

Preneoplastic and small neoplastic lesions in
 the pancreas. EUS detection and features

L Palazzo
 Paris, France

Background

- 10% of pancreatic Ca (PCa) are related to hereditary factors
- Family members of these patients with hereditary disorders worry about their own risk
- Some families have genetic syndromes with known germ line mutations
- More common are families with multiple family members with PCa and no identifiable genetic syndrome

Goals of the lecture

- Identify who to screen
- When do we start screening?
- What do we look for?
 - Pathology
 - EUS
- Follow up programmes

Who to screen?

| Syndrome (genes) | Lifetime risk of PCa |
|--|----------------------|
| Hereditary pancreatitis (PRSS1) | 40% |
| FAMMM syndrome (CDKN2A/p16) | 15-20% |
| Peutz-Jeghers syndrome (STK11/LKB1) | 35% |
| Hereditary breast/ovarian ca (BRCA1&BRCA2), with at least one first or second degree relative with PCa | 3_10% |
| Ataxia telangiectasia (ATM) | ? |
| HNPCC (MLH1,MSH2,MSH6,PMS2) | ? |
| Li-Fraumeni syndrome (TP53) | ? |

FAMMM : familial atypical multiple mole melanoma
 HNPCC: hereditary non polyposis colorectal cancer

Who to screen?

- Non syndromic familial pancreatic cancer
 - ≥ 3 first, second, third-degree relatives with Pca in the same lineage
 - 2 relatives in the same lineage (directly connected) affected with PCa, at least one first-degree relative of the candidate
 - A subject with at least a 10-fold greater PancPRO* risk of developing Pca with respect to general population

Wang et al*PancPRO : risk assessment for individuals with a family history of Pca. J Clin Oncol 2007

When do we start screening?

- Start 50 years or 10 years younger than youngest PCa, except Peutz Jeghers syndrome (40 years)
- Start younger in smokers?

What do we look for?

- Mass
 - Adenocarcinoma
 - Neuroendocrine tumors
- Cysts
 - Single
 - Multiple IPMN
 - Multiple PanIN (22% PanIN 3 in 24 patients operated on among 275 patients screened at Johns Hopkins University)

