OASIS Event

"European Consortium Selection"
IMAGING AND BIOPHOTONICS

Example of EU biophotonics projects in collaboration with Cerimed:
EndoTOF PET - US

Pr.René LAUGIER
La Timone Hospital

ENDO TOFPET US

Endoscopic TOFPET & Ultrasound

A dedicated detector for pancreas and prostate biomarkers developments

FP7 project, Grant Agreement n °256984

P. Lecoq

CERN, Geneva, Switzerland

Pr. René LAUGIER

Timone Hospital

Marseilles

The CONSORTIUM

Part. no.	Organisation type	Short Name	Organisation legal name	Principal investigator	City, Country
1 coord	University Hospital	UnivMed	Université de la Méditerranée, Aix-Marseille II Team 1a. UnivMed/AP-HM Team 1b. UnivMed/Cerimed Team 1c. UnivMed/CRO2	R. Laugier R. Laugier V. Vidal E Mas	Marseille, France
2	International Research Organisation	CERN	European Organization for Nuclear Research	P. Lecoq	Geneva, Switzerland
3	University Hospital	CHUV-UNIL	Centre Hospitalier Universitaire Vaudois et Université de Lausanne	J. Prior	Lausanne, Switzerland
4	Research Organisation	DESY	Deutsches Elektronen-Synchrotron	E. Garutti	Hamburg, Germany
5	Higher Education	Delft TU	Delft Technical University	E. Charbon	Delft, Netherlands
6	SME	Fibercryst	Fibercryst	D. Perrodin	Villeurbanne, France
7	SME	KLOE	Kloe SA	P. Coudray	Montpellier, France
8	Higher Education	LIP	Laboratório de Instrumentação e Física Experimental de Partículas	J. Varela	Lisbon, Portugal
9	SME	SurgicEye	SurgicEye GmbH	J. Traub	München, Germany
10	University Hospital	TUM	Technische Universität München Team 10a. TUM/NUK Team 10b. TUM/CAMP	M. Schwaiger M. Schwaiger N. Navab	München, Germany
11	Higher Education	UHEI	University of Heidelberg	H.C. Schultz-Coulon	Heidelberg, Germany
12	Higher Education	Unimib	University Milano Biccoca	M. Paganoni	Milano, Italy

- EndoTOFPET-US collaboration
  - Grant # 256984

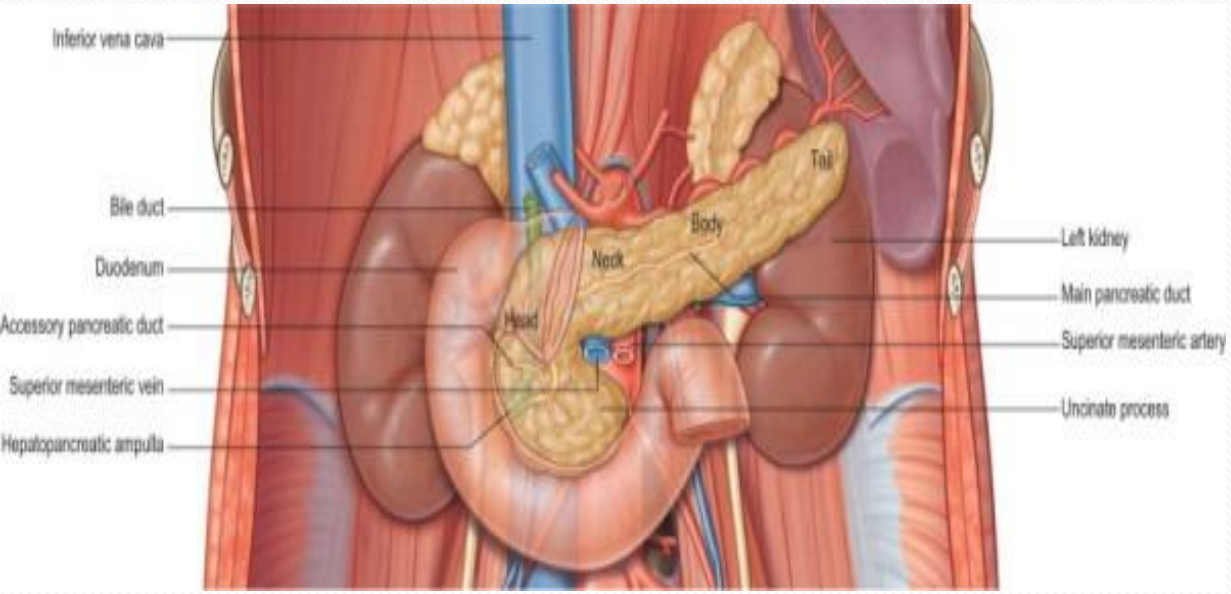
- PICOSEC Marie Curie TN
  - Grant # 289355

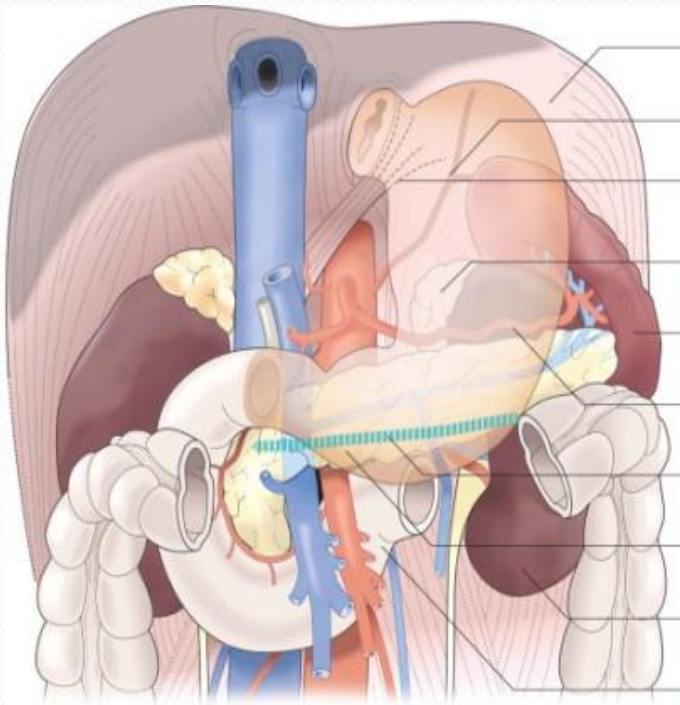
- ERC Advanced Grant -TICAL
  - Grant # 338953

What the rationale ?

Pancreas is difficult to examine !

- Retroperitoneal organ, deep and hiden
- Not directly accessible to endoscopy

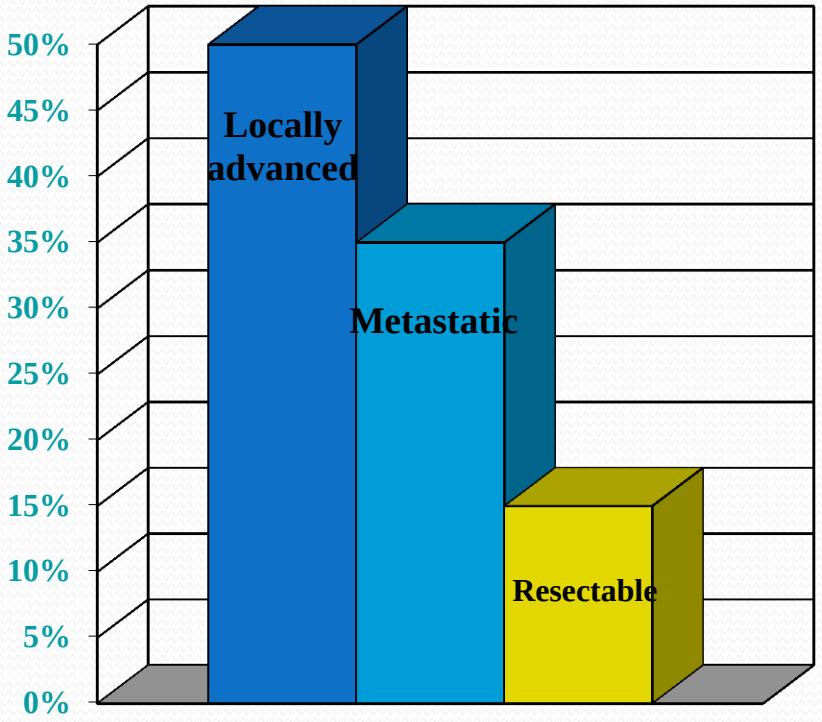




Because pancreatic cancer is a big problem !

Epidemiological data

- > 3050 new cases/year in France
- Enhancing incidence
- 2 nd digestive cancer in mortality,
- 6th in frequency
- Poor prognosis
- Lack of improvement in the early diagnosis

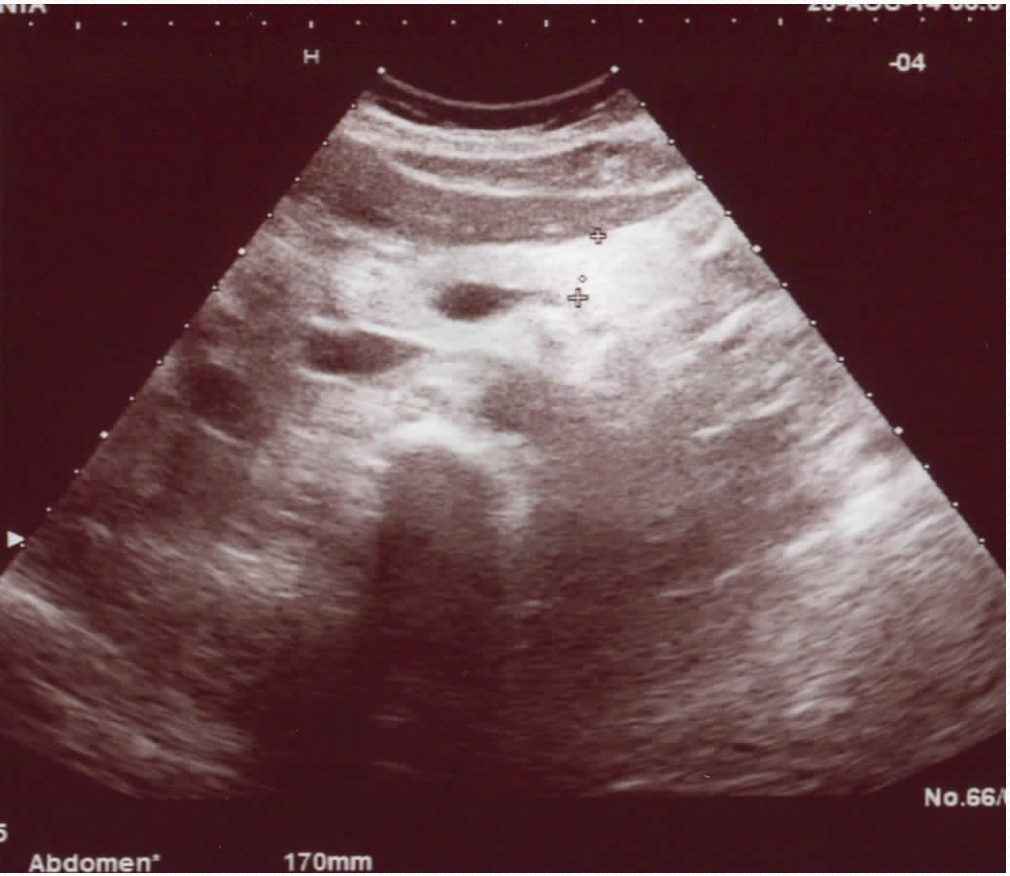


frequency

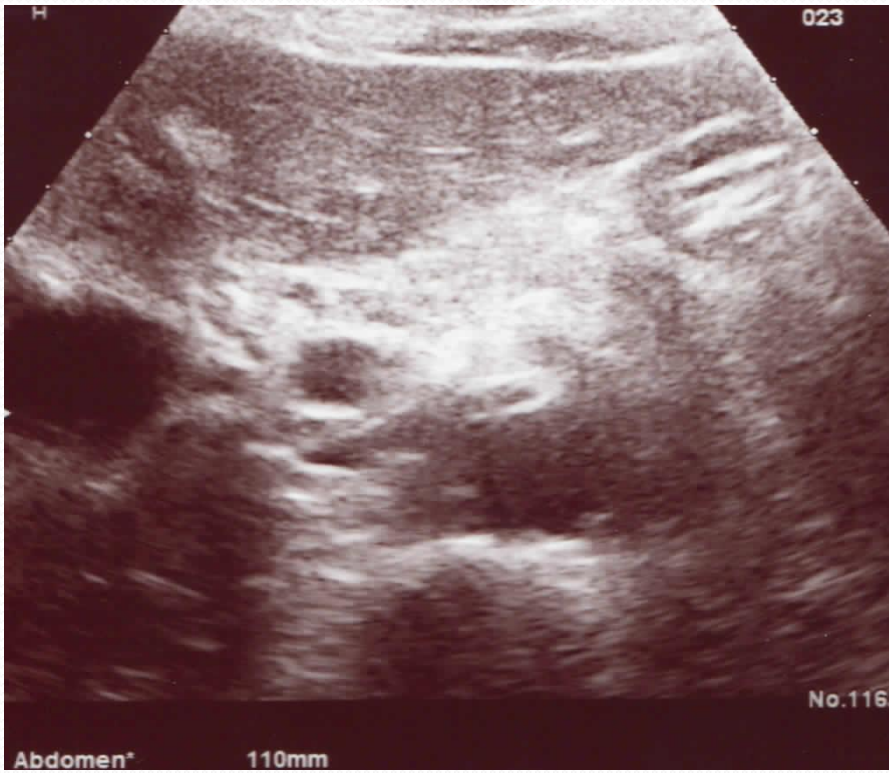
Because clinical symptoms are scarce!

