Drs **Frances Tse** and **Charles Menard**

Interventional EUS

Disclosures

Frances Tse

Has no relevant financial relationships with any commercial interests

Charles Ménard

Has no relevant financial relationships with any commercial interests

Objectives

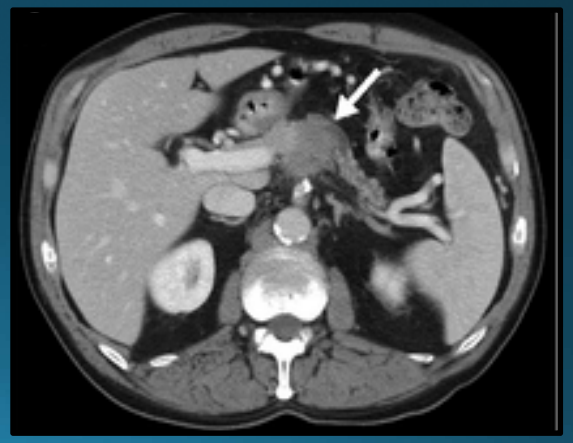
1. Review the indications, efficacy and techniques of EUS guided celiac plexus neurolysis
2. Comment on the role of EUS-guided fiducial placement in radiation therapy
3. Discuss the evidence and technical advances in EUS-guided pancreatic fluid collection drainage
4. Identify the indications and risks associated with EUS bilio-pancreatic access and drainage

CanMED roles

- Medical expert
- Collaborator
- Scholar

Case

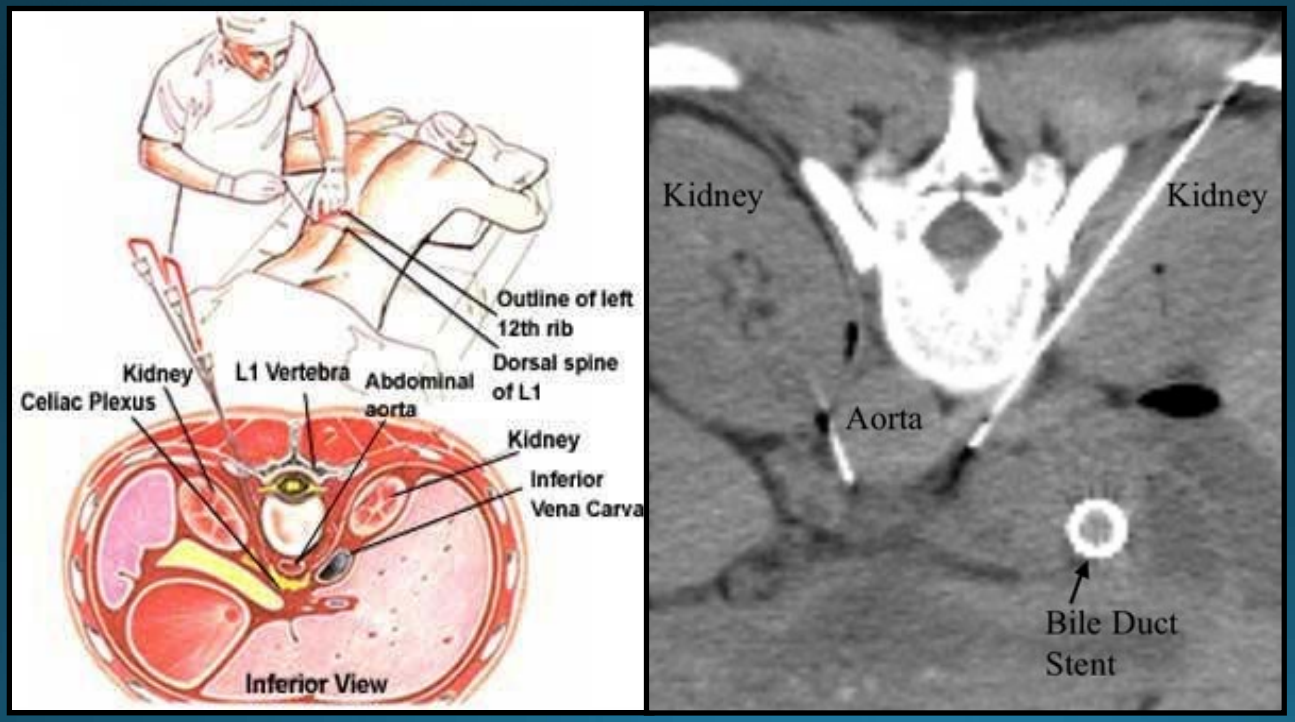
- 60 year old man presents with 6 months of vague abdominal discomfort accompanied by weight loss.
- CT: 3.5cm mass in the pancreatic neck encasing 180 degrees of the SMA with occlusion of the splenic vein and dilatation of the distal PD, no regional LN or distant mets.
- EUS guided biopsy: adenocarcinoma
- The tumor is deemed unresectable
- Patient begins chemotherapy



