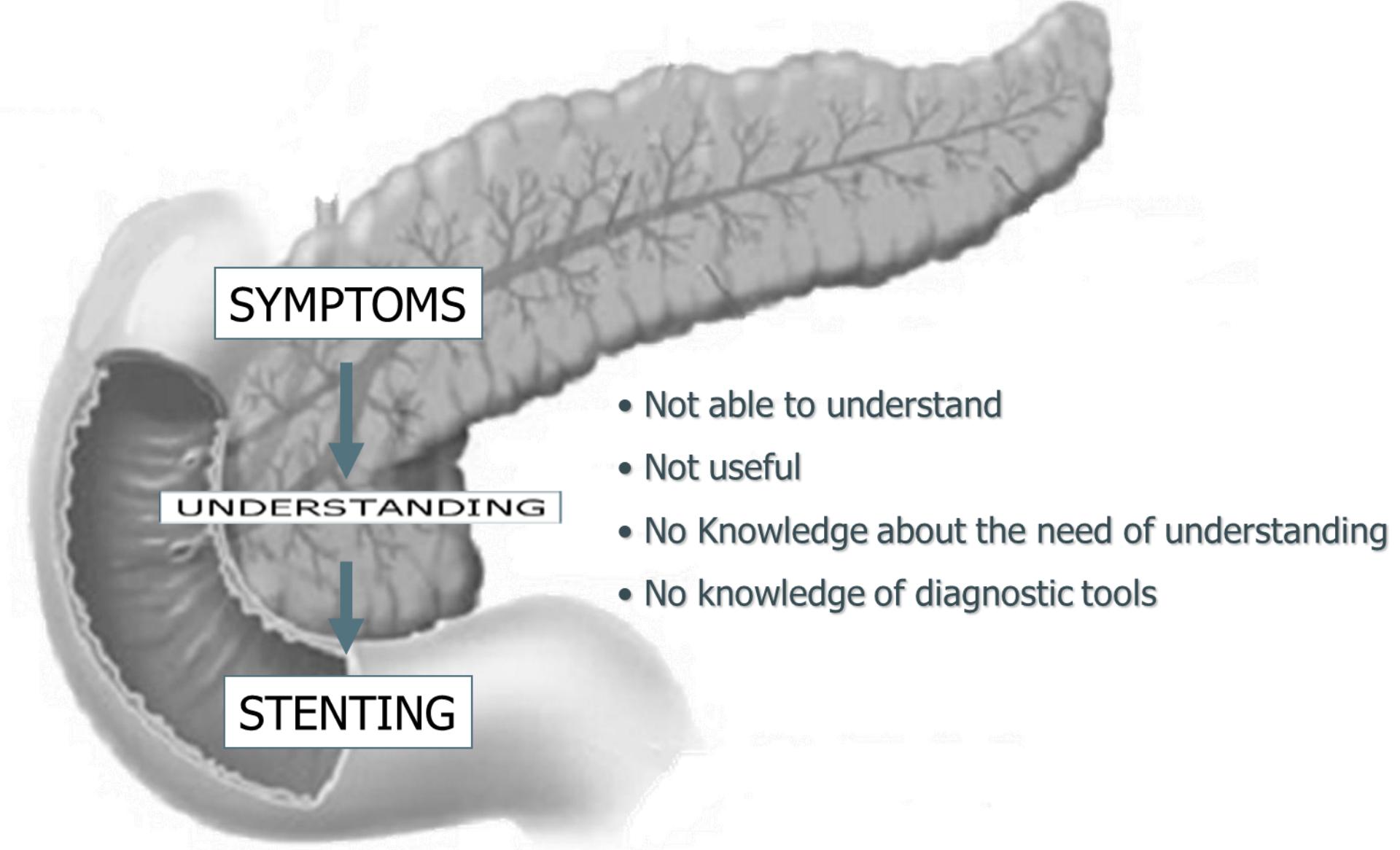
SYMPTOMS



UNDERSTANDING



STENTING



SYMPTOMS

UNDERSTANDING

STENTING

- Not able to understand
- Not useful
- No Knowledge about the need of understanding
- No knowledge of diagnostic tools



**Indicazioni
Tecniche
Complicanze**

Causes of malignant bile duct strictures

Intrahepatic bile ducts	Cholangiocarcinoma Hepatocellular carcinoma Metastatic disease
Extrahepatic bile duct	Cholangiocarcinoma Pancreatic cancer Ampullary malignancy Gallbladder cancer Metastatic disease
Hilar region	Cholangiocarcinoma Bulky porta hepatis lymphadenopathy

GASTROENTEROLOGY
CLINICS OF NORTH AMERICA

Webb, Suanders 2013

Preprocedural checklist

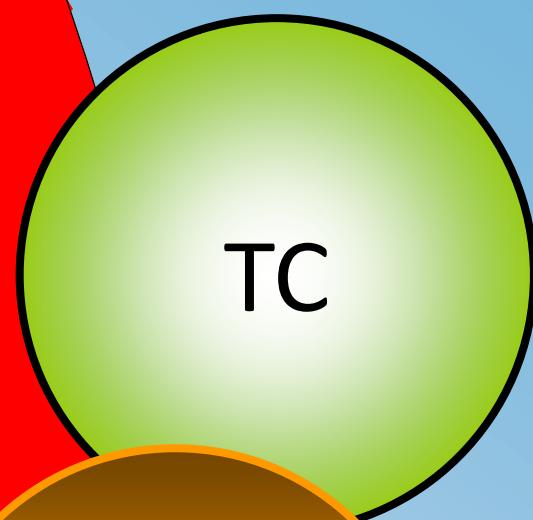
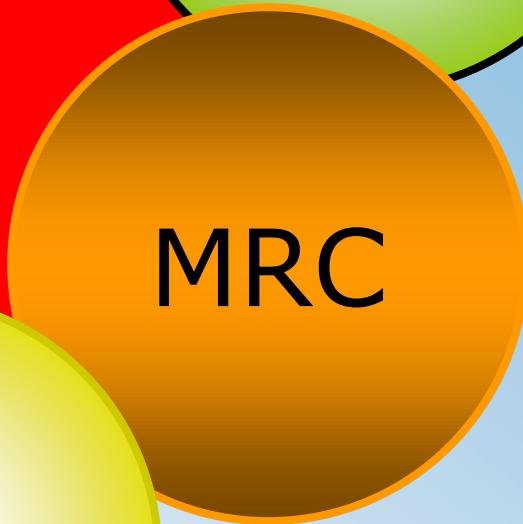
- Lesion resectability and goals of care
- Life expectancy given stage of disease and comorbidities
- Location and length of the lesion
- Plastic versus self-expanding metal stent
- Covered versus uncovered
- Cost comparisons
- Physician comfort level with the procedure



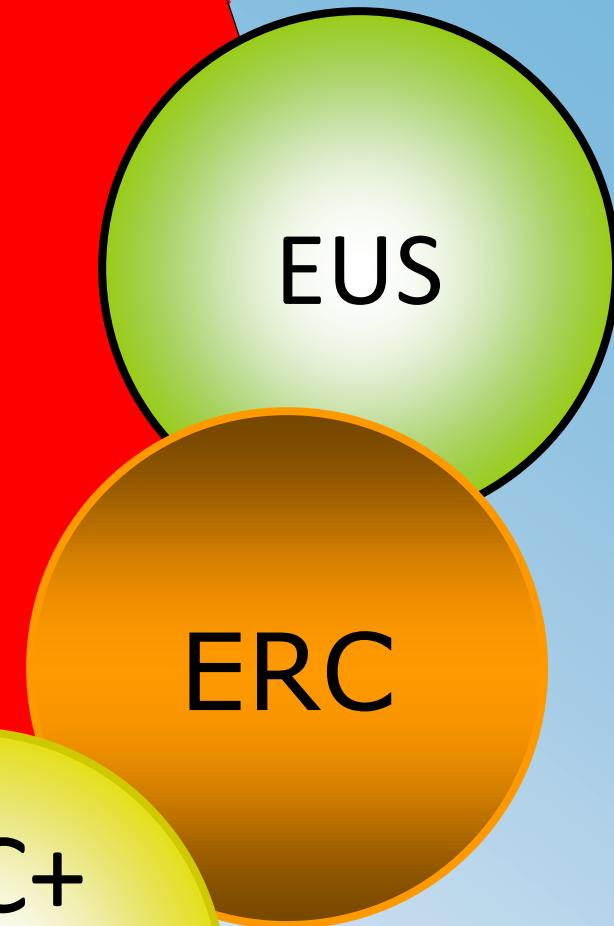
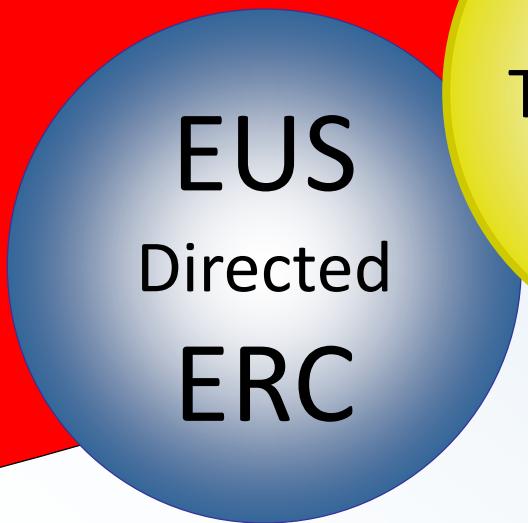
Webb, Suanders 2013