- **Early clinical symptoms do not exist :**
- Signs often only appear when neighbouring organs are involved : too late
- **Pain** : very evocative (solar type) but very late
- **Jaundice** : non specific and always late
- **Biology** : CA 19-9 non specific and very late

Ultrasonography is not sensitive enough

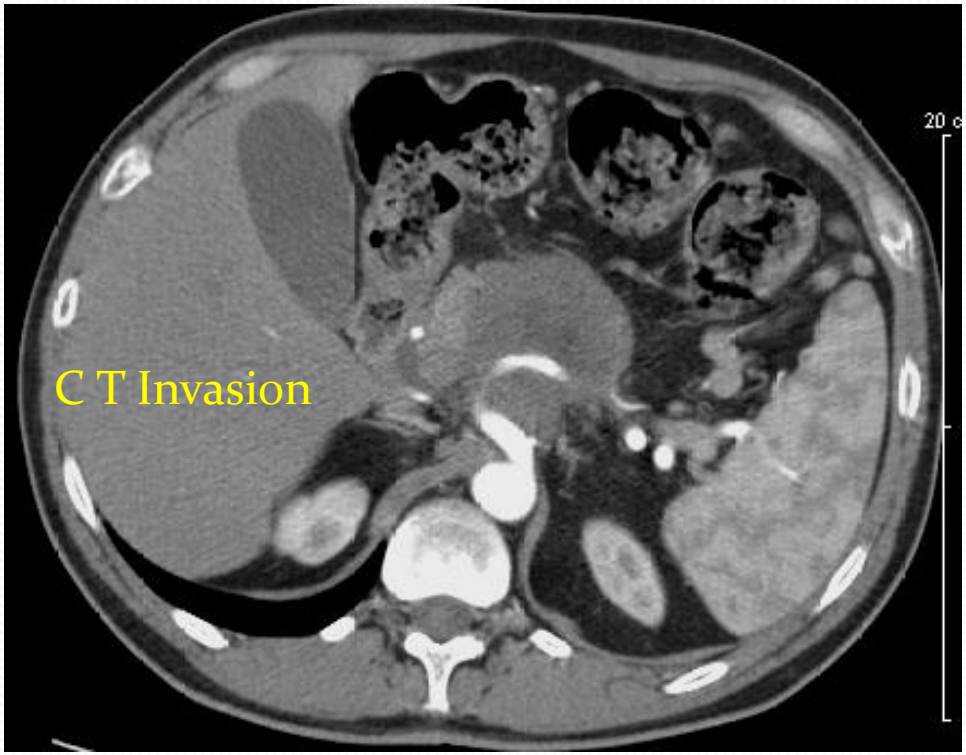


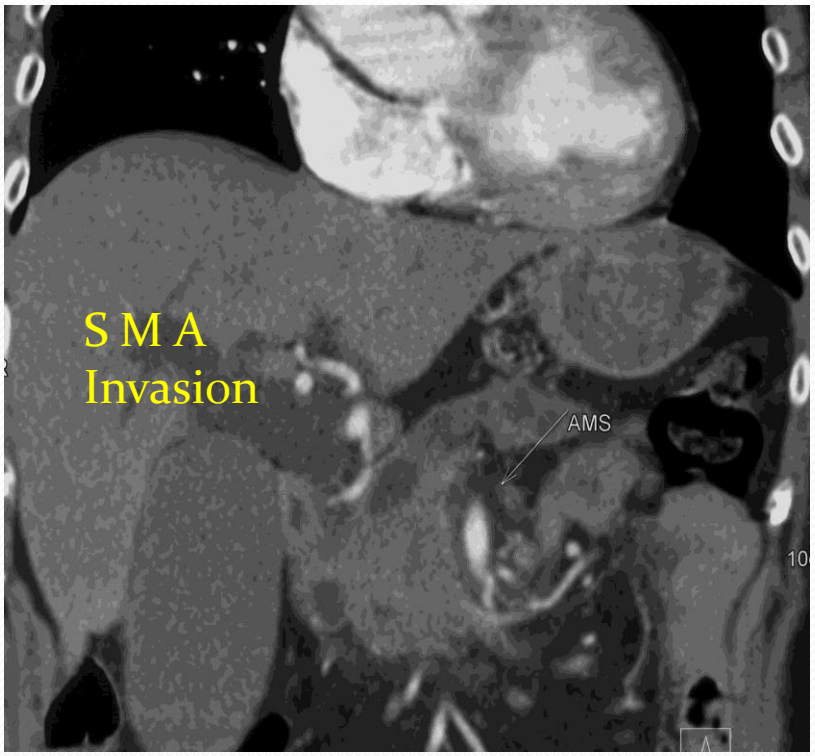
Low sensibility, only when tumor exceed 20 mm



CT Scan: confirmation and staging for operability but only for diagnosed lesion

Precision : 83-93 % Good for resectability evaluation



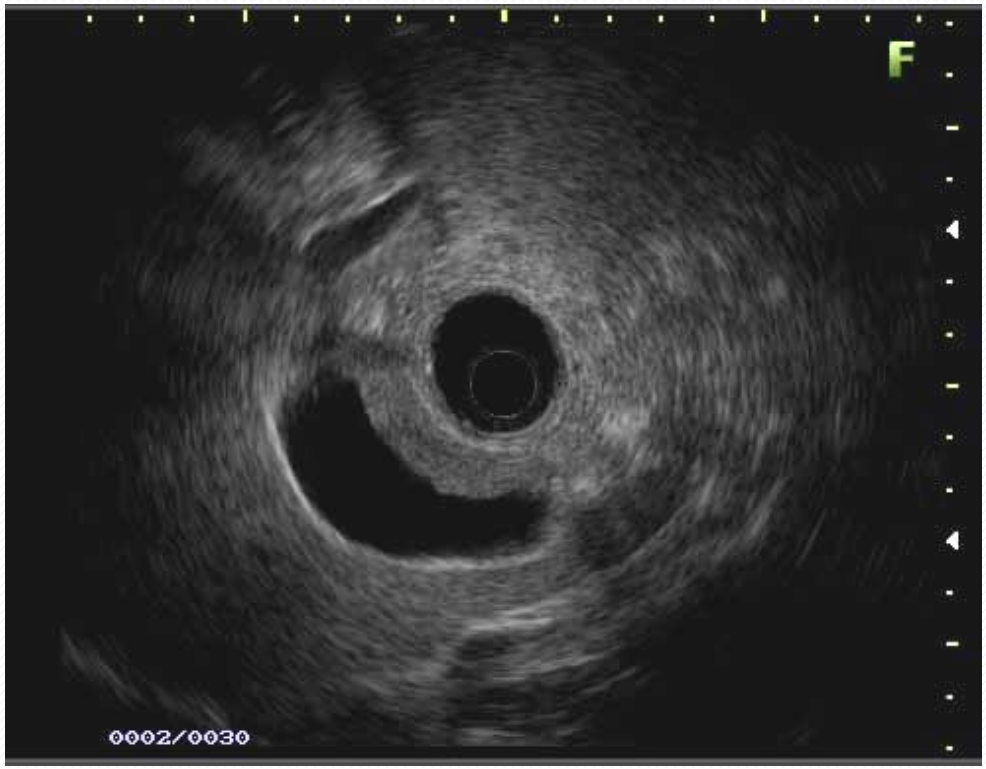


Endosonography:

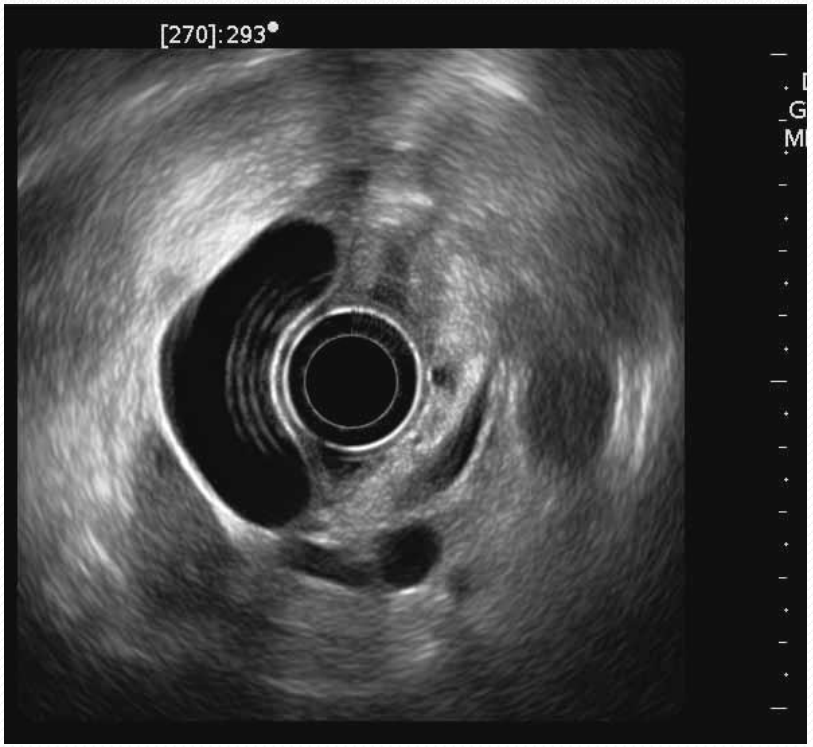
Combines endoscopy and US

Radial Linear

- **Endosonography**: radial probe

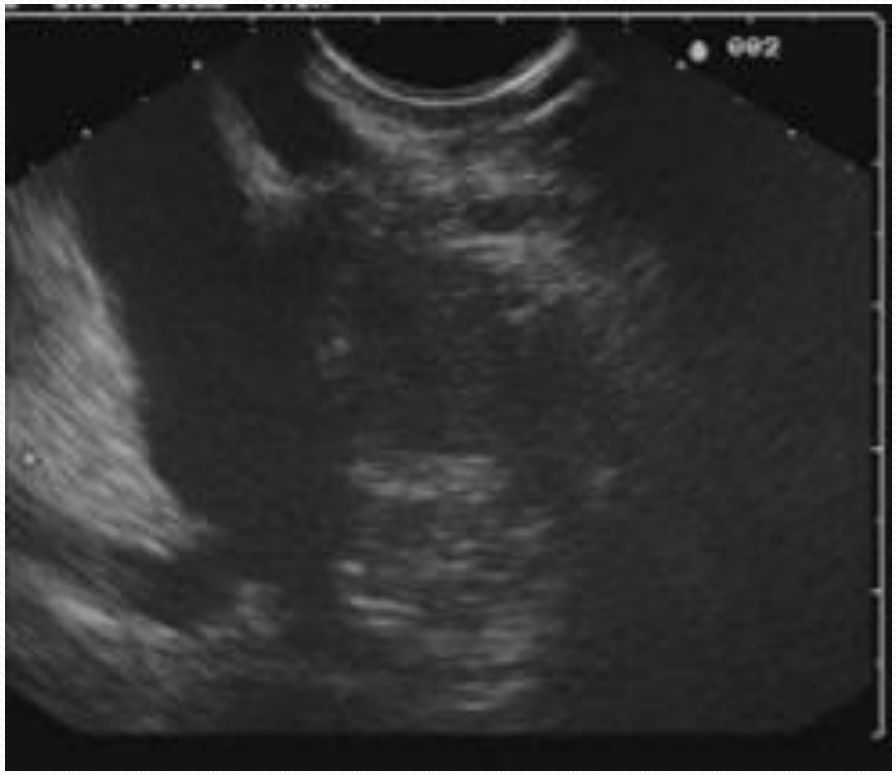


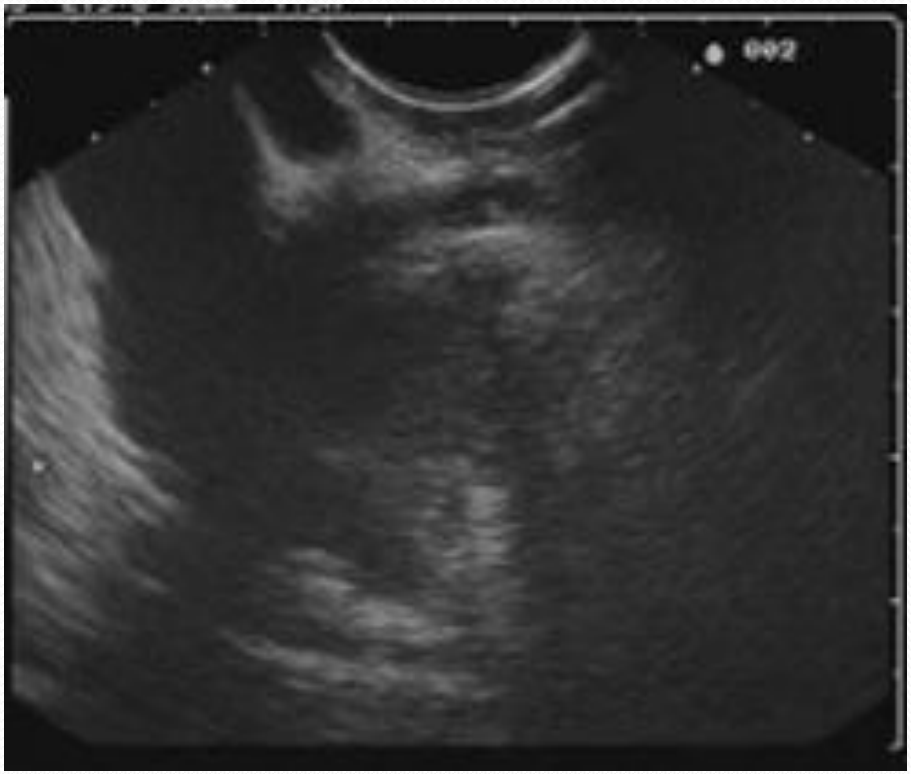
7. MHz



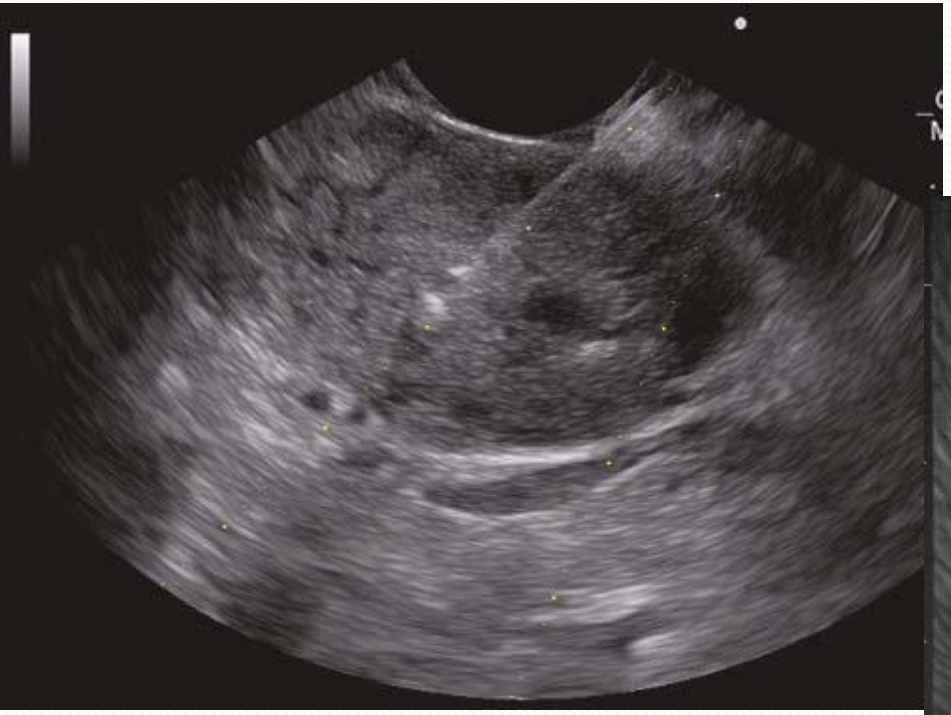
12 MHz

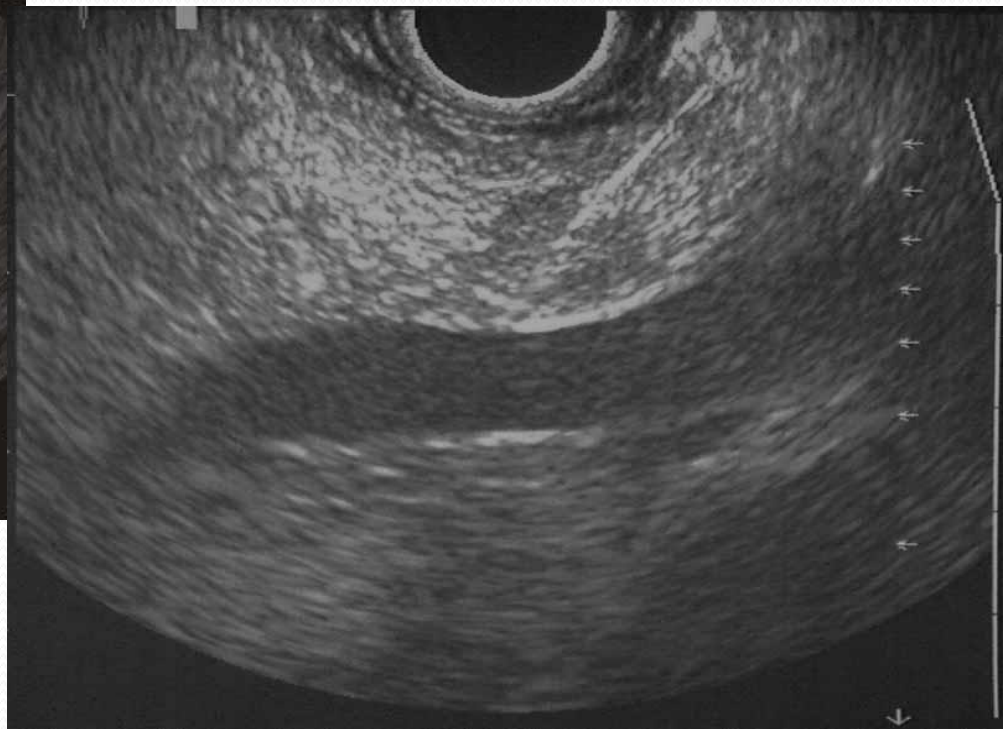
- **Endosonography**: linear probe



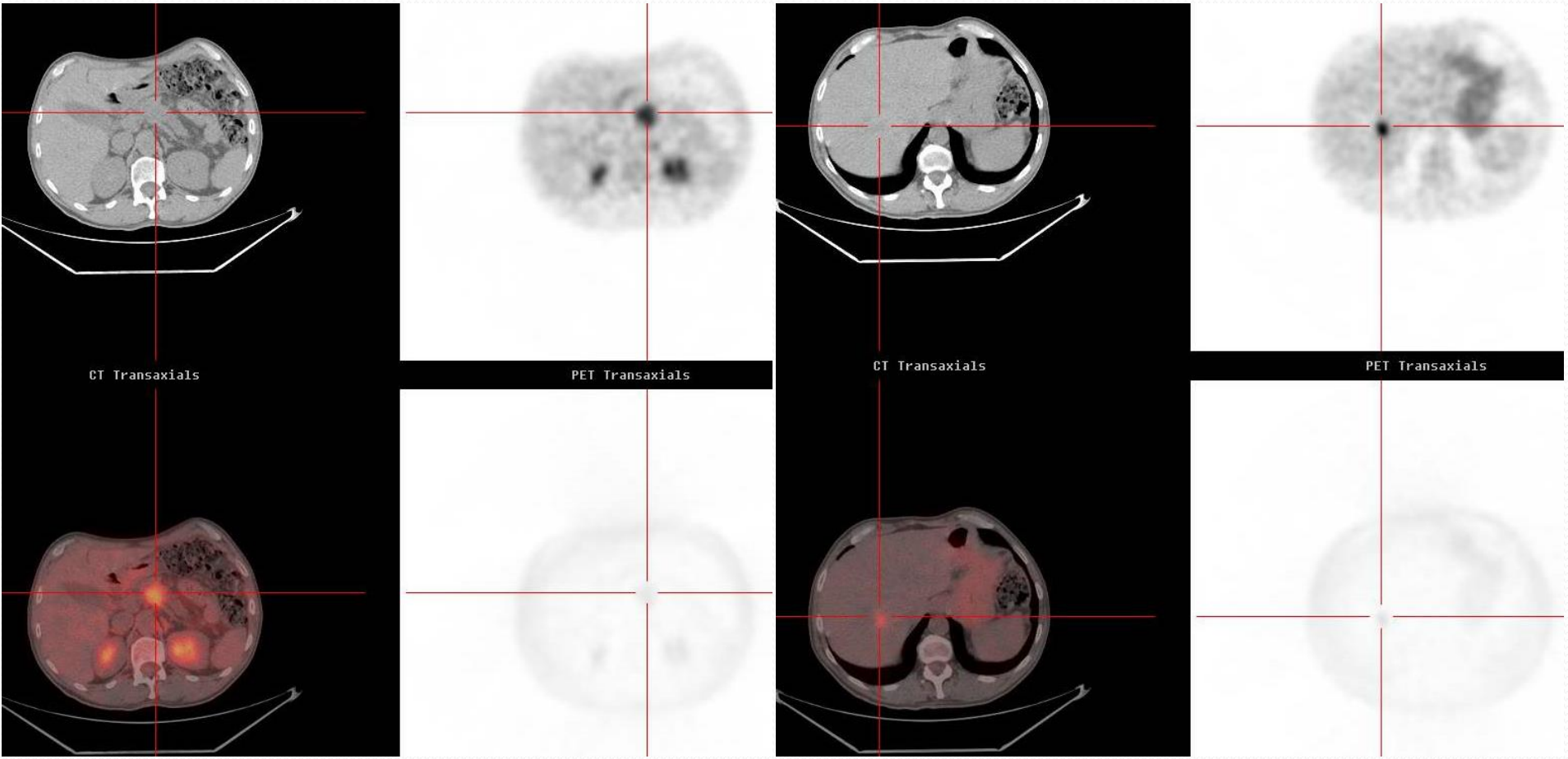


- **Endosonography**: the linear probe allows a direct cytology guidance for a puncture