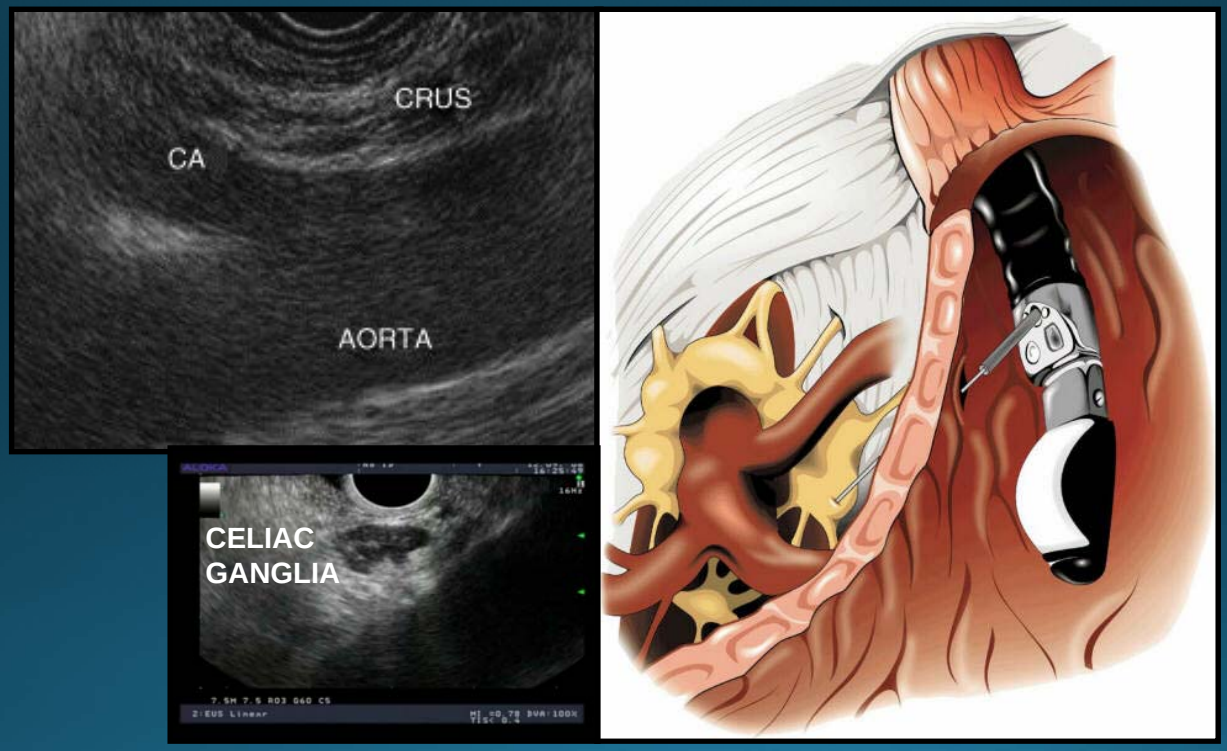
Case

- Two months later…
- He presents with worsening severe upper abdominal pain with radiation to his back requiring high dose narcotic medications leading to drowsiness and constipation
- Restaging CT: stable disease and the proximal SMA continues to be involved by tumor.
- Patient is asking if there are other options besides narcotics for managing his pain
- Oncologist is considering CyberKnife radiotherapy, and asking if you can assist in placing fiducials

