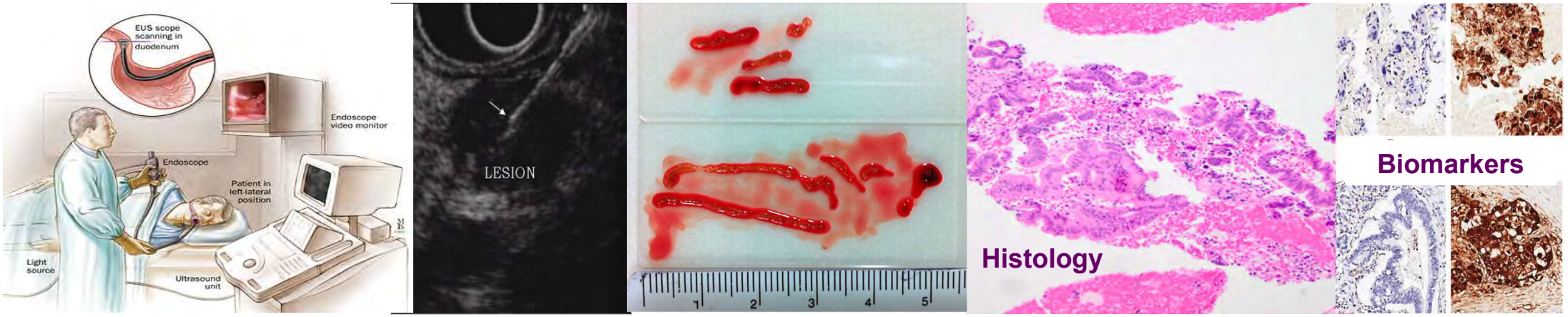
EUS guided FNA of GI diseases

Challenges for endoscopists and pathologists

Do we really need rapid on-site assessment?



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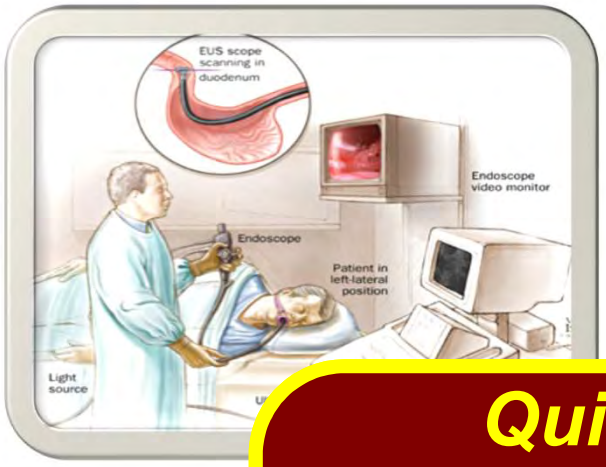
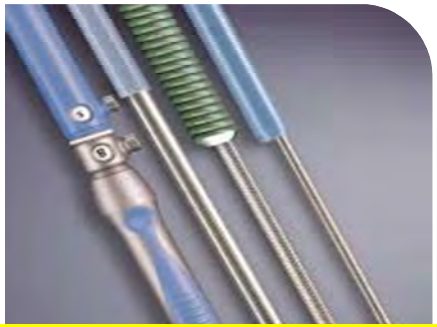
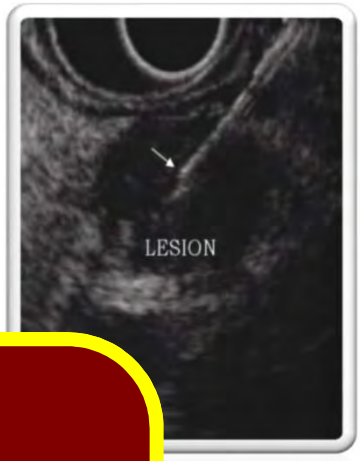
Outline

- *Challenges in EUS FNA for endoscopists*
- *Challenges in EUS FNA for pathologists*
- *Impact of Rapid Onsite Cytological Evaluation (ROSE) for the endoscopists and pathologist*
- *Alternative approach if ROSE is not presence*
  - **Does cytology still needed?**
  - **Macroscopic Onsite (core) Evaluation (MOSE)**
  - **Routine core needle (FNB) biopsy**

Current status of EUS guided FNA







Quick, easy to use, and safe

Diagnostic outcome:

- **Sensitivity = 76-98%**
- **Specificity = 60-100%**
- **PPV = 93-100%**

EUS-guided FNA is better than percutaneous approach for GI and Pancreatico-biliary neoplasm

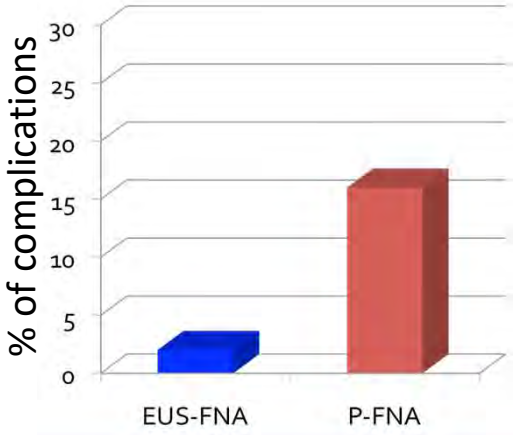
Diagnostic yield from needle biopsy is higher with EUS guided approach:

- ***EUS-FNA:*** ***84%***
- CT / US FNA: 62%

Horwhat et al. GIE 2006

Peritoneal carcinomatosis at time of surgery	
Percutaneous FNA (P-FNA)	16 %
EUS-FNA	***2 %***

Micames et al. GIE 2003



EUS guided tissue acquisition is ….an ART!

No single "gold standard" needle, technique or scope position!

Best outcome and the choice of needle, technique and tissue processing will depends on may factors:

- Location and size of lesion
- Indication of procedure
  - Need for biomarkers or genomics analysis
- Presence of ROSE
- Inability to stop anti-platelet or anti-coagulant therapy
- Endoscopist's experience *(this will overcome all others!)*

Needle and technique factors in EUS FNA outcomes

- **Type of needle**
  - Size
  - Flexibility
  - Shape of needle tip

Techniques

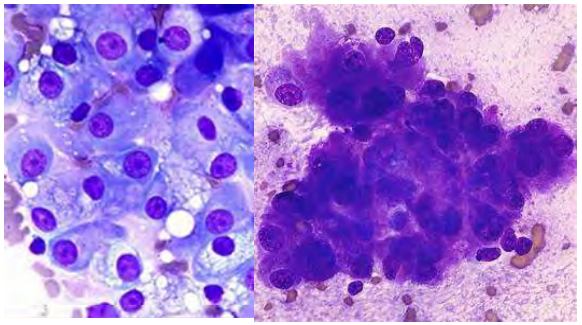
- Number of pass
- Stylet
- Suction, slow pull vs. none
- “Fanning”
- Ancillary imaging techniques to guide the site of biopsy
  - Elastography
  - Contrast
- Site of needle puncture

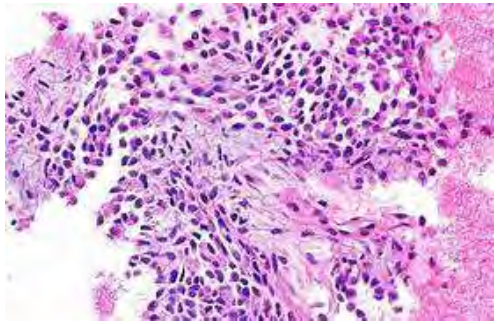
Type of specimens from different needles

Sharp tip needles

Small calibre (25G/22G)
Highly flexible and easy to use
Tiny to small amount of tissue
Suitable for cytological evaluation

FNA needles

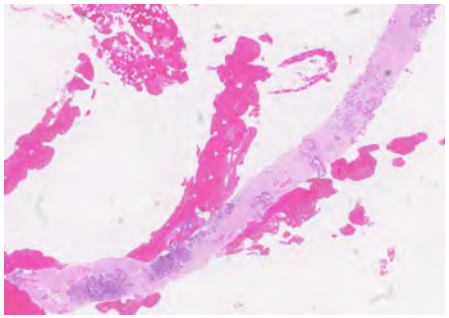


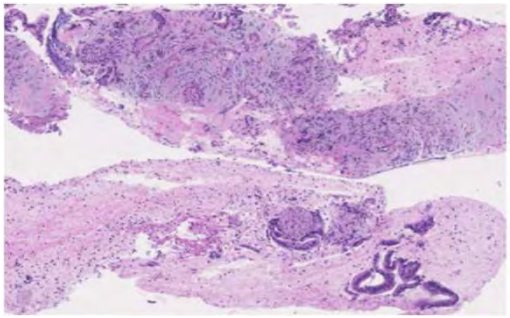


Modified tip needles

- Medium calibre (22G/20G/19G)
- Less flexible and sharp
- Harder to use
- Acquire core tissue
- Suitable for histology

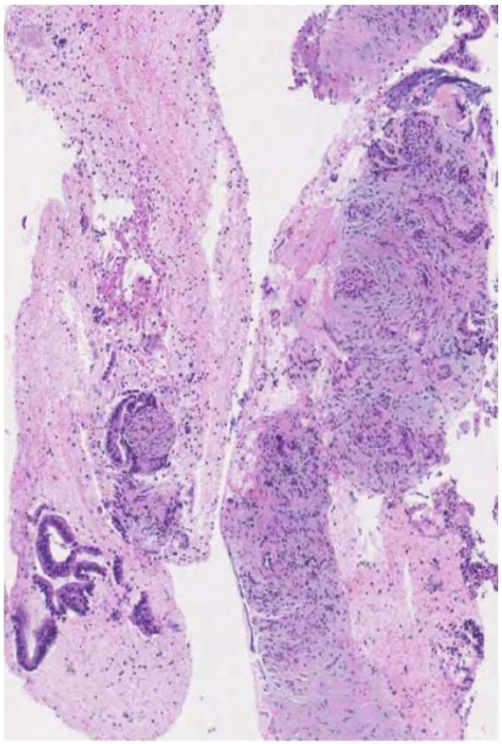
FNB needles





Van Riet, Larghi, Nguyen et al. GI Endoscopy 2019

EUS Tru-cut needle



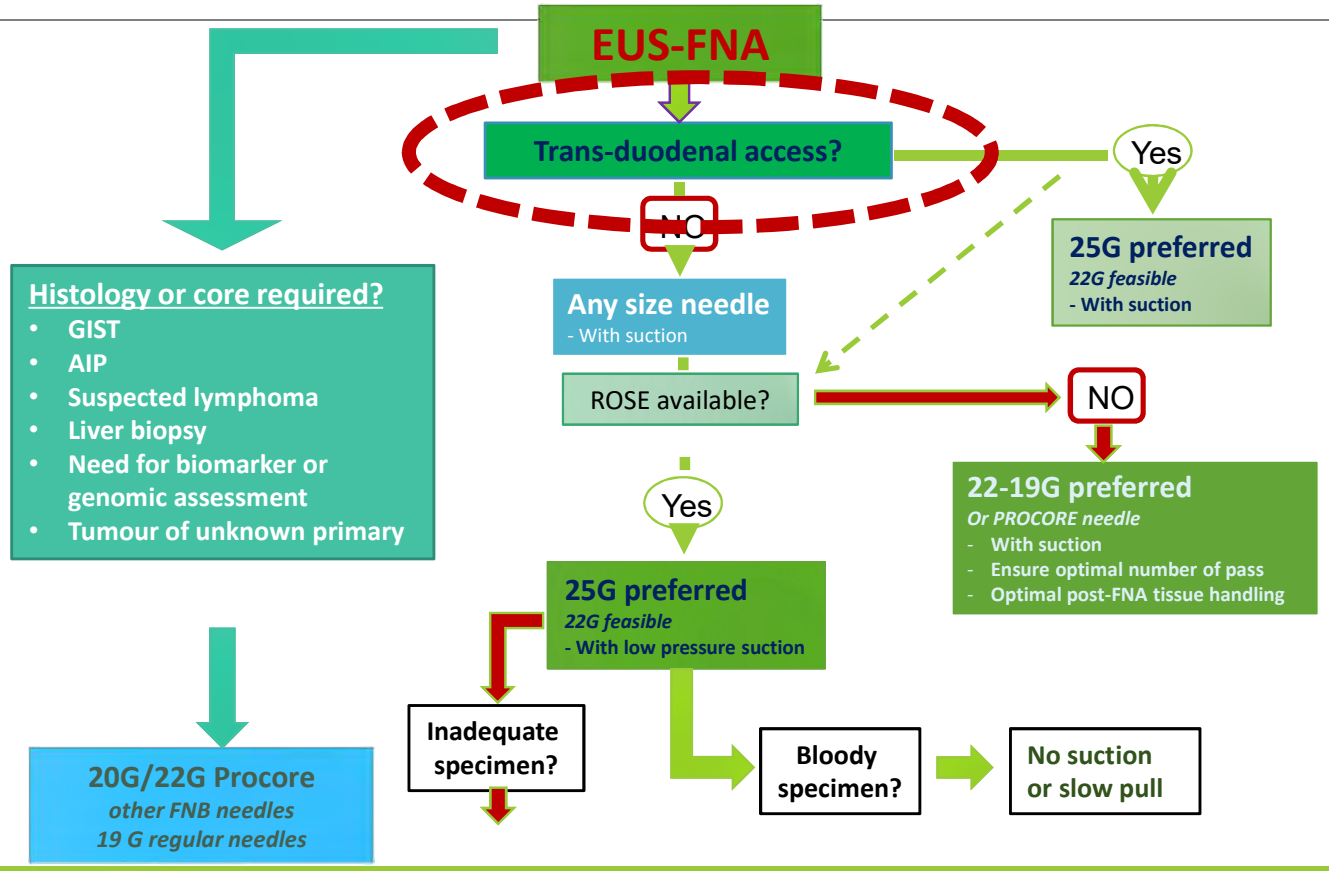
Good core tissue

Compromised by:

- Technically difficult with high failure rate
- Extremely rigid
- Almost impossible for lesions located in pancreatic head or uncinate process

No longer use, and is replaced by the newer tip-modified needle.

Algorithm that based on scope position to determine type and size of needle…



Number of pass?

Relevant only when ROSE is not available

Recommend performing 3 needle passes for lymph nodes and liver lesions, at least 5 needle passes for solid pancreatic masses (mostly used 22G)

- *Pancreatic lesion: Four passes of 25G is sufficient?.*

  Suzuki et al. Dig Endosc 2012

Less for Core (FNB) needle

- ***Single-pass studies: 87% for 19G , 90% for 20G, 88% for 22G Procore***

  Iglesias-Garcia et al. Endoscopy 2011 Larghi et al. Endoscopy 2014 Larghi et al. EuroEUS 2015

- ***Even with ROSE, 22G Procore required fewer passes than FNA***
  - *1 vs. 2 passes; P<0.0001;*
  - *Procore had higher % diagnosis on 1st pass: 73% vs. 37%; P<0.001*

  Lee et al. Endoscopy 2014

Technique: Fanning?