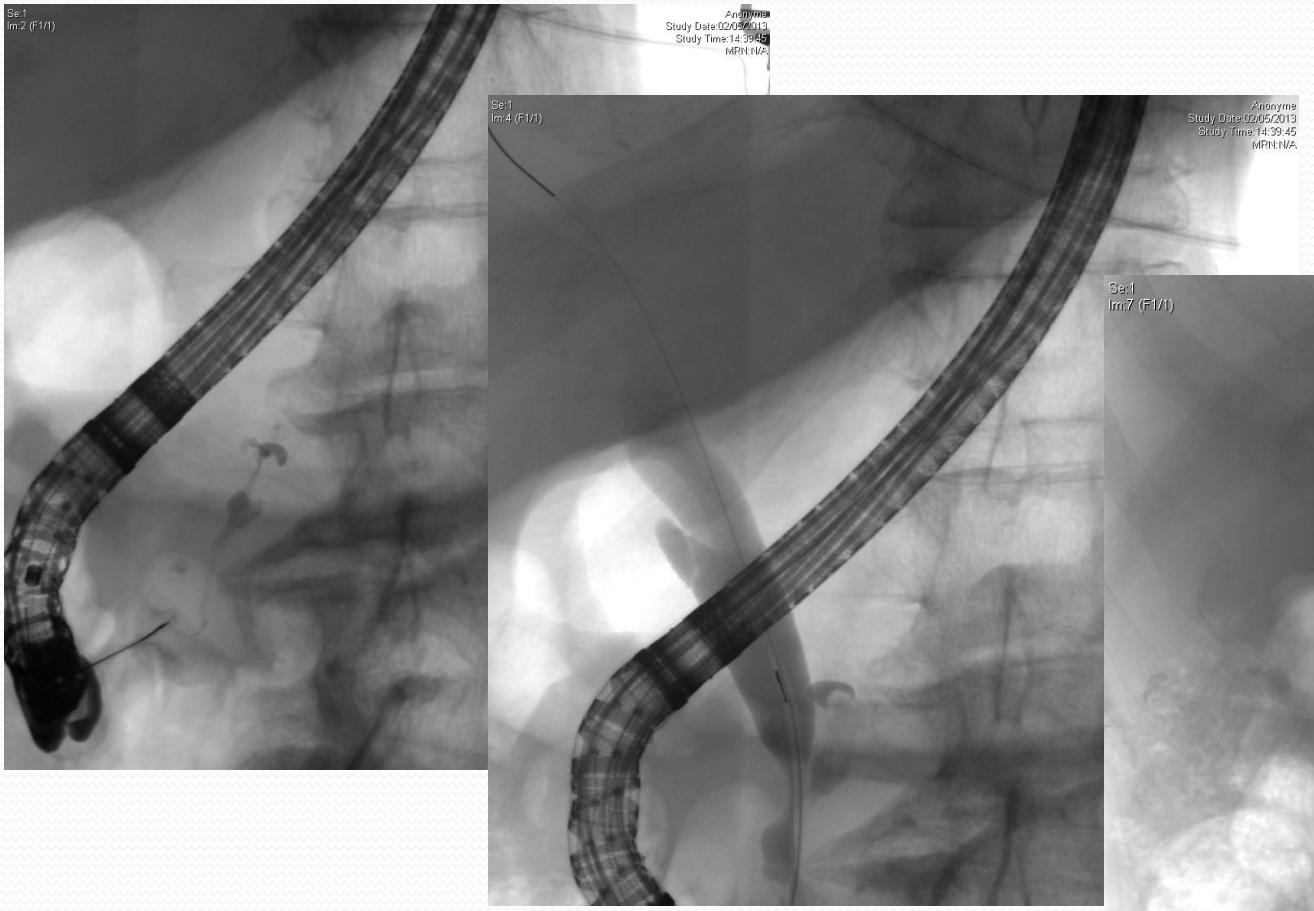


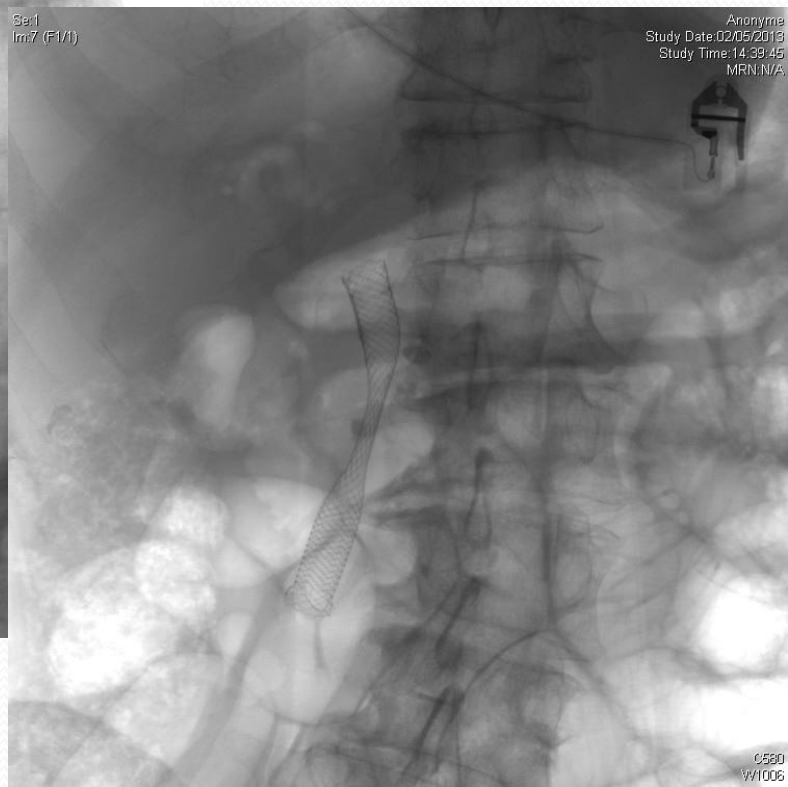


- **Positon Emission Tomography: Only for staging primitive pancreatic lesion and metastasis**



- E R C P: no longer for diagnosis but only for treatment



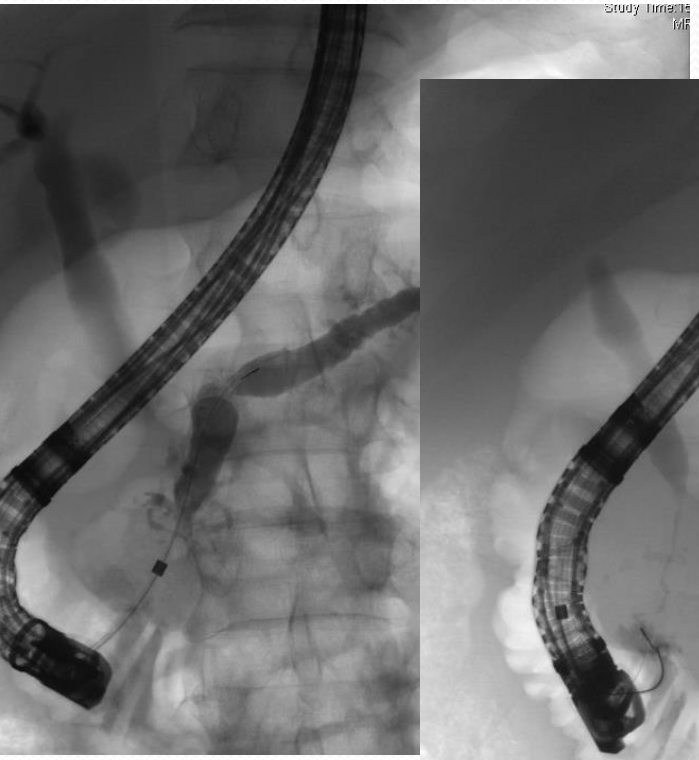


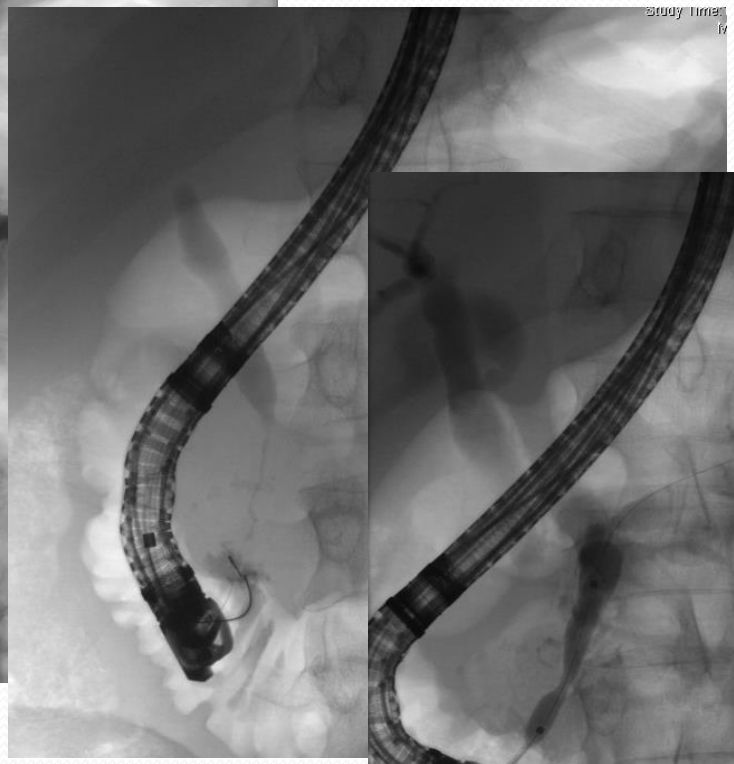
Is a pancreatic cancer screening possible ?

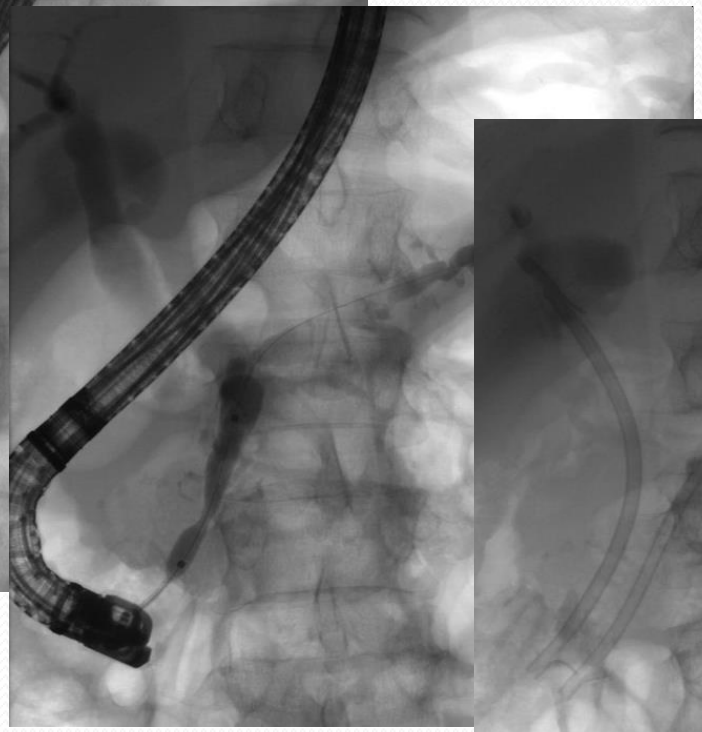
- **Not for the general population , BUT**
- Some sub populations are of interest for the GE:

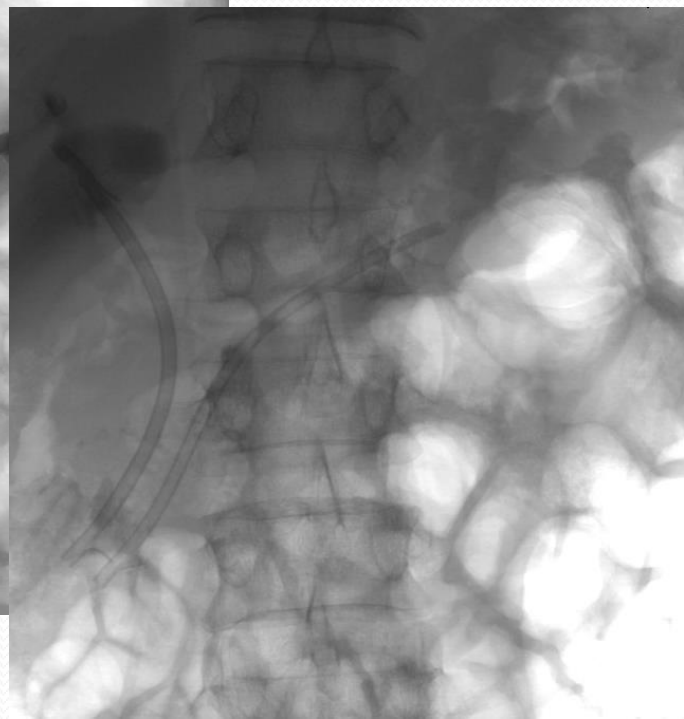
  * Chronic pancreatitis patients, at a late stage, with a stricture of MPD or MBD or both
  * IPMN: mixt and branch duct types
  * Chronic Hereditary Pancreatitis
  * Mucinous neoplasms
  * Endocrine tumors

Chronic pancreatitis patients, at a late stage







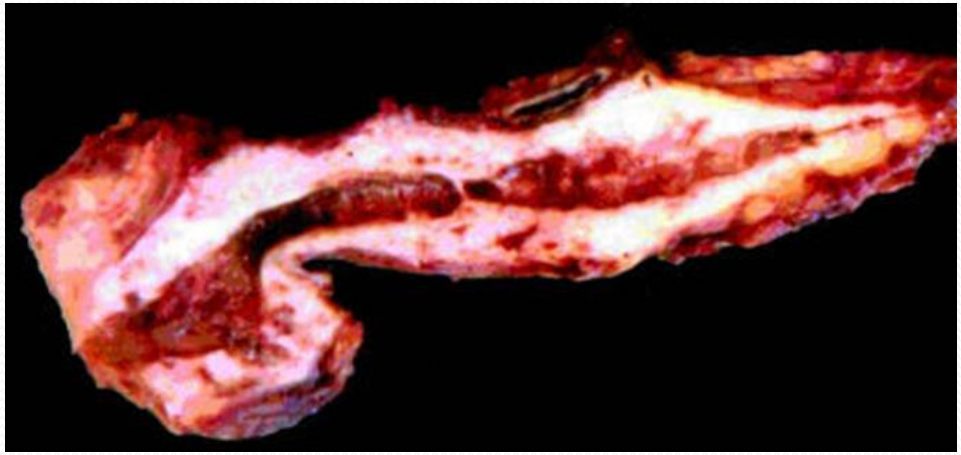


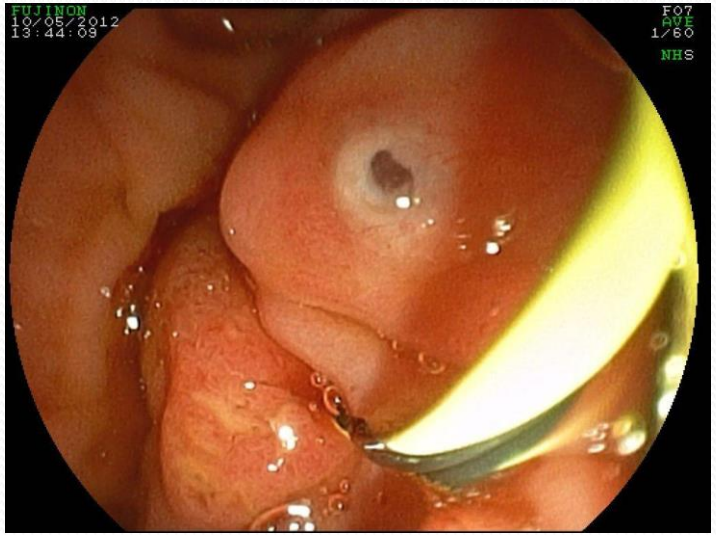
Relevance of a stricture ??

Surveillance or surgery ??