CPN – Traditional Approach



EUS-CPN

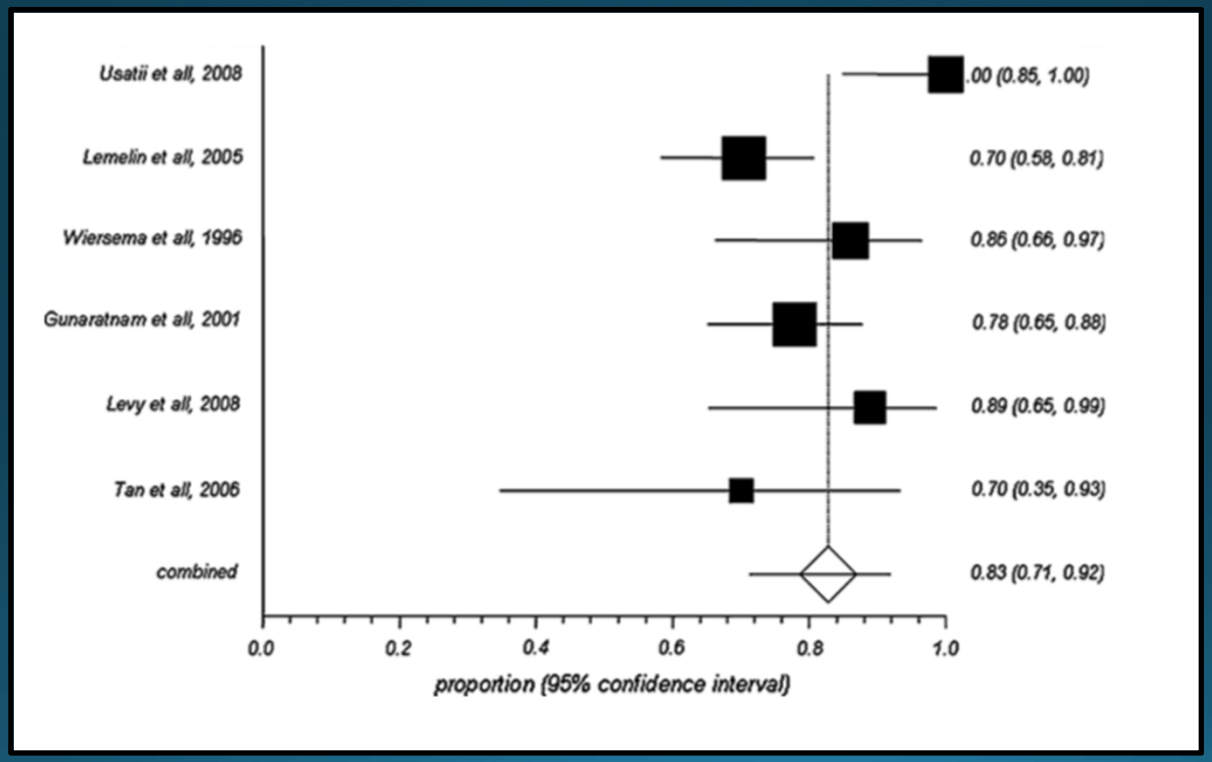


Wiersema. GIE 1996

EUS-CPN in Pancreatic Cancer Pain

- Efficacy
- Complications
- Different EUS approaches
  - Celiac ganglion neurolysis vs. Celiac plexus neurolysis
  - Bilateral vs. Central injection
  - Dose of alcohol and anesthetic
  - Type of needle