N=54, ROSE, Pancreatic mass
Randomised:

- "Fanning" = 26 vs. Standard = 28

Results:

Diagnostic accuracy

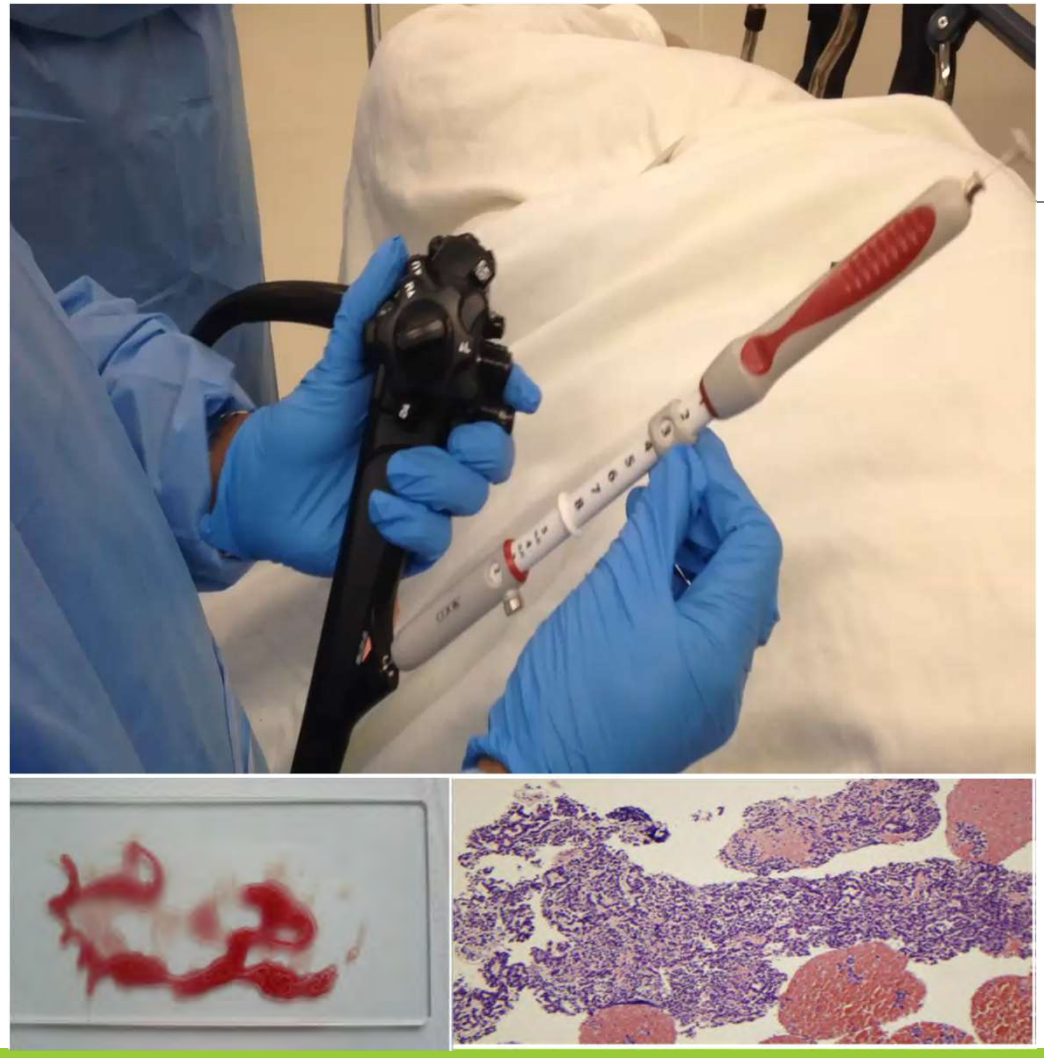
- 96% vs. 77% (P=0.05)

Lesser no. pass required for diagnosis and ***higher % of diagnosis on 1st pass***

- 86% vs. 58% (P=0.02)

Bang et al. Endoscopy 2013: 45; 445

Slow pull or capillary suction



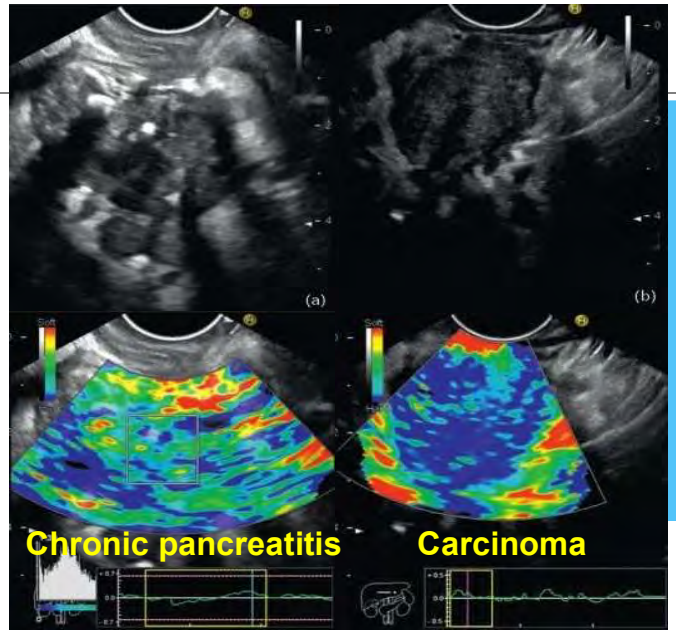
Nakai et al. Dig Dis Sci 2014

- Retrospective study, pancreatic mass
- 181 suction vs. 186 slow pull FNA
- Both 25G and 22G were examined.

Results: Slow pull is associated with

- Less blood contamination but also less cellularity but higher diagnostic yield only with 25G?
- No impact with 22G

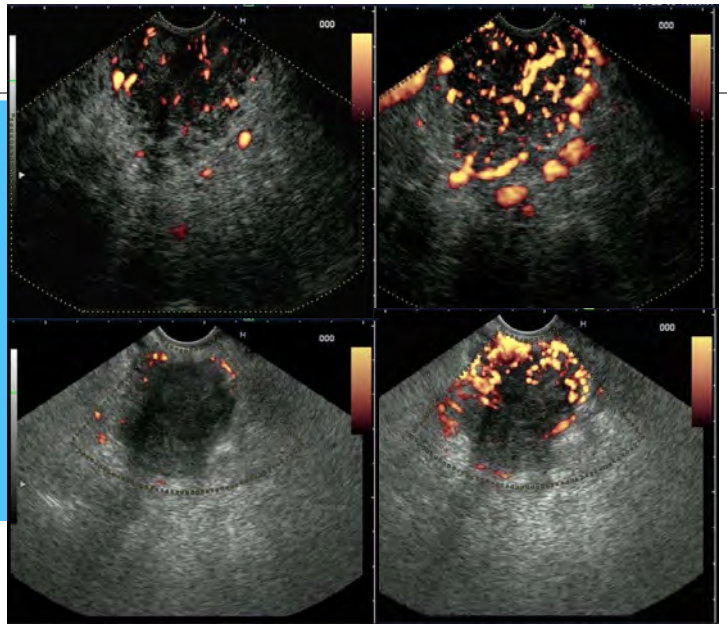
Advanced imaging assisted in difficult cases



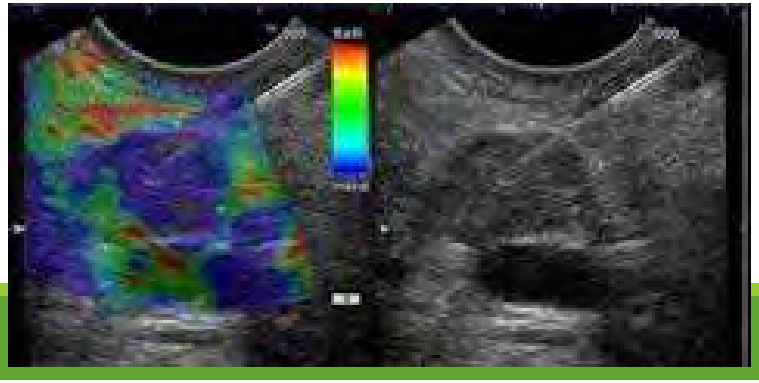
Iglesias-Garcia et al. Gastroenterology 2010

Predict the likelihood of malignancy prior to FNA

Pre-Sonovue Post-Sonovue



Guide placement of needle during FNA



“Only blood…”

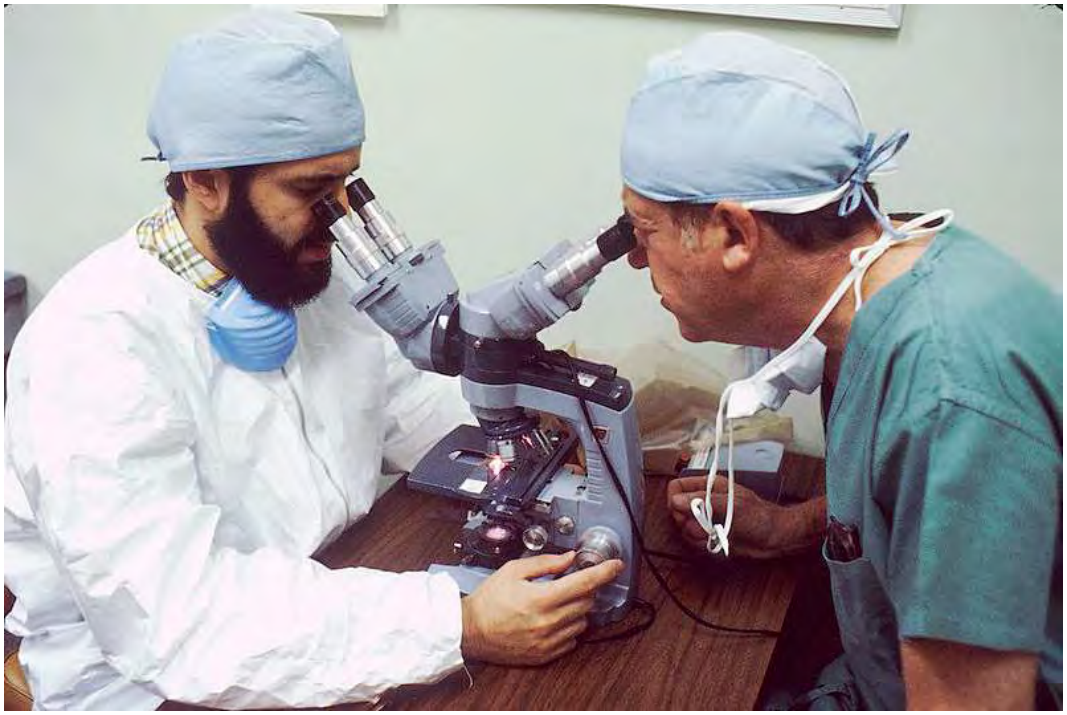
“No diagnostic tissue…”

“Atypical cells but non-diagnostic”

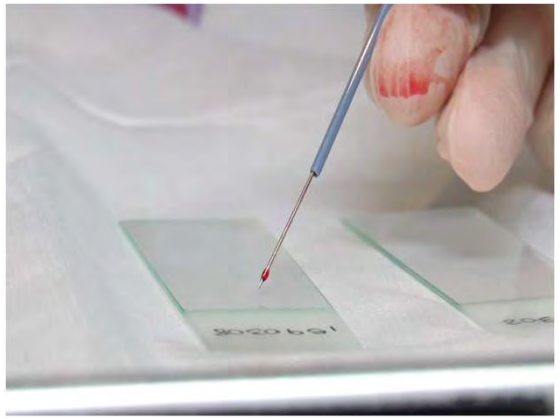
“Insufficient material for diagnosis”

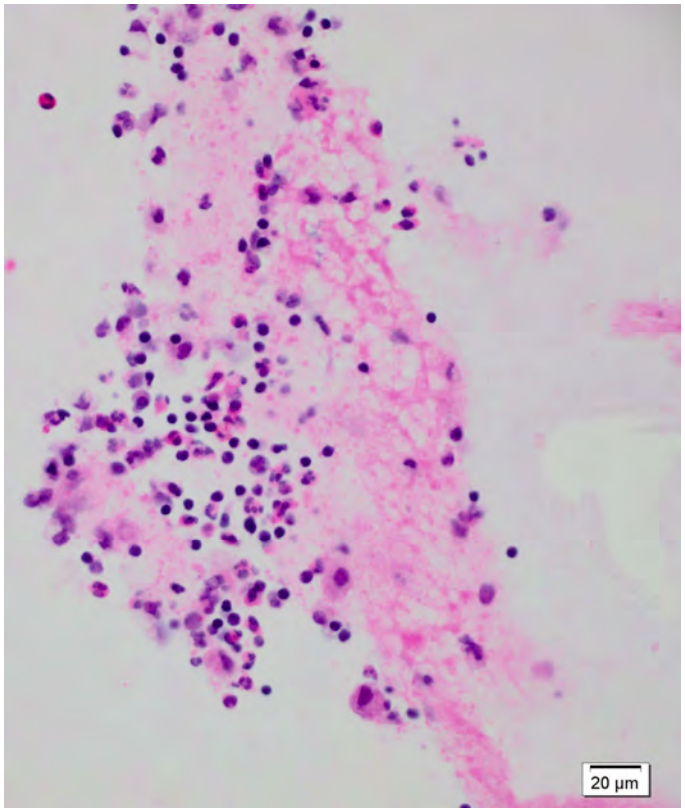
“Atypical cells, highly suspicious of malignant process”

How to overcome the endoscopist's frustration?



EUS FNA and Rapid On-site Cytology Evaluation (ROSE)





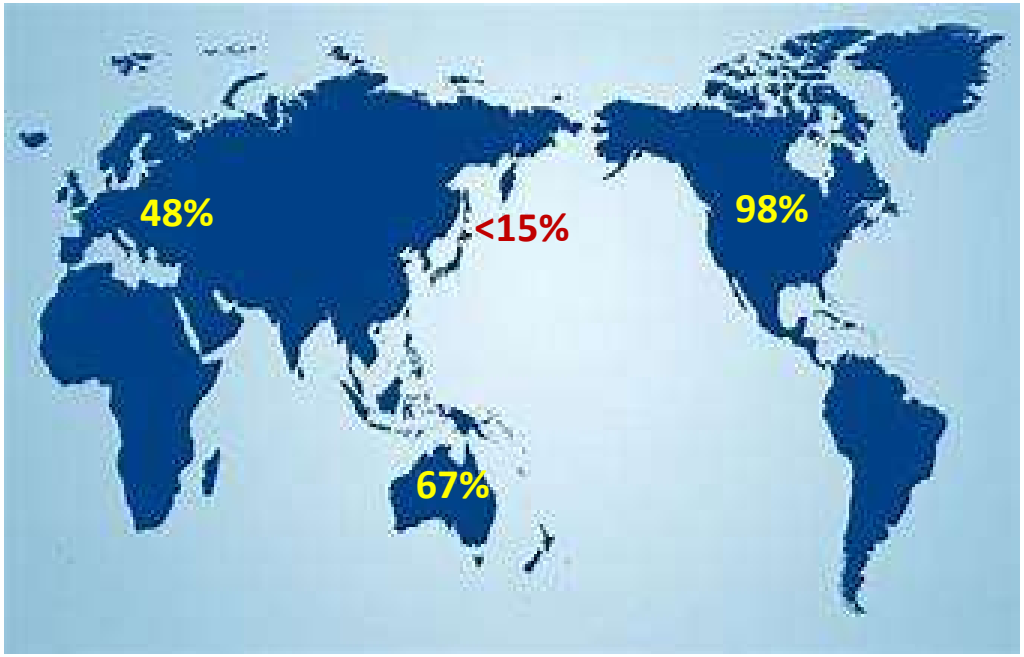
Benefits of Rapid On-site Cytology Evaluation (ROSE)

Non-randomized data

Author	Number	Diagnostic yield with vs. without OCP, %
Klapman et al.,[96] 2003	198	78 vs. 32, p=0.001
Alsohaibani et al.,[97] 2009	104	77 vs. 53, p=0.01
Iglesias-Garcia et al.,[98] 2011	182	97 vs. 86, p=0.01

- ***Provides an immediate cytological diagnosis***
- ***Guiding the need for further FNA***
- ***Optimizing the diagnostic yield***
- ***Minimize the need for repeat EUS***

Practice of ROSE around the world



Availability of ROSE for EUS FNA practice

"Limited pathology staffing"
= 74%

"Disbelieve in its additive value"
= 32%

"High costs"
= 24%

"Additional procedure time"
= 24%

"ROSE" is *COSTLY* !!!

Non-inferiority study: FNA with ROSE vs. standard 7 passes

142 patients were randomized:

- cytopathologist arm (n=73) vs. 7 passes arm (n=69).