* IPMN

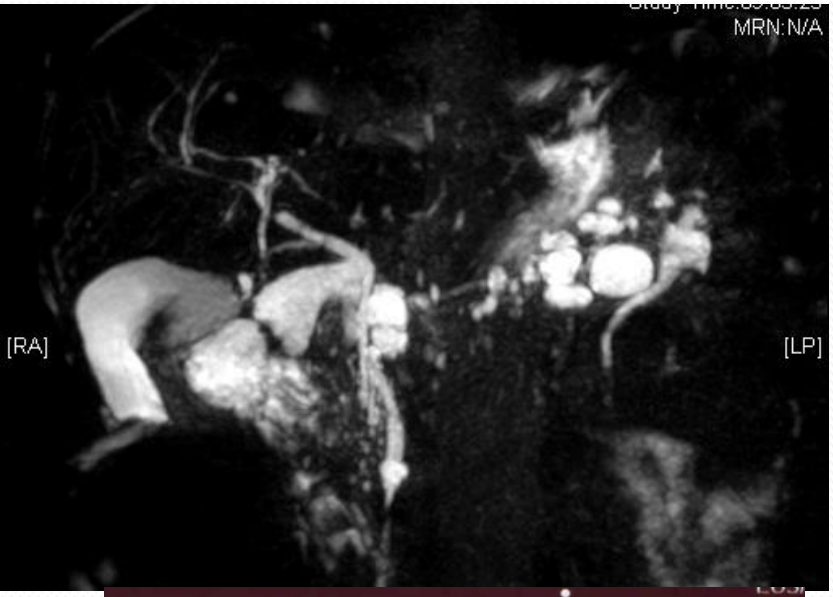
- Transformation of the cubic type epithelium of the ducts into a mucinous type
- Acute bouts of pancreatitis and duct dilation
- Mucus secretion

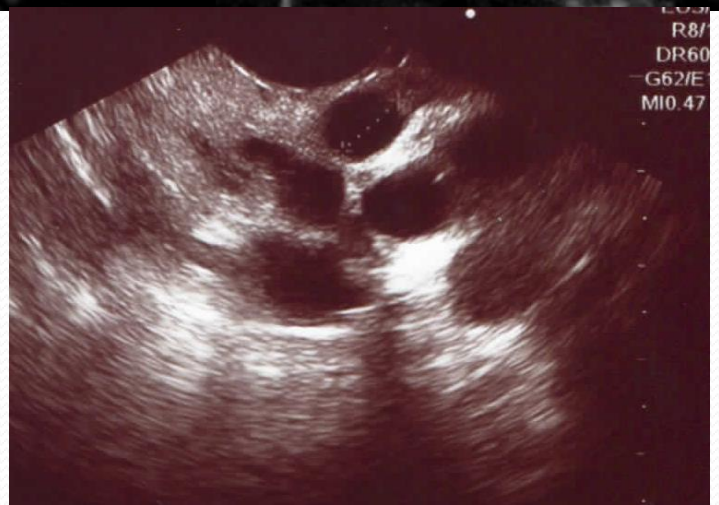




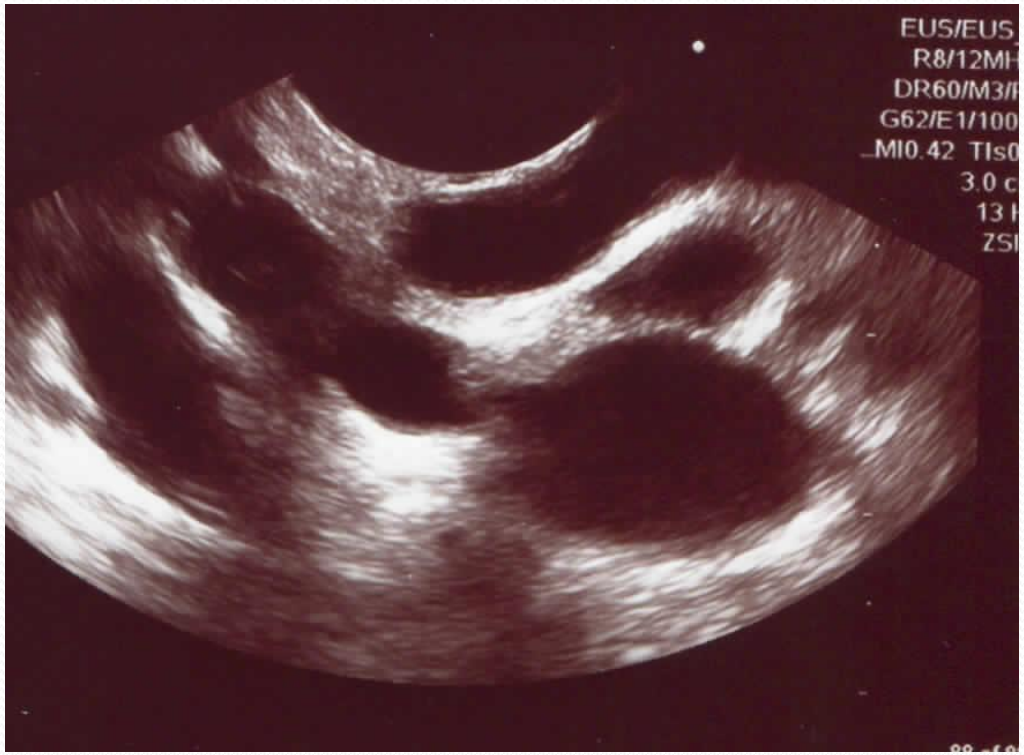
- Risk of degeneration into a cancer
- Main duct++, branch duct and mixt types: surveillance

* IPMN mixt and branch duct forms: MRI and EUS +++

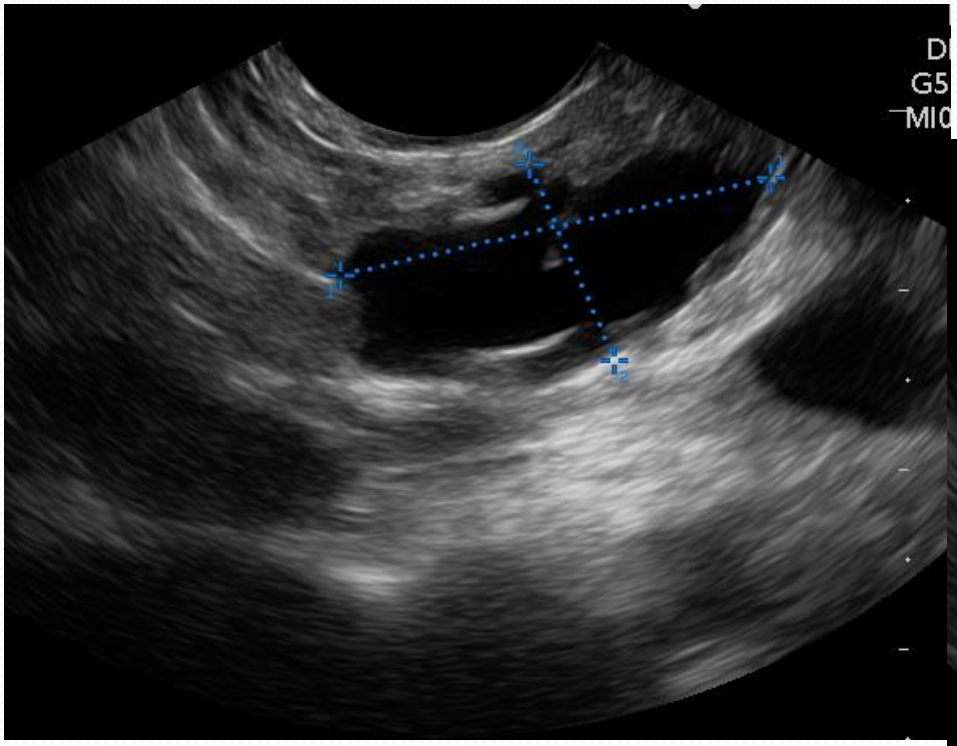




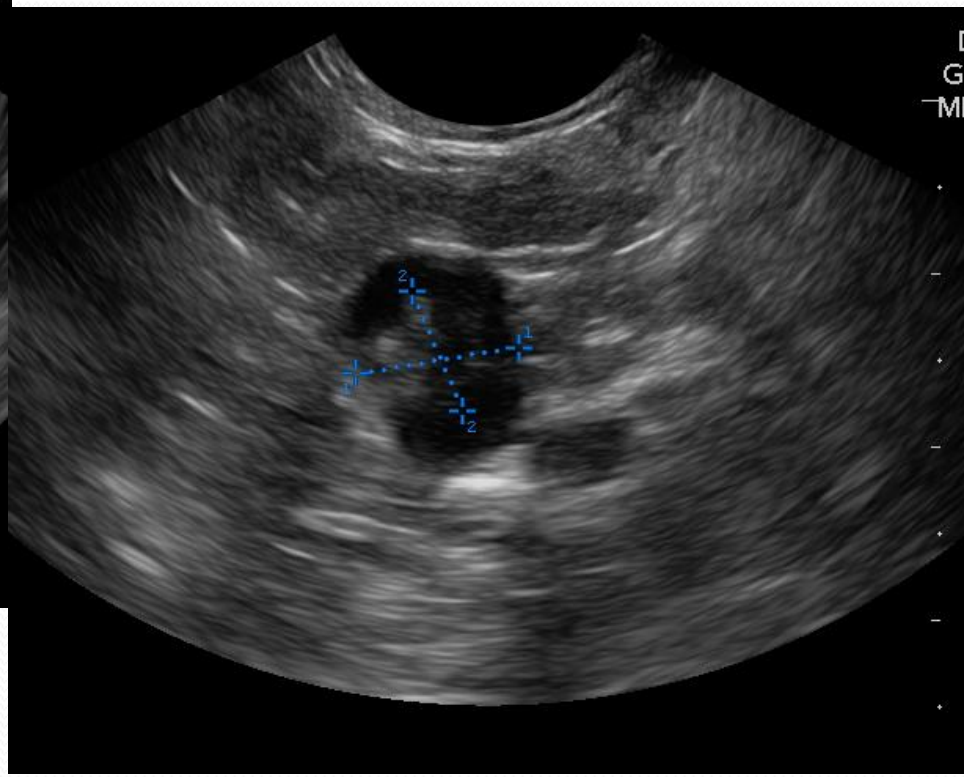
No cancer ? Surveillance ?



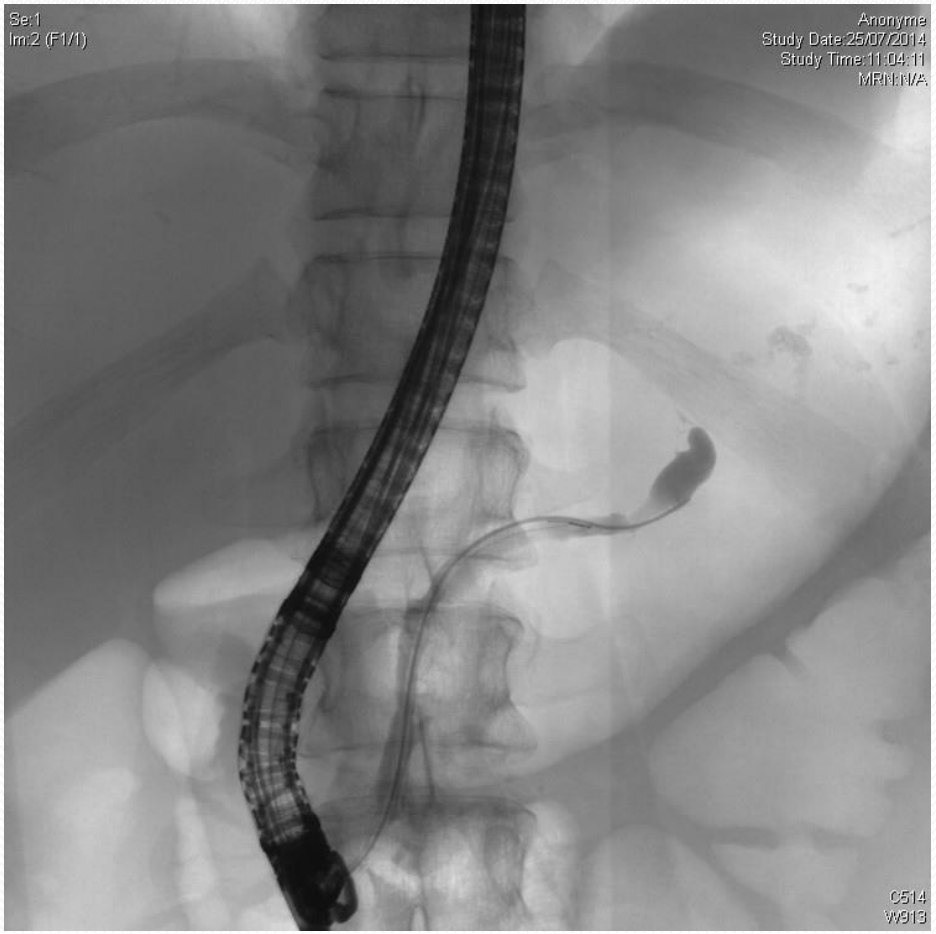
* IPMN mixt and branch duct forms: MRI and EUS +++



Nodule or mucus ??