Non endoscopic biliary imaging modalities

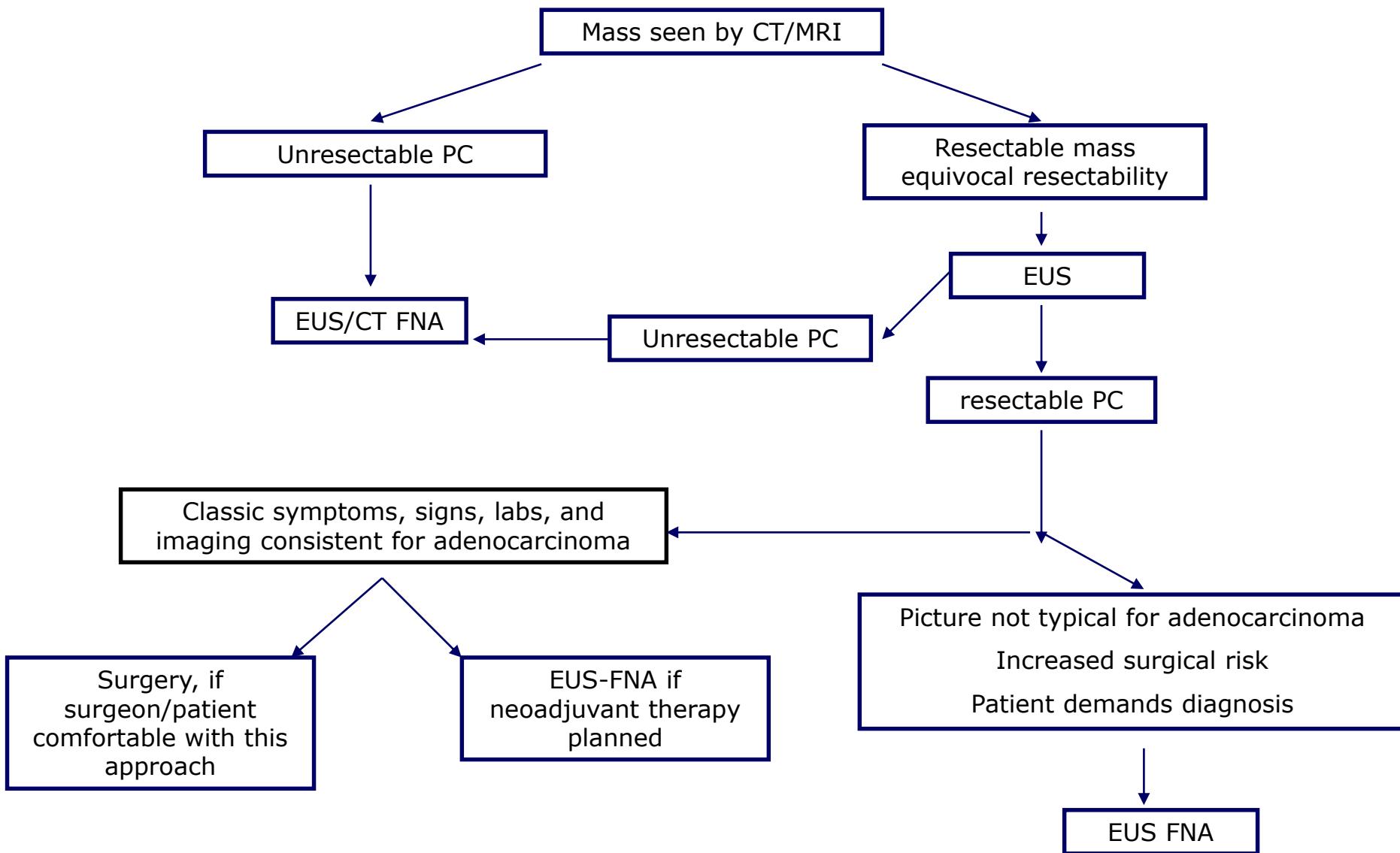


Endoscopic biliary imaging modalities





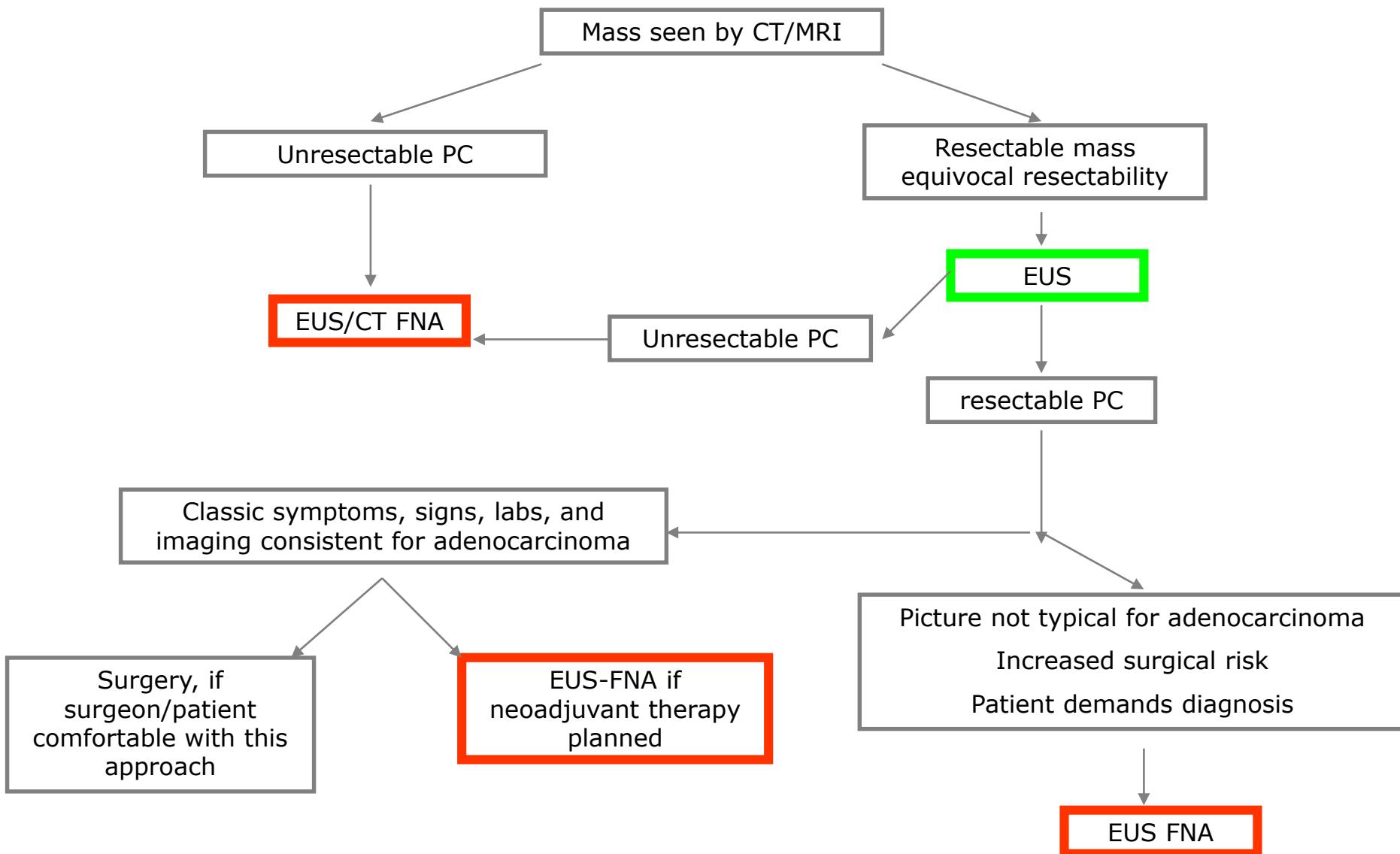
Algorithm for Suspected Panc Mass





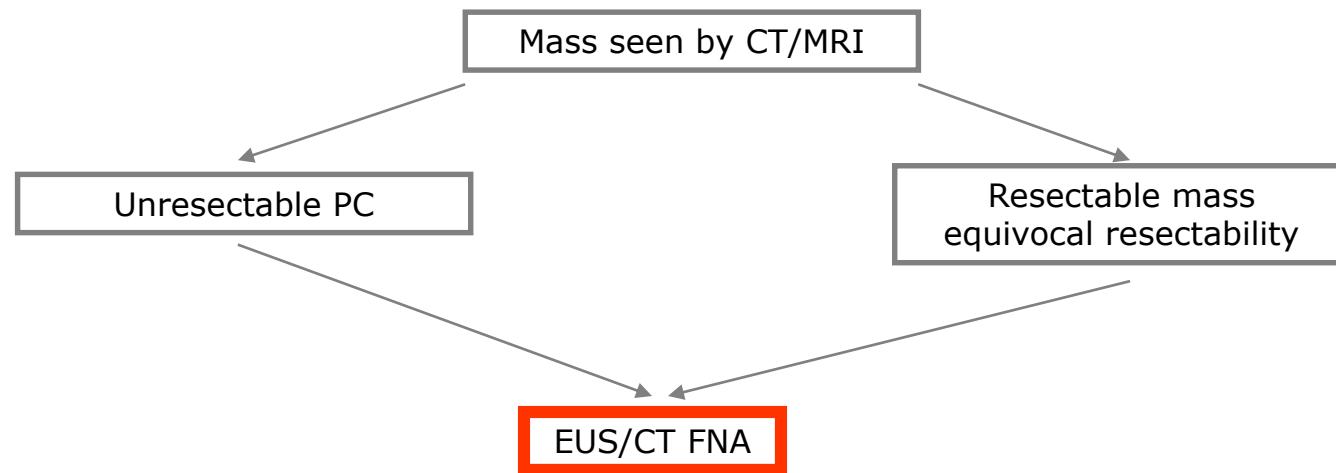


Algorithm for Suspected Panc Mass



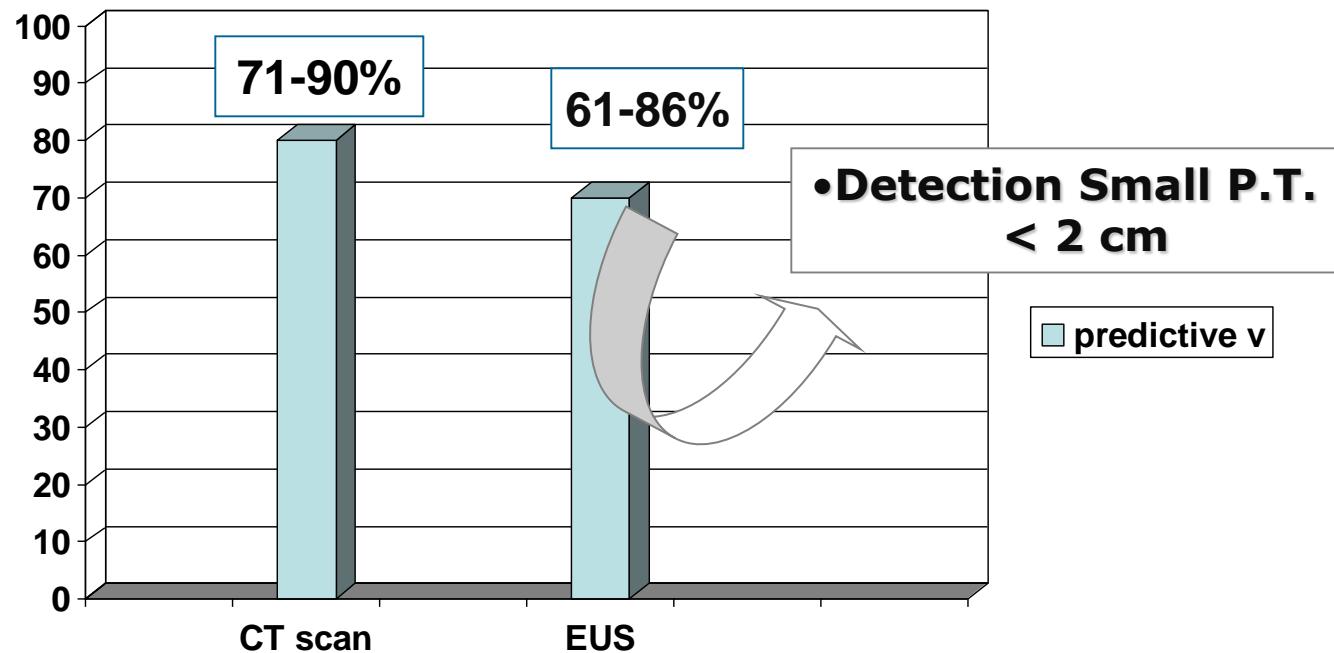


Algorithm for Suspected Panc Mass



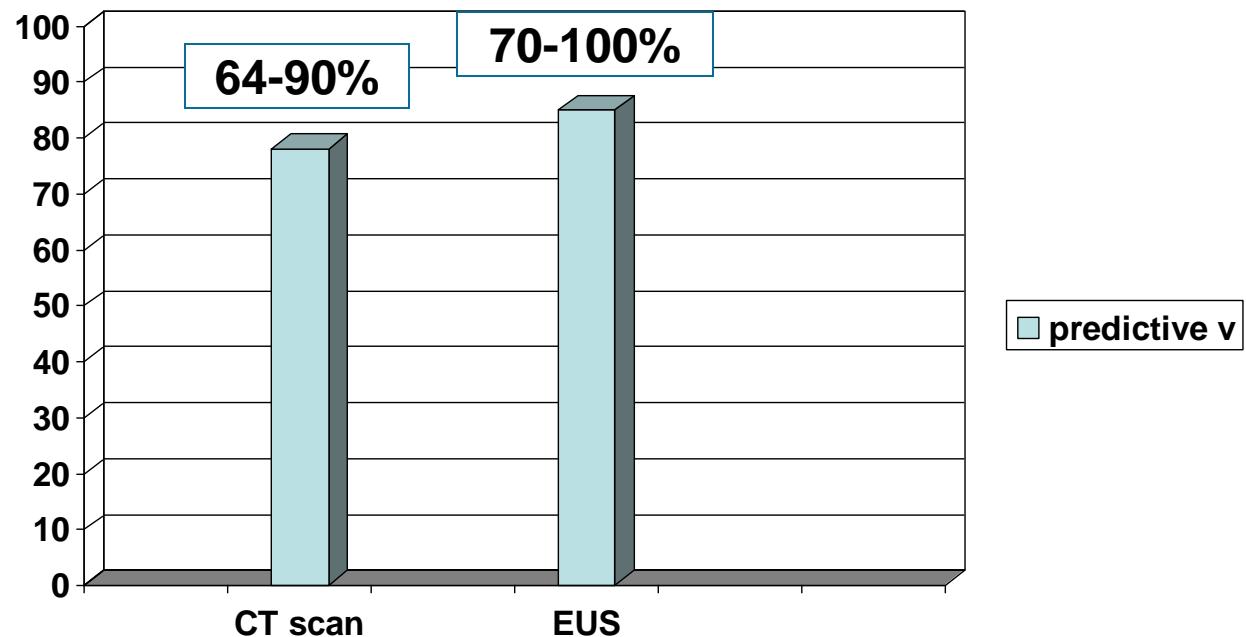
Staging of Solid Pancreatic Tumors

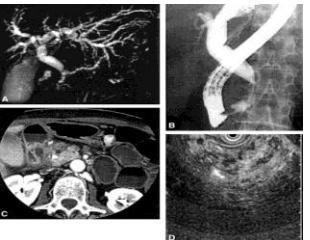
Resectability



Staging of Solid Pancreatic Tumors

Unresectability





Pancreatic Cancer

DIAGNOSTIC ACCURACY

	EUS	TC
Detection	97%	73%
Resectability	91%	83%
Vascular Invasion	91%	64%

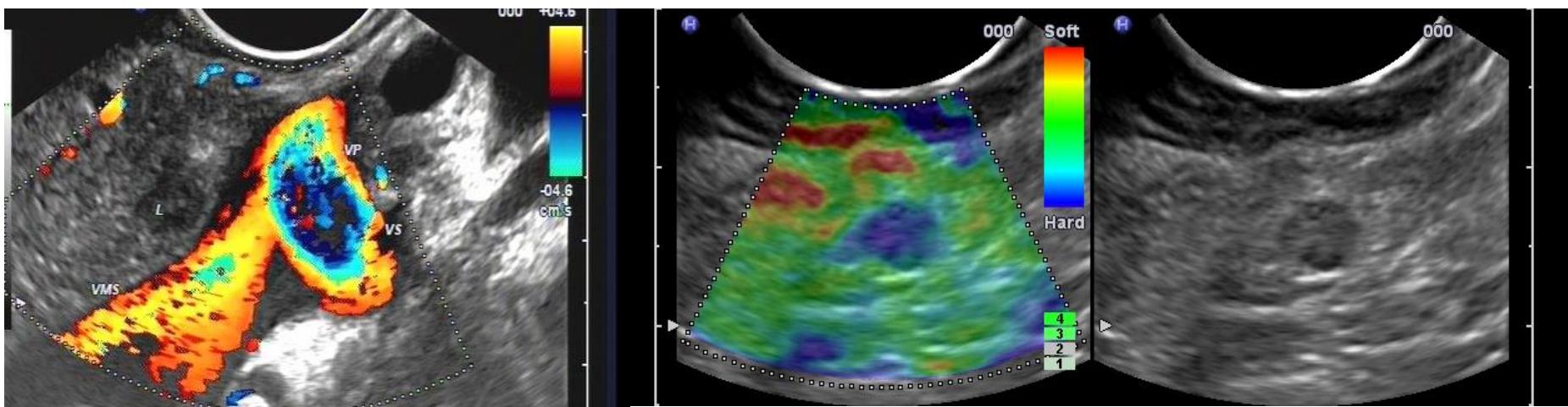
EUS vs MDHCT

MDHCT missed 47% lesions < 25 mm and 21% overall

DeWitt J et al. Ann Intern Med 2004

MDHCT missed 60% of lesions < 2 cms

Agarwal B, AM J Gastro 2004



EUS in patients with non specific change of the pancreas on CT

Author	N° Patients	FNA	Rate of malignancy
Reddymasu 2011	320 patients Enlarged MDCT	30/320	9%
Horwhat 2009	69 patients Enlarged pancreas	19/69	8.7% (6/69)
Singh 2008	107 patients Enlarged pancreas	???	22%
Ho	50 patients	11/50	8% (4/50)

EUS - negative

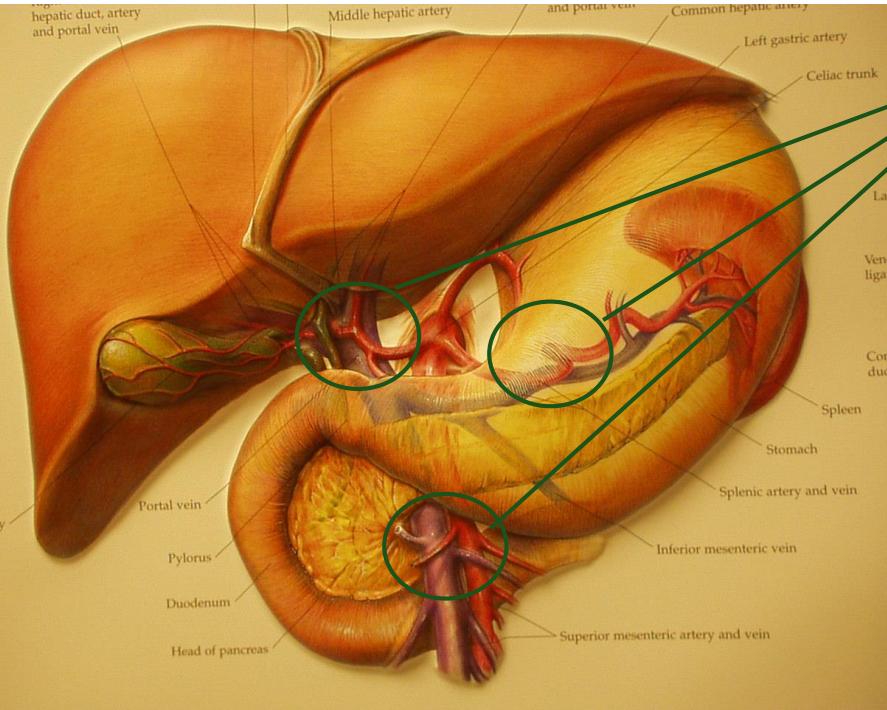
- Negative predictive value of EUS in patients with clinical suspicion of pancreatic cancer

In a follow – up period of 25 months NO patient developed Cancer

NPV (rule out cancer) 100%

J Klapman et al; Am J Gastro 2005;100:1-4

Pancreatic Cancer



Vascular Invasion

Sensitivity: **50-90%**

Specificity: **90-100%**

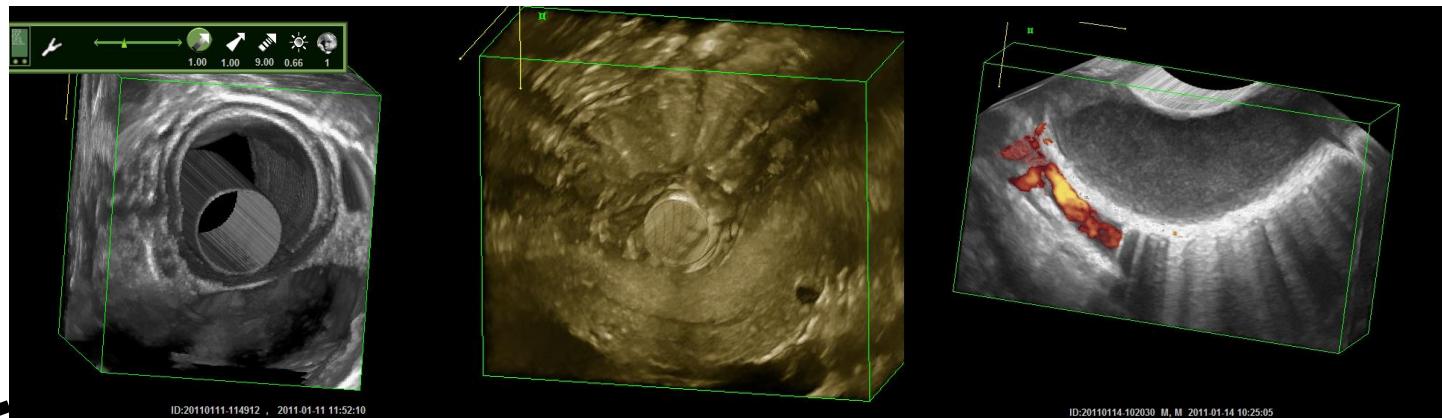
PV/confluence:EUS superior

SMV:Equivalent (~CT)

Celiac trunk:Equivalent (~CT)

HA, SMA:CT superior

Three-Dimensional Linear Endoscopic Ultrasound Feasibility of a Novel Technique Applied for the Detection of Vessel Involvement of Pancreatic Masses



	Linear EUS	3D	Surgery
Tumor invasion	10 (3FP) + (1FP) (+1)	6 (+1)	7
Tumor compression	 6 (+2) + (+1)	10 (-1)(1FN) (+1)	9
No vessel involvement	6 (+1) (1FN)	6 (+1) (-1)	6

Indications for the use of EUS-FNA

- ✓ To document a diagnosis of malignancy in a patient with an unresectable mass as a prerequisite for adjuvant chemotherapy or radiation therapy
- ✓ To exclude other tumor types
- ✓ patients who are reluctant to undergo major surgery without a definitive diagnosis
- ✓ To document the absence of malignancy when the pretest probability of malignancy is low
- ✓Neoadviant therapy

Pancreatic Cancer Clinical Impact of EUS-FNA

99 patients eligible for surgery

Metastatic distant lymph nodes	6
Liver metastasis	4
Malignant ascites	1
Retroperitoneal infiltration	1
•	

**EUS FNA influenced
Management in 12%**

Performance of EUS-FNA: Solid Pancreatic Tumors



- Celiac mesenteric region
- Hepatic pedicule
- Entire pancreas
- Lymph nodes
- Aspirate ascitic Fluid
- Left liver node

Celiac
Lumboaortic
Retroduodenopancreatic
Superior Mesenteric
Mediastinal

NODE

Malignant infiltration occurs in up to

30%

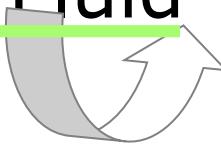
<5 mm LNs,

lung, esophageal, gastric, pancreatic, rectal carcinoma.

Cui XW et al. World J Gastroenterol 2013; 19: 4850
Hocke M et al. Endosc Ultrasound 2017; 6: 4

Performance of EUS-FNA: Solid Pancreatic Tumors

- Celiac mesenteric region
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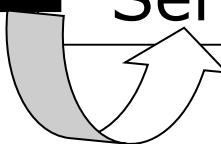
Peritoneal
Carcinomatosis

Performance of EUS-FNA: Solid Pancreatic Tumors

- Celiac mesenteric region
- Hepatic pedicule
- Entire pancreas
- Lymph nodes
- Aspirate ascitic Fluid
- Left liver node



Small metastasis
Sensibility: 100%



Resectable Tumors Should FNA be performed?

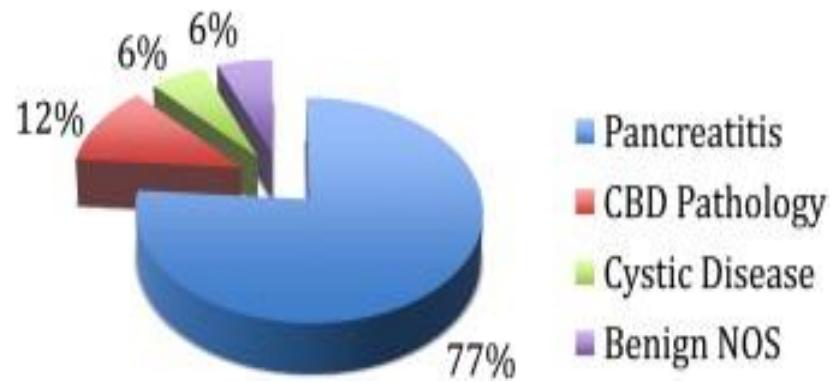
503 pts

Adenocarcinoma	78,5%
Mucinous cystic neoplasm	5,4%
Metastatic tumor	3,9%
Neuroendocrine tumor	3,8%
Poorly differentiated carcinoma	3,0%
Lymphoma	2,8%
Serous Cystadenoma	1,8%
Solid pseudopapillary tumor	0,8%

When to perform a pancreatoduodenectomy in the absence of positive histology? A consensus statement by the International Study Group of Pancreatic Surgery

Horacio J. Asbun, MD,^a Kevin Conlon, MD,^b Laureano Fernandez-Cruz, MD,^c Helmut Friess, MD,^d Shailesh V. Shrikhande, MD,^e Mustapha Adham, MD,^f Claudio Bassi, MD,^g Maximilian Bockhorn, MD,^h Markus Büchler, MD,ⁱ Richard M. Charnley, MD,^j Christos Dervenis, MD,^k Abe Fingerhut, MD,^l Dirk J. Gouma, MD,^m Werner Hartwig, MD,ⁱ Clem Imrie, MD,ⁿ Jakob R. Izbicki, MD,^h Keith D. Lillemoe, MD,^o Miroslav Milicevic, MD,^p Marco Montorsi, MD,^q John P. Neoptolemos, MD,^r Aken A. Sandberg, MD,^s Michael Sarr, MD,^t Charles Vollmer, MD,^u Charles J. Yeo, MD,^v and L. William Traverso, MD,^w for the International Study Group of Pancreatic Surgery, Jacksonville, FL, Dublin, Ireland, Barcelona, Spain, Munich, Hamburg, and Heidelberg, Germany, Mumbai, India, Lyon and Poissy, France, Verona and Milan, Italy, Newcastle-upon-Tyne, Glasgow, and Liverpool, UK, Athens, Greece, Amsterdam, The Netherlands, Boston, MA, Belgrade, Serbia, Stockholm, Sweden, Rochester, MN, Philadelphia, PA, and Boise, ID

Conclusion. In the presence of a solid mass suspicious for malignancy, consensus was reached that biopsy proof is not required before proceeding with resection. Confirmation of malignancy, however, is mandatory for patients with unresectable disease to be treated with neoadjuvant therapy before exploration for resection. When a diagnosis of AIP is highly suspected, a biopsy is recommended, and a short course of steroid treatment should be considered if the biopsy does not reveal features suspicious for malignancy. (Surgery 2014;155:887-92.)