Diagnostic yield for definite diagnosis was similar

- cytopathology guidance=78.1% vs. 7 passes = 78.3%

Median charge with onsite cytopathology was significantly greater than performing 7 passes

- **ROSE= $1058** versus **7-passes = $375** (P<0.001)

ROSE service imposes significant cost to the hospital

→ a major factors for high patient-load, busy hospital

Lee et al. Dig Endosc 2015

Multi-centre, randomized US trial:

EUS-FNA with and without ROSE

US, MCT, RCT, All masses, FNA needles (no FNB)

241 patients were randomized to either: ROSE+ (n=121) or ROSE- (n=120)

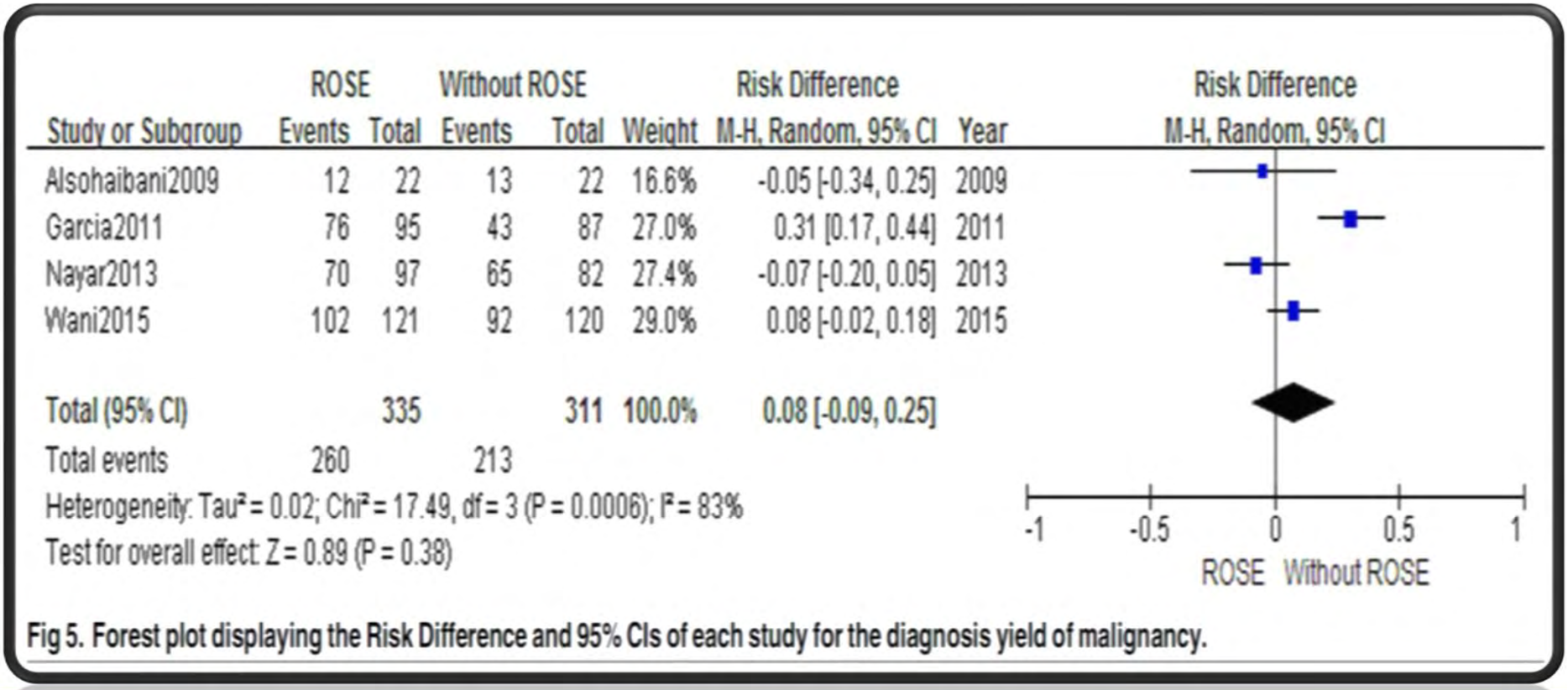
No significant difference

- ***diagnostic yield*** (ROSE+ 75.2% vs. ROSE- 71.6%, P=0.45)
- proportion of inadequate specimens (9.8 vs. 13.3%, P=0.31).
- cytologic characteristics of cellularity, bloodiness, number of cells/slide, and contamination
- procedure time
- adverse events
- number of repeat procedures and costs

Fewer EUS-FNA passes in ROSE+ group (4 vs. 7, P<0.0001).

Wani et al. Am J Gastro 2015

Meta-analysis:
FNA +/- ROSE



Study or Subgroup	ROSE Events	ROSE Total	Without ROSE Events	Without ROSE Total	Weight	Risk Difference M-H, Random, 95% CI	Year
Alsohaibani2009	12	22	13	22	16.6%	-0.05 [-0.34, 0.25]	2009
Garcia2011	76	95	43	87	27.0%	0.31 [0.17, 0.44]	2011
Nayar2013	70	97	65	82	27.4%	-0.07 [-0.20, 0.05]	2013
Wani2015	102	121	92	120	29.0%	0.08 [-0.02, 0.18]	2015
Total (95% CI)		335		311	100.0%	0.08 [-0.09, 0.25]	
Total events	260		213				

Heterogeneity: Tau² = 0.02; Chi² = 17.49, df = 3 (P = 0.0006); I² = 83%

Test for overall effect: Z = 0.89 (P = 0.38)

Fig 5. Forest plot displaying the Risk Difference and 95% CIs of each study for the diagnosis yield of malignancy.

Kong et al. Plos one 2016

Other weaknesses of ROSE and cytological assessment

- ***No ability to differentiate between in-situ vs. invasive cancer***
- ***Limited ability to specifically diagnosis***
  - Benign lesions
  - Inflammatory condition
  - Lymphoma
  - Sarcoma/stromal tumour
- ***Limited ancillary testing and tumour profiling***

❑ ***Halt the progression of "Personalized Oncology therapy"***

Thieme

Technical aspects of endoscopic ultrasound (EUS)-guided sampling in gastroenterology: European Society of Gastrointestinal Endoscopy (ESGE) Technical Guideline – March 2017

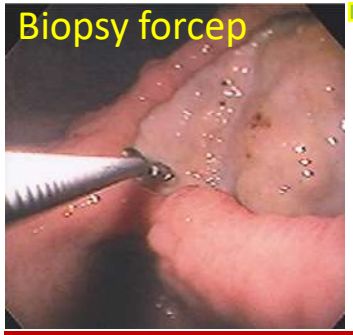
On-site cytologic evaluation

RECOMMENDATION

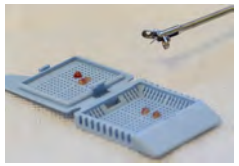
ESGE equally recommends EUS-guided sampling with or without on-site cytologic evaluation (moderate quality evidence, strong recommendation).

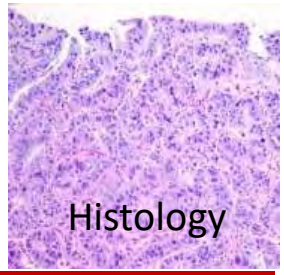
How can we overcome the lack of ROSE?

Routine practice of tissue acquisition in *luminal Gastroenterology*

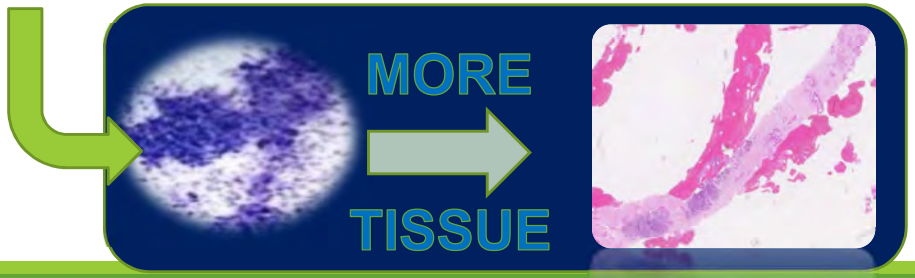


No ROSE service

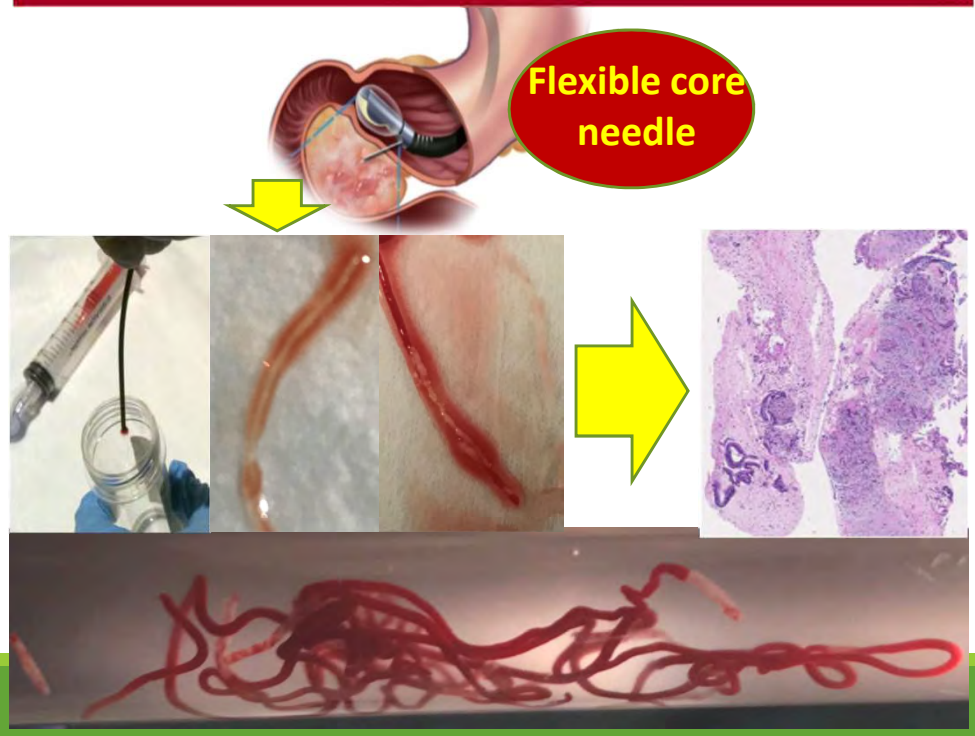




Tissue diagnosis achieves in >95%

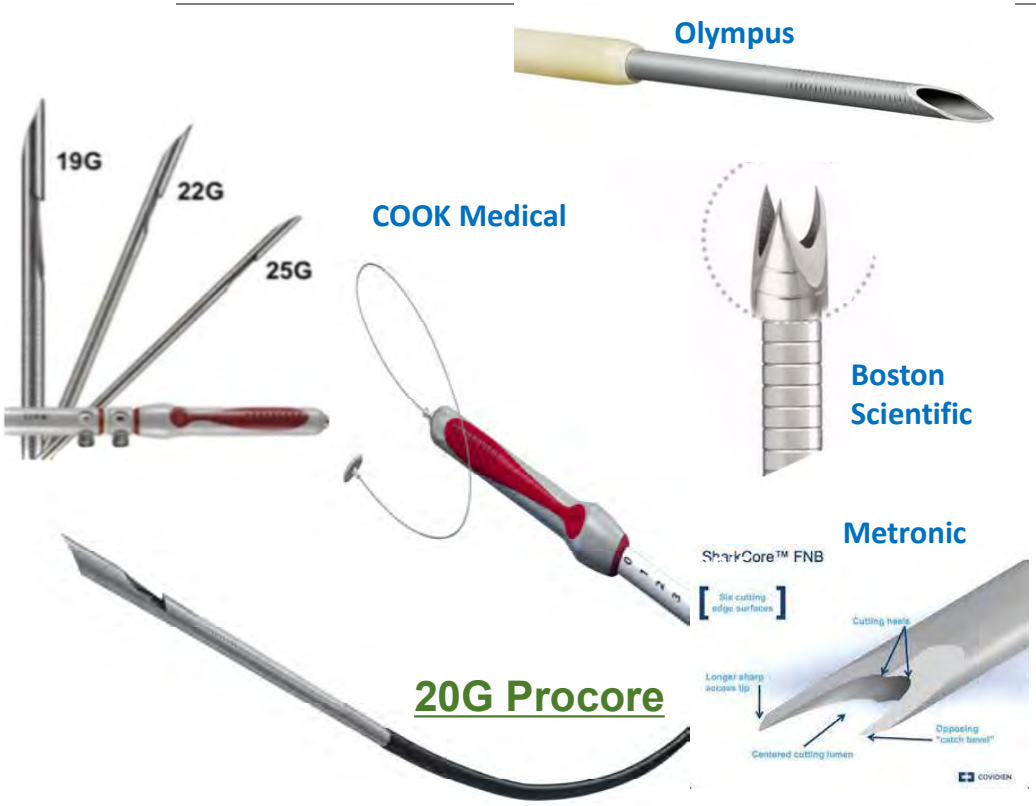


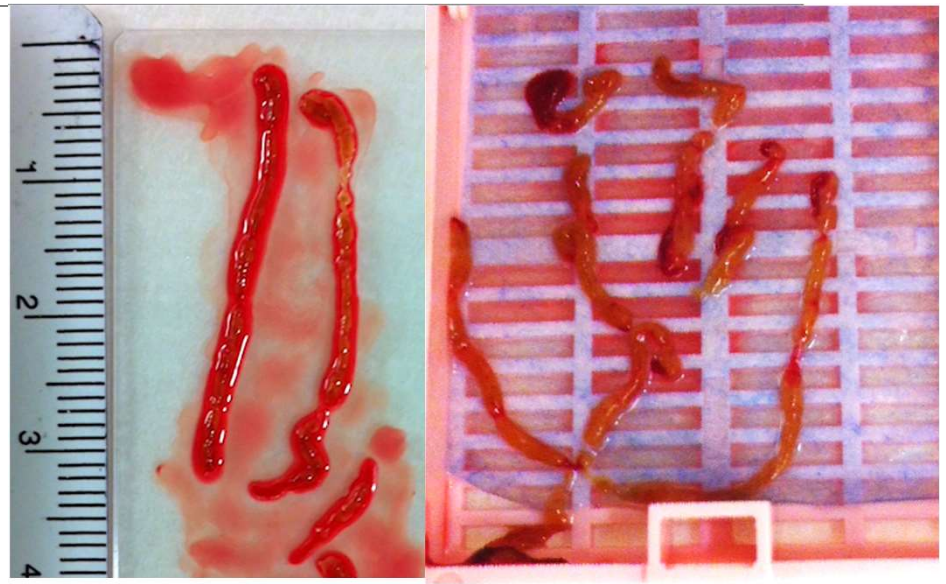
Ideal *trans-luminal* tissue acquisition via *EUS approach*



Advances in EUS needle technology

...an ideal EUS core needle...





1. ***Core biopsy without ROSE:***
2. **Maximize specificity and accuracy (>90%)**
   - **Improve inter-observer variation**
3. **Allow routine biomarkers and genomic analyses**
   - **Critical for current oncological care of GI cancers**
4. **Easy to use, reproducible and safe**

"ASPRO study"

MULTICENTER INTERNATIONAL RANDOMIZED TRIAL COMPARING A 25G EUS FINE NEEDLE ASPIRATION DEVICE WITH A 20G EUS FNB DEVICE

608 patients referred for EUS guided biopsy
- 312 pancreatic lesions (51%),
- 147 lymph nodes (24%),
- 149 other solid lesions (25%).

Randomized 1:1

306 for FNA with 25G Echotip

302 for FNB with 20G Procore

20G Procore

Measured outcomes:

Primary: diagnostic accuracy for malignancy and the Bethesda classification (non-diagnostic, benign, atypical, malignant)

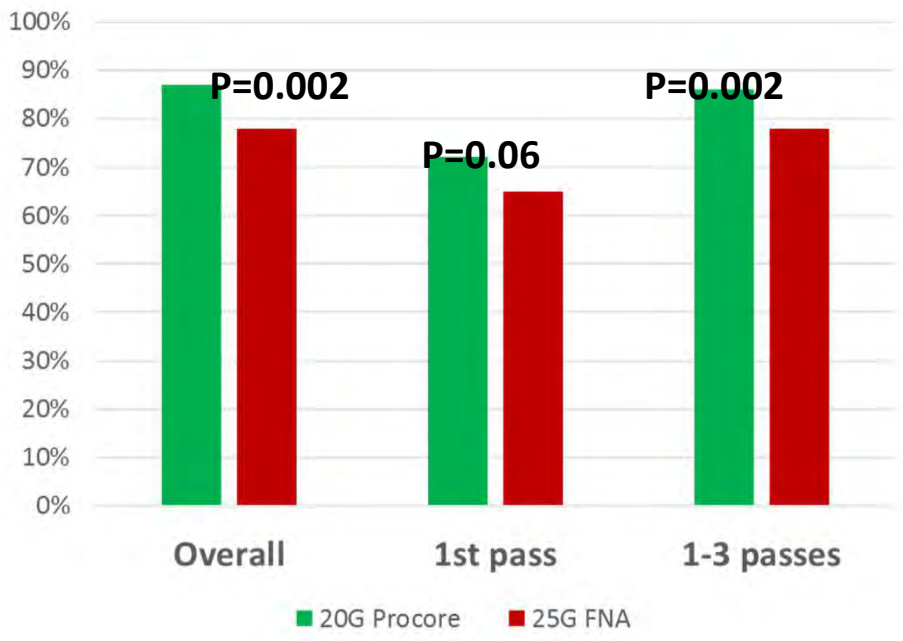
Secondary: needle safety, yield per pass, sample sufficiency, cellularity, and histological tissue core yield.