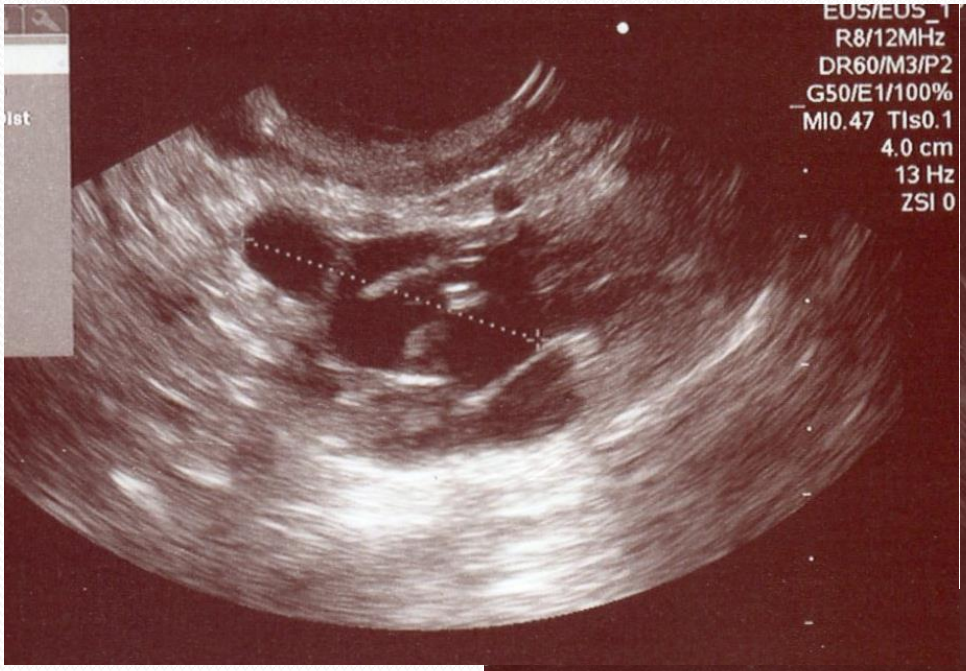


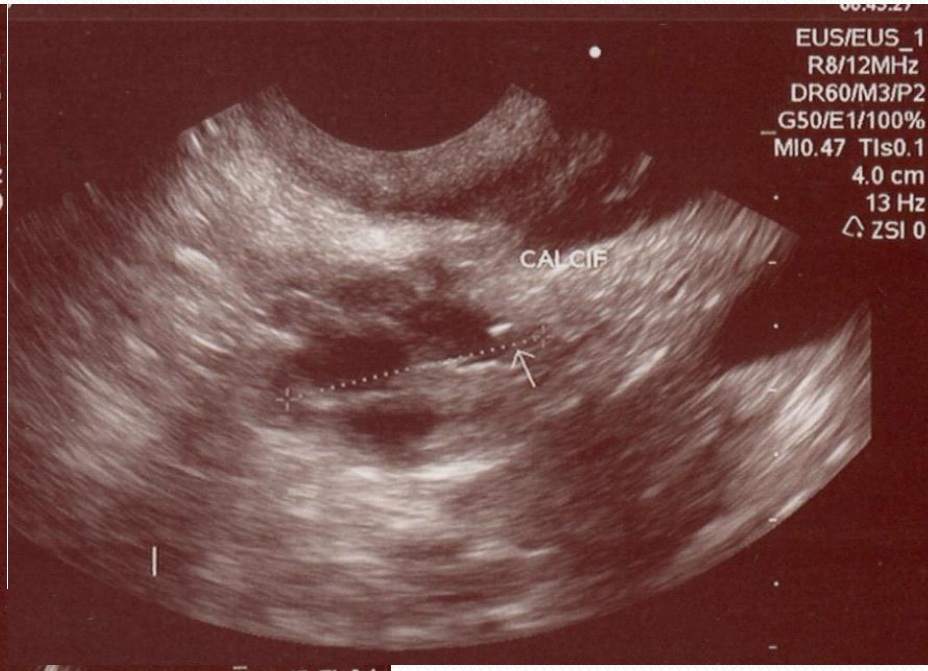
Chronic hereditary pancreatitis

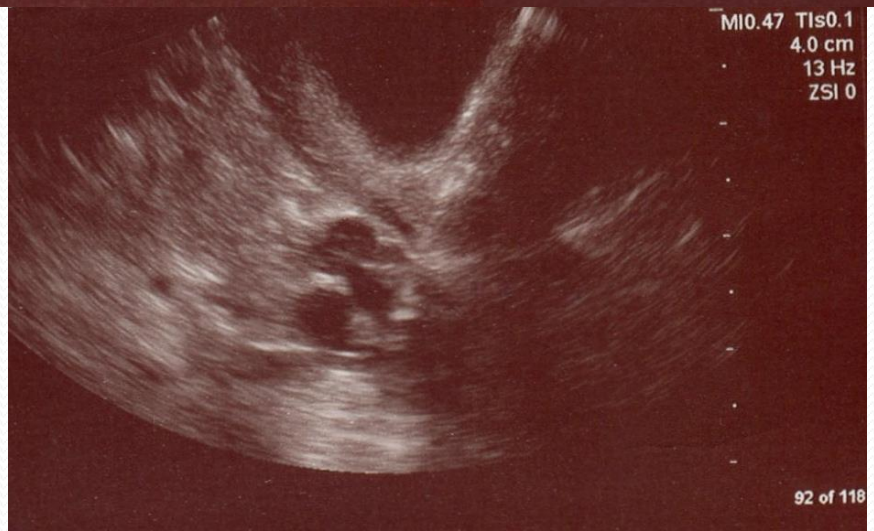


- Chronic pancreatitis but very high risk of cancer
  > 50 Years:
- What nature for this stricture ???

Mucinous cyst adenoma



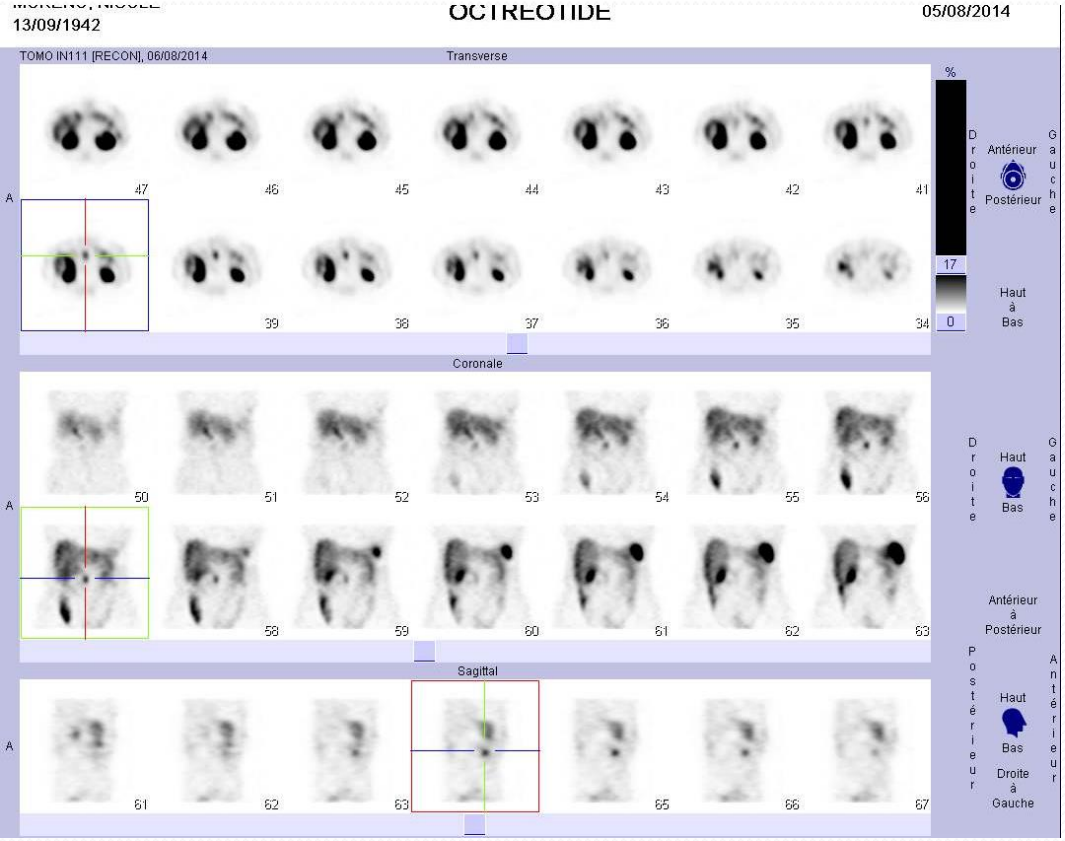


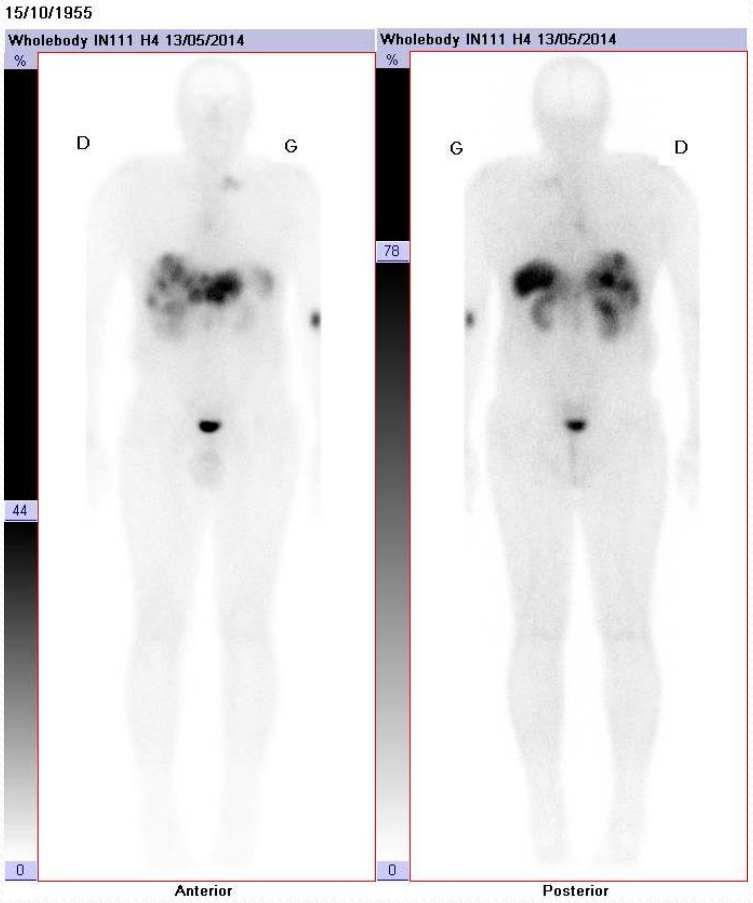


- **Octreoscan for endocrine tumors:**

confirmation and staging

but some are benign for a long time





CLINICAL RATIONALE : exists

- Pancreas is a difficult organ with late symptoms
- Surveillance of pancreatic patients is difficult despite immense improvements of technology
- TEPscan and EUS have followed a very rapid development but are unable to allow a good FU
- EndoTOF PET-US may help us to solve difficult problems of therapeutic indications: surveillance or surgery ?

The AIM : Imaging tool for pancreas and prostate cancer biomarker development

Tool

- Endo = echo endoscope (EUS)
  - 1 for pancreas
  - 1 for prostate

Spatial resolution
Biopsy

- US = Ultrasound

Anatomic +
Molecular imaging

- PET
  - Endoscopic head close to organ
  - External plate for coincidences

- TOF = Time-of-Flight

Other organs
background rejection

Imaging tool for pancreas and prostate cancer biomarker development

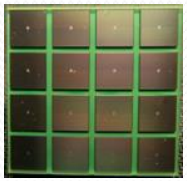
Objectives

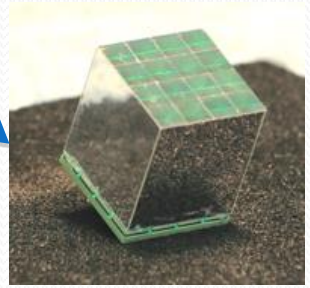
- Develop new biomarkers for pancreas and prostate cancer
  - Ex: mAb16D10 antibody for pancreatic cancer
  - Ex: ^{68}Ga – PSMA for prostate
- Introduce PET as an endoscopic imaging tool
- Develop intra-operative interventional imaging techniques ?