Final diagnosis in benign disease after pancreatectomy for suspected malignancy.

Asbun HJ et al. Surgery 2014

Differential diagnosis of small solid pancreatic lesions

Christoph Frank Dietrich, MD, PhD,^{1,2} Anand Vasante Sahai, MD, PhD,³ Mirko D'Onofrio, MD,⁴ Uwe Will, MD, PhD,⁵ Paolo Giorgio Arcidiacono, MD, PhD,⁶ Maria Chiara Petrone, MD,⁶ Michael Hocke, MD, PhD,⁷ Barbara Braden, MD, PhD,⁸ Eike Burmester, MD,⁹ Kathleen Möller, MD,¹⁰ Adrian Săftoiu, MD, PhD,^{11,12} Andre Ignee, MD,² Xin-Wu Cui, MD, PhD,^{1,2} Sevastita Iordache, MD,¹¹ Andrej Potthoff, MD,¹³ Julio Iglesias-Garcia, MD, PhD,¹⁴ Pietro Fusaroli, MD, PhD,¹⁵ Yi Dong, MD, PhD,^{2,16} Christian Jenssen, MD¹⁷

TABLE 1. Clinical and pathologic characterization of 394 patients with solid pancreatic lesions

No.	All (%) 394	Benign (%) 179/394 (45)	Malignant (%) 215/394 (55)	PDAC (%) 146/394 (37)	NET (%) 156/394 (40)	Met (%) 28/394 (7)
All, median \pm SD, (range), no.	64					
Focal pancreatitis, median \pm SD, (range), no.	25					
SMCA, median \pm SD, (range), no.	15					
IPMN mucin filled, median \pm SD, (range), no.	8					
No.						
SPT, median \pm SD, (range), no.					5	
Intrapancreatic accessory spleen, median \pm SD, (range), no.					4	
Lipoma, median (range)					2	
Hamartoma, median (range)					2	
NHL, median (range)					2	
Necrosis, no.					1	

Resectable Tumors Should FNA be performed?

Adenocarcinoma	78,5%
Mucinous cystic neoplasm	5,4%

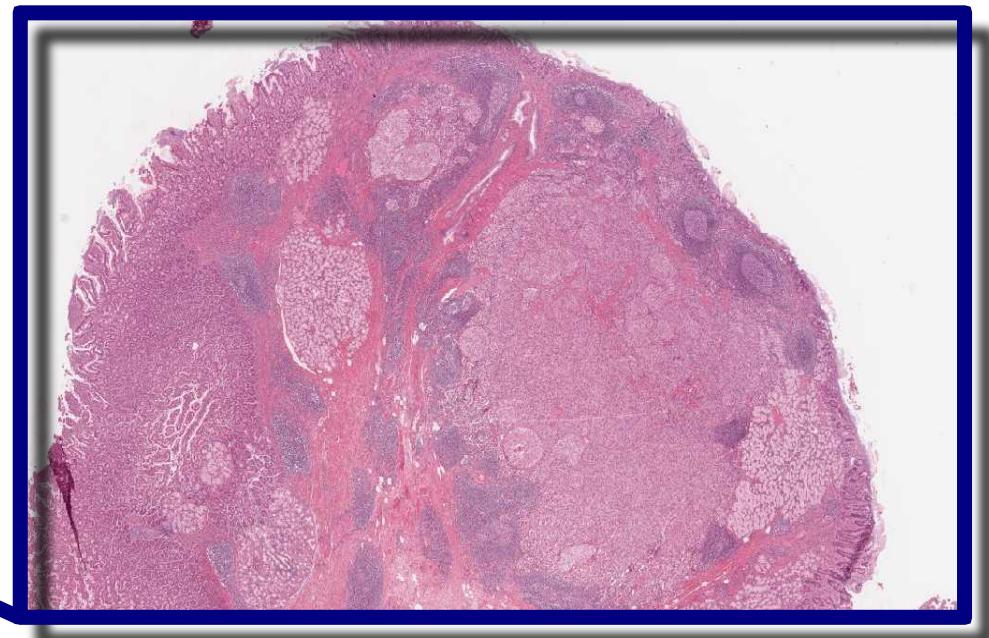
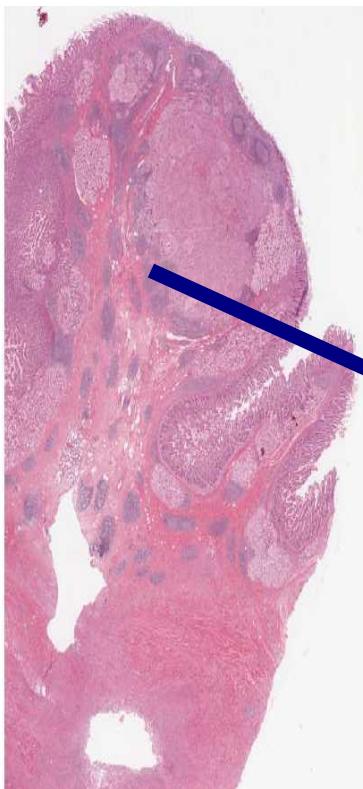
Benign lesions

- Pseudotumor Chronic pancreatitis
- Groove pancreatitis
- PAI tipo I e II

Solid pseudopapillary tumor)	0,8%
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GEP-NETs

Paranganglioma Gangliocitico Ampollare



Chronic pancreatitis

Shounak Majumder, Suresh T Chari

“Only 20% of chronic pancreatitis are detected by screening. In this article, we review the clinical features, pathophysiology, and management of chronic pancreatitis, and how a specific set of tests should affect clinical practice.”



Chronic calcifying pancreatitis

- Alcohol
- Smoking
- Genetic
- Idiopathic
 - Juvenile-onset
 - Tropical
 - Senile-onset

Chronic obstructive pancreatitis

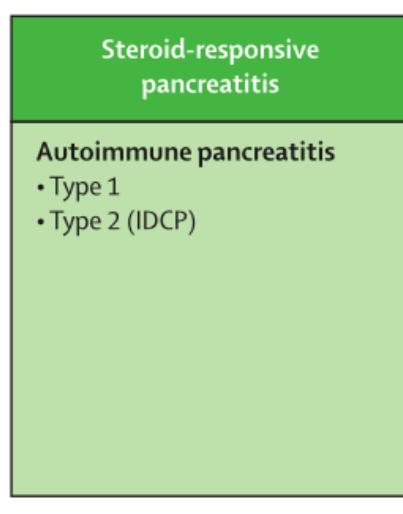
- Stricture**
- Blunt trauma
 - Endoscopic stenting
 - Acute pancreatitis
 - Anastomotic stricture

Tumour

 - Adenocarcinoma
 - IPMN
 - Serous cystadenoma
 - Islet cell tumour

Steroid-responsive pancreatitis

- Autoimmune pancreatitis**
- Type 1
 - Type 2 (IDCP)



	Type 1	Type 2
Median age of onset	Seventh decade	Third decade
Sex difference	Male predominant (3:1)	Equal predisposition (1:1)
Other organ involvement	Common (60%)	None
Inflammatory bowel disease	Less than 10%	About 30%
Serum IgG4 increase (>1·40 g/L)	Commonly present (>80%)	Usually absent (<10%)
Histological hallmarks		
Granulocyte epithelial lesion	Absent	Present
IgG4 staining	Prominent	Scant
Response to corticosteroid treatment	Universal	Universal

EUS-guided FNA for diagnosis of solid pancreatic neoplasms: a meta-analysis

TABLE 2. Classification of FNA cytology*

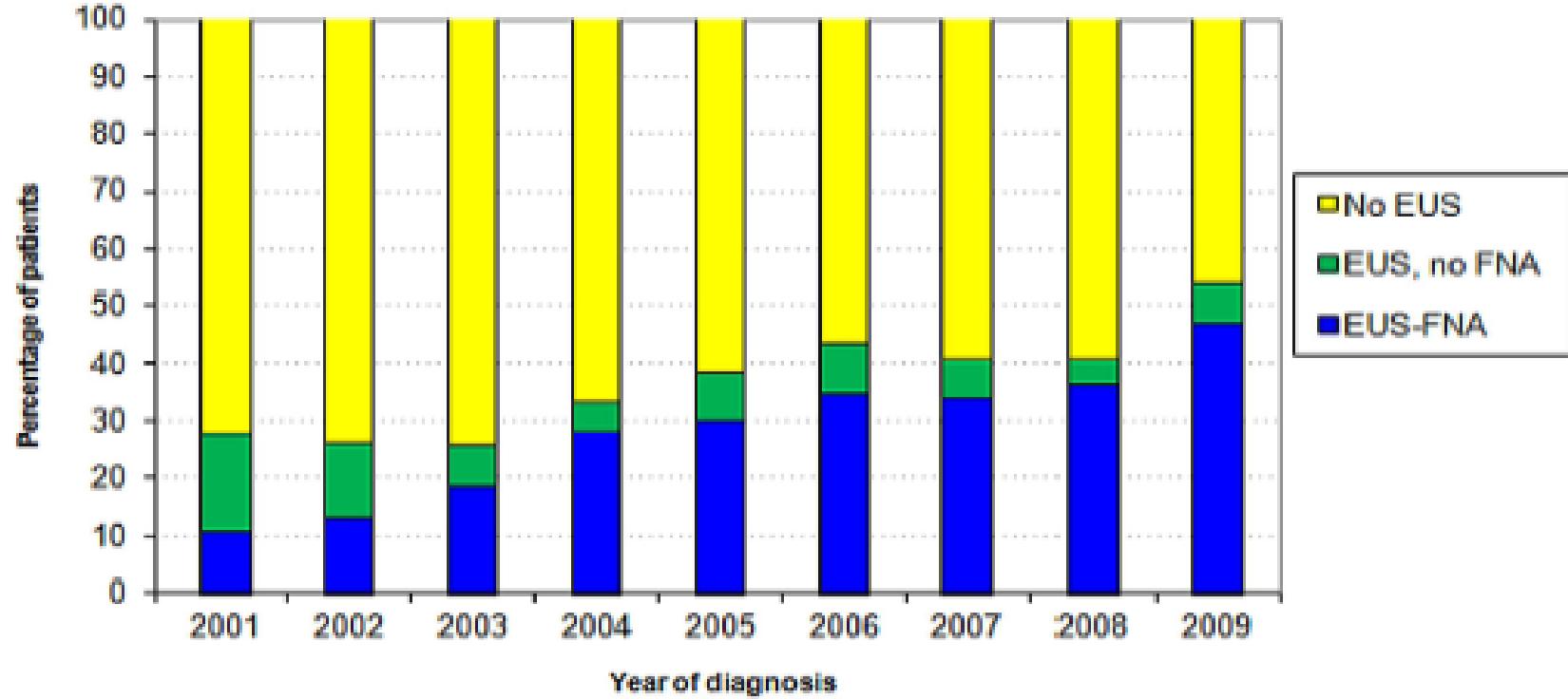
Classification 1	Classification 2
Inadequate, negative	Inadequate, negative
Benign on EUS-FNA, negative	Benign on EUS-FNA, negative
Suspicious/atypical results on EUS-FNA, negative	Suspicious/atypical results on EUS-FNA, positive
Malignancy on EUS-FNA, positive	Malignancy on EUS-FNA, positive

EUS-FNA, EUS-guided FNA
*Classification 1 is more strict

ic,¹ Mark J. W. McPhail, MRCP, PhD,² Lucia Possamai, MRCP,¹ Petros Vlavianos, MD, FRCP,² Kevin J. Monahan, MRCP, PhD³

	Sensibilità	Specificità	VPP	VPN
Classif. 1	85%	98%	99%	64%
Classif. 2	91%	94%	98%	72%

Trends in the use of EUS-FNA in patients with locoregional pancreatic cancer who underwent curative intent surgery

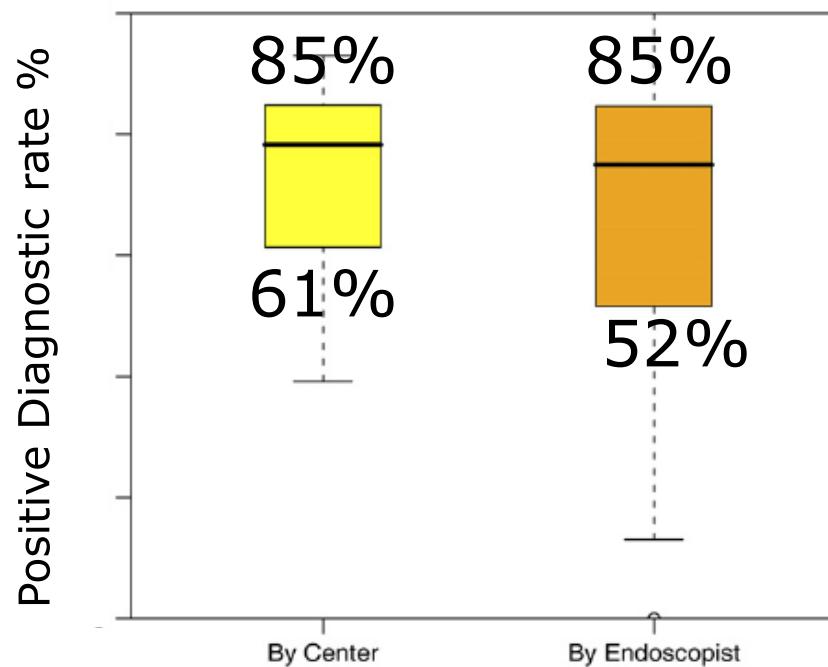


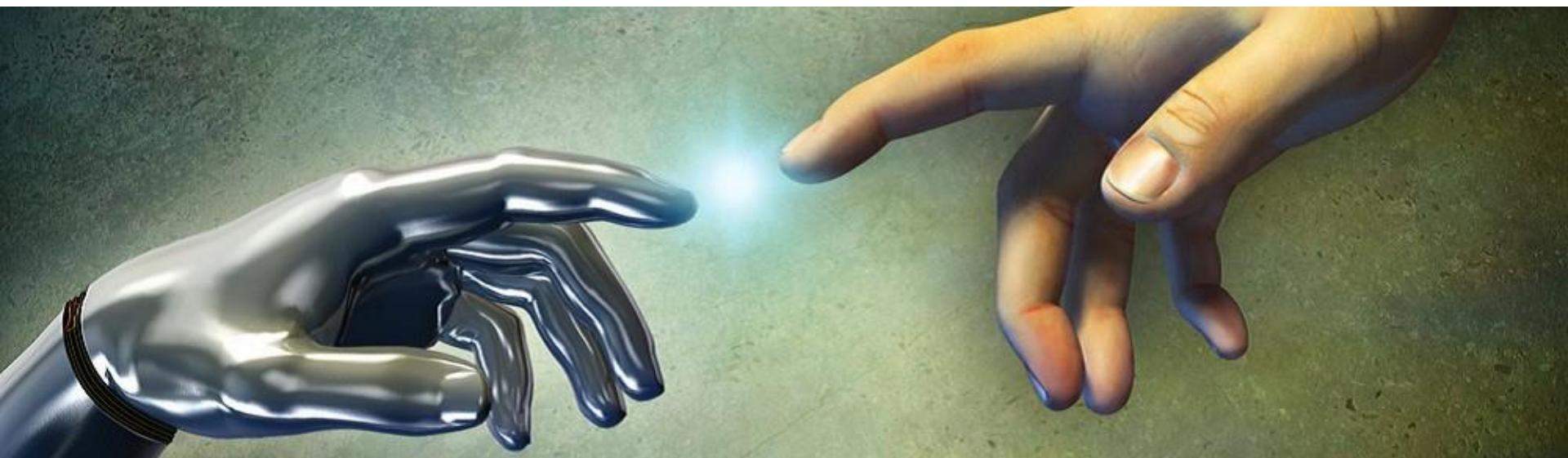


EUS-guided FNA: a benchmark for quality performance measurement

1075 ptz

21 centers/41endoscopist





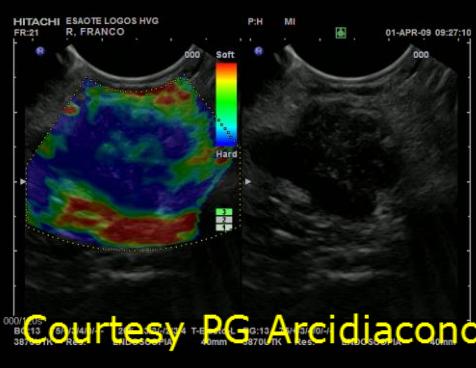
Differential Diagnosis

- ✓ Pancreatic cancer
- ✓ Cholangiocarcinoma



ACCURACY	
EUS	78%
IDUS	86%

P<0.002

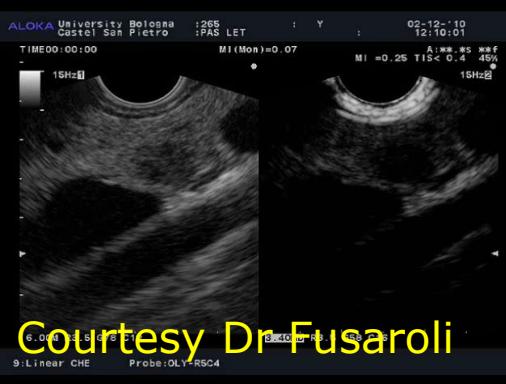


Courtesy PG Arcidiacono

Cancer vs Chronic Pancreatitis Elastosonography

Author (yr)	No. Pts	Sen (%)	Spe (%)	PPV (%)	NPV (%)	Acc (%)
Saftoi, '08	68	91.4	87.9	88.9	90.6	89.7
Hirche, '08	70	41	53	--	--	45
Giovannini, '09	121	92.3	80	93.3	77.4	89.4
Iglesias-Garcia, '09	130	100	85.5	90.7	100	94
Iglesias-Garcia, '10*	86	100	92.9	96.7	100	97.7

* Second generation EUS elastography



Cancer vs Chronic Pancreatitis Contrast-Enhanced Harmonic EUS

Courtesy Dr. Fusaroli

Author (yr)	No. Pts	Sen (%)	Spe (%)	PPV (%)	NPV (%)	Acc (%)
Hocke, '06	86	73.2	83,3	--	--	--
Fusaroli, '10 Hypoenhancing lesion* Hyperenhancing lesion*	90	96	64	78	93	82
		39	98	94	68	72
		69	90	56	95	88
Napoleon, '10*	35	72	100	100	77	86
Seicean, '10*	24	80	91.7	92.8	78	--