Van Riet, Larghi, Nguyen et al. GI Endoscopy 2018

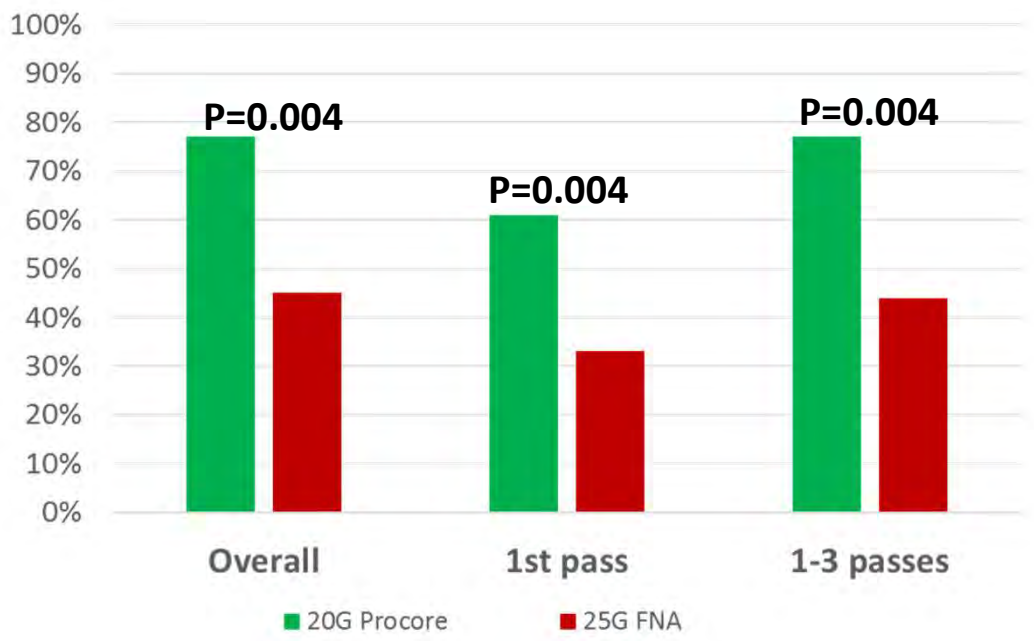
"ASPRO STUDY"

Performance of the new 20G Procore needle

DIAGNOSTIC ACCURACY



PRESENCE (%) OF TISSUE CORE



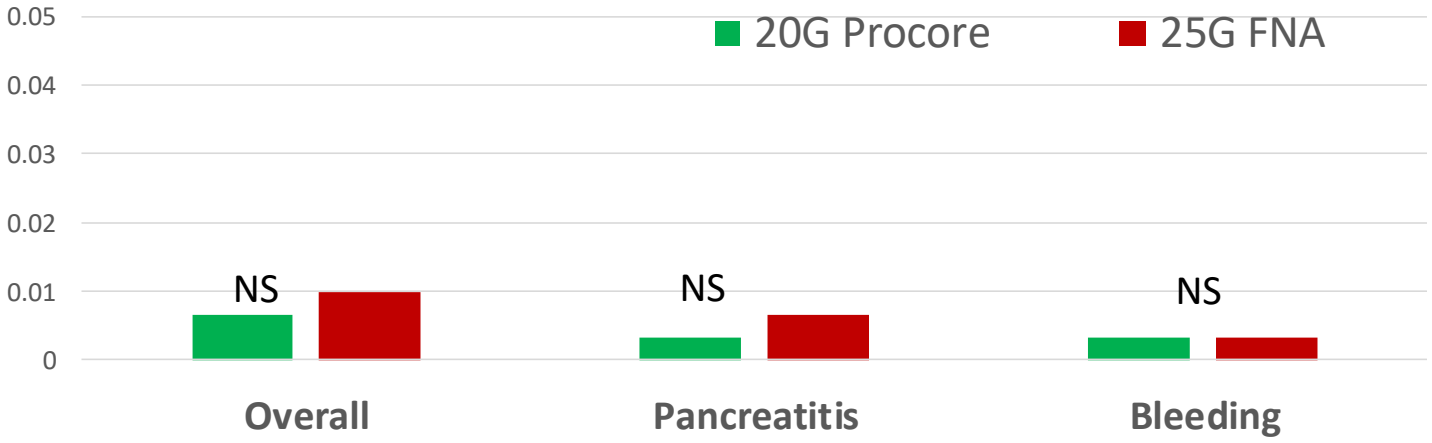
van Riet, Larghi, Nguyen et al. GIE2018

"ASPRO STUDY"

Technical success and complications

	20G Procore (n=302)	25G FNA (n=306)	
Technical success rate (%)	298 (**99%**)	306 (**100%**)	0.043

Complication is Rare = 5/608 (0.8%)



van Riet, Larghi, Nguyen et al. GIE2018

Lack of ROSE did not alter diagnostic yield when FNB needles are used!

	Correct diagnosis, % (n/n)	Odds ratio (95% CI)	P-value
Application of ROSE			
Yes	79% (237/299)	0.97 (0.51-1.76)	0.917
No	85% (232/273)	*	

van Riet, Larghi, Nguyen et al. GIE2018

Subgroup	Diagnostic yield (95% CI, I^2)		
	All	Franseen-tip	Fork-tip
ROSE			
Yes	93.7 (87.4-97.0, 77.4)	96.2 (88.1-98.9, 51.5)	91.2 (79.4-96.6, 71.7)
No	95.9 (88.0-98.7, 7.3)	94.1 (80.5-98.4, 0.0)	98.8 (88.1-99.9, 0.0)
Statistical difference (*P*)	0.25	0.26	0.26
Needle pass			
≤2	90.6 (78.1-96.3, 75.9)	89.5 (66.1-97.4, 80.6)	93.9 (74.4-98.8, 60.8)
>2	93.3 (88.5-96.2, 85.7)	94.4 (85.5-97.9, 91.1)	91.2 (83.5-95.5, 74.9)
Statistical difference, (*P*)	0.54	0.46	0.68

Mohan et al. Endosc Ultrasound 2019

FNB (Procore) needles
ROSE did not improve diagnostic yield

Retrospective from Italian centres

333 patients with pancreatic solid mass lesions

140 cases with ROSE v.s 193 cases without ROSE.

No difference in tissue adequacy

- 92.1 % (ROSE) vs. 88.1 % (no ROSE) (p = 0.227).

No difference between the ROSE vs. no ROSE in:

- Sensitivity = 90.7% vs. 87.2%
- Specificity = 100% vs. 100%
- **accuracy = 92.1 % vs. 88.1 %**

No difference in acquire tissue core

- 61.4% (ROSE) vs. 53.4 % (no ROSE) (p = 0.143).

Fabbri et al. Sugr Endosc 2017

Ongoing MCT-RCT trials: *FNB and ROSE*

FROSENOR study (leading site = Larghi)

A Multicenter Randomized Trial, Comparing EUS Fine Needle Biopsy (EUS-FNB) with Rapid on-Site Evaluation (ROSE) versus EUS-FNB Alone for the evaluation of Patients with Solid Pancreatic Lesions.

Sample size = 730;

16 sites (Europe, Asia, Australia)

1:1 randomization between FNB/ROSE vs. FNB alone

Crino et al. Dig Liver Dis. 2019

BEAT-ROSE study (leading site = Nguyen)

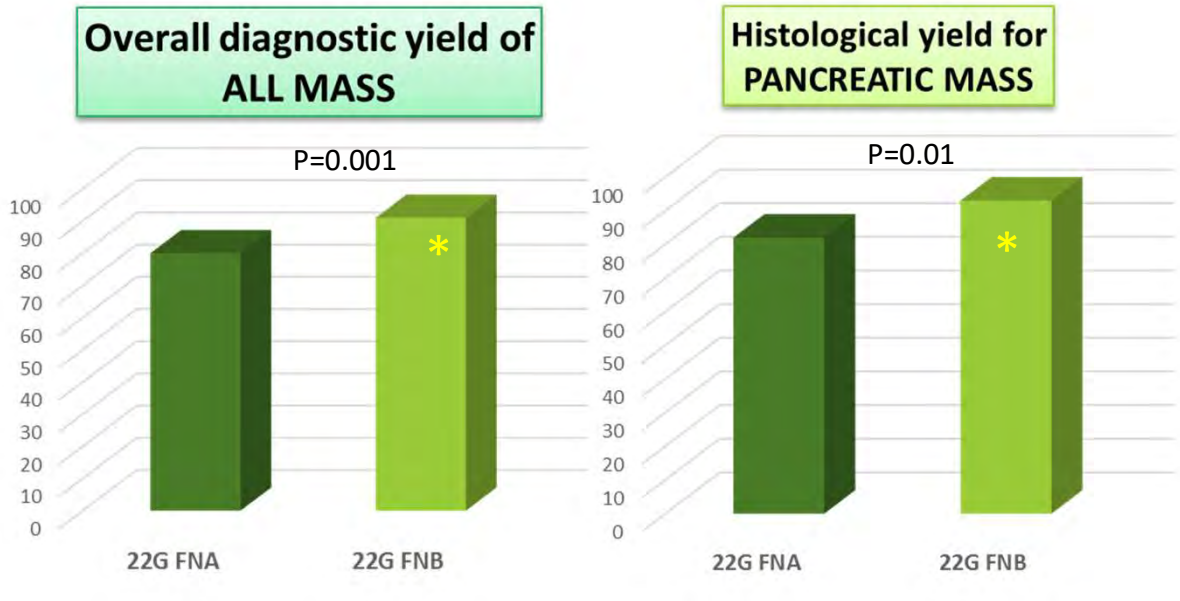
Evaluation of fine needle biopsy (FNB) for EUS guided tissue acquisition of pancreatic masses to negate the need for rapid on-site evaluation: a multi-centre randomized control trial

- Sample size = 598;
- 12 sites in Australian and Asia-Pacific region
- 1:1 randomization between FNA/ROSE vs. FNB alone

FNB gives higher diagnostic and histological yield for pancreatic mass

- RCT of 5 centres
- n = 408; solid mass (>1 cm), 4 passes each patients
- No ROSE
- Randomized to:
  - FNA (22G, n = 190)

  or
  - FNB (22G Procore n = 187)



No difference in diagnostic yield between EUS-FNA and EUS-FNB for ***non-pancreatic masses***.

Cheng et al. Clin Gastroenterol Heptol 2017

Fork tip needle

- **Multicenter retrospective study**
  - **147 patients: 101 EUS-FNB (Fork-tip) vs. 46 EUS-FNA needles.**
  - **All solid masses**
  - **80% without ROSE**
- **Compared to FNA needle, Fork-tip <u>FNB needle had higher</u>:**
  - **Diagnostic yield (89% vs 37% (P = 0.001))**
  - **Cytopathology yield (92% vs 46% (P = 0.001))**
  - **IHC yield (89% vs 41% (P = 0.001))**

Trindade et al. Endoscopy Int Open 2019

- **Multicenter prospective study**
  - **100**
  - **3 centers**
- **Solid pancreatic masses (28.5 mm (SD 11.7))**
- **<u>Diagnostic accuracy was 93%.</u>**
- **Core specimens in 67% of patients**
  - **poor agreement with MOSE (kappa, 0. 12; 95% CI: 0.03-0.28).**

Di Leo et al. Dig Dis Liver 2019

Franseen tip needle

- Prospective multi-centre study (n=200; FNB of solid lesions with ROSE).
- Tissue obtained by EUS-FNB was adequate for evaluation and ***diagnosis by ROSE in 197/200 cases (98.5%).***
- *Core of tissue was obtained in 131/145 (90%) of cases*

Adler et al. Endosc Ultrasound 2019

Prospective tandem study:

- N=56; pancreatic solid mass
- First pass = 22G Franseen needle
- Second pass = 22G FNA needle
- Formalin fixed for histology
- No ROSE

No ROSE	Franseen needle (*n*=56), *n* (%)	Standard needle (*n*=56), *n* (%)	*P*
Sensitivity	42/52 (80.7)	31/52 (59.6)	0.018
Specificity	4/4 (100)	4/4 (100)	NS
PPV	42/42 (100)	31/31 (100)	NS
NPV	4/14 (28.6)	4/25 (16.0)	0.351
Accuracy	44/52 (84.6)	33/52 (63.5)	0.014

Matsuno et al. Endosc Ultrasound 2019

Randomized comparison: *Franseen vs. standard FNA needles*

- N= 46, solid lesion (mainly pancreatic) randomized to either:
  - 22G Franseen needle
  - 22G Standard needle
  - 2 passes per lesion, presence of ROSE

	Franseen (46)	Standard (46)	p-value
Diagnostic Cell Block	**97.8%**	**82.6%**	**.03**
Tumor	0.68 mm^2	.099 mm^2	.0001
Retained Architect	93.5%	19.6%	.0001
Total Tissue	6.1 mm^2	0.28 mm^2	.0001

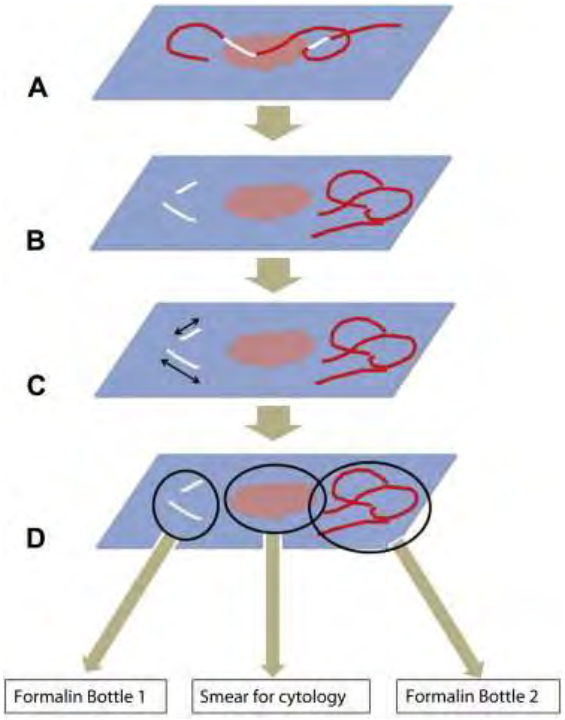
Bang et al. Gut 2018

19G Needle and "core" specimen

Study, Year	Needle Size (G)	Number of Patients	Histologic Adequacy (%)	Location of Biopsy
Iwashita et al,[47] 2012	19	44	43	Pancreas[a]
Yasuda et al,[45] 2006	19	104	98	Lymph nodes
Rong et al,[44] 2012	22	54	70.4	Pancreas
Bang et al,[43] 2012	22, FNA	28	66.7	Pancreas
	22, FNB	28	80	
Larghi et al,[46] 2011	19	120	97.5	Various
Varadarajulu et al,[48] 2012	19[b]	38	94.7	Subepithelial masses Pancreatic (head and uncinate lesions)

Use of 19G needles is limited by its poor technical success and risk of bleeding/pancreatitis

Macroscopic Onsite Examination (MOSE) as an alternative technique for assessing specimens from FNB needles.

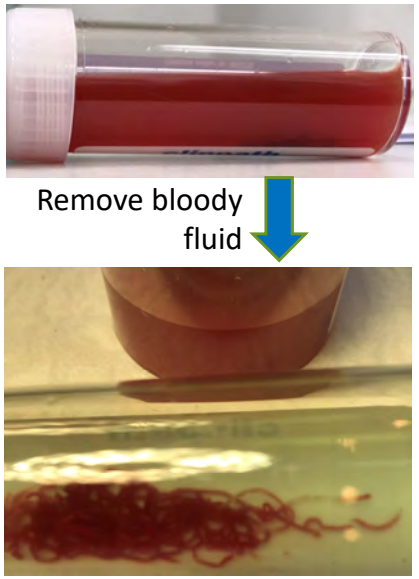


Conventional (slides)

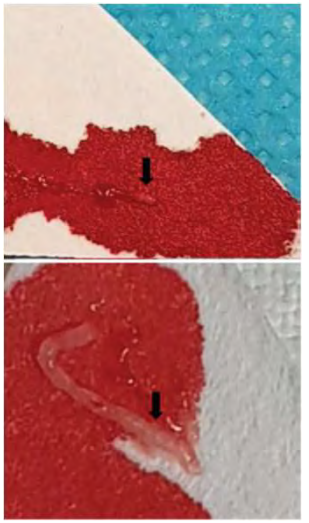
Modified technique of MOSE

Direct inspection in formalin

Remove bloody fluid



Filter paper technique



Iwashita et al. GIE 2015

Oh et al. Endosc Ultrasound 2019

Direct MOSE to guide the number of pass

- 46 consecutive patients with 54 solid lesions were biopsied using FNB needle (22G Franseen). Retrospective reviewed.
- If no macroscopic core was visualized, a second pass was performed.
- ***Core tissue was visualized in 93% (50/54) of targets with a single pass***
  - Histologic core fragments confirmed in 94% (47/50).
- ***Overall correlation between MOSE and histologic core fragments was 94% (48/51).***
- Diagnostic adequacy was 98% (53/54) with one biliary target biopsied without significant material.
- The overall diagnostic accuracy was 94 %, with 100% specificity.