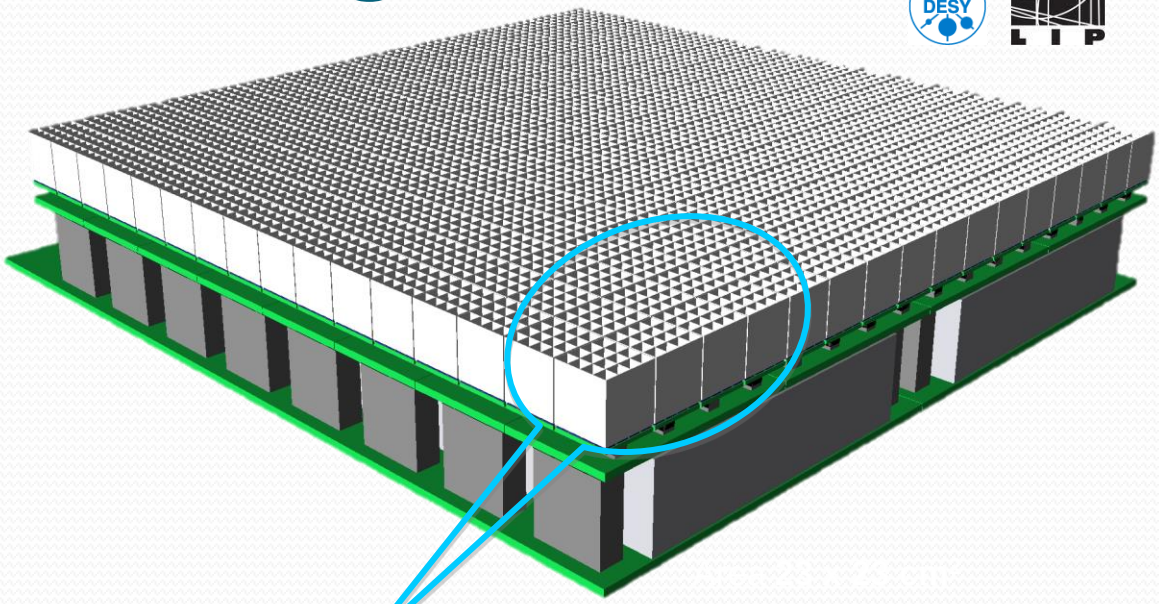
Technical challenges

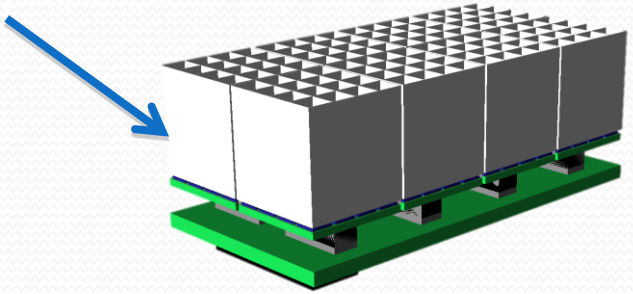
- Non symetric PET
- High level of miniaturization imposed by anatomy
  - Thin crystal pixels for high granularity of the endoscopic probe with ≤ 1mm spatial resolution
  - High level of electronics and mechanical integration (5µm precision)
- Electronic collimation with < 200ps timing resolution
  - for background rejection outside 3cm ROI
- Ultrafast light detection: Multi-digital SiPM
  - for single optical photon counting and ultimate timing resolution
- Tracking of all movables parts
  - for ≤ 1mm determination of their relative positions