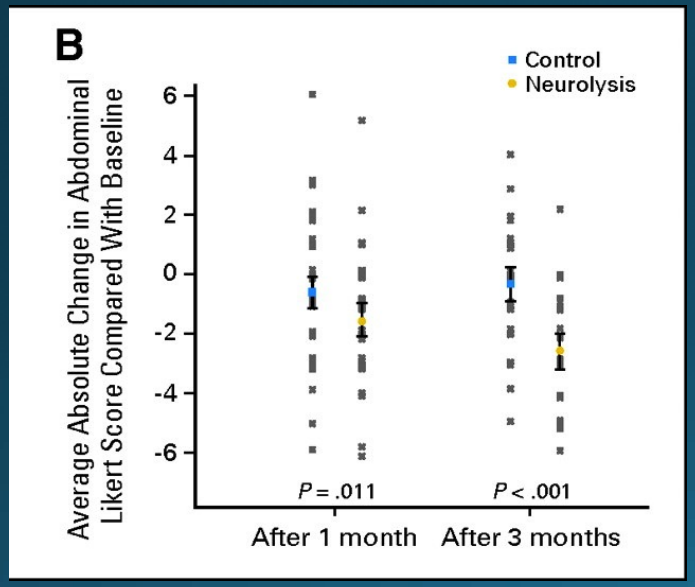
Efficacy of EUS-CPN



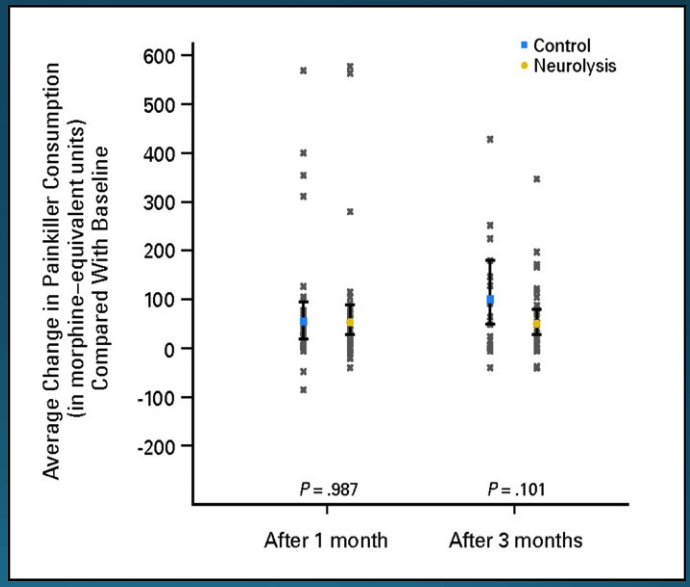
Puli. Dig Dis Sci 2009

Should EUS-CPN be done earlier?

Double-blinded RCT, N = 48



Decrease in Pain



Decrease in Morphine consumption

Wyse JM et al. J Clin Oncol 2011

Complications of EUS-CPN

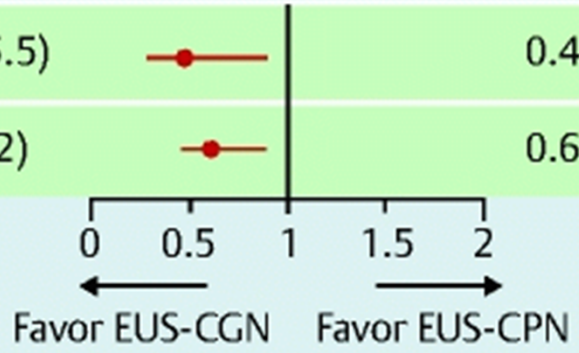
- 15 studies (N = 661)
  - Diarrhea (10%)
  - Hypotension (5%)
  - Transient pain exacerbation (4%)
  - Intoxication (1%)
- Serious complications were rare (0.2%)
  - Retroperitoneal bleeding, infections, ischemia

O"Toole. Endoscopy 2009
Alvarez-Sanchez. Surg Endosc

Celiac Ganglia Neurolysis (CGN)