Leung et al. Endoscopy Int Open 2019

Tissue specimen from FNB improves inter-observer agreement

	Kappa value *expert vs non-expert*
20-gauge ProCore FNB	
Diagnostic classification	0.62 = 0.59
Sufficient quality in 91%*	0.51 > 0.42
Tissue cores in 70% *	0.41 > 0.26
≥50% target cells 70%	0.33 = 0.27
Additional analysis in 76%*	0.51 > 0.38
25-gauge Echotopic FNA	
Diagnostic classification*	0.48 > 0.35

No differences between pathologists

Non-expert pathologists performed less well

*P<0.05; 25G vs. 20G Procore)

Histology provided better agreement than cytology, but only when a core specimen was obtained with FNB (P = 0.004 vs P = 0.432).

van Riet, Larghi, Nguyen et al. Dig Endosc 2019

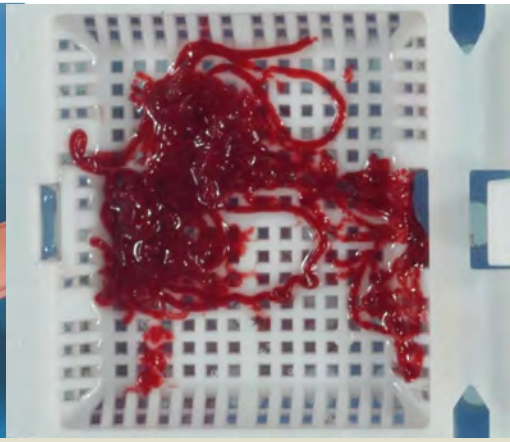
RAH approach for EUS FNA/FNB sampling and tissue processing

Predominantly core (FNB) needles with direct histology tissue processing

20G Procore (at least 2 passes) *

* If FNA needle use, at least 4 passes.

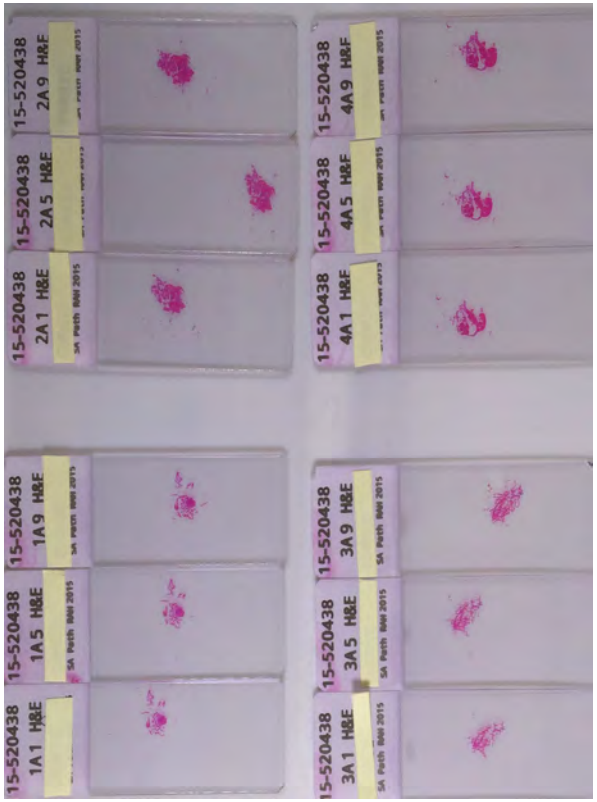
Extraction of aspirate by flushing the needle with small amount of 0.9% saline solution into fixative solution.

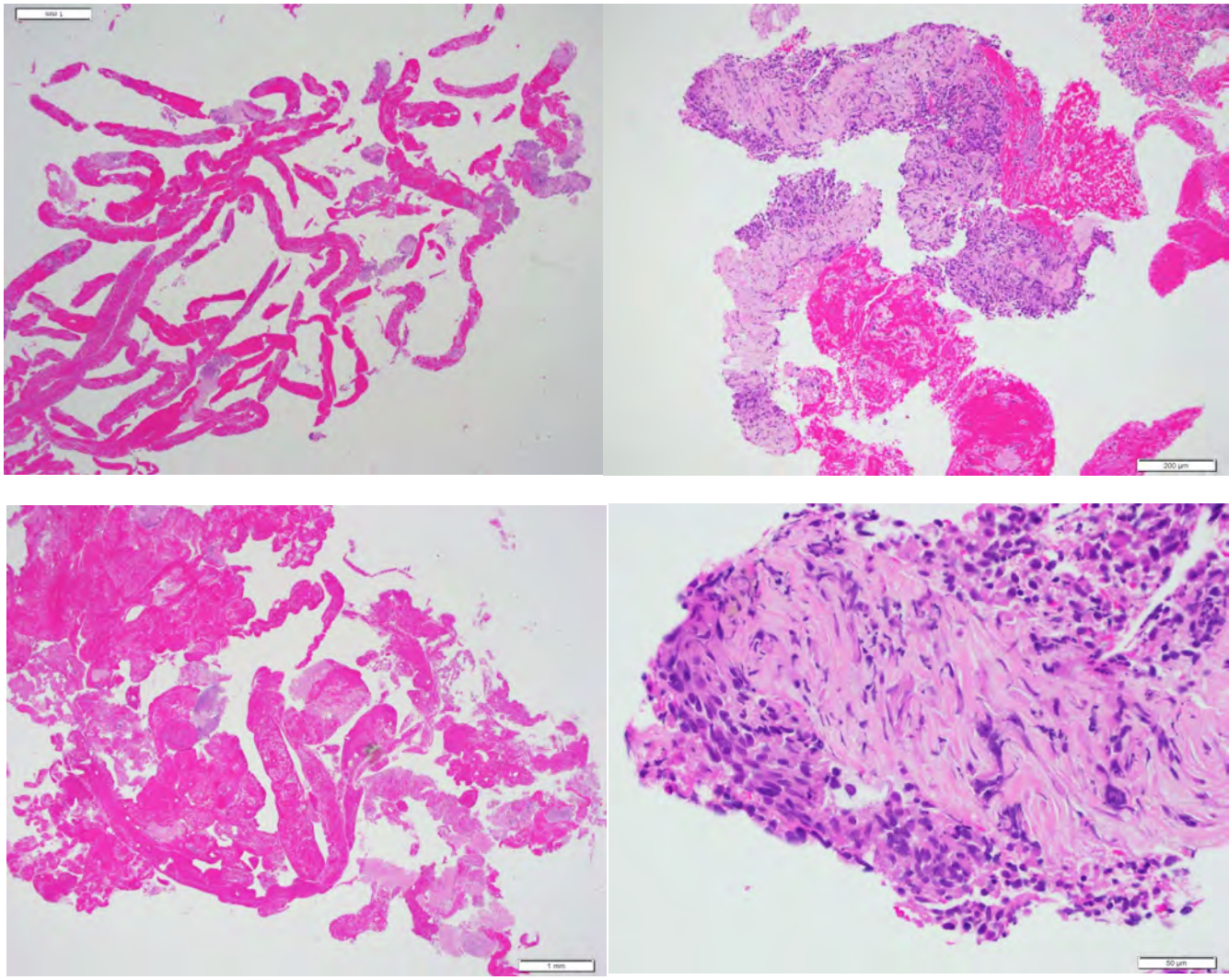


- No smears from aspirate
- No on site assessment by cytologist
- Entire material for paraffin block

Nguyen NQ, Schoeman MN, Ruszkiewicz A. Gastrointest Endosc. 2013

RIBBON OF 12 (1ST 5TH AND 9TH - HE STAIN, SPARES ON "CHARGED" SLIDES



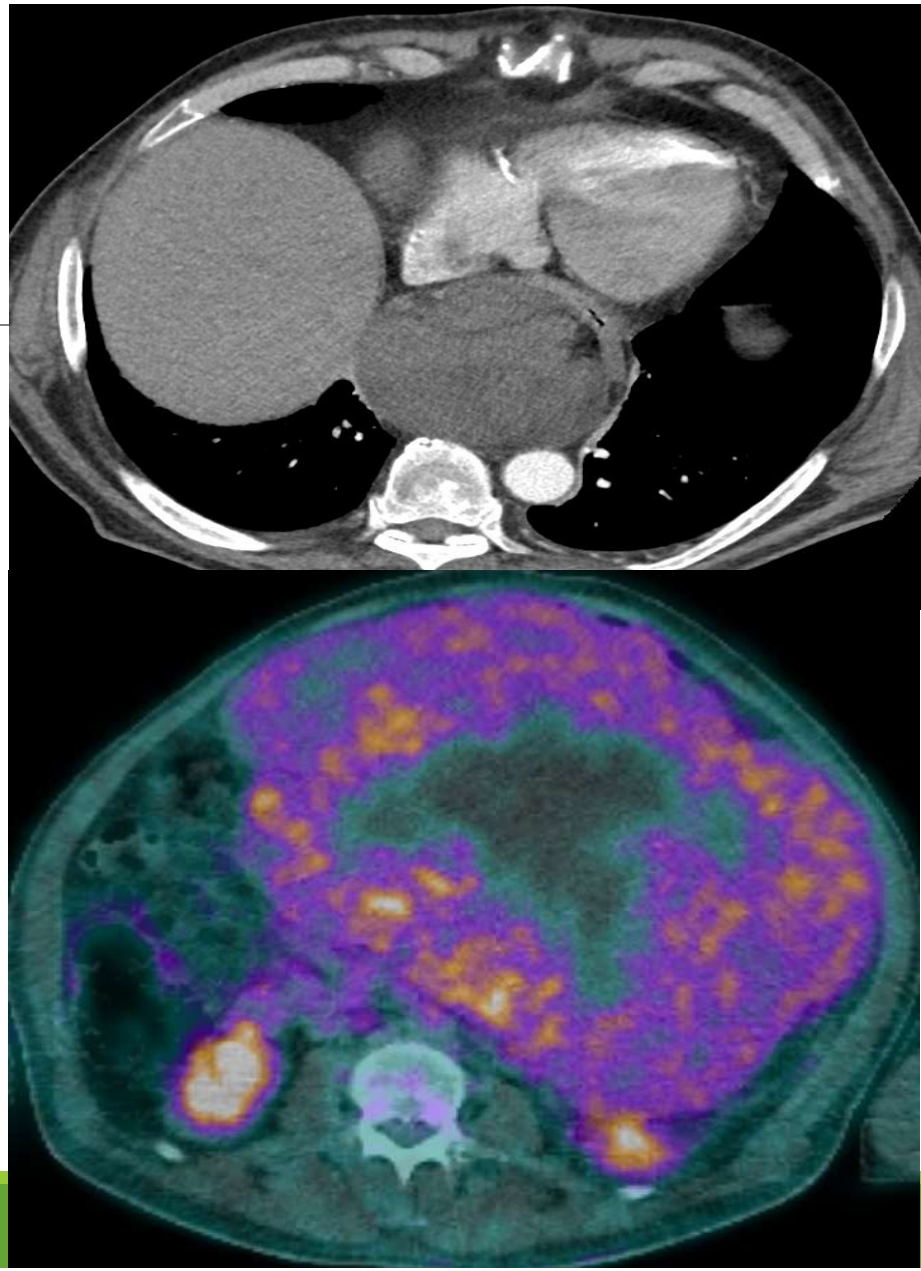


Nguyen NQ, Schoeman MN, Ruszkiewicz A. Gastrointest Endosc. 2013

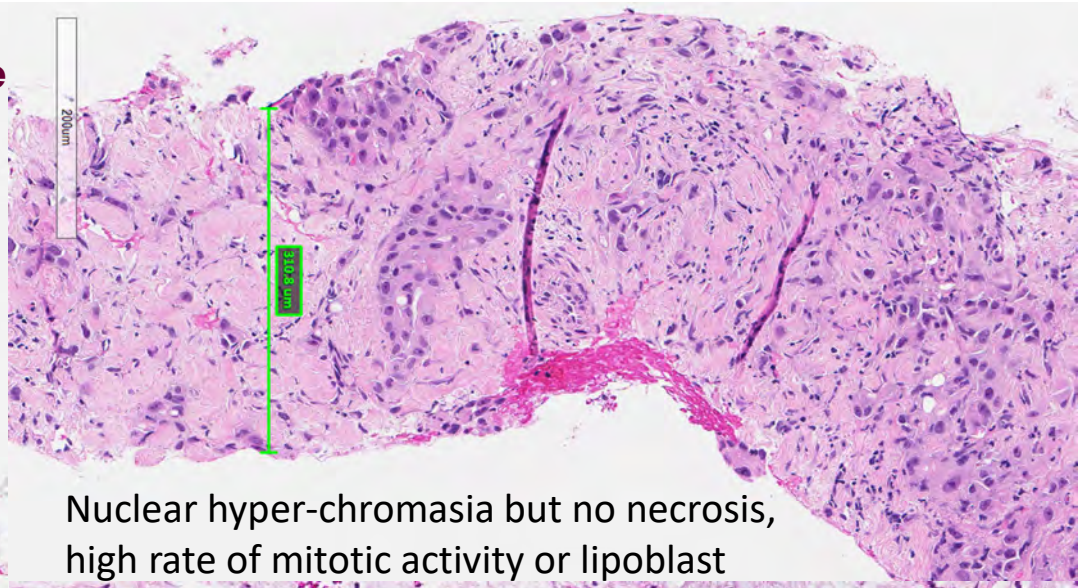
Case illustrations

Massive abdominal mass...

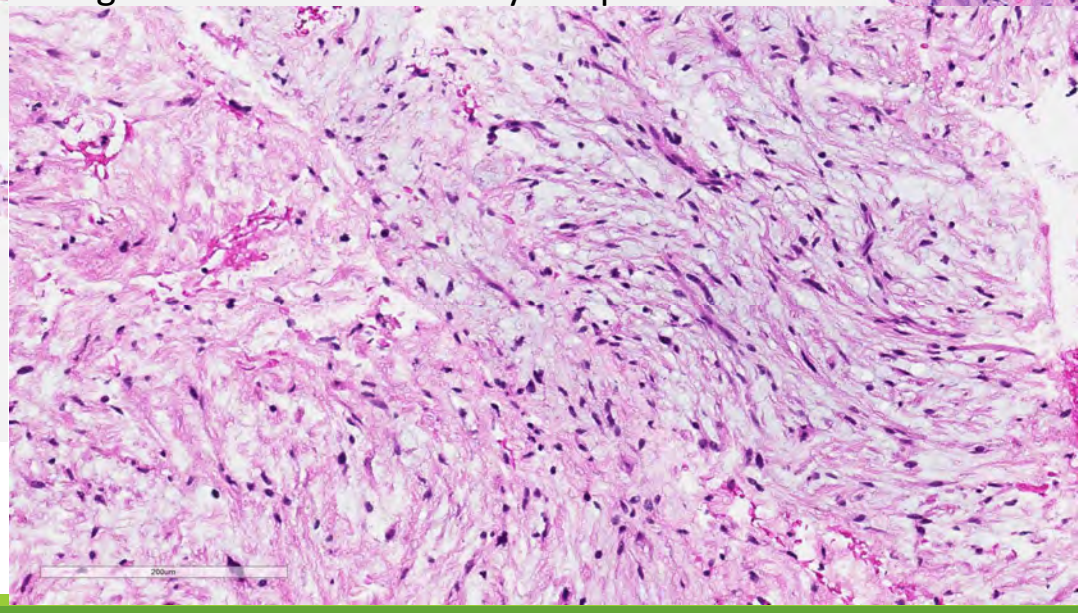
- 67 man
- 6 months of upper abdominal pain
- increasingly abdominal distension
- markedly reduced appetite and oral intake
- CBE, ECaU, LFT - all normal
- Imaging:
  - CT and MRI
  - PET scan



A single pass of 22G Core needle



Nuclear hyper-chromasia but no necrosis,
high rate of mitotic activity or lipoblast