Predictors of *Adeno Ca and #NET

CHE-EUS in pancreatic tumors

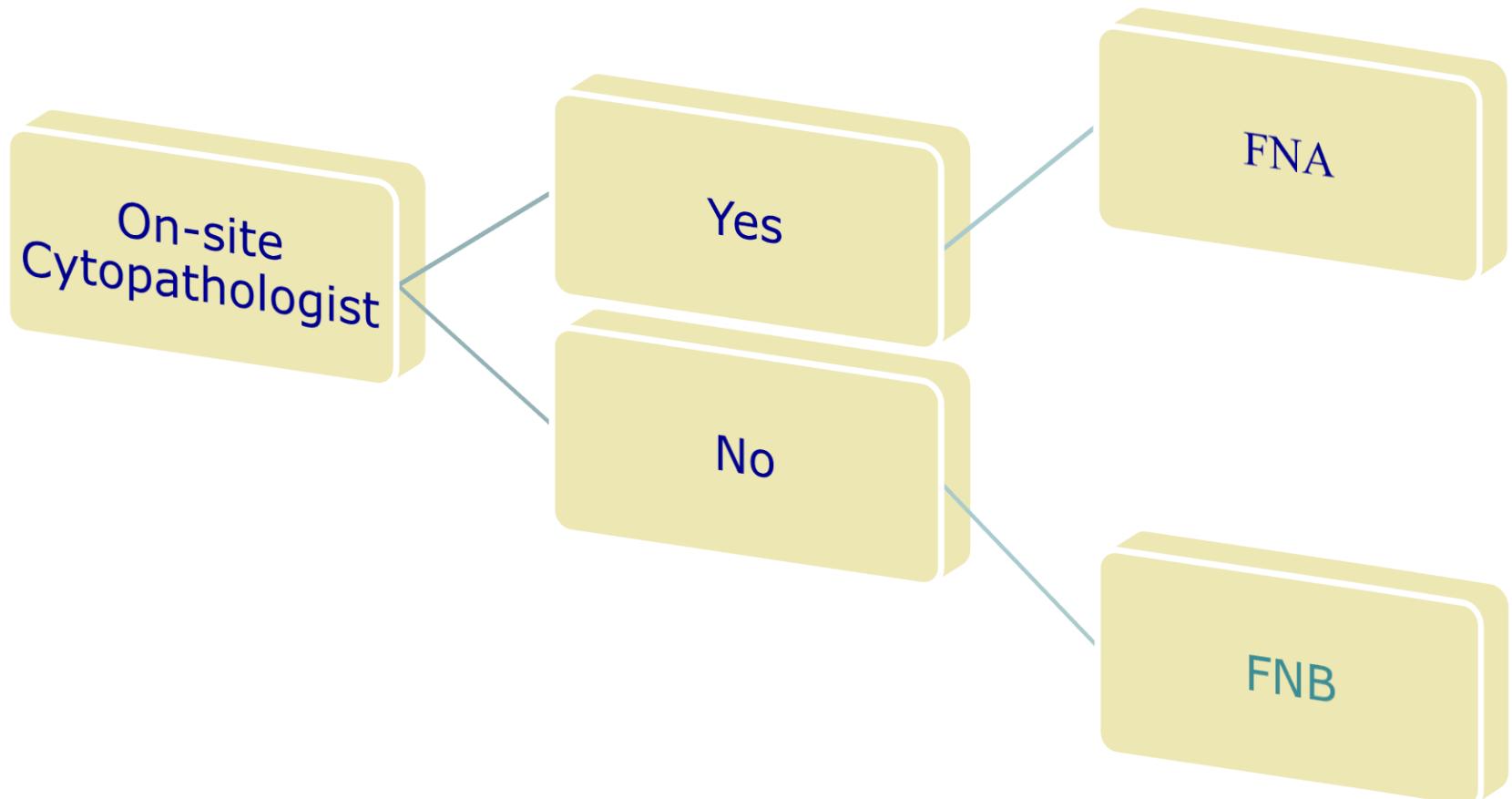
- ✓ Identified pancreatic tumor
- ✓ Increased detection (difficult cases)
- ✓ Help EUS-FNA
- ✓ Rule out cancer

NEDDLES

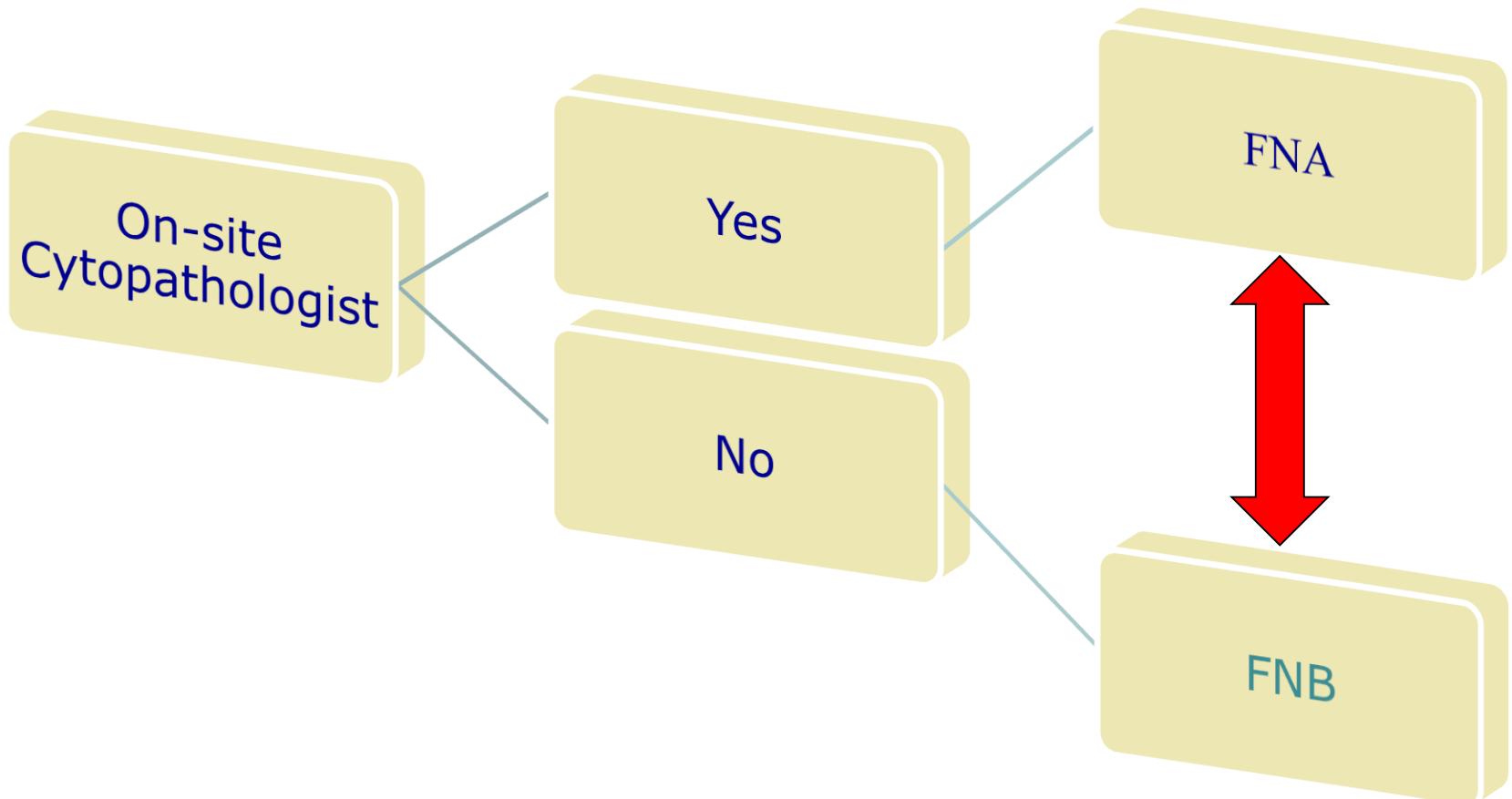


- 25 G
- 22 G
- 19 G
- Tru-cut
- Echo-Brush

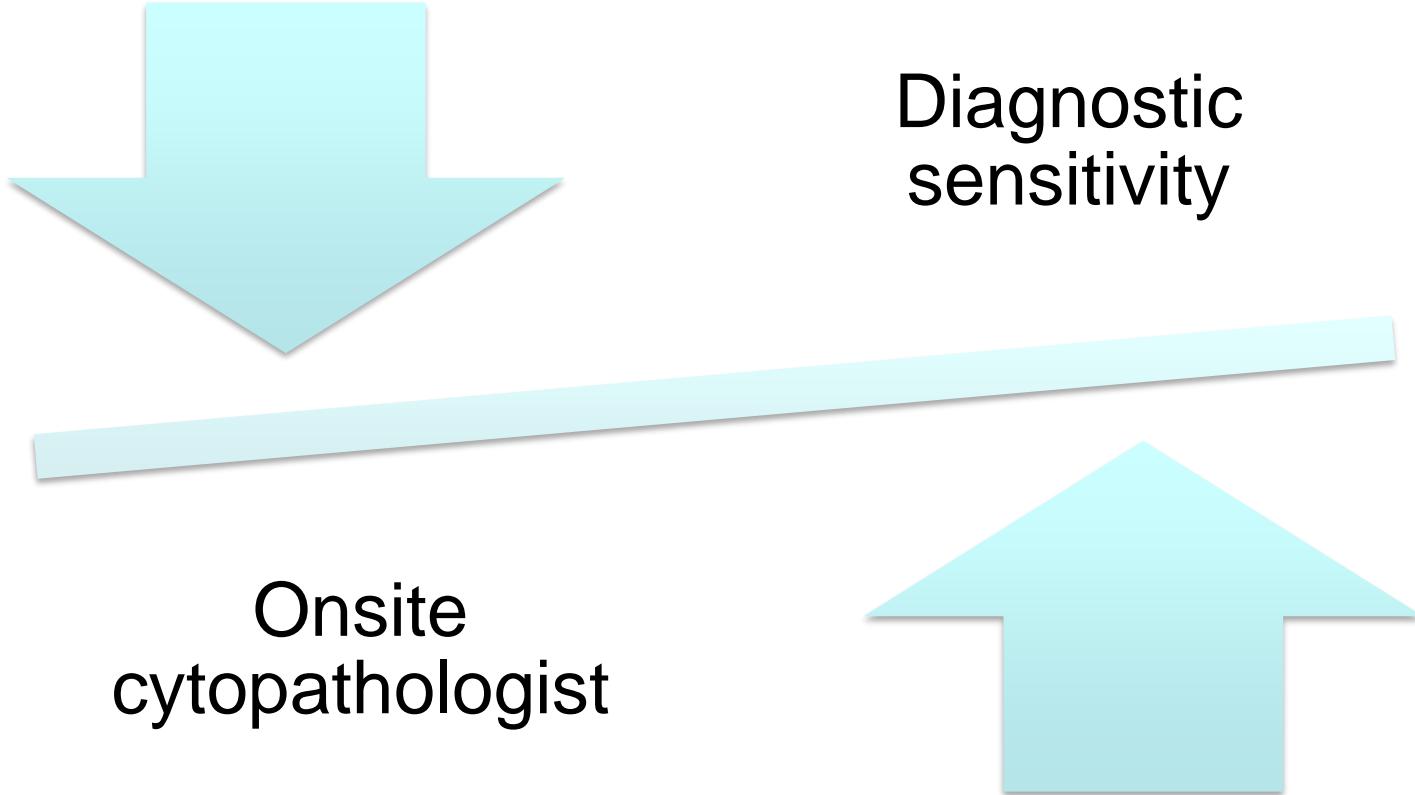
ROSE: the big dilemma



ROSE: the big dilemma



Do you have a onsite pathologist?



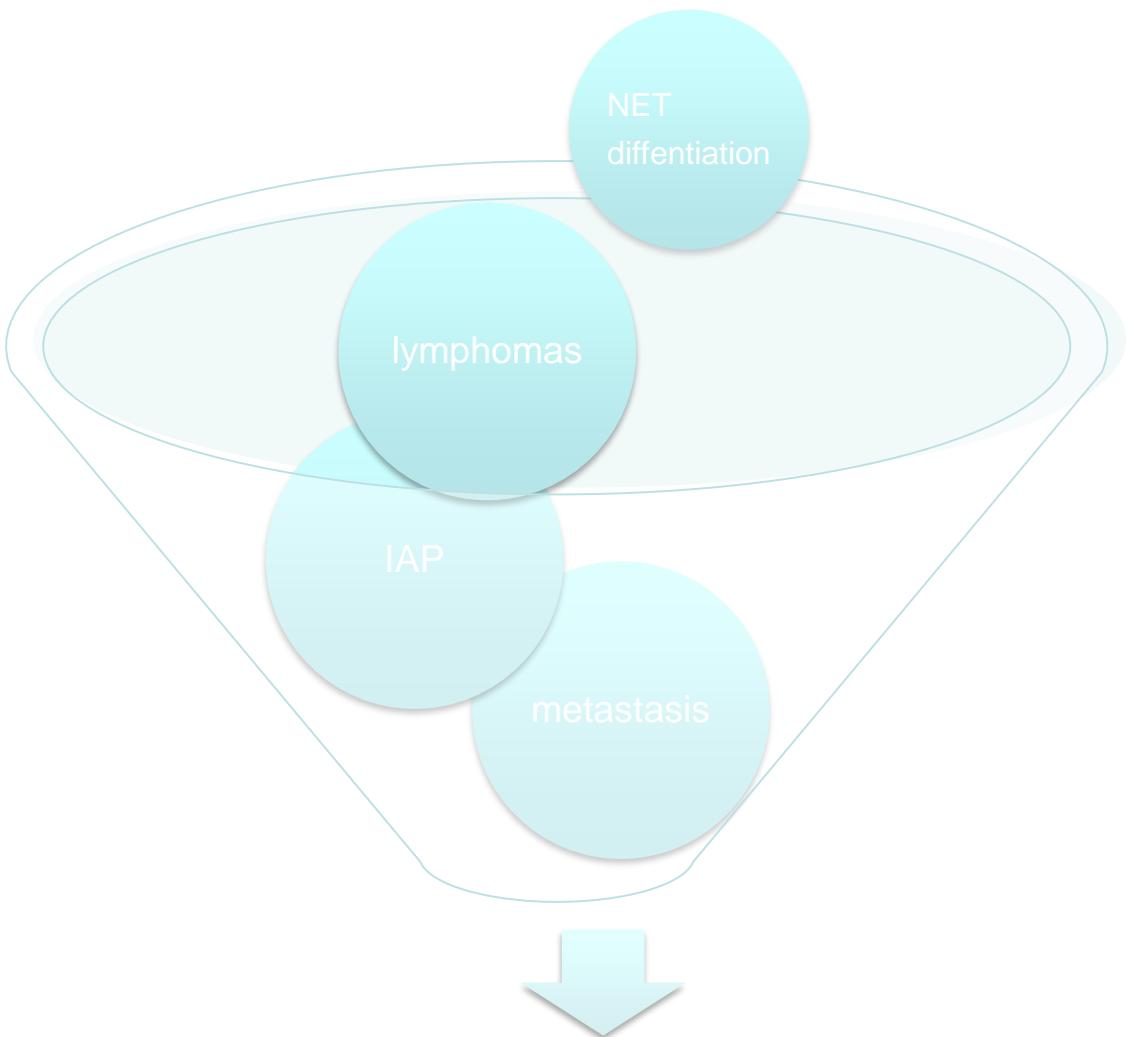
Survey

Available	Normal	Selected cases
ROSE	28%	15.1%

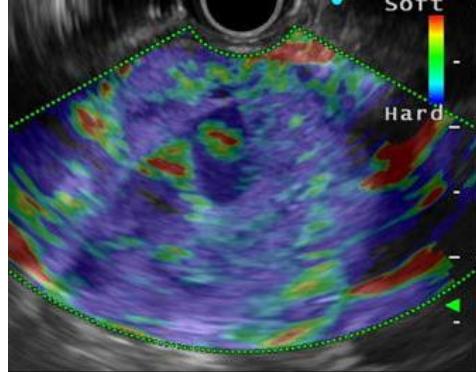
Dumonceau.