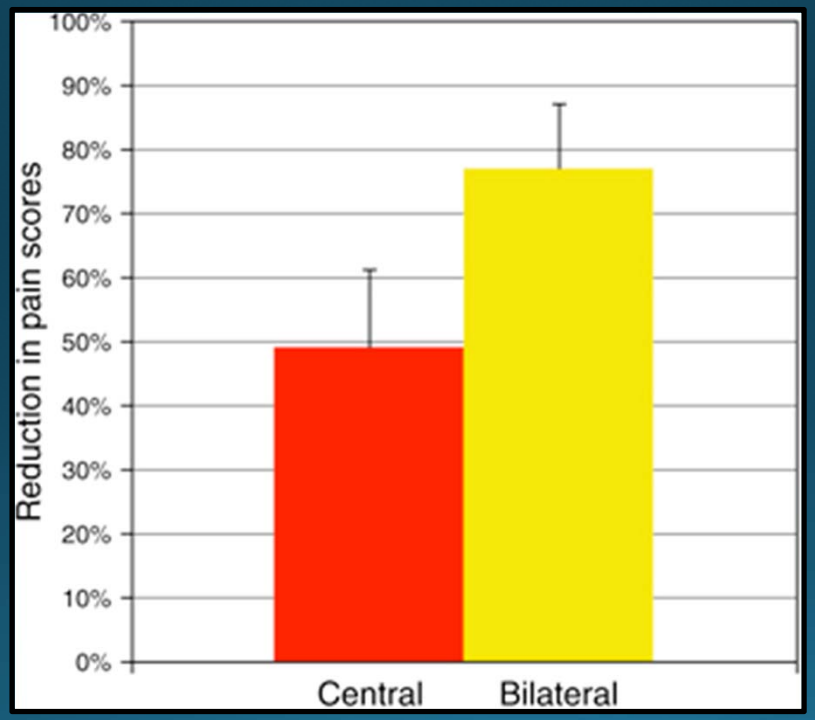
CGN vs. CPN

Endpoint	Number (%) EUS–CGN	EUS–CPN	Risk ratio [95% CI]	*p* value
Positive response	25/34 (73.5)	15/33 (45.5)	0.49 [0.26–0.89]	0.026
Complete response	17/34 (50.0)	6/33 (18.2)	0.61 [0.46–0.87]	0.010



Doi. Endoscopy 2013

Bilateral vs. Central Injection



Sahai. Endoscopy 2009

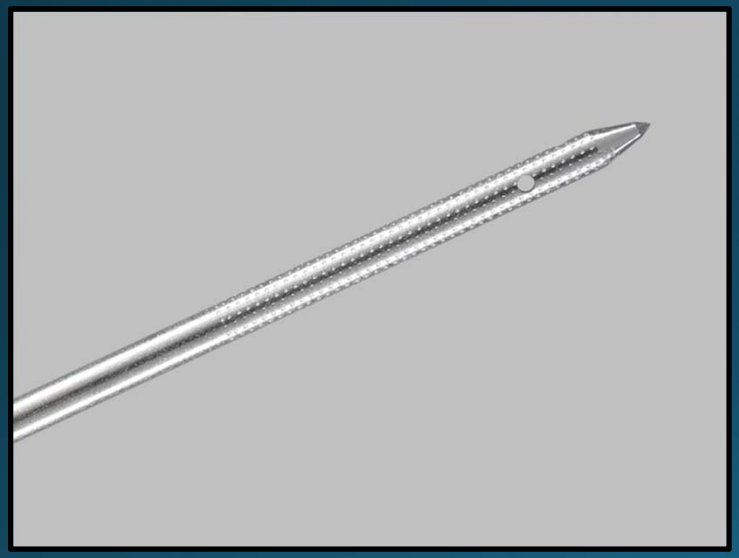
Dose of Alcohol and Anesthetic

- No difference in pain relief and complications between 10 vs. 20 mL of 98% alcohol (ganglia or central injection)

LeBlanc. Diagn Ther Endosc 2013

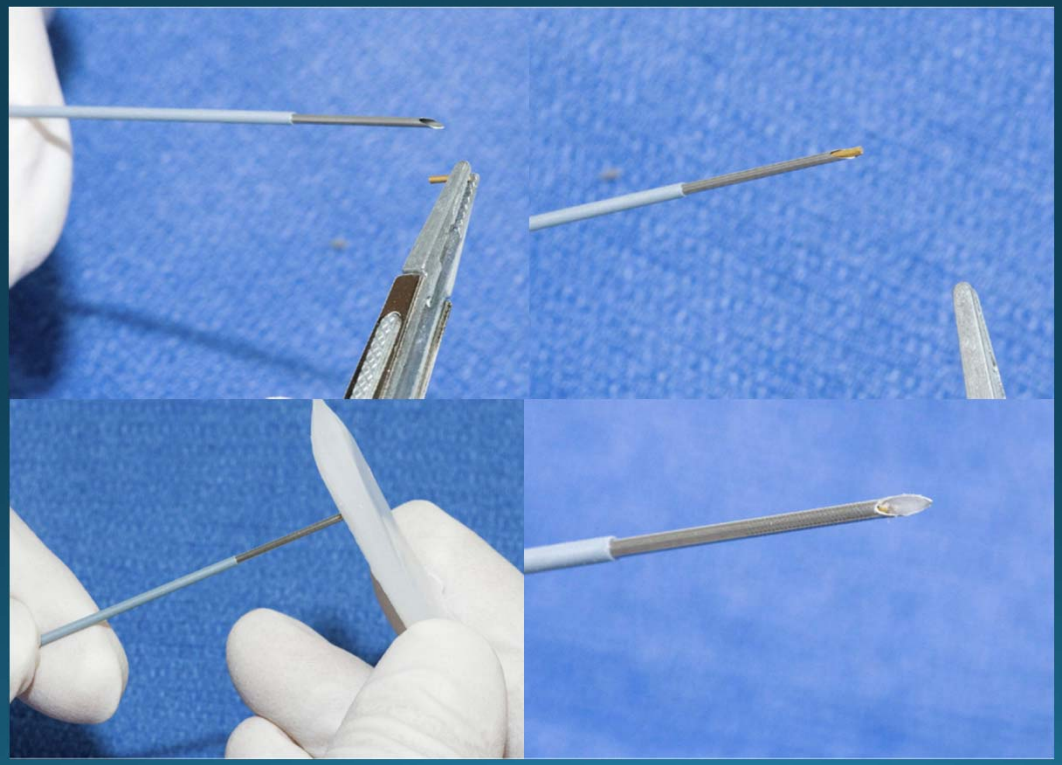
- No studies assessing effectiveness of different anesthetics or dosage