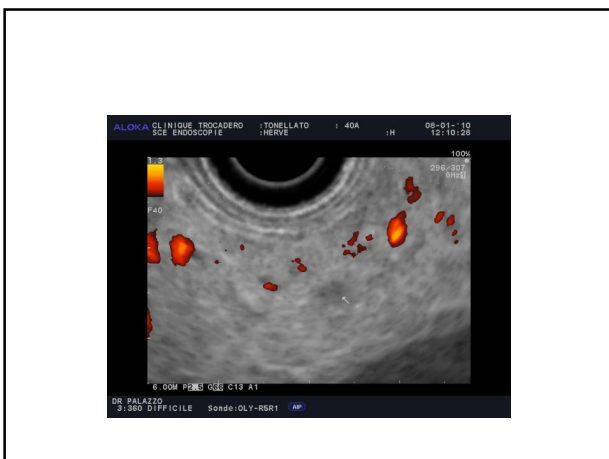
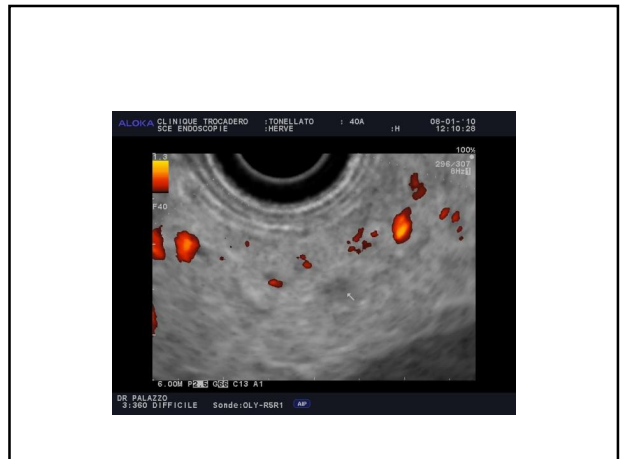
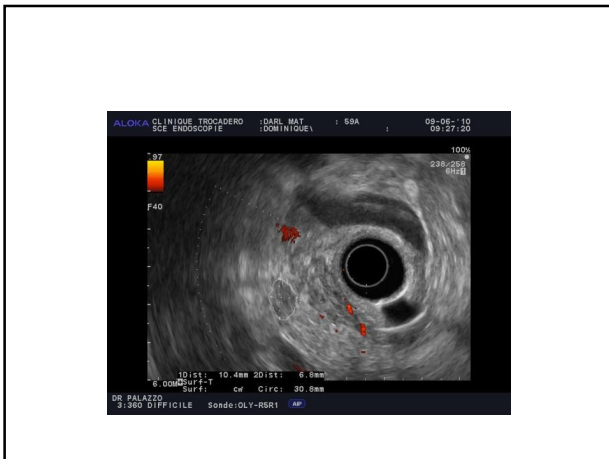
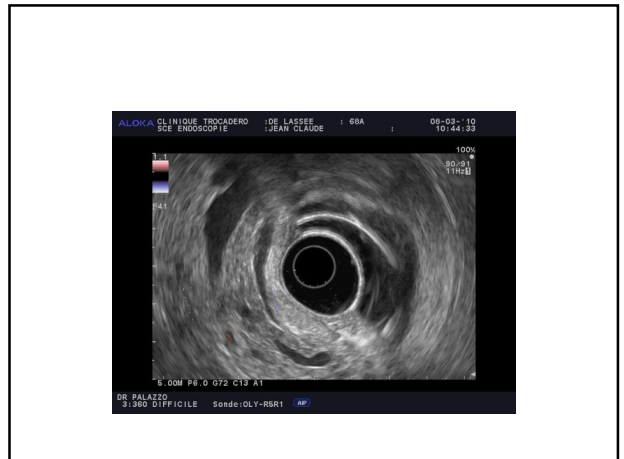
Brune et al Am J Pathol 2006