Cores of monotonous spindle cell proliferation

-with a myxoid background

Immunohistochemistry and molecular evaluation

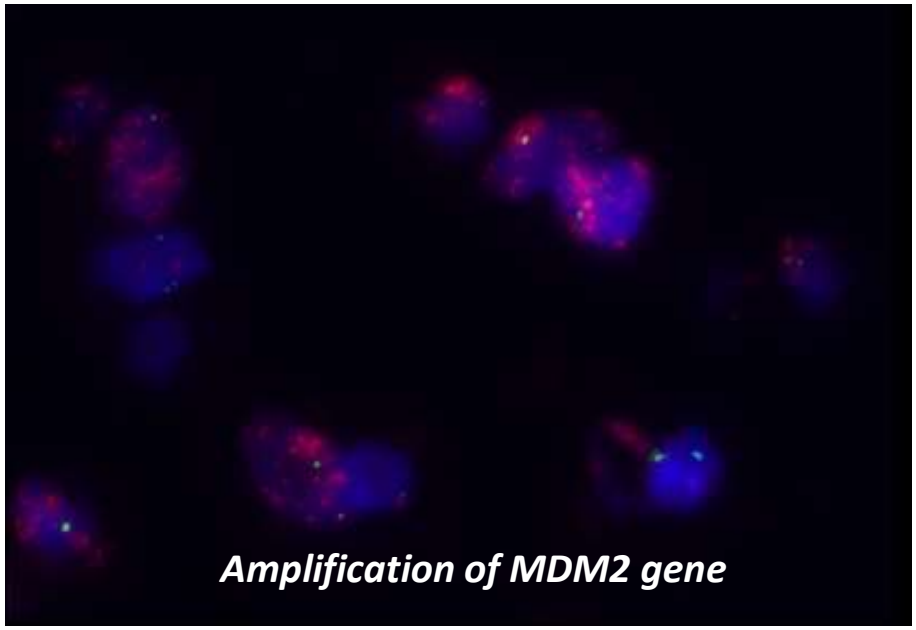
Immuno-histochemistry assessment:

Negative stain for:

- Desmin
- DOG1
- C-kit
- AE1/3

Not GIST

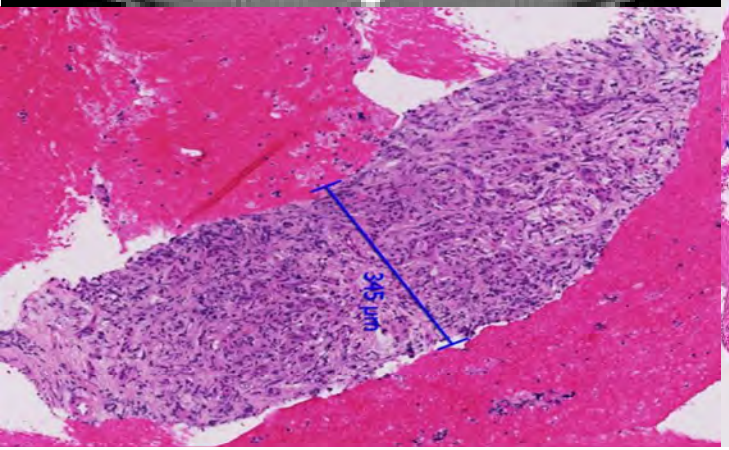
SISH and FISH analyses:

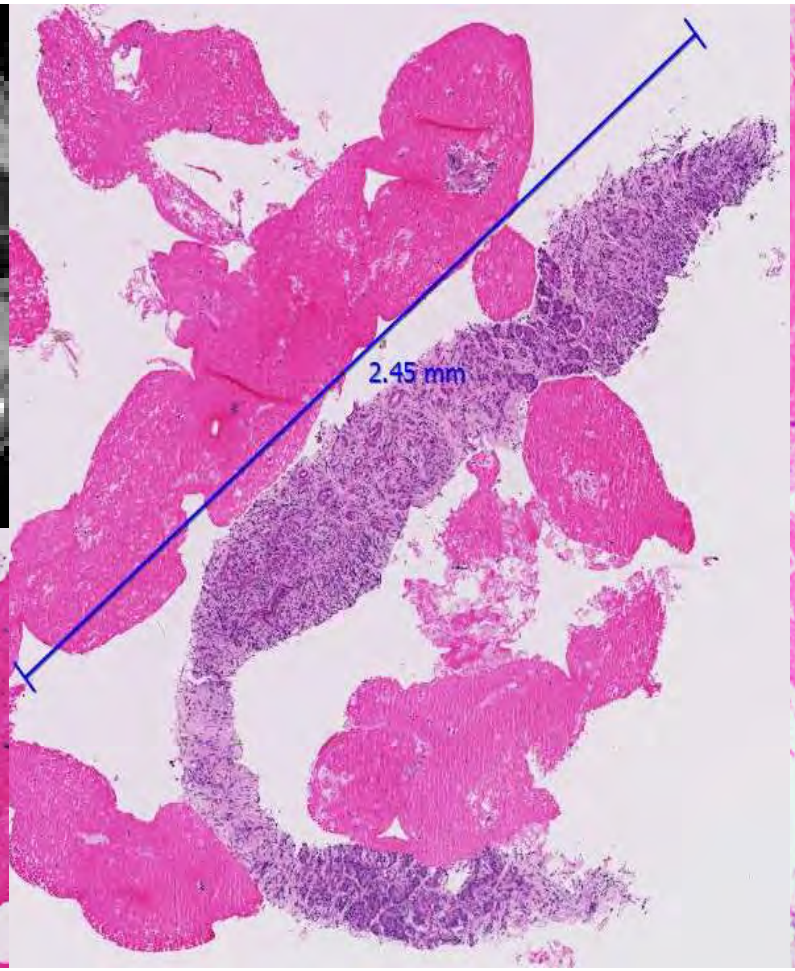


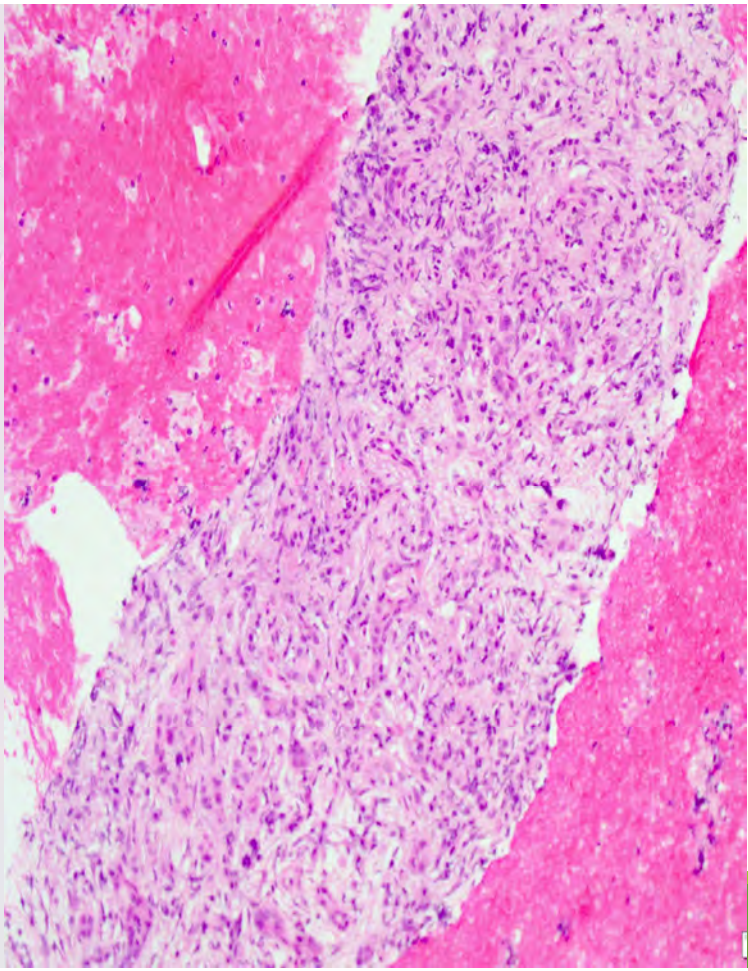
Amplification of MDM2 gene

Dedifferentiated liposarcoma → Surgery, completely resected

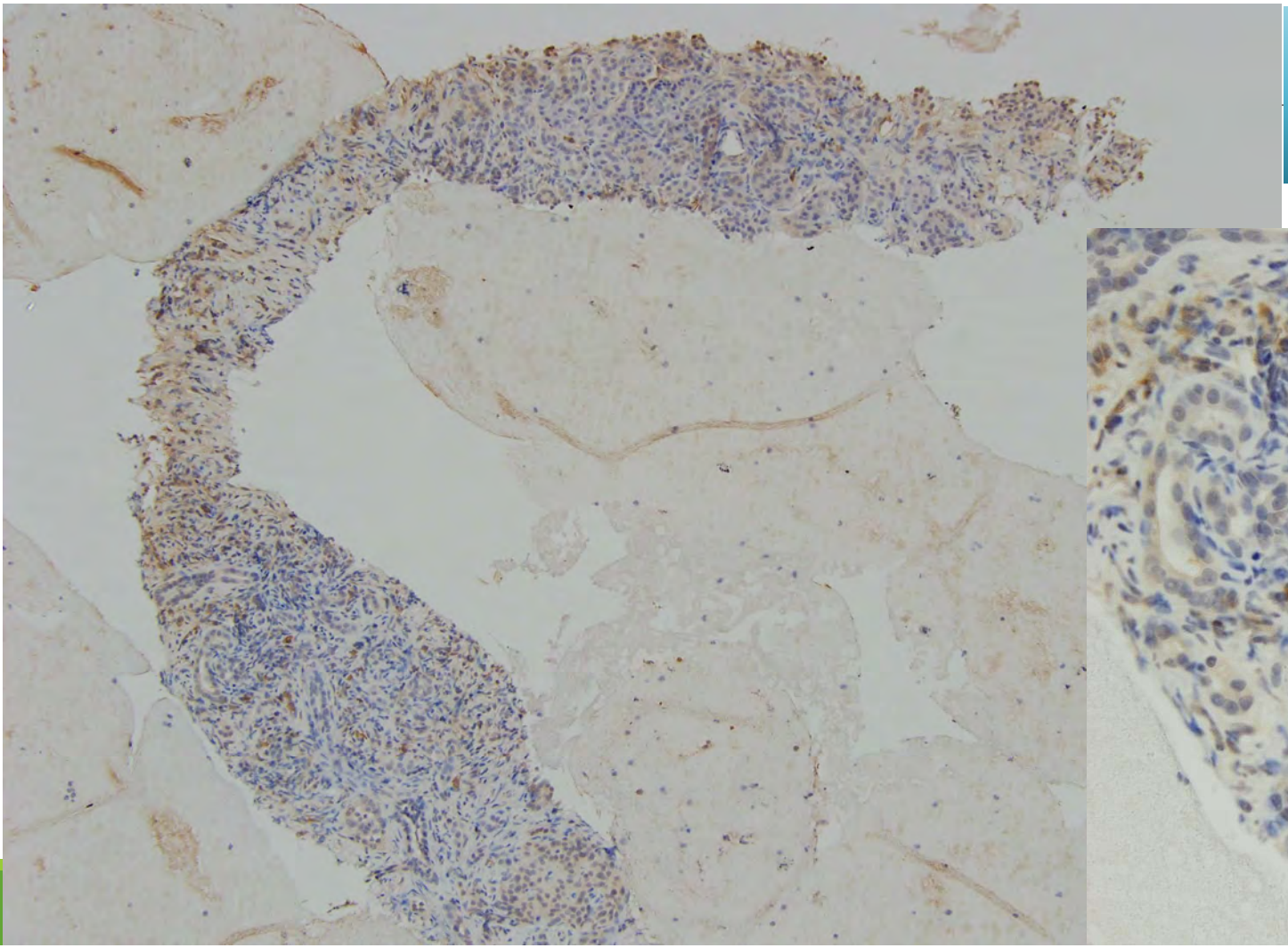
Jaundice with a “sausage shape” pancreas