Type of Needle

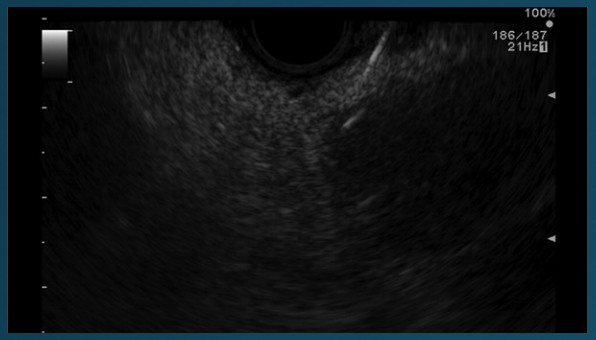


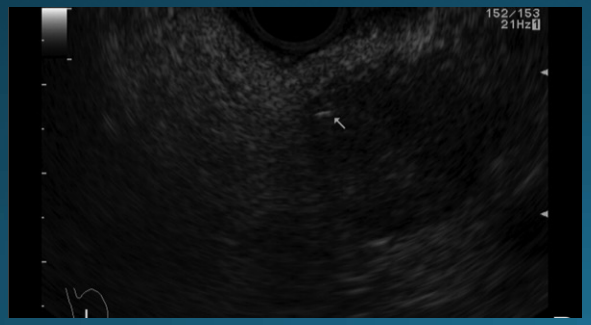
- No studies comparing needle types or sizes in CPN or CGN

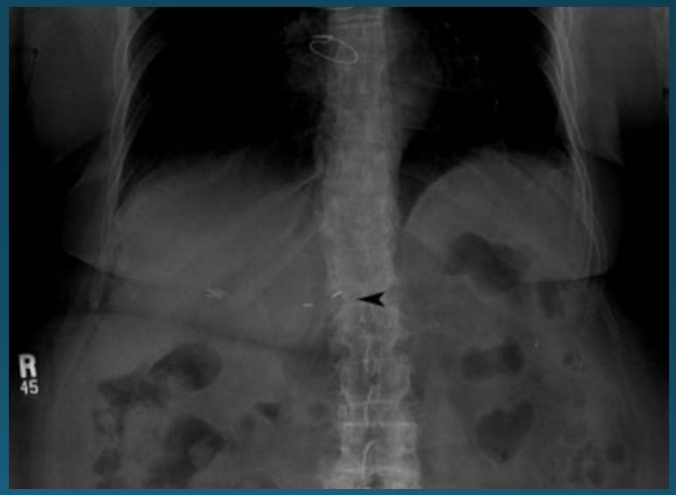
EUS-guided Fiducial Placement



EUS-guided Fiducial Placement







Sanders. GIE 2010.
Koong. Int J Radiat Oncol Biol Phys 2004
Koong. Int J Radiat Oncol Biol Phys 2005
Didolkar. J Gastrointest Surg 2010
Rwigema. Am J Clin Oncol 2011