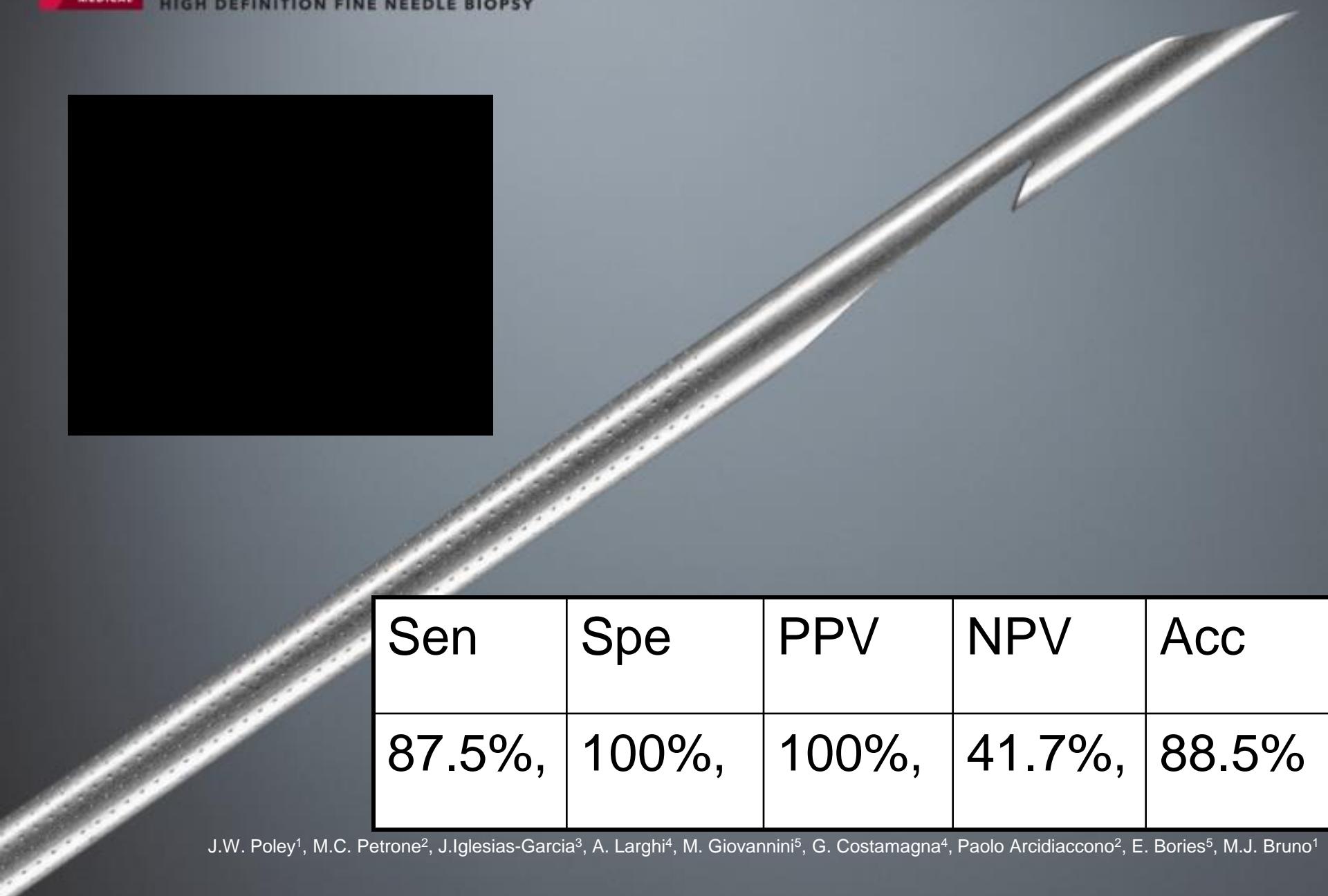
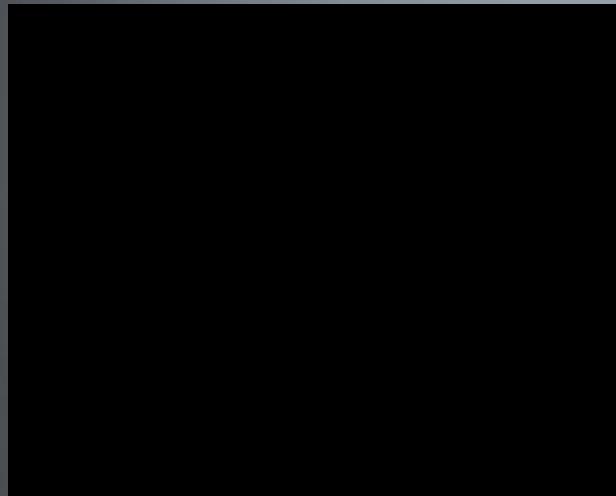


2012



Rare Conditions

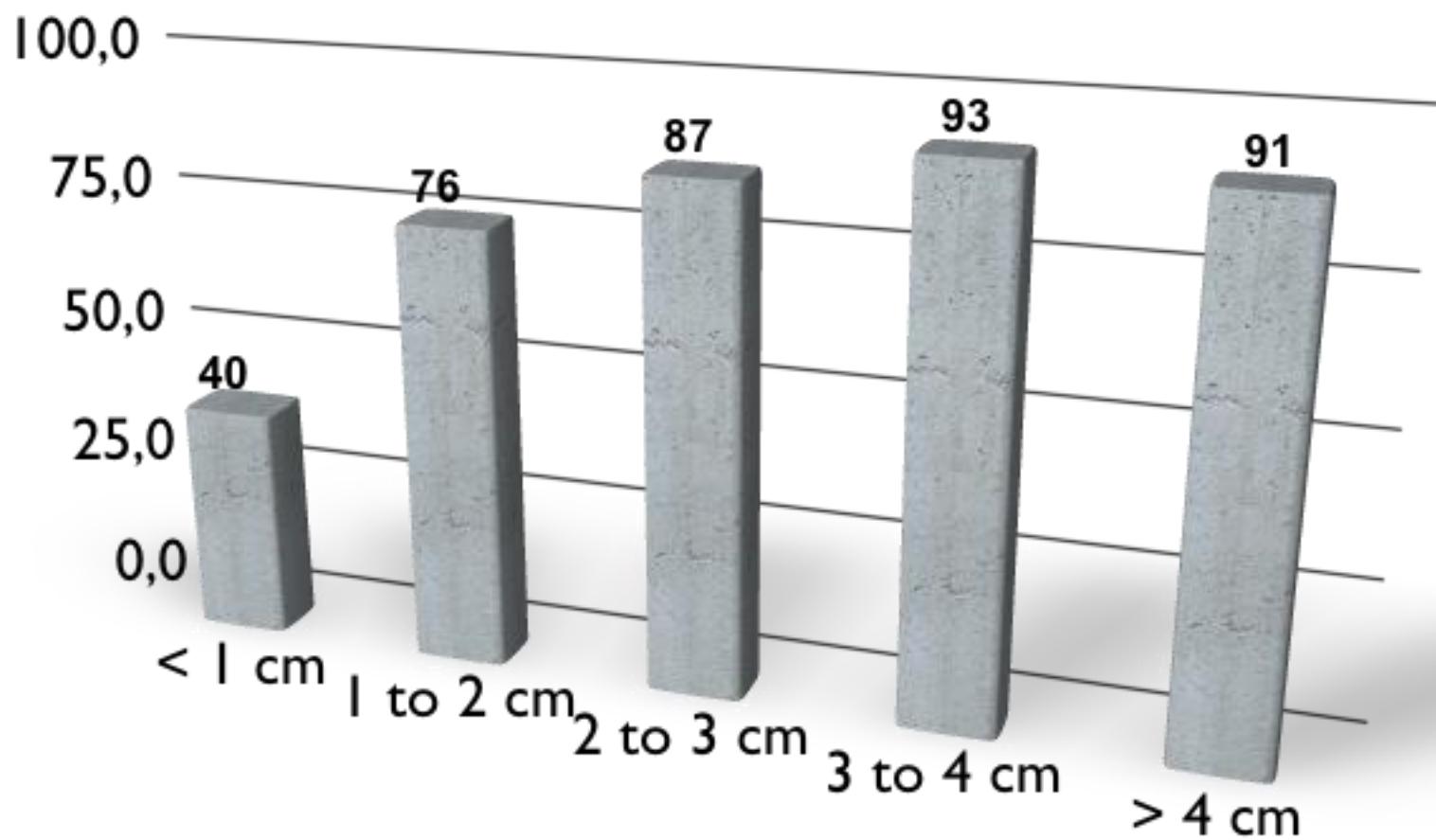
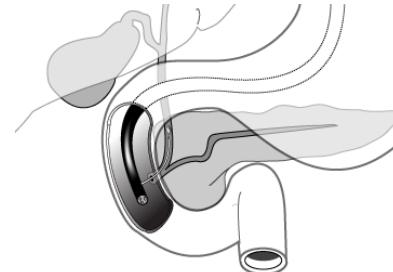




Sen	Spe	PPV	NPV	Acc
87.5%,	100%,	100%,	41.7%,	88.5%

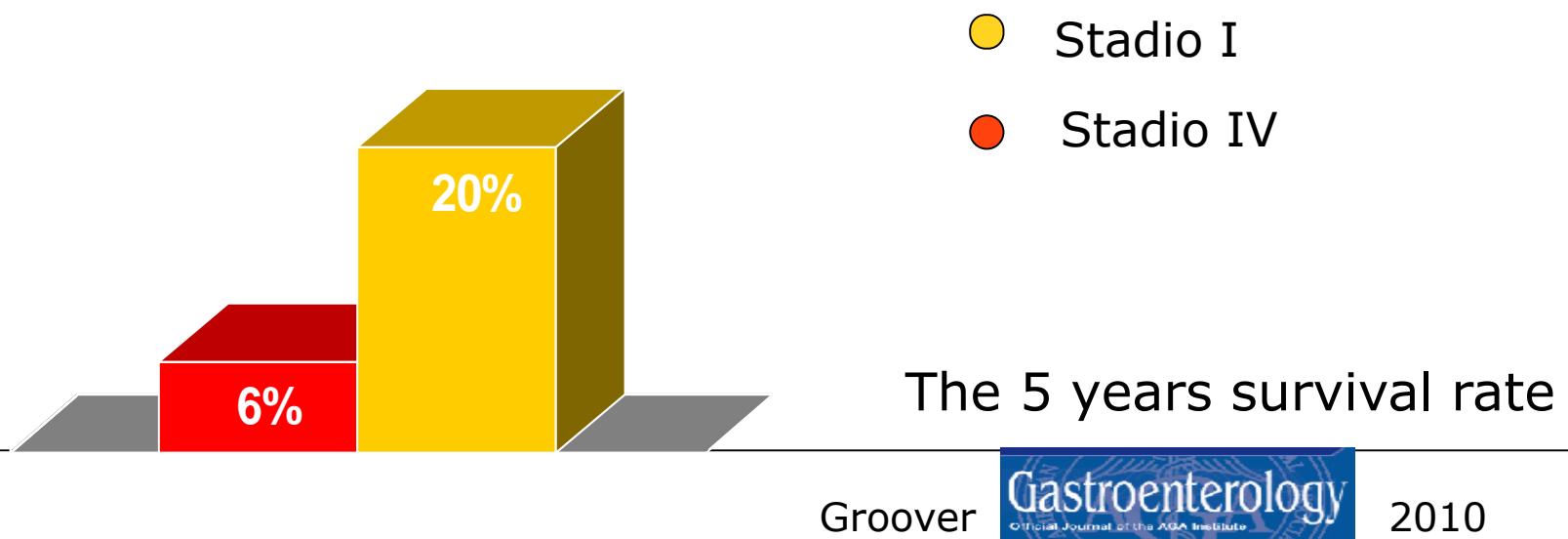


sensitivity



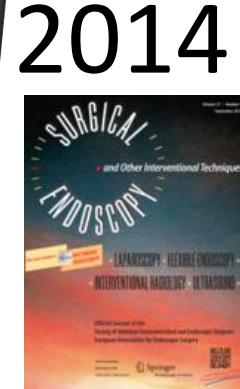
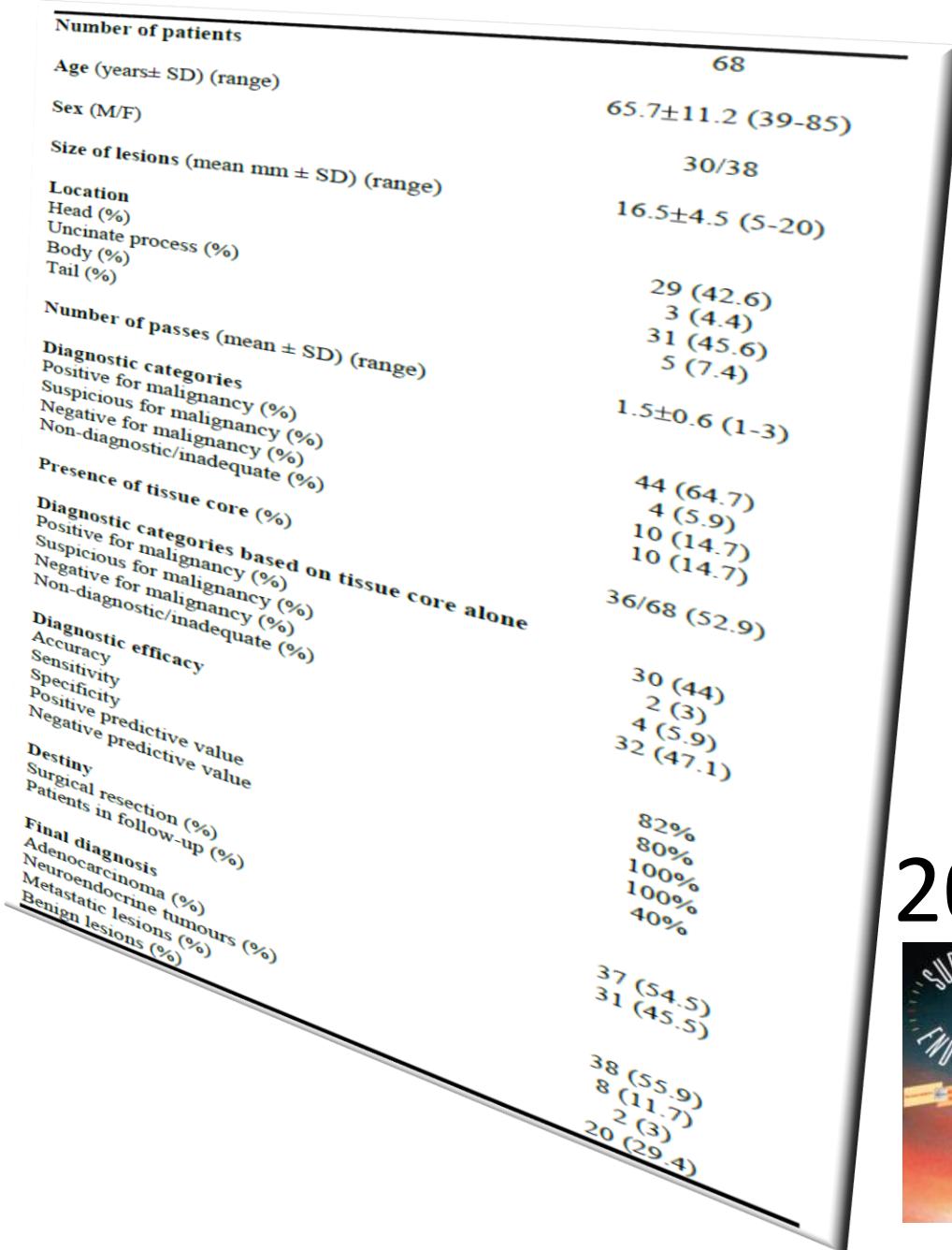
Surgical outcomes

15%-20%: candidates for pancreatectomy at the time of diagnosis



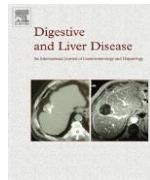


EUS-FNB of Small Solid Pancreatic Lesions using a 22-Gauge Needle with Side Fenestration



Endoscopic ultrasound-guided fine needle aspiration and biopsy using a 22-gauge needle with side fenestration in pancreatic cystic lesions

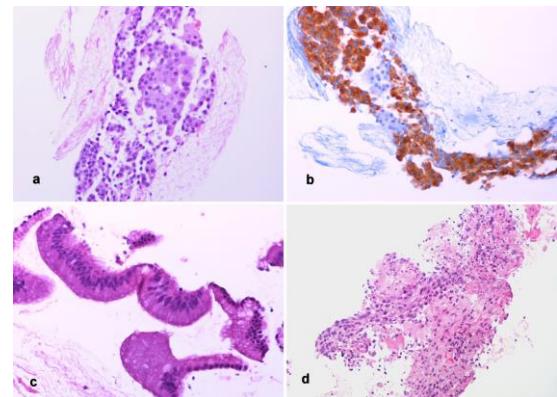
Luca Barresi ^{a,*}, Ilaria Tarantino ^a, Mario Traina ^a, Antonino Granata ^a, Gabriele Curcio ^a, Neville Azzopardi ^a, Paola Baccarini ^b, Rosa Liotta ^c, Adele Fornelli ^b, Antonella Maimone ^d, Elio Jovine ^e, Vincenzo Cennamo ^d, Carlo Fabbri ^d



2013

Fine needle aspiration and biopsy cytohistologic diagnosis.

Inadequate specimens	21 (35%)
Mucinous cysts with no malignancy	20 (33.3%) ^a
Mucinous carcinoma (in situ or invasive)	6 (10%)
Ductal adenocarcinoma with cystic degeneration	2 (3.3%)
Neuroendocrine cystic tumour	3 (5%)
Solid pseudopapillary tumour	1 (1.6%)
Benign PCLs	7 (11.6%) ^b

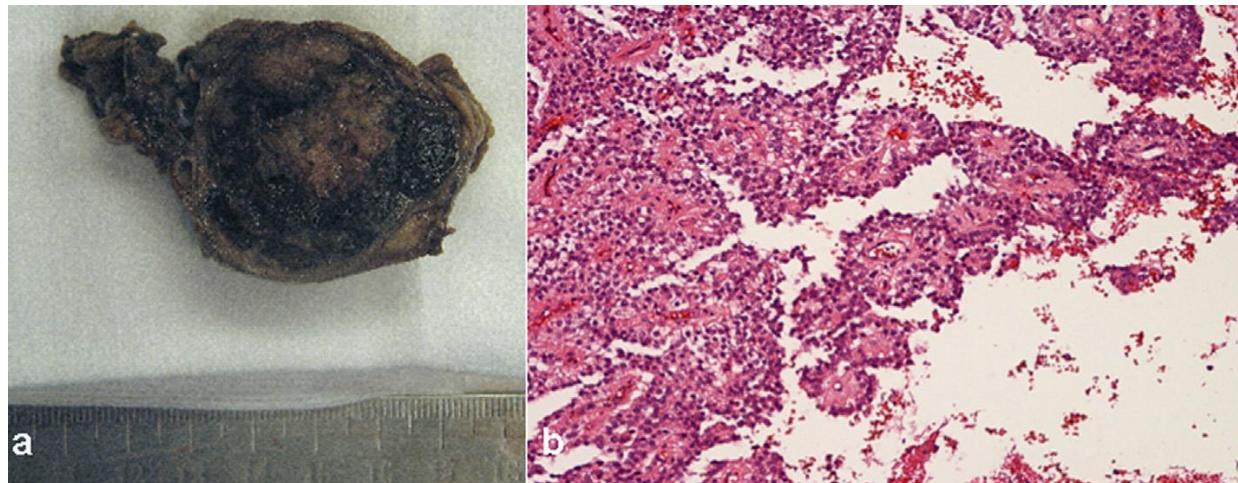


	CEA ≥ 192 ng/ml	CEA ≤ 192 ng/ml	Unavailable
Mucinous PCLs (n = 29)	9 (32.1%)	7 (26.9%)	13 (44.8%)
Mucinous malignant cysts (n = 9)	4 (44.4%)	2 (22.2%)	3 (33.3%)

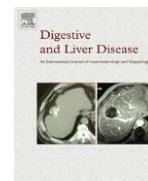
	K-ras mutation		
	Present	Absent	Unavailable
Mucinous PCLs (n = 29)	5 (17.8%)	7 (25%)	17 (58.6%)
Mucinous malignant cysts (n = 9)	1 (11.1%)	4 (44.4%)	4 (44.4%)



Preoperative diagnosis of a solid pseudopapillary tumour of the pancreas by Endoscopic Ultrasound Fine Needle Biopsy:
A retrospective case series



Antonella Maimone^a, Carmelo Luigiano^b, Paola Baccarini^c, Adele Fornelli^d,
Vincenzo Cennamo^a, Annamaria Polifemo^a, Marta Fiscaletti^e, Dario de Biase^c,
Francesca Jaboli^f, Clara Virgilio^b, Liliana Stelitano^b, Nicola Zanini^g,
Michele Masetti^g, Elio Jovine^g, Carlo Fabbri^{a,*}



2014

core'

[cò·re]

DEFINIZIONE

~Variante pop. e poet. di cuore.

Mostra dettagli ▼

Core | Definition of Core by Merriam-Webster Traduci questa pagina

<https://www.merriam-webster.com/dictionary/core> ▾

Define core: a central and often foundational part usually distinct from the enveloping part by a difference in nature : such as ... — core in a sentence

Core | Define Core at Dictionary.com Traduci questa pagina

www.dictionary.com/browse/core ▾

Core definition, the central part of a fleshy fruit, containing the seeds. See more.