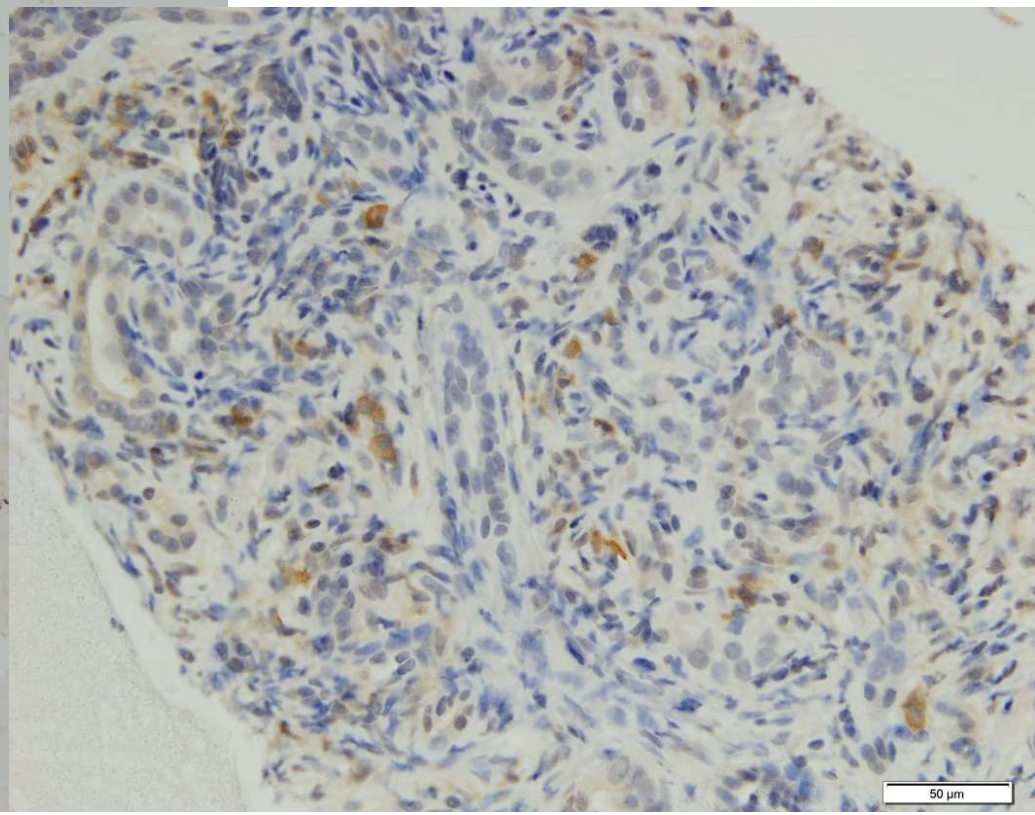




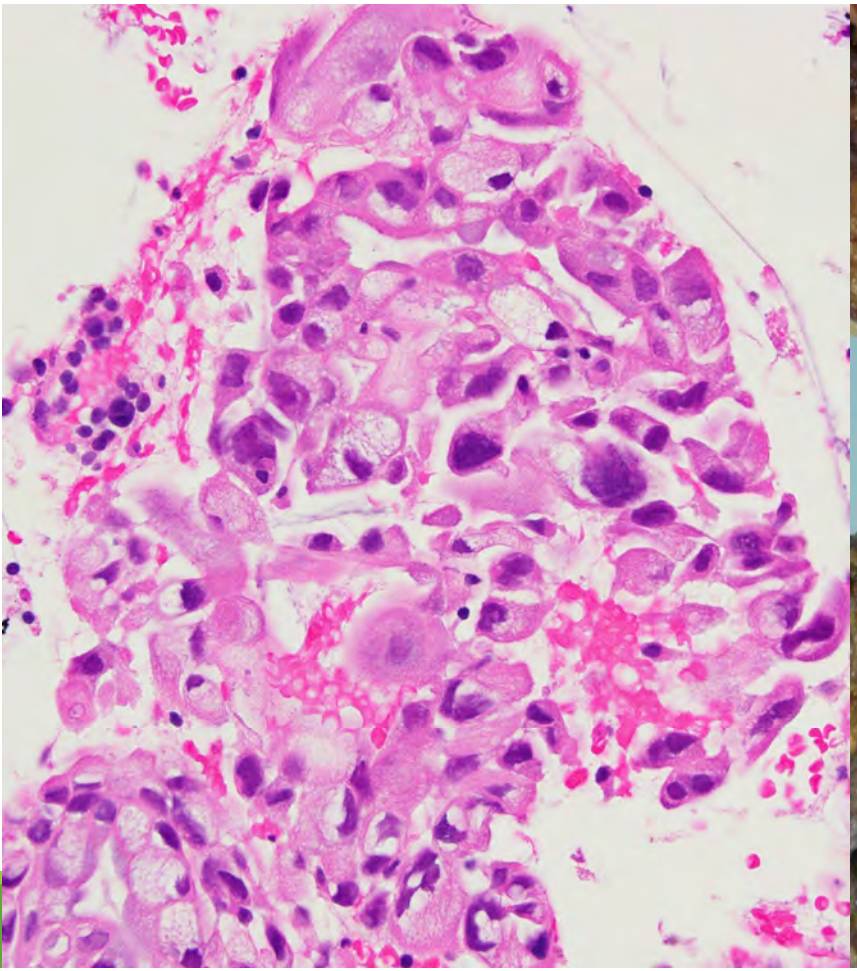
Immunohistochemistry stain

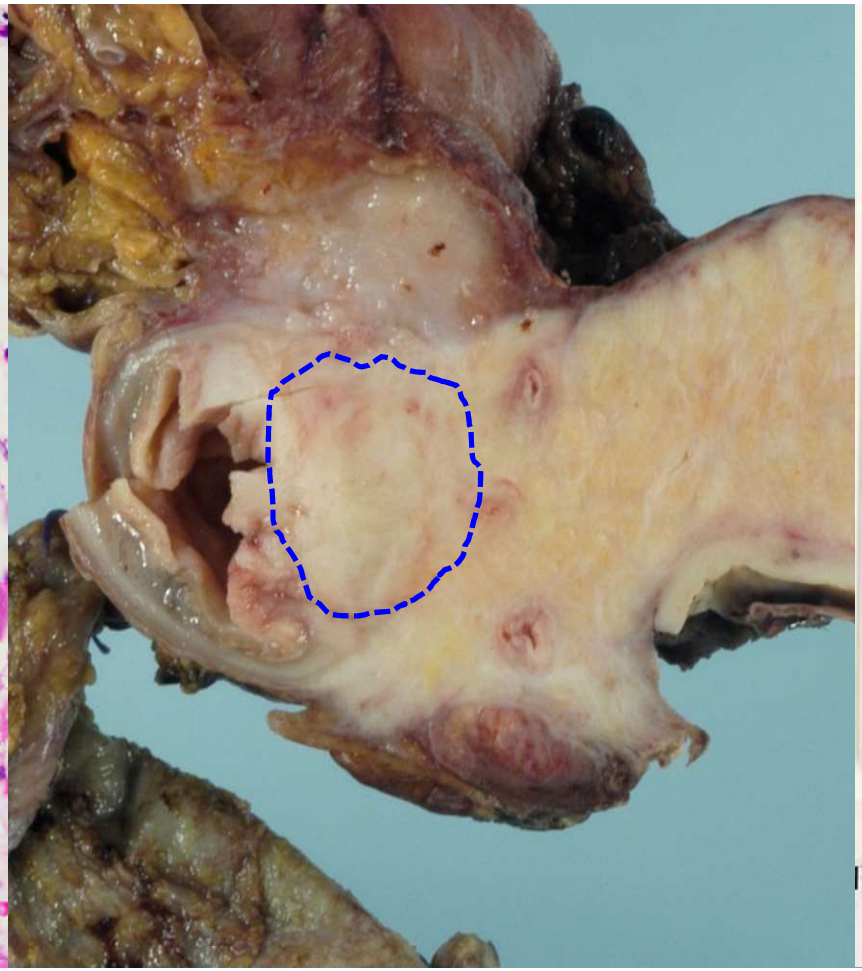


AIP without elevation of serum IgG4



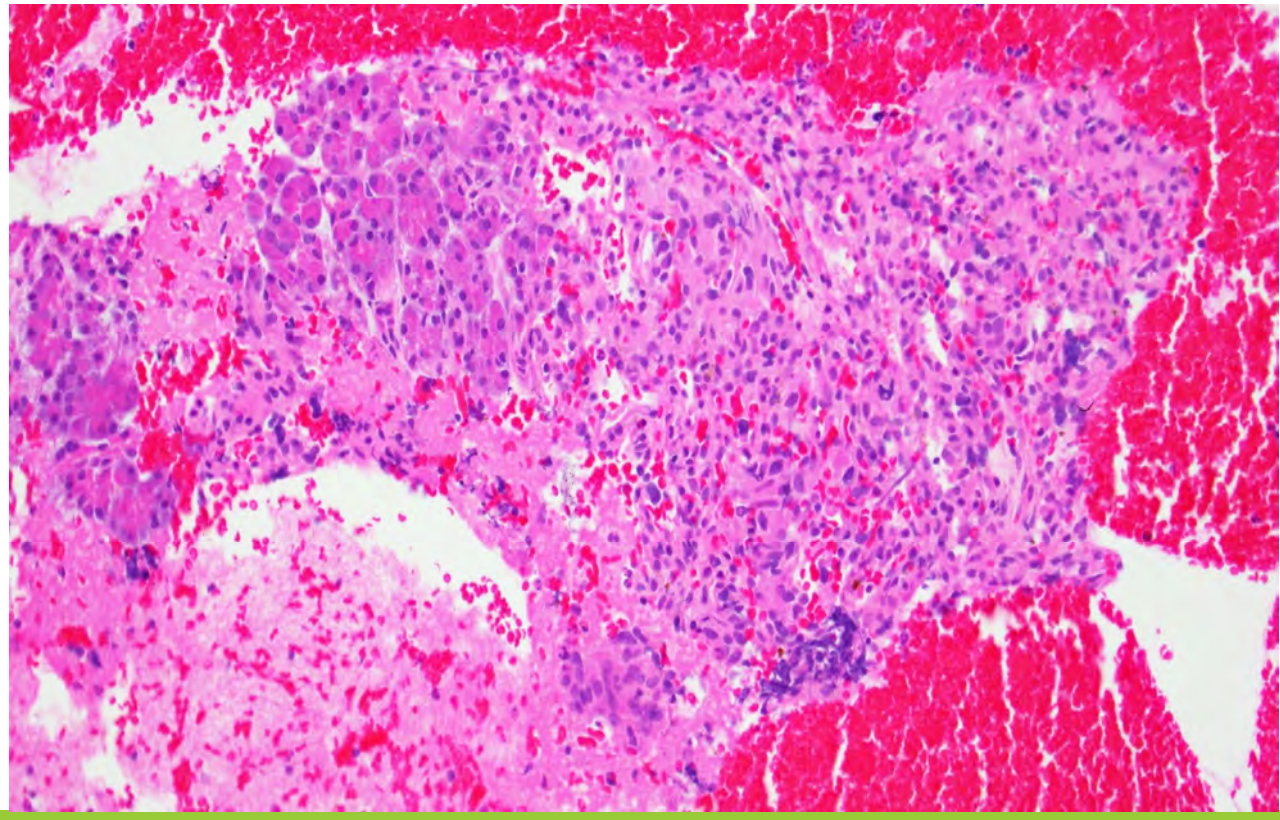
A surprising finding of... adenosquamous carcinoma...

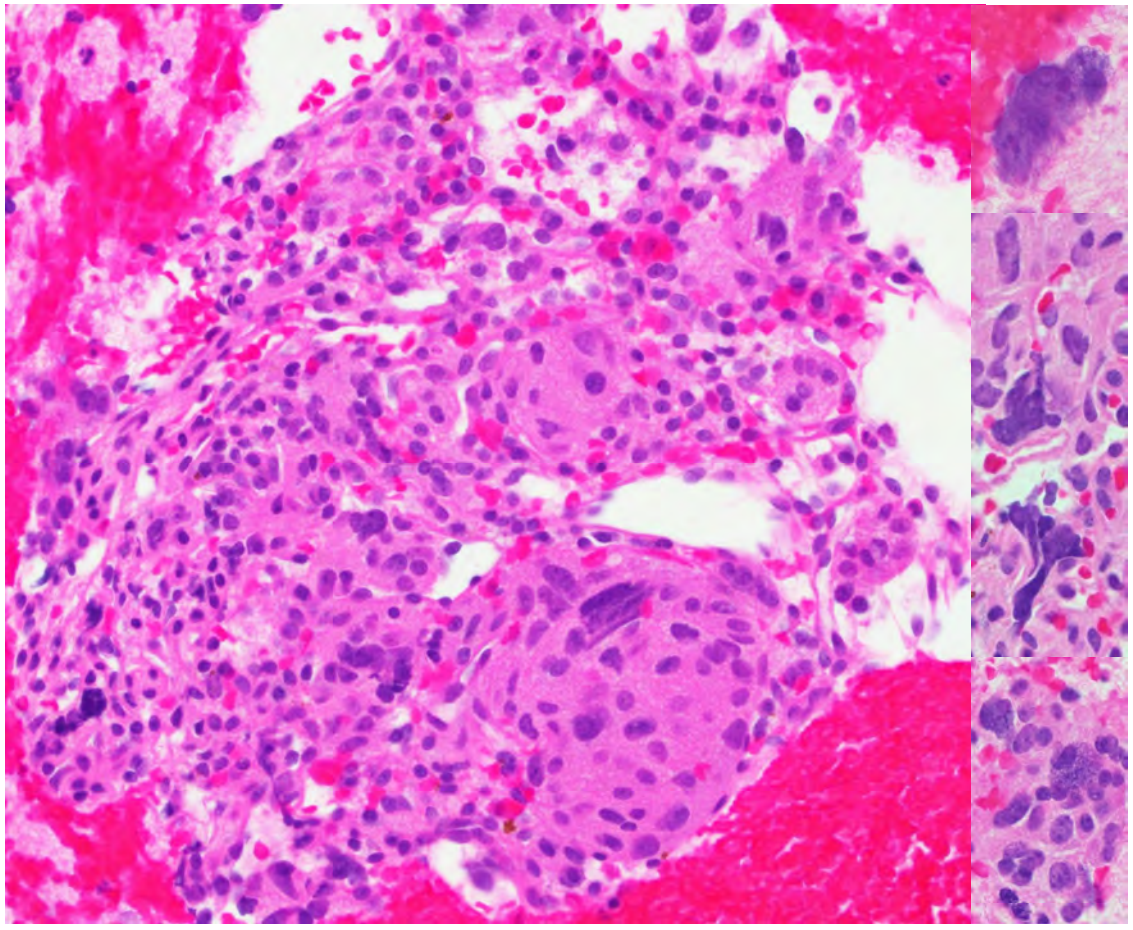


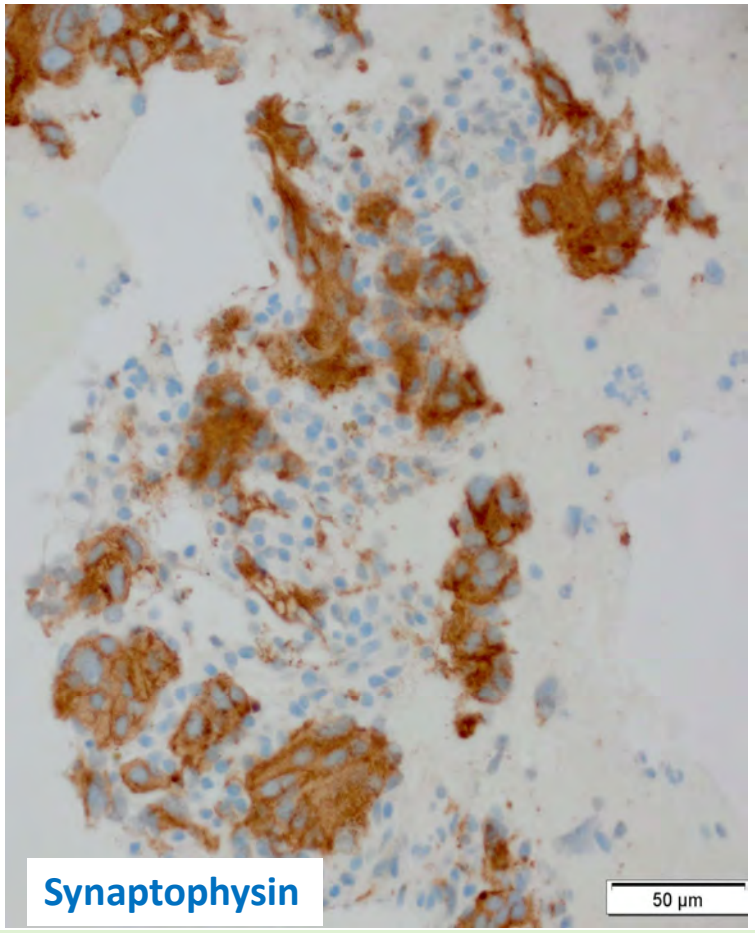


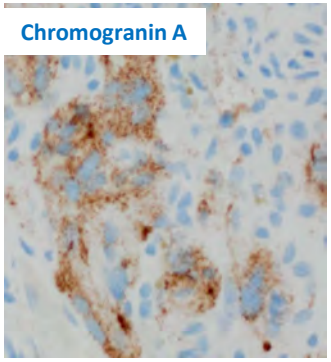
Direct histology for conventional FNA needle is also useful…

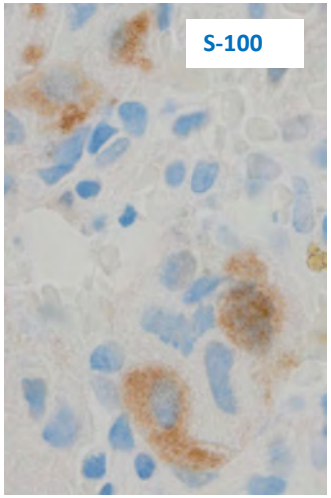
- 62/F
- Surgery 7 months ago for ovarian papillary serous carcinoma
- Completed 1st chemotherapy course
- 8mm pancreatic head lesion PET +ve
- ? Metastatic deposit
- EUS FNA biopsy (22G).









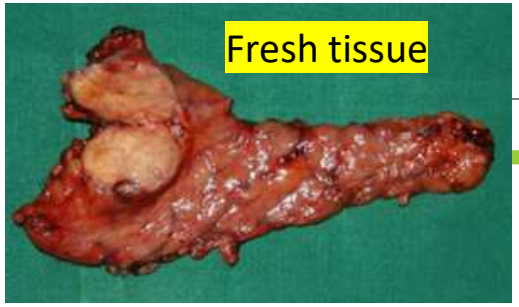


Extra-adrenal Paraganglioma

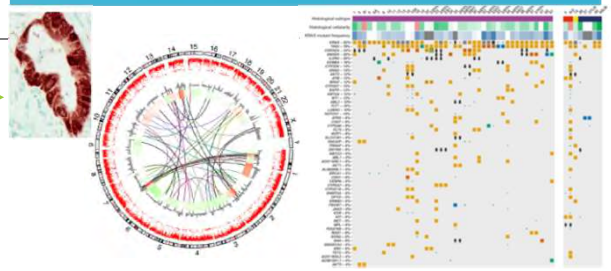
- Rare neuroendocrine neoplasms arising in extra-adrenal chromaffin cells of autonomic nervous system

Future implications of EUS guided core biopsy

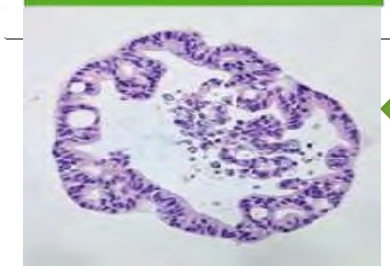
Provides tissue for Precision Oncology



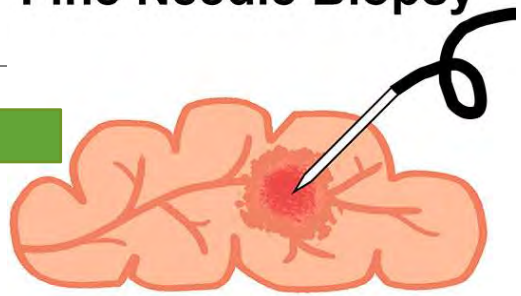
Biomarker or genomic assessment



Tumour organoid

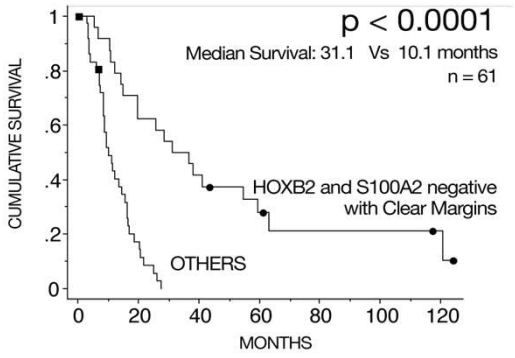


Fine Needle Biopsy



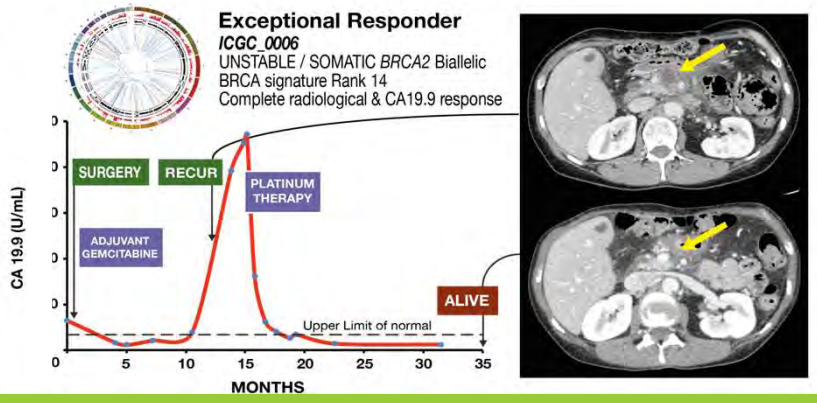
Inform outcomes and stratify appropriate therapy for patient