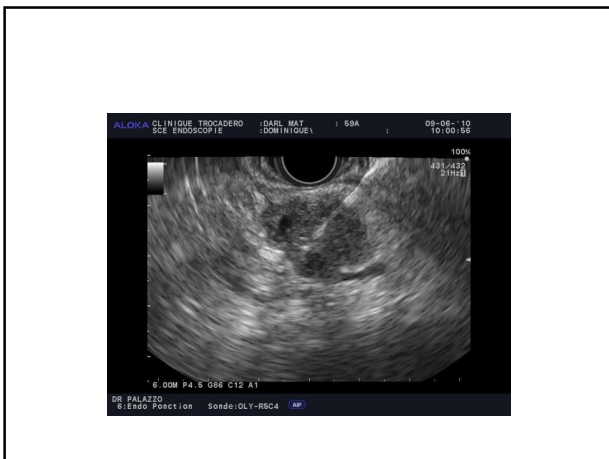
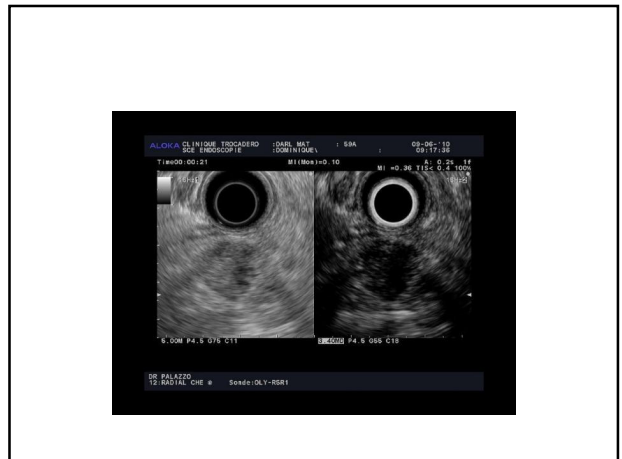
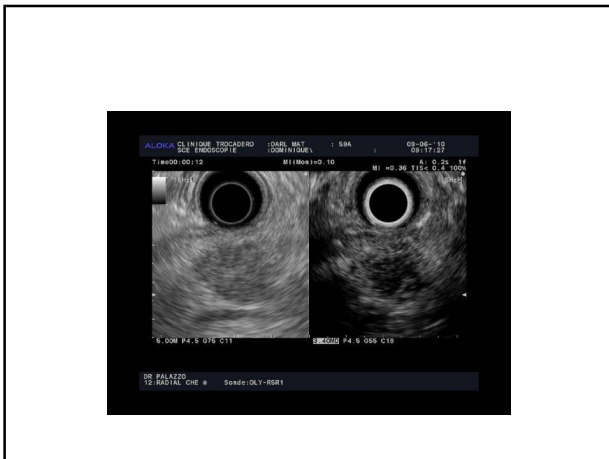
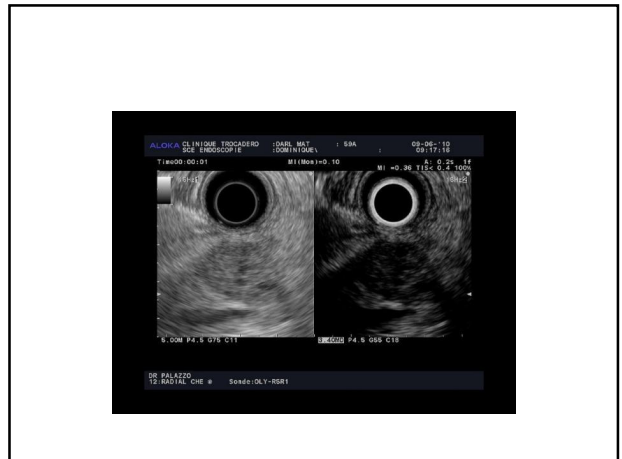
Canto et al, Clin Gastro Hepatol 2006

What do we look for?

- « Chronic pancreatitis »
 - Lobulo centric parenchymal atrophy (LCA)
 - PanIN density in resection specimen: 15% (1-28%)
 - Different Kras mutations
- Ductal changes
 - PD dilatation
 - PD focal narrowing
 - Focal polypoid PD wall thickening
 - PD echogenic material







- ### Johns Hopkins experience
- 275 patients screened
 - 24 patients had 29 operations
 - 17 FPCa
 - 2 PJS
 - 3 BRCA2
 - 2 HNPCC
 - 2 total pancreatectomy
 - 18 partial resection
 - 6 partial then completion resection
 - No significant morbidity, no mortality

Johns Hopkins experience

| N= 24 | LGD | MGD | HGD | PCa |
|----------------------|-------------|------------|-----------|-----|
| Ductal Ca | | | | 3 |
| IPNM | 8 | 2 | 3 | |
| PanIN | 1 | 12 | 7 | |
| % patient with PanIN | 4.3% | 73.9% | 21.7% | |
| | PanIN 1 | PanIN 2 | PanIN 3 | |
| Nb of PanIN (range) | 962 (3-219) | 148 (1-36) | 34 (1-14) | |

Follow-up programmes

- EUS and MRI (MRCP) yearly
- Suspected neoplastic lesions : ERCP
 - No abnormality: repeat EUS at 3, 6, 9,12 months
 - Abnormality: repeat EUS and EUS-guided FNA then surgery if confirmed
- Obvious neoplastic lesions: EUS-guided FNA then surgery if confirmed

Conclusions

- Yearly EUS screening has to be promoted in FPCa
- We are looking for IPMN and chronic pancreatitis changes
- Studies have to be performed in sporadic Pca to evaluate the risk of kindred relatives which is perhaps higher than expected