Core - definition of core by The Free ... Traduci questa pagina

www.thefreedictionary.com/core ▾

CORE (kôr) abbr. Congress of Racial Equality core (kôr) n. 1. The central or innermost part: a rod with a hollow core; the hard elastic core of a baseball. 2. The ...

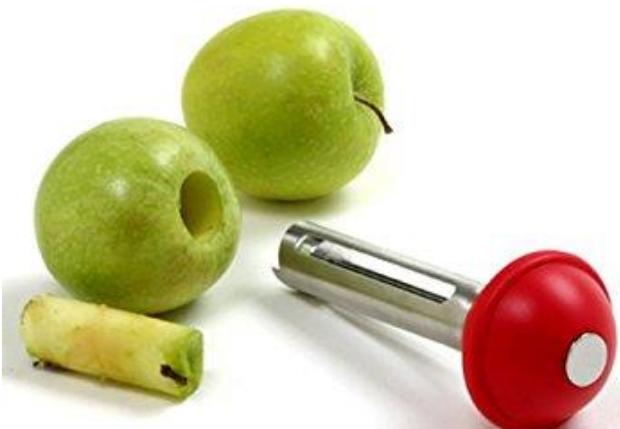
core Meaning in the Cambridge English ... Traduci questa pagina

dictionary.cambridge.org/dictionary/english/core ▾

core meaning, definition, what is core: the basic and most important part of something
Learn more.

Core: Definizione e significato di Core – Dizionario ...

dizionari.corriere.it/dizionario_italiano/C/core.shtml







**Presence of Core
30-80%**



Core tissue

a common-sense definition
it must contain
epithelium and stroma

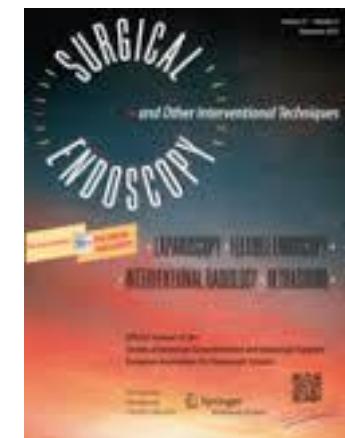




Dimensions, however, are variable.
For this reason we proposed a minimum length of 550 microns, which roughly corresponds to the diameter of a microscopic high-power field



Fabbri et al,

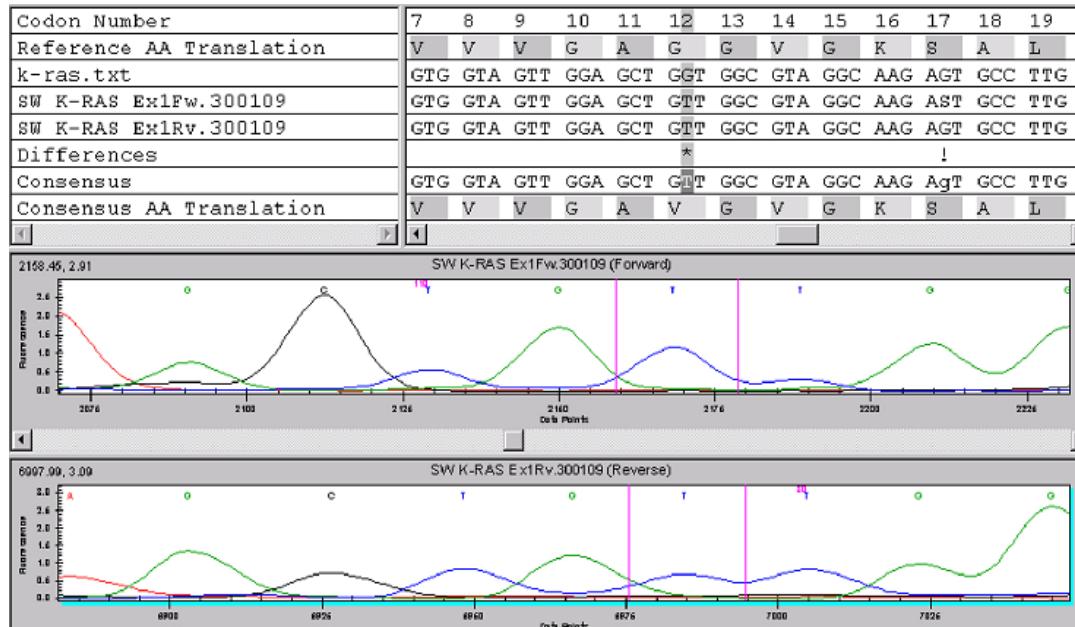


Molecular Techniques

GASTROINTESTINAL ENDOSCOPY	
Fasanella 2009	<ul style="list-style-type: none">Pancreatic endocrine tumor EUS-guided FNA DNA microsatellite loss and mortality
Clinical Gastroenterology and Hepatology	<ul style="list-style-type: none">Differentiating neoplastic from benign lesions of the pancreas: translational techniques
Kalid 2009	
Pathology International	<ul style="list-style-type: none">Diagnostic approach to pancreatic tumors with the specimens of endoscopic ultrasound-guided fine needle aspiration
Ito 2009	
GASTROINTESTINAL ENDOSCOPY	
De Witt 2009	<ul style="list-style-type: none">EUS for pancreatic endocrine tumors: do we need to know our pancreatic endocrine tumor's DNA?

Molecular Techniques

K-ras analysis

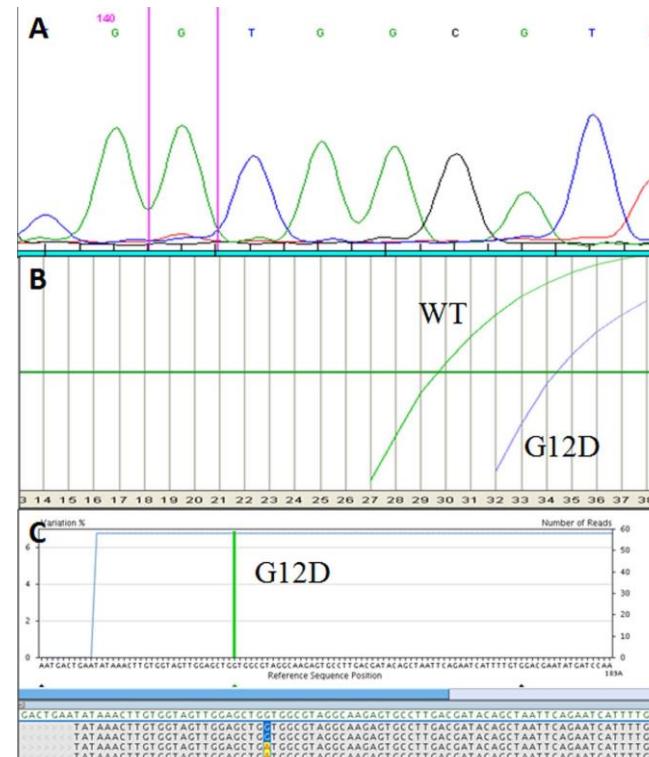


Next Generation Sequencing Improves the Accuracy of KRAS Mutation Analysis in Endoscopic Ultrasound Fine Needle Aspiration Pancreatic Lesions

Dario de Biase^{1,2*}, Michela Visani², Paola Baccarini¹, Anna Maria Polifemo³, Antonella Maimone⁴, Adele Fornelli⁵, Adriana Giuliani⁶, Nicola Zanini⁷, Carlo Fabbri³, Annalisa Pession^{2†}, Giovanni Tallini^{1†}

Performance	KRAS Ex 2			KRAS Ex 2 and Ex 3		
	454 NGS	ASLNA	Sanger	454 NGS	ASLNA	Sanger
SPEC (%)	100.00	100.00	100.00	100.00	100.00	100.00
SENSIT (%)	52.78	52.78	44.19	73.68	52.78	42.11
PPV (%)	100.00	100.00	100.00	100.00	100.00	100.00
NPV (%)	55.26	55.26	36.84	65.52	55.26	46.34
ACC (%)	70.18	70.18	57.89	82.46	70.18	70.18
FDR (%)	0.00	0.00	0.00	0.00	0.00	0.00

Number of KRAS mutated samples using:		
Final End-Point	454 NGS (%)	ASLNAqPCR (%)
Adenocarcinomatous and pre-neoplastic lesions (n = 38)	28 (73.7)	21 (55.3)
PDAC (n = 20)	14 (70)	12 (60)
IPMN (n = 12)	10 (83.3)	5 (41.7)
Inop. Neoplasia (n = 6)	4 (66.7)	4 (66.7)
Not-adenocarcinomatous lesions (n = 7)	0 (0)	0 (0)
pNET (n = 5)	0 (0)	0 (0)
SPPT (n = 2)	0 (0)	0 (0)
Benign Lesions (n = 12)	0 (0)	0 (0)
NA (n = 3)	3 (100)	3 (100)
		1 (33.3)



STRENGTHS strong points



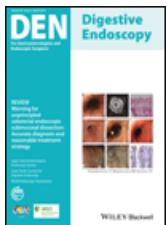


Team work and cytopathology molecular diagnosis of solid pancreatic lesions

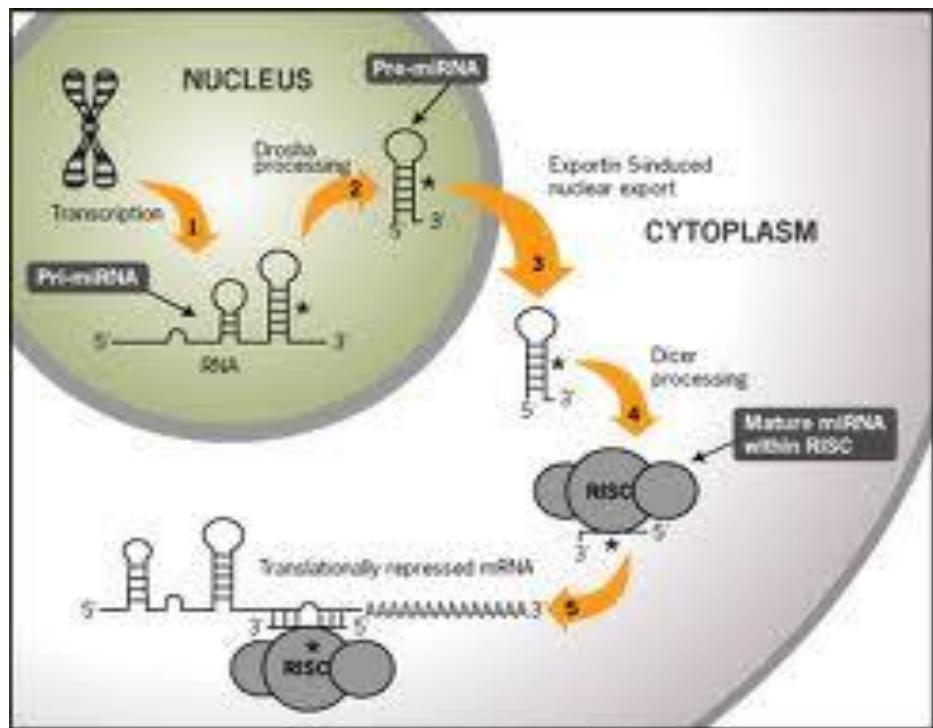
Carlo Fabbri,¹ Giulia Gibiino,⁶ Adele Fornelli,² Vincenzo Cennamo,¹ Daniela Grifoni,³ Michela Visani,⁴ Giorgia Acquaviva,⁴ Matteo Fassan,⁷ Sirio Fiorino,⁵ Silvia Giovanelli,¹ Marco Bassi,¹ Stefania Ghersi,¹ Giovanni Tallini,⁴ Elio Jovine,¹ Antonio Gasbarrini⁶ and Dario de Biase³

PRE-ANALYTICAL EVALUATION: EVERYTHING YOU ALWAYS WANTED TO KNOW ABOUT THE ENDOSCOPIC MATERIAL FOR MOLECULAR ANALYSIS (BUT YOU WERE AFRAID TO ASK YOUR MOLECULAR BIOLOGIST)

2017



The Near Future



The MicroRNA(miRNAs)
regulate the expression of
oncogenes and
tumors suppressor

The miRNAs have characteristic expression profiles in
some
carcinomas, and several species are dysregulated in
Pancreatic Ductal Adenocarcinoma.

The Near Future

The MiRNA expression have accurately predicted the presence of malignancy in 89% of cancer specimens in the cellblock

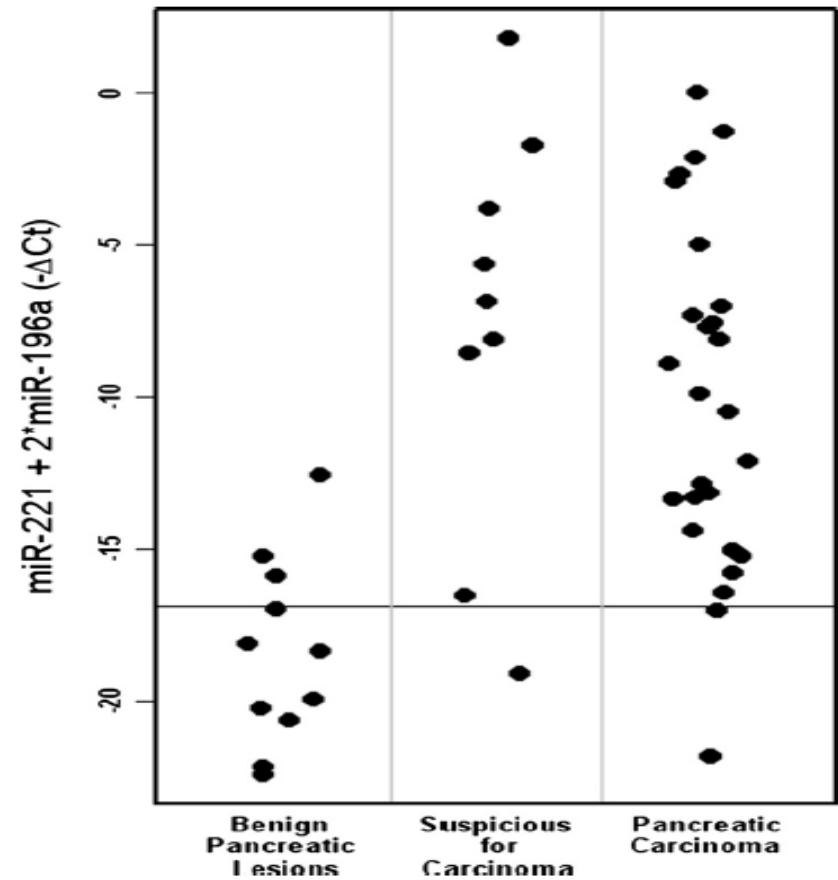


Table 3-4 Applications of Molecular Diagnostics for Gastrointestinal Cancers

TECHNIQUE	DISORDER	GENE(S) DETECTED	s or Altered Proteins
PCR-Based Strategies to Detect Germline DNA Alterations	Germline DNA Analysis for Hereditary GI Cancer Syndromes		
FAP, AFAP Single-strand conformation polymorphism analysis	MYH polyposis	APC	ture of single-stranded DNA caused by cleavage
Lynch, HNPCC	Peutz-Jeghers syndrome	<i>hMSH2</i> , <i>hMLH1</i> , <i>hMSH6</i> , <i>hPMS2</i>	le-stranded DNA altered by mutations
Denaturing gradient gel electrophoresis	Cowden's disease	<i>MYH</i>	ation caused by mutations
Heteroduplex analysis	Juvenile polyposis	<i>LKB1</i>	atches in heteroduplexes
Heteroduplex mismatch cleavage	Hereditary gastric cancer	<i>PTEN</i>	de sequence
Direct DNA sequencing	Hereditary pancreatic cancer	<i>SMAD4</i> , <i>BMPR1A</i>	ed by enzymatic cleavage
PCR-Based Strategies to Detect Allele-Specific Oligonucleotides	MEN1	<i>E-cadherin</i> <i>p16^{INK4A}</i> , <i>BRCA2</i> <i>Menin</i>	s with wild-type or mutant sequence
Protein-Based Strategies	Molecular Analysis for the Diagnosis of Sporadic GI Cancers		from nonsense mutation and a premature
In vitro translation (IVT)	Colon cancer	<i>K-ras</i> , <i>APC</i> , <i>TP53</i>	caused by mutation
Yeast and bacterial colorimetry	Stool DNA testing		f gene product in tumor sample
Immunohistochemistry	Tumor DNA MSI testing		
	Tumor immunohistochemistry for <i>hMSH2</i> , <i>hMLH1</i> , <i>hMSH6</i> , <i>hPMS2</i> protein		

Table 3-4 Applications of Molecular Diagnostics for Gastrointestinal Cancers

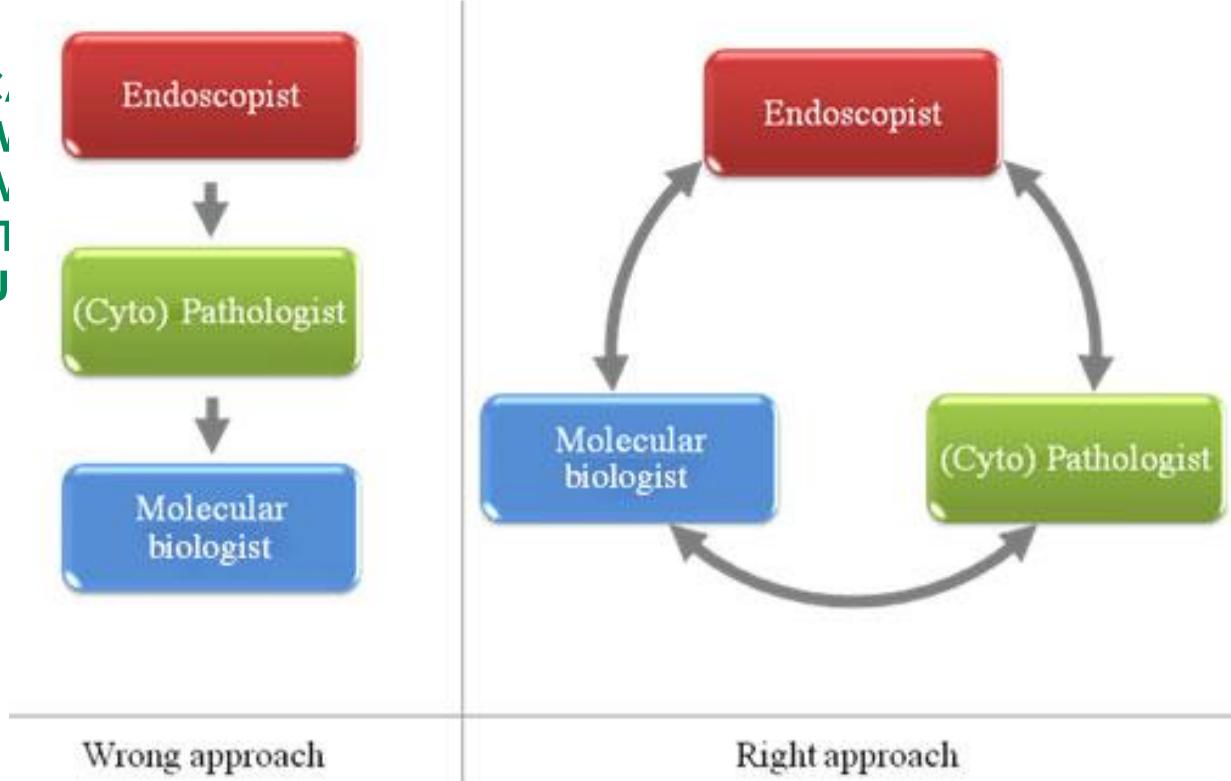
DISORDER	GENE(S) DETECTED
Germline DNA Analysis for Hereditary GI Cancer Syndromes	
FAP, AFAP	APC
Lynch, HNPCC	<i>hMSH2</i> , <i>hMLH1</i> , <i>hMSH6</i> , <i>hPMS2</i>
MYH polyposis	MYH
Peutz-Jeghers syndrome	<i>LKB1</i>
Cowden's disease	<i>PTEN</i>
Juvenile polyposis	<i>SMAD4</i> , <i>BMPR1A</i>
Hereditary gastric cancer	<i>E-cadherin</i>
Hereditary pancreatic cancer	<i>p16^{INK4A}</i> , <i>BRCA2</i>
MEN1	<i>Menin</i>
Molecular Analysis for the Diagnosis of Sporadic GI Cancers	
Colon cancer	
Stool DNA testing	<i>K-ras</i> , APC, TP53
Tumor DNA MSI testing	
Tumor immunohistochemistry for <i>hMSH2</i> , <i>hMLH1</i> , <i>hMSH6</i> , <i>hPMS2</i> protein	