External plate design

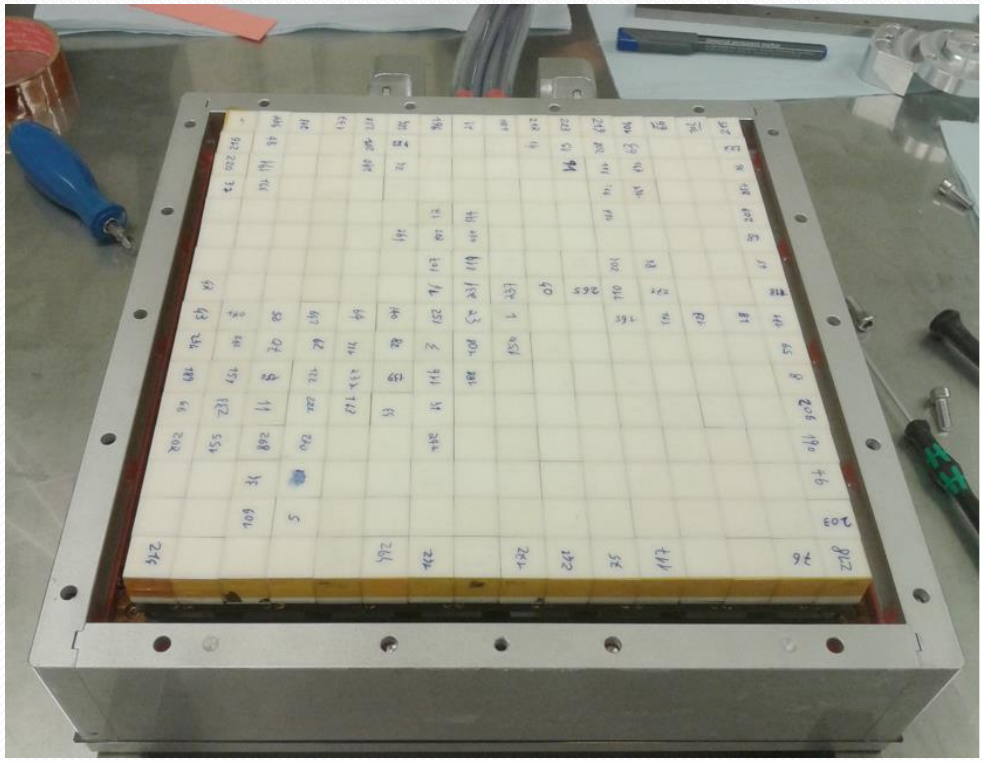


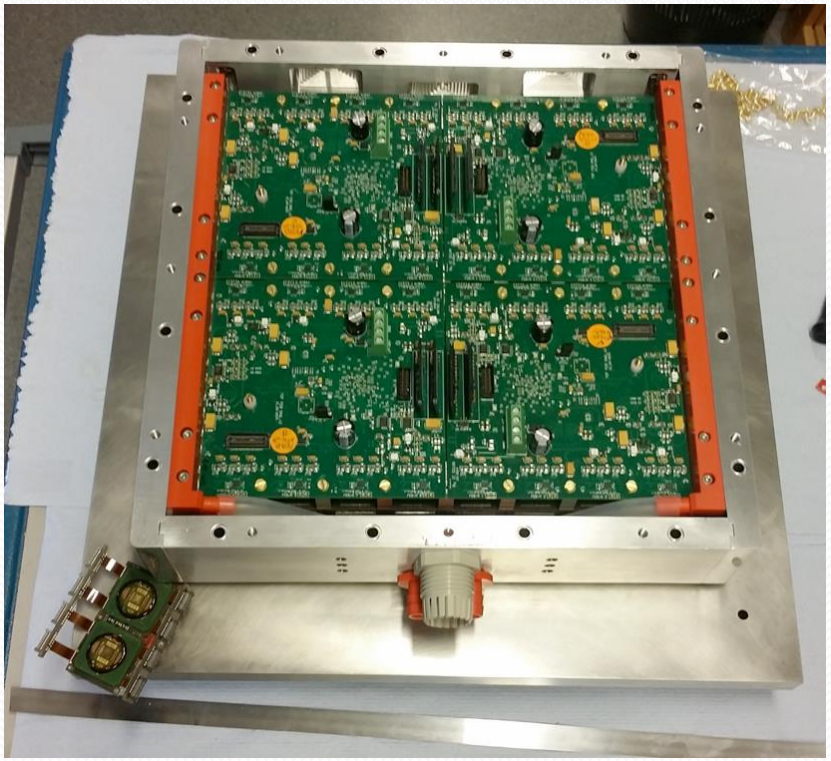




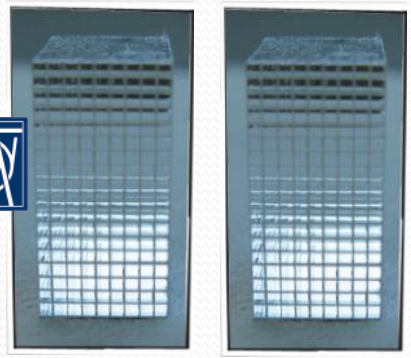


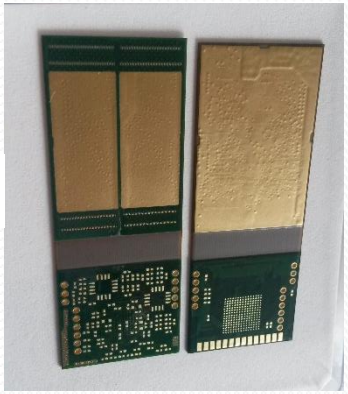
External plate

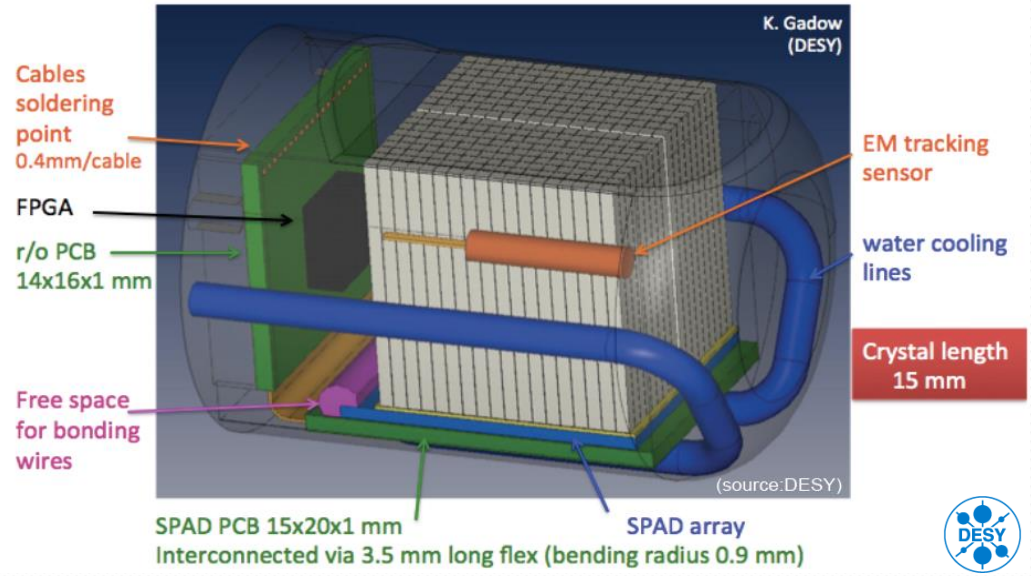




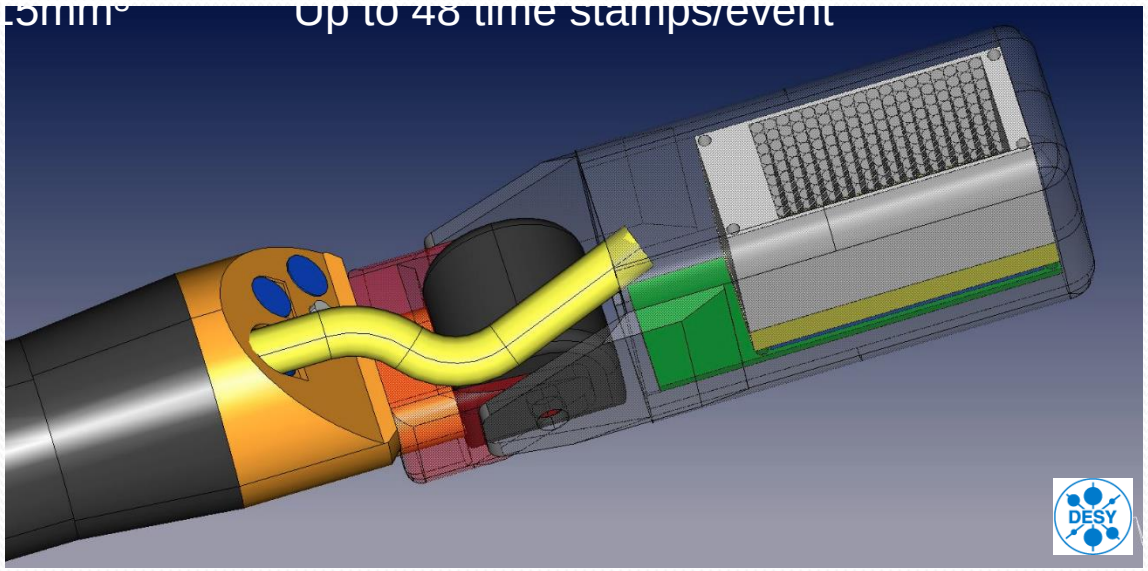
Endoscopic probe: Prostate



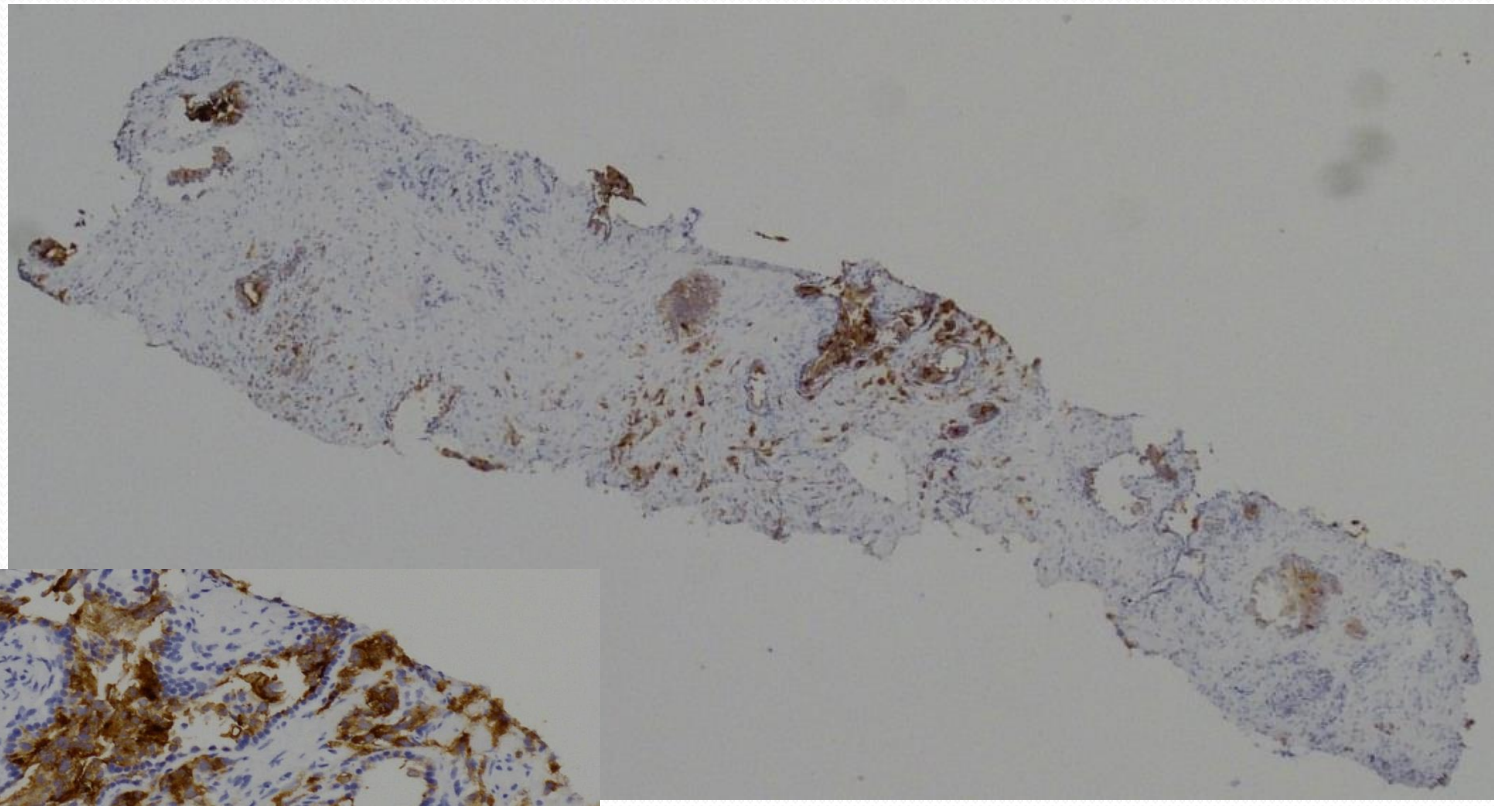


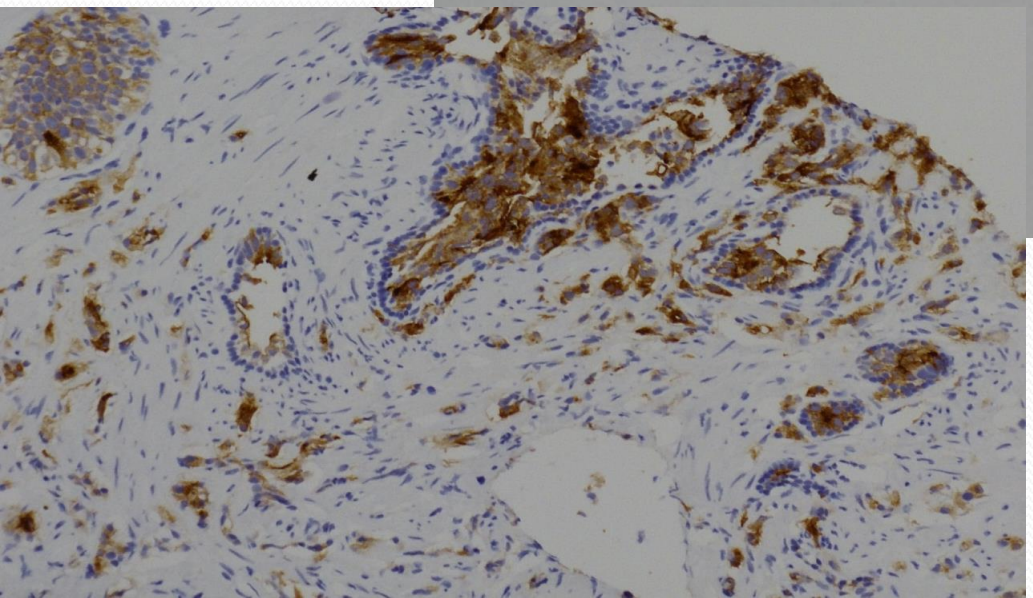


Endoscopic probe:Pancreas



Biological challenge: tumor heterogeneity: role for biomarkers





^{68}Ga-PSMA PET/MRI

Pelvis dimensions (prostate level)	• H: 35.6 cm • V: 21.4 cm
Torso dimensions	• H: 36 cm • V: 24 cm
Distance between prostate and urinary bladder	• Center urinary bladder-center prostate : 5.7 cm • Lower limit urinary bladder-upper limit prostate : 1.4 cm

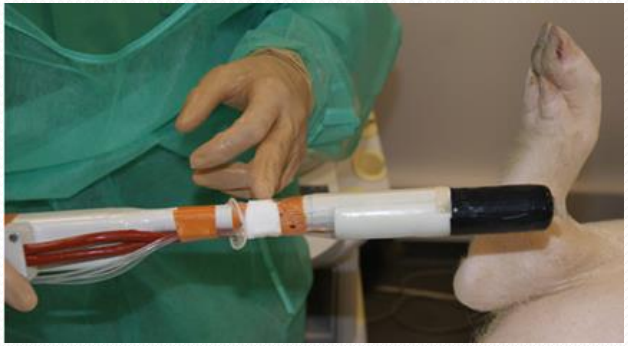
Prostate volume	44 cm^3
Prostate upatke	1,14 kBq/cm^3
Urinary bladder volume	270 cm^3
Urinary bladder uptake	4.8 kBq/cm^3
Prostatic lesion volume	7.7 cm^3
Prostatic lesion uptake	3.53 kBq/cm^3
Thickness of pelvic bone (prostate level)	2.28 cm

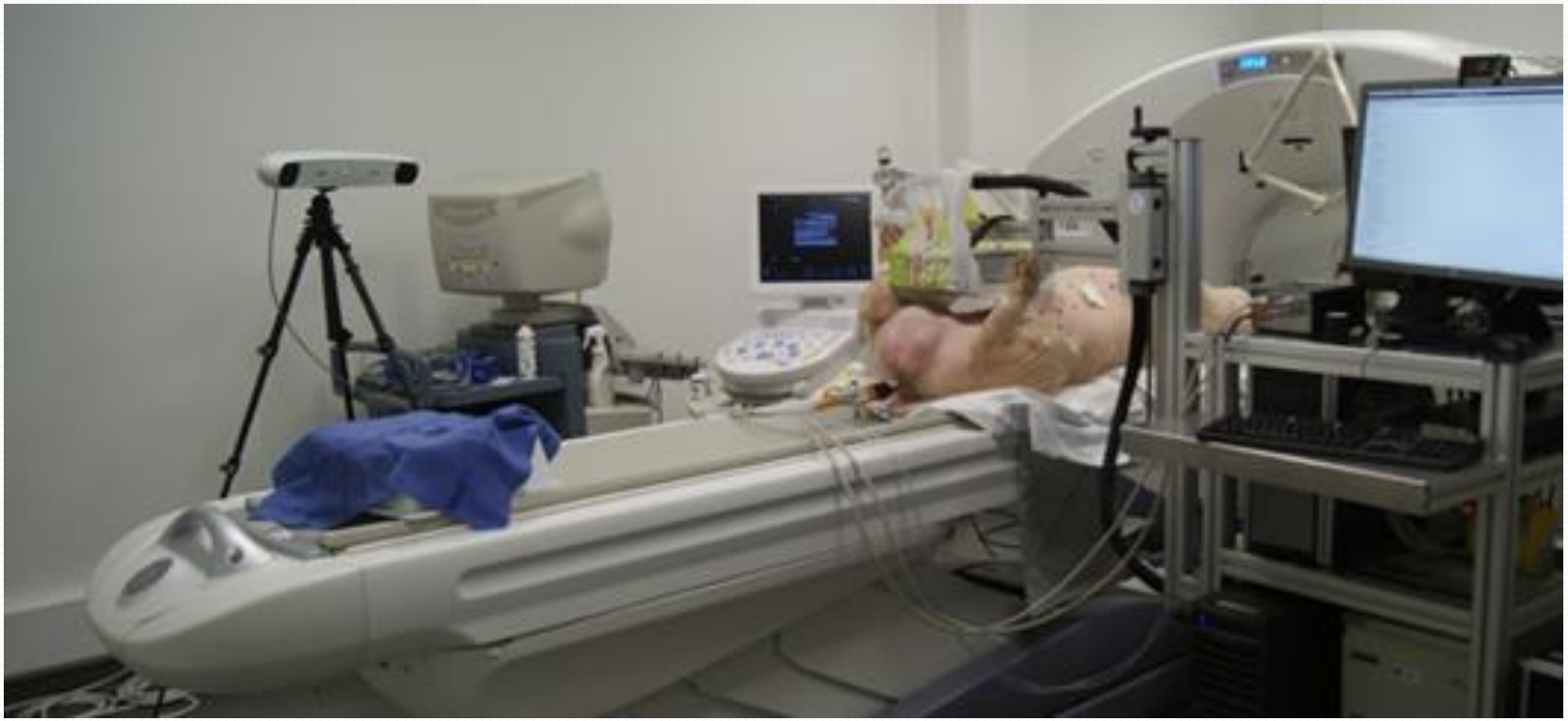
50kBq

1.3MBq

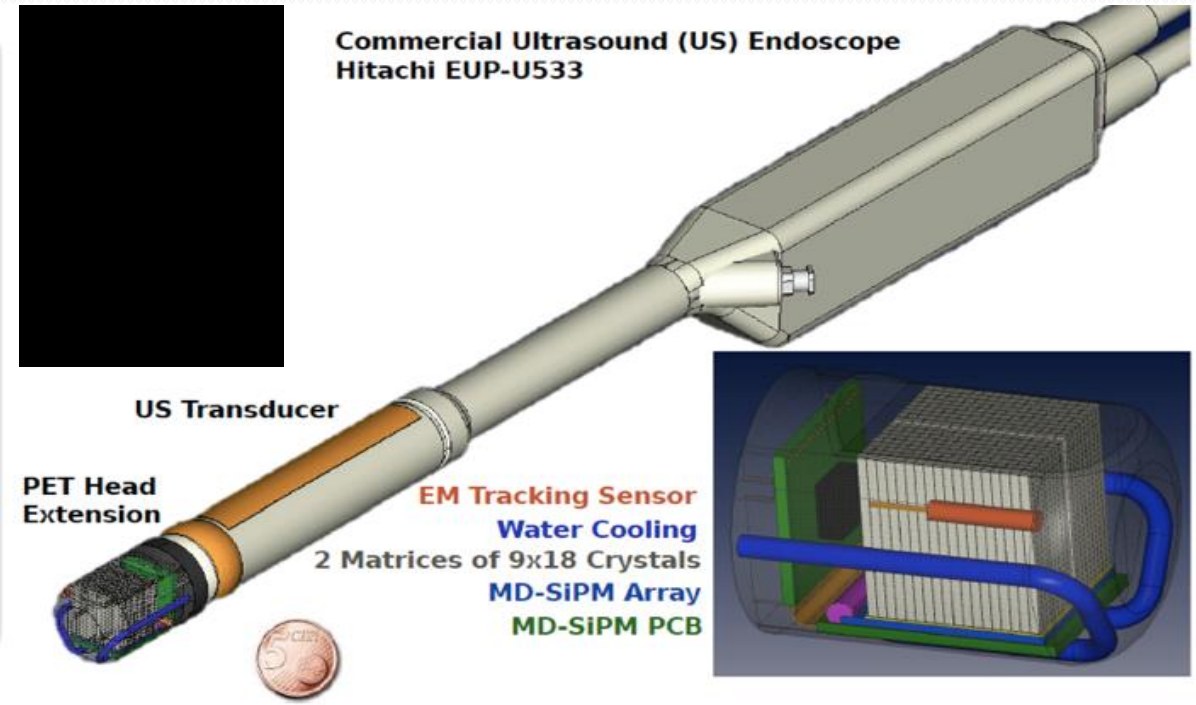
27kBq

First preclinical tests on pigs





Endoscopic probe: Prostate



Conclusions

- EndoTOFPET-US in two versions for developing new biomarkers:
  - Prostate
  - Pancreas
- First time endoscopic configuration for a PET
  - Asymetric PET
  - High level of miniaturization and integration
- TOF performance close to 200ps
- Opportunity to compare analog and digital approaches in a clinical environment