Whipple Pancreaticoduodenectomy



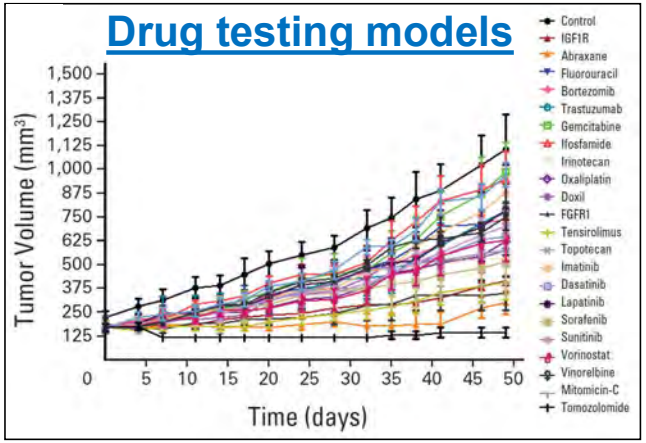
Biankin, Kench, Colvin, Scarlett, Nguyen et al. Gastroenterology 2009

Unstable chromosomal PDAC response to platinum based chemotherapy



Waddell……Nguyen… et al. Nature 2015

Drug testing models



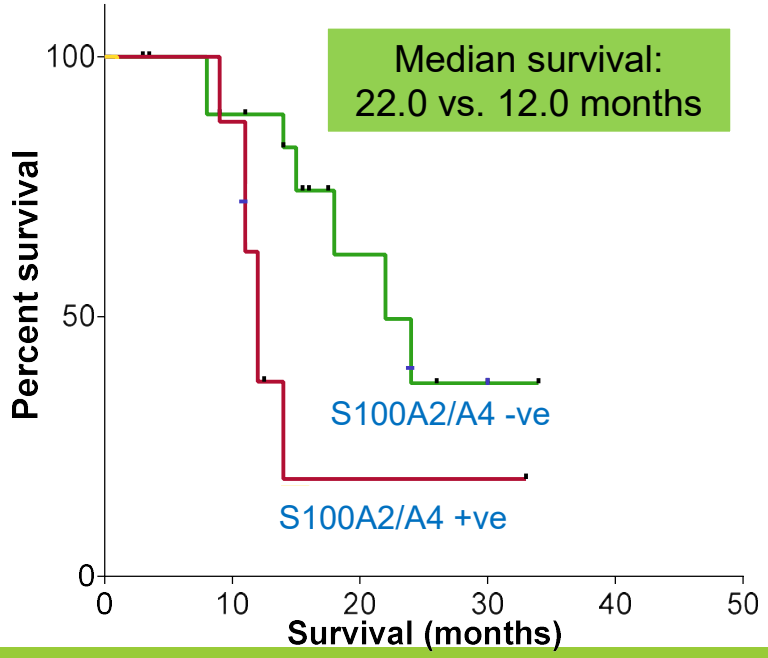
Rubio-Viqueira et al. Mol Cancer Ther 2007
Boj et al. Cell 2015: 160, 324-338

IMPACT OF S100A2/4 ON OUTCOME OF PANCREATECTOMY

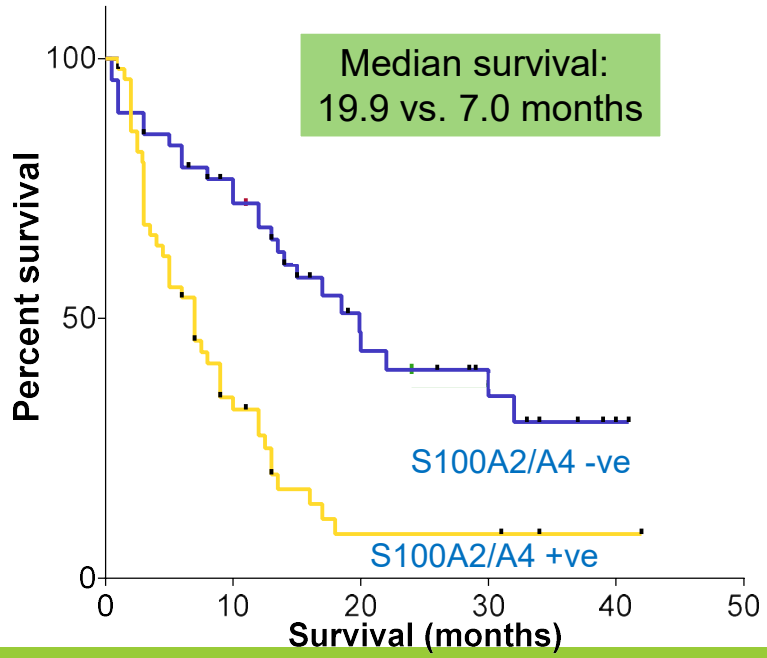
Prospective longitudinal study; 189 patients with pancreatic cancer
EUS biopsy with FNB needle (22G, 20G PROCORE)

1. IHC studies (S100A2/A4)
2. Genomic analysis from micro-dissection of fresh tumor tissue

Resection cohort (n=28)



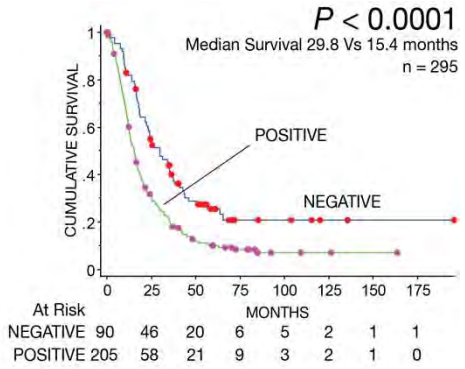
Non-resectable cohort (N=161)



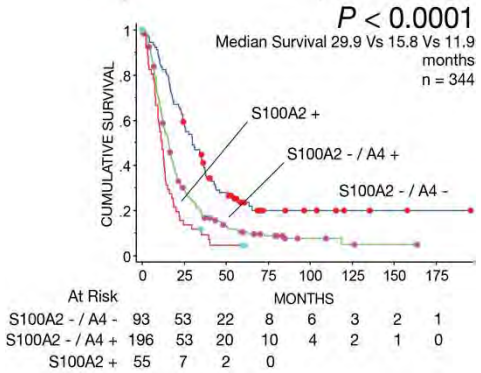
Nguyen et al. DDW 2017

Molecular nomogram to predict outcome of pancreatectomy

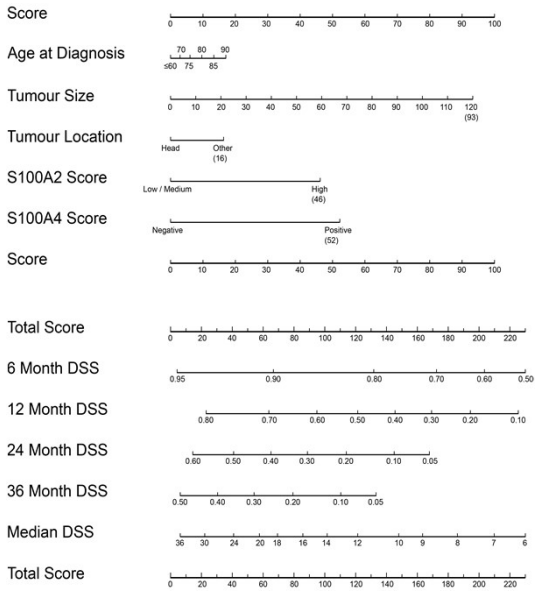
S100A4



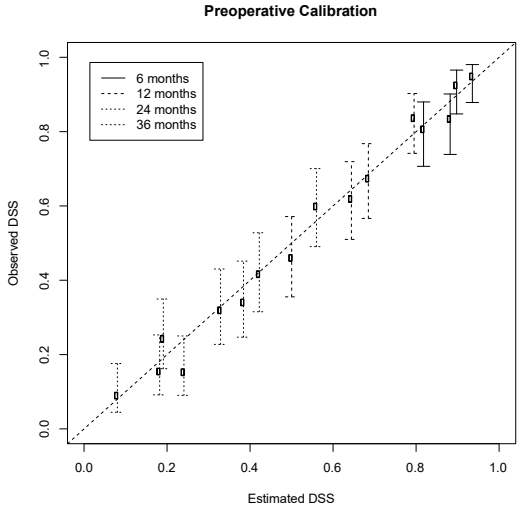
S100A2 and A4



Molecular Nomogram



Good correlation between the estimated and observed DSS



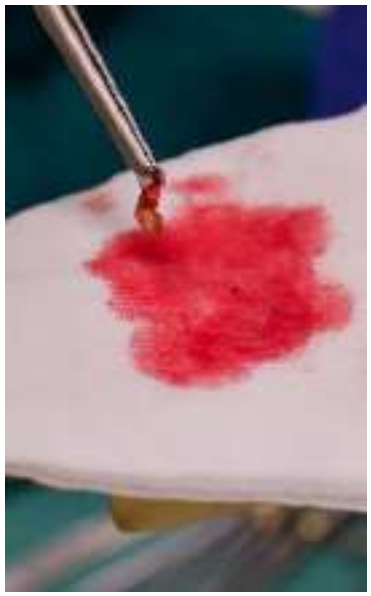
Chang, Nguyen et al. Ann Surg 2018

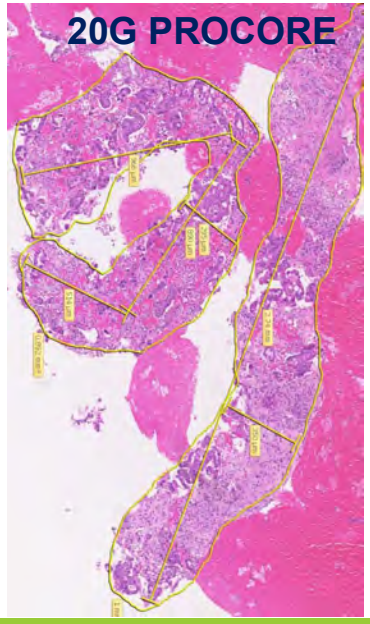
How much tissue do I need to biomarker or genomic testing?

Minimum requirement for genomic sequencing:

- 100 ng or more of total DNA
- ~500,000 ***cancer*** cells

- **One microliter or 1 cubic mm of blood contains about 4 million red blood cells**
- **One microliter or 1 cubic mm of tissue contains about ~1-2 million cells**





Feasibility for Precision Oncology Care

EUS needle type	Size (G)	Fresh Frozen Specimen	
		DNA yield [mean, range (ng)]	RNA yield [mean, range (ng)]
Boston Acquire®	22	1,819 (133–7,350)	191 (30–1,187)
Sharkcore®	19	2,170 (11.4–6,000)	N/A
Sharkcore®	22	2,939 (1,134–7,595)	481 (40–1,790)
Cook Procore®	20	1745 (290–4,750)	18 (3.6–44)

Patient cohort	Needle size (G)	Formalin fixed paraffin embedded specimem	
		DNA yield [mean, range (ng)]	RNA yield [mean, range (ng)]
Training set (n=14)	22	1,819 (133–7,350)	191 (30–1,187)
PRECISION-Panc EUS set (n=27)	22	2,694 (102–28,600)	N/A
PRECISION-Panc Core set (n=19)	Various	550 (0–1,730)	

For next-generation sequence, a minimum of **100ng** of either DNA or RNA are required

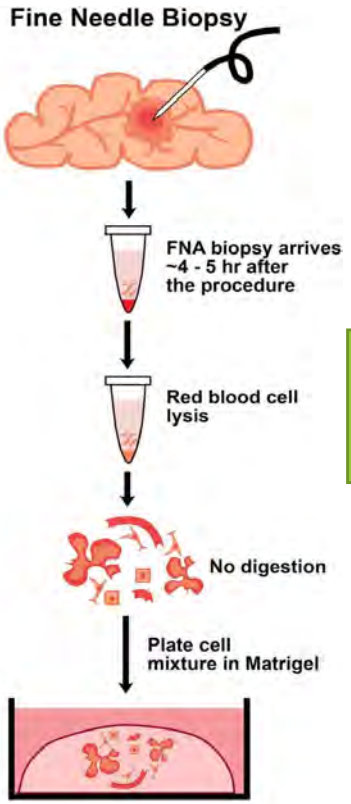
31 of 43 patients (72%) had samples with sufficient quantity DNA for WGS

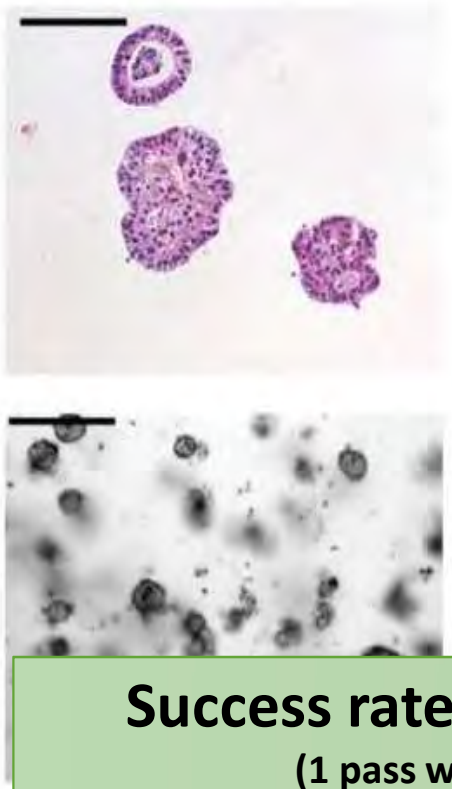
Dryer et al. Chin Clinic Oncol 2019

Genomic mutations to guide targeted therapy

Target	Treatment
KRAS wild-type	EGFR inhibitors (e.g., panitumumab, cetuximab, erlotinib)
DNA repair pathway defects (*BRCA1, BRCA2, PALB2, ATM*)	DNA damaging agents (e.g., mitomycin C, platinums) PARP inhibitors (e.g., olaparib)
HER2 amplification	Anti-HER2 antibodies/tyrosine kinase inhibitors (e.g., trastuzumab/lapatinib)
MET activation (mutation, overexpression, amplification)	MET inhibitors
Mismatch repair gene deficits (*MLH1, MSH2, MSH6, PMS2*)	Immunotherapy
PIK3CA amplification/mutation +/− *PTEN* loss	mTOR inhibitors (e.g., everolimus)
CDKN2A loss	CDK4/6 inhibitors (e.g., palbociclib)
BRAF mutation	BRAF inhibitors (e.g., dabrafinib), MEK inhibitors (e.g., trametinib)
FGFR1 amplification	FGFR inhibitors

High feasibility of creating PDAC organoids from EUS FNB specimens





- N=38 histologically confirmed PDAC
- 2 extra passes of **22-gauge** FNB needle (Procore)
- Within 2 weeks, isolation of **organoids** was achieved in 33 of 38 tumors (87%).
- Establishment of PDA **organoid** lines for ≥5 passages of growth (P5, five passages) was reached in 25 of 38 tumors (66%).
- There were no serious adverse events.

Success rate is even better with the 20G Procore

(1 pass with 75% rate of >5 passages, unpublished data)

Tiriac et al. GI Endoscopy 2018

CONCLUSIONS

The challenges to both endoscopist and pathologist for EUS guided biopsy can be overcomes by advances in EUS-needle technology and appropriate post-FNA/B tissue processing

- *Data from RCTs indicate ROSE is not essential*

- *Direct histology processing has many advantages, especially for specimens taken from new core needles*

- *Routine use of FNB offer other advantages*
  - Increases specificity and improves inter-observer variability
  - Allow ancillary testing for Personalized Oncological treatment

THANK YOU!