Team work and cytopathology molecular diagnosis of solid pancreatic lesions

Carlo Fabbri,¹ Giulia Gibiino,⁶ Adele Fornelli,² Vincenzo Cennamo,¹ Daniela Grifoni,³ Michela Visani,⁴ Giorgia Acquaviva,⁴ Matteo Fassan,⁷ Sirio Fiorino,⁵ Silvia Giovanelli,¹ Marco Bassi,¹ Stefania Ghersi,¹ Giovanni Tallini,⁴ Elio Jovine,¹ Antonio Gasbarrini⁶ and Dario de Biase³

**PRE-ANALYTIC,
YOU ALWAYS HAVE
AN ENDOSCOPIC ANALYSIS (BUT
YOUR MOLECULAR**



Istotipo	Caratteri lesione	Procedura chirurgica
Insulinoma	< 2 cm, superficiale, No Wirs > 2 cm o coinvolg. Wirsung	Enucleoresezione Resezione
Gastrinoma	Qualsiasi localizzazione Local. Esclusiva linfonodale	Resezione tipica Exeresi linfonodi
Tumori non funzionanti	< 2 cm, superficiale, No Wirs > 2 cm o coinvolg. Wirsung	Enucleoresezione Resezione tipica
VIPoma Glucagonoma SMSoma	Qualsiasi localizzazione	Resezione tipica



Simultaneous EUS-FNA Diagnosis and TNM Staging of a Pancreatic Neuroendocrine Tumor in a Patient with an Unrecognized MEN Type 1

Francesco Ferrara,¹ Carmelo Luigiano,¹ Antonella Maimone,¹
Marco Bassi,¹ Anna Maria Polifemo,¹ Paola Baccarini,² Vincenzo
Cennamo,³ Nadia Cremonini,⁴ and Carlo Fabbri¹



(a)



(a)



(a)



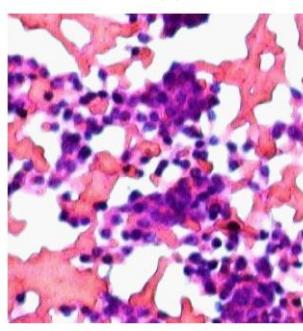
(b)



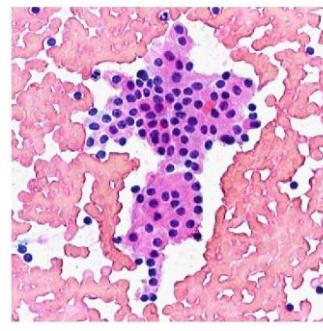
(b)



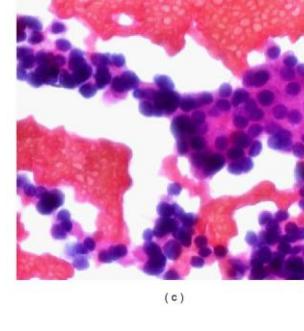
(b)



(c)



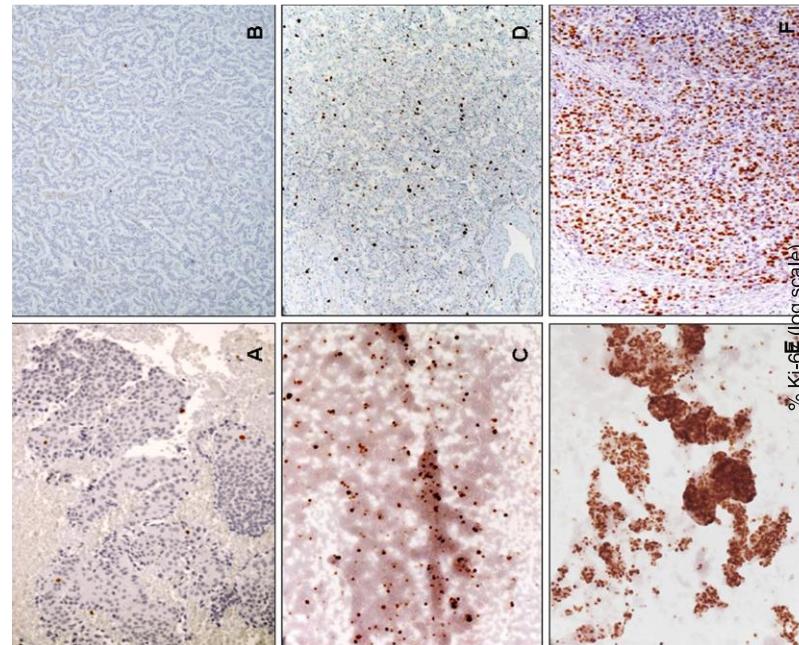
(c)



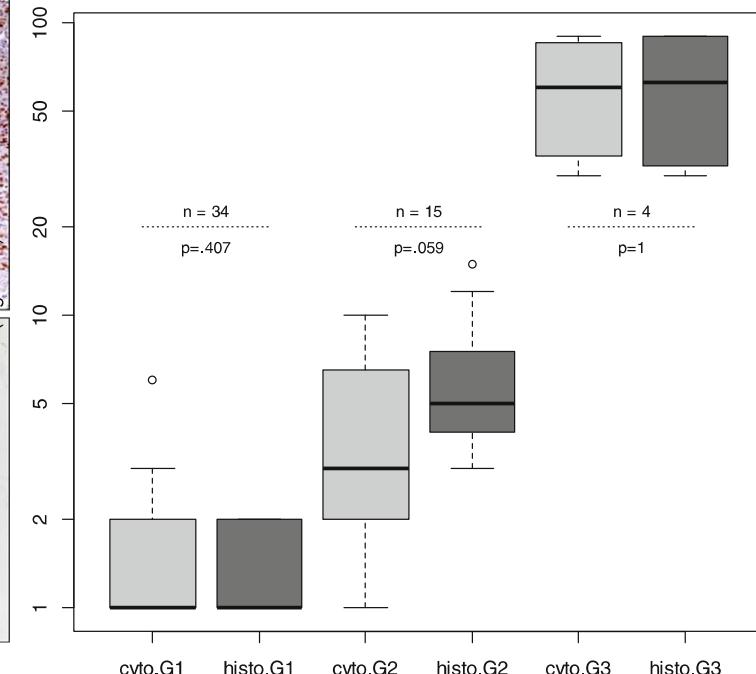
(c)

Ki-67 cytological index can distinguish well-differentiated from poorly differentiated pancreatic neuroendocrine tumors: a comparative cytohistological study of 53 cases

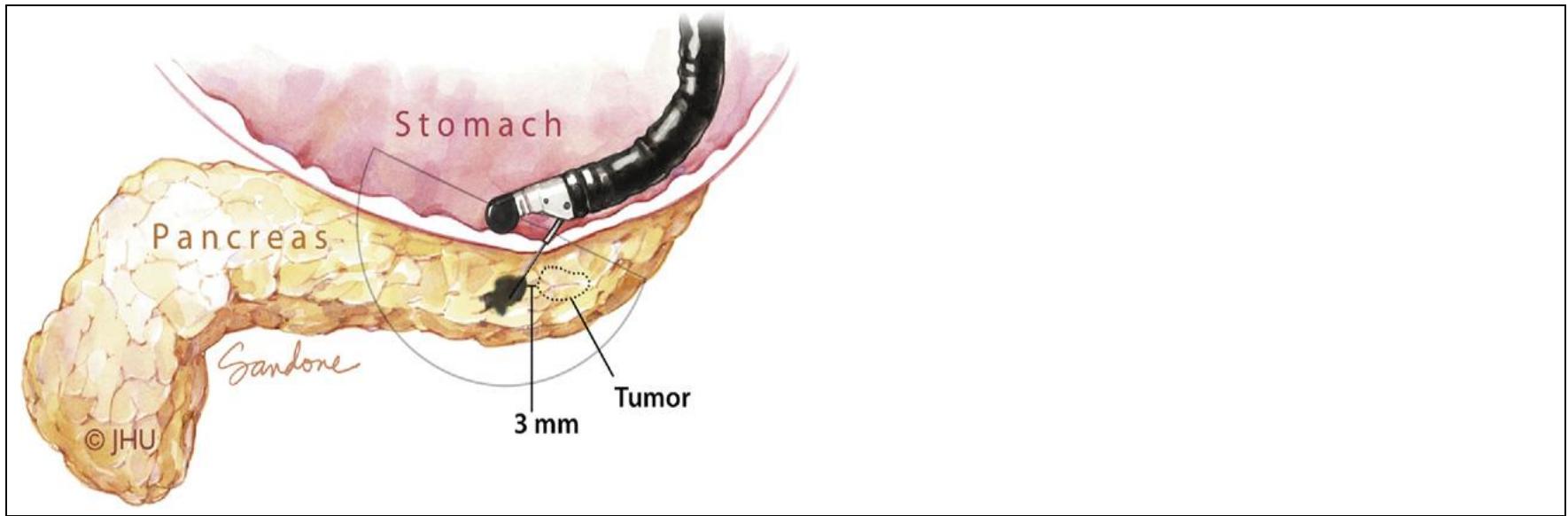
Gabriele Carlinfante · Paola Baccarini · Debora Berretti · Tiziana Casetti ·
Maurizio Cavina · Rita Conigliaro · Alessandro De Pellegrin · Luca Di Tommaso ·
Carlo Fabbri · Adele Fornelli · Andrea Frasoldati · Giorgio Gardini · Luisa Losi ·
Livia Maccio · Raffaele Manta · Nico Pagano · Romano Sassatelli · Silvia Serra ·
Lorenzo Camellini



Distribution of Ki-67 by measurement source and grading



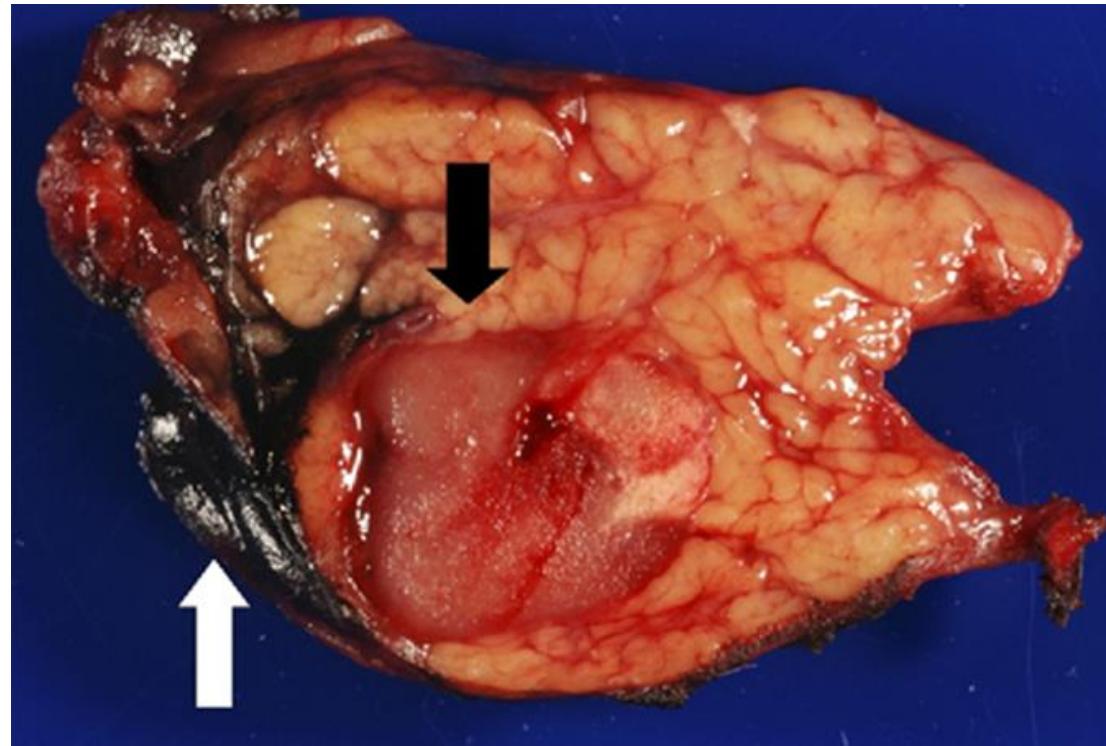
Tattooing before laparoscopic distal pancreatic resection



Pancreatology. 2013 Jul-Aug;13(4):449.

Body tattooing: efficacy of a “new” practice.

Fornelli A¹, Fabbri C, Zanini N, Jovine E.



Pancreatology



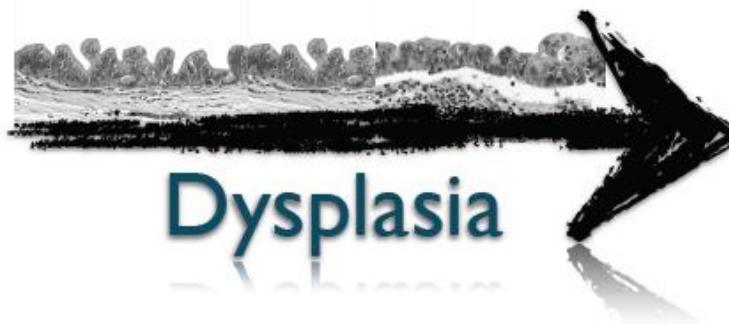
precancerous lesions
of
GI tract



precancerous lesions
of
GI tract

HOLLISS

COLON



Screening PC

Potential intervention

Risk assessment
and prevention

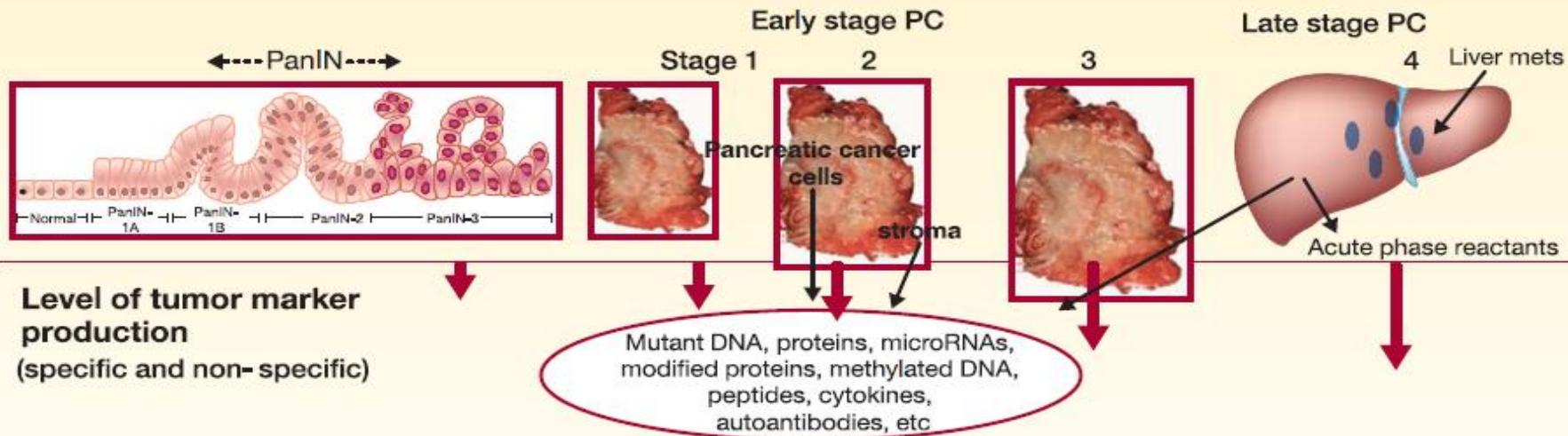
< 2 cm

Screening

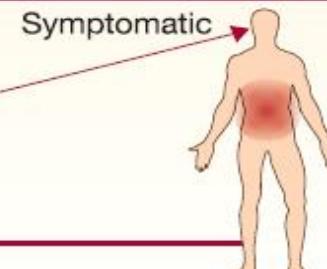
Surgical resection
and adjuvant therapy

Palliative
chemotherapy,
other therapies

Natural history of pancreatic cancer development and progression



Clinical presentation



Screening/Follow up

Surgery

Principles of screening

To be considered an important health problem, a disease need not necessarily have a high degree of prevalence...

.....but also conditions with serious consequences to the individual may warrant relatively uneconomic screening measures.

Screening pancreatic cancer



Brentnall

Ann Intern Med 1999



Kimmey

Gastr Endosc 2002



Langer

Gut 2009

Canto

Clin Gastroen Hepatolog 2004

Canto

Gastroenterology 2012

Canto

Clin Gastroen Hepatolog 2006

Al-Sukhni

J Gastrointest Surg 2012

Ludwing

Am J Gastroent 2011

Poley

A J Gastroemter 2009

Verna

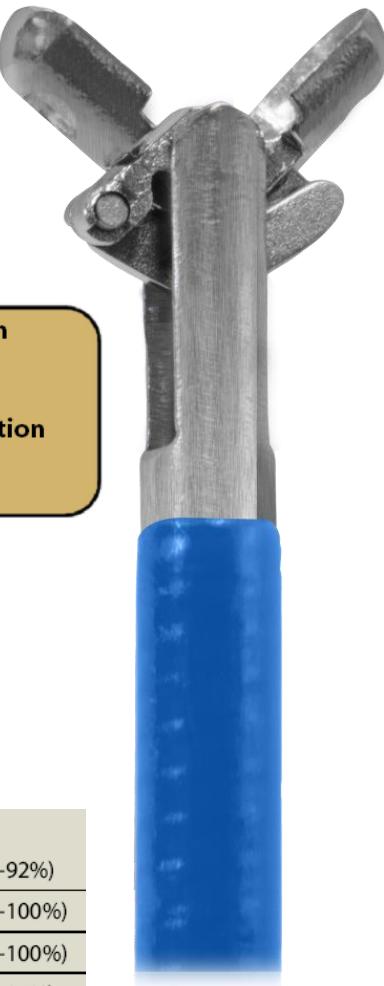
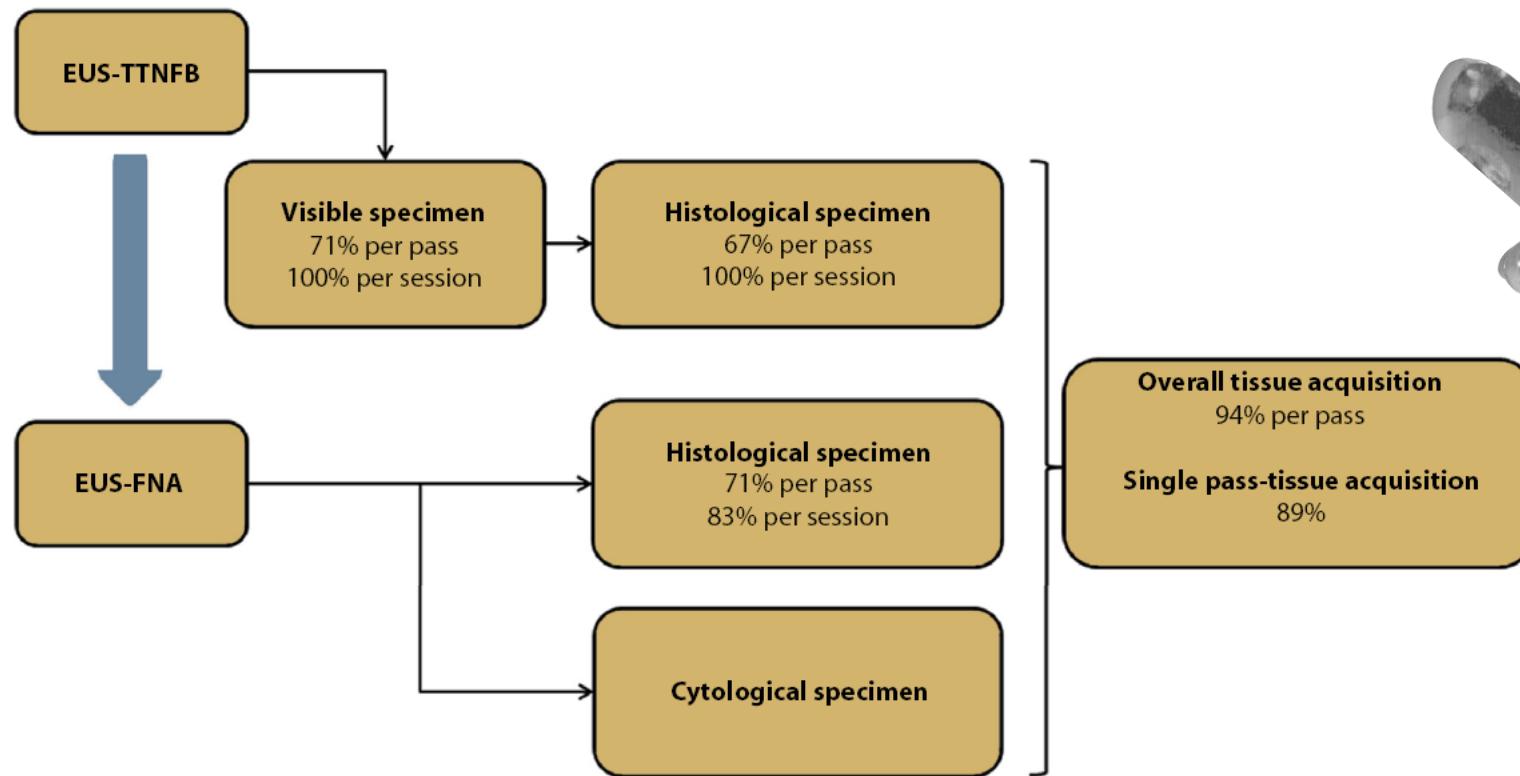
Clinical Cancer Contr 2010

Needle Forceps Biopsy

EUS-TTNFB

19g





Diagnostic yield of EUS-TTNFB and EUS-FNA

	Per pass	Per session
Sensitivity	83% (95% CI, 68%-83%)	92% (95% CI, 77%-92%)
Specificity	100% (95% CI, 70%-100%)	100% (95% CI, 71%-100%)
Positive predictive value	100% (95% CI, 82%-100%)	100% (95% CI, 84%-100%)
Negative predictive value	75% (95% CI, 52%-75%)	86% (95% CI, 61%-86%)
Accuracy	89% (95% CI, 69%-89%)	94% (95% CI, 75%-94%)

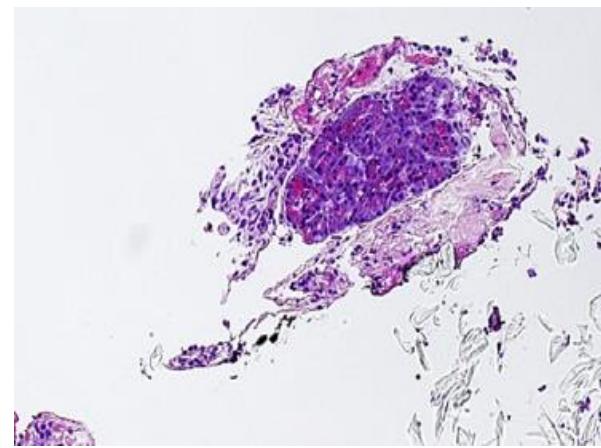
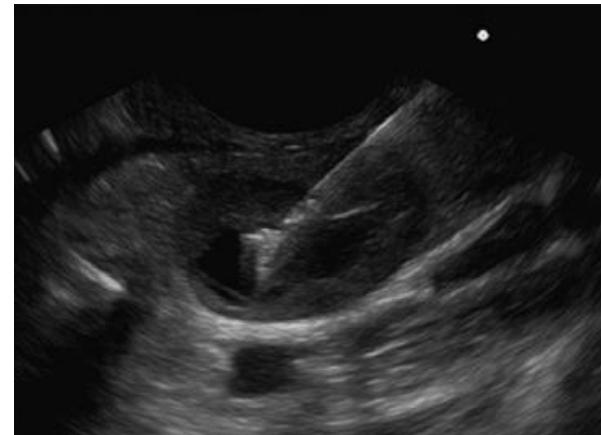
Data are shown in percentage (95% confidence interval).

EUS-TTNFB, EUS-guided through-the-needle forceps biopsy; EUS-FNA, EUS-guided FNA; CI, confidence interval.

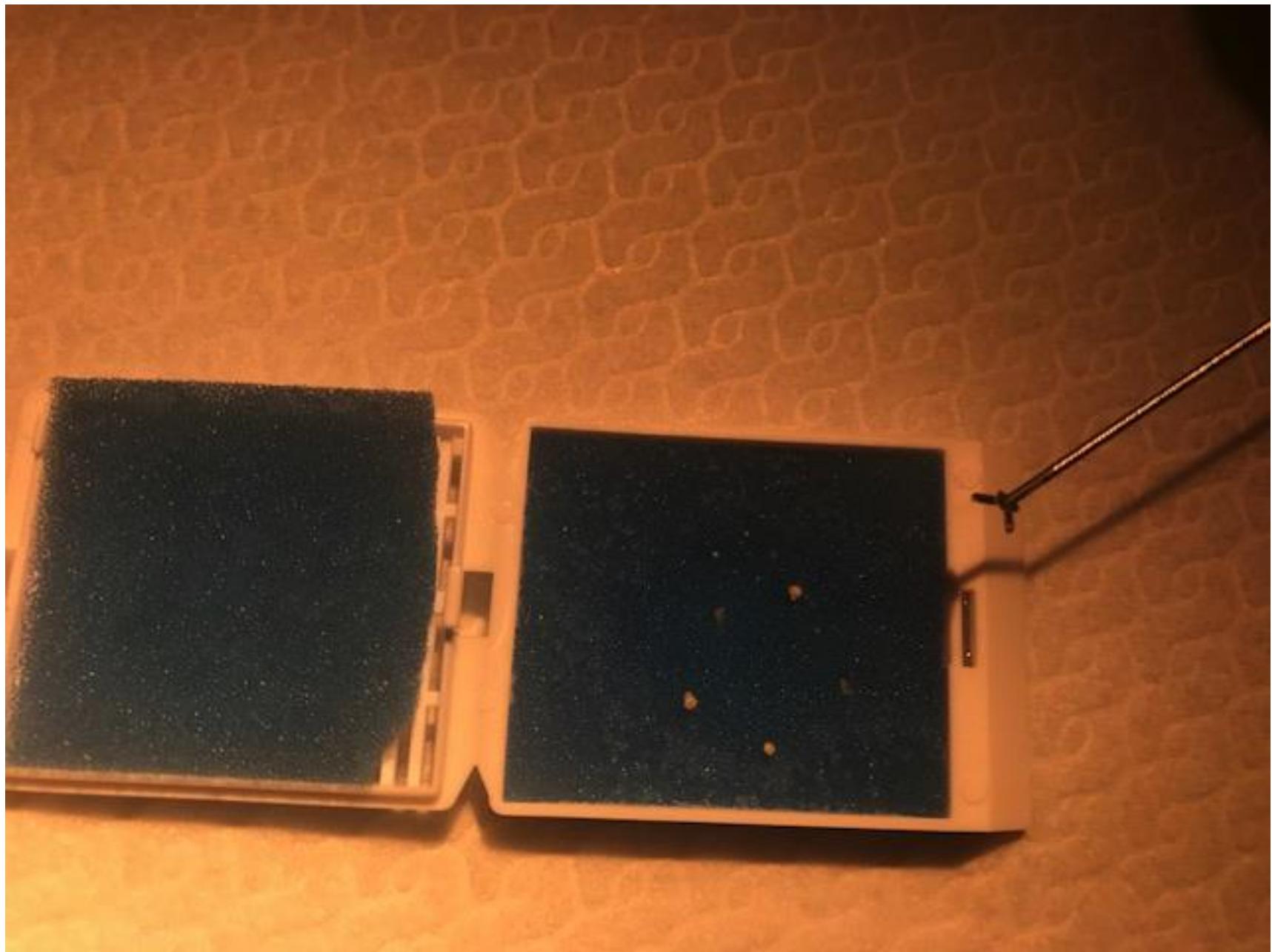
Nakai, 2016

Patient and tumor characteristics

Age, median (range), y	64 (44-84)
Male, no. (%)	12 (71)
Tumor size, median (range), mm	30 (13-80)
Initial session or salvage/no.	15/3
Tumor location, no.	
Pancreas head	2
Pancreas body	10
Pancreas tail	2
GI submucosa	1
Intra-abdominal	2
Puncture site, no.	
Transgastric	15
Transduodenal	3
Final diagnosis, no.	
Pancreatic adenocarcinoma	7
Autoimmune pancreatitis	4
Pancreatic sarcoma	1
Pancreatic neuroendocrine tumor	1
Necrotic tumor	1
GI stromal tumor	1
Schwannoma	1
Mesothelioma	1

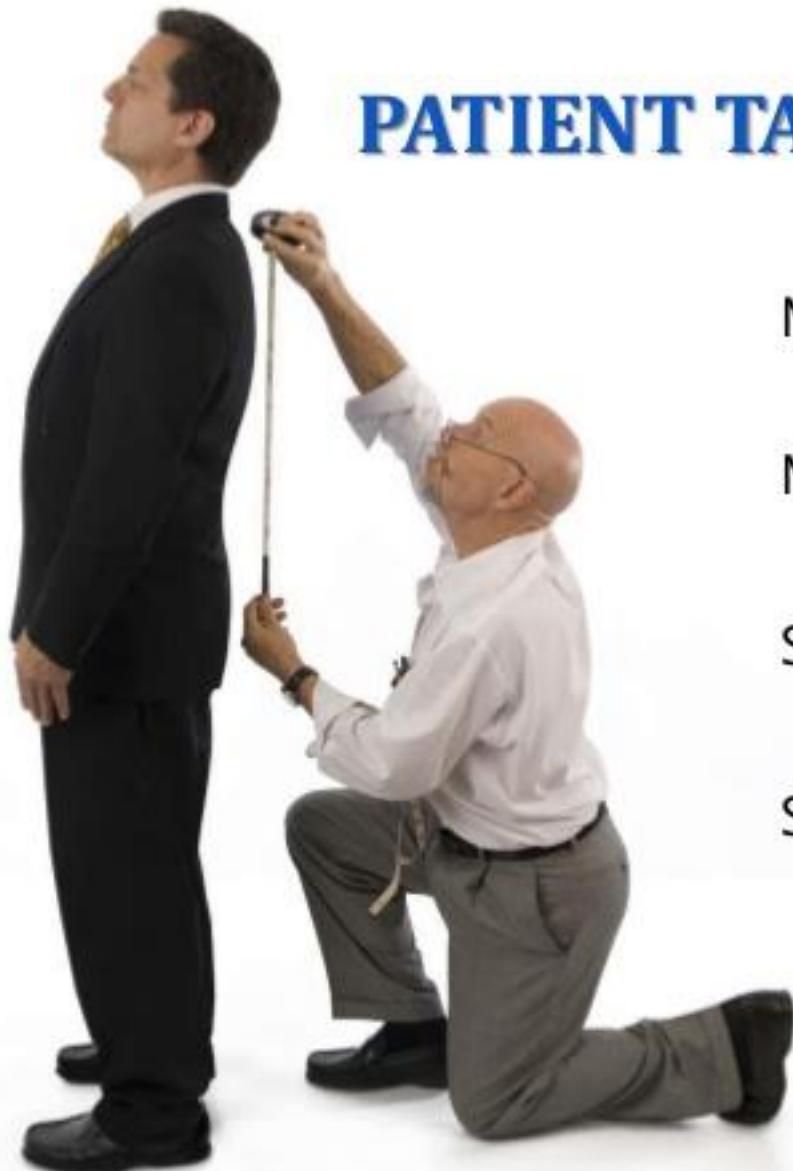


Nakai, 2016









PATIENT TAILORED Approach

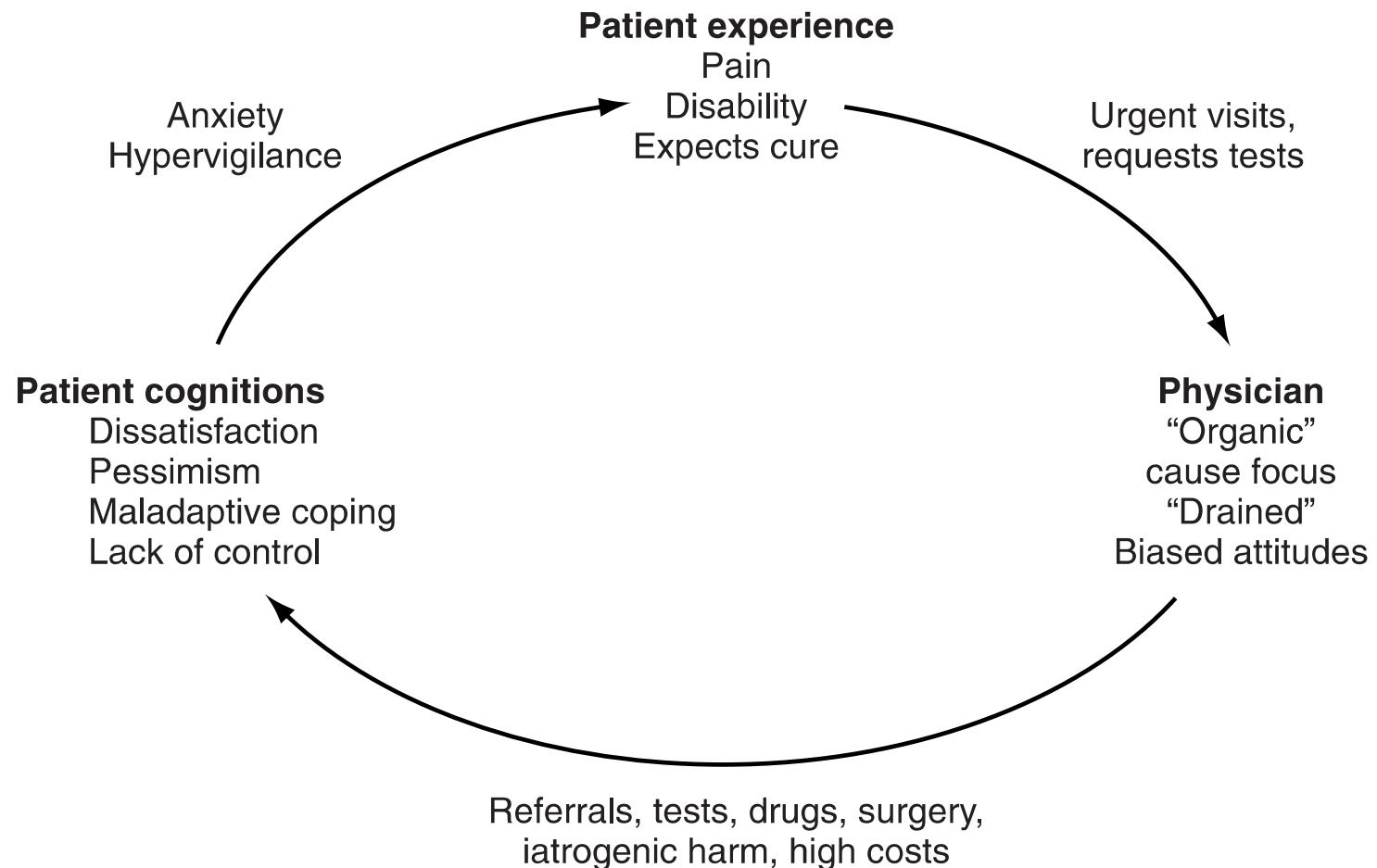
Multi-modal treatment

Multi-component treatment

Self-management strategies

Symptom based approach





Teamwork: Hard to get, easy to lose





Thanks