EUS-guided Brachytherapy

Authors	Therapy	N	Tumor response (%)	Adverse events
Sun et al Endoscopy 2006	Iodine seeds implantation	15	Partial (27) Minimal (20) Stable (33)	Pancreatitis and pseudocyst (3)
Jin et al Endoscopy 2008	Iodine seeds implantation plus chemo	22	Partial (13) Stable (46) Progression (41)	Hyperamylasemia Mild fever Seeds translocation

Improvement in pain x 1 month
No improvement in survival

EUS-guided delivery of Anti-tumor Agents

Study	Therapy	N	Tumor response (%)
Chang 2000	Cytoimplant (activated allogenic mixed lymphocyte culture)	8	Partial (25), Minimal (12), Stable (37)
Farrell 2006	TNFerade (adenovirus vector)	51	Partial (13), Stable (73)
Posner 2007	TNFerade	51	Stable (73), Progressive (27)
Hecht 2003	ONYX-015	21	Partial (10), Minor (10), Stable (30), Progression (50)
Goldberg 1999	RF ablation	8	N/A
Chan 2006	PDT	3	N/A
Matthes 2007	OncoGel	3	N/A
Sun 2007	Solid polymer embedded 5-FU	6	N/A
Nonogaki 2007	Immature dendritic cells	5	Partial (20), Stable (40)

Case

- Three months later…
- Patient returns with an episode of severe acute pancreatitis complicated by a large pseudocyst causing gastric outlet obstruction
- What are your options?

PFC: When to drain

- Pain, obstructive symptoms, organ failure, refractory infection
- Encapsulation usually later than 4 weeks
- Worse outcomes if necrotic content
- Obtain precisions on PFC content with MRI or EUS
  - 87% with debris at 6 weeks
  - 44% with debris at 6 months

Varadarajulu. J Gastrointest Surg. 2011 Nov;15(11):2080-8
Bang. Clin Endosc. 2014 Sep; 47(5): 429–431
Rana. Ann Gastroenterol. 2014;27(3):258-261

PFC: How to drain
EUS vs blind EGD vs surgical

- EUD superior or equal to CTD and safer for:
  - Non-bulging PC
  - Portal hypertension/gastric varices/collaterals
  - Previous failed attempts of CTD
- EUS comparable to surgery with shorter stay, lower cost, better QOL

Varadarajulu. Gastrointest Endosc. 2008 Dec;68(6):1102-11
Park. Endoscopy. 2009 Oct;41(10):842-8
Pananmonta. Eur J Gastroenterol Hepatol 2012; 24: 1355-1362
Varadarajulu, Gastroenterology. 2013;145:583–590

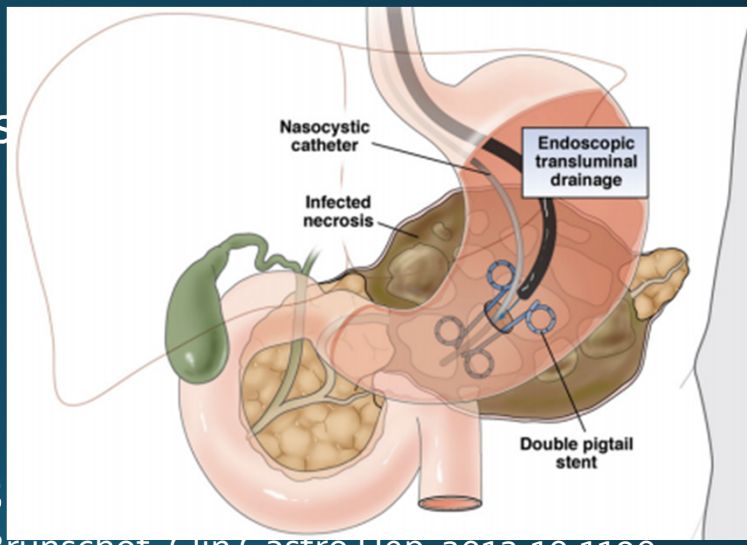
PFC: How to drain
EUS-guided PFC drainage

- Success rates: 90-97%
- Recurrences: 8%
- Complications: 1-18% (bleeding, infection, stent migration, perforation, pneumoperitoneum, death 0.2%)

Fabbri, World J Gastroenterol 2014 July 14; 20(26): 8424-8448

PFC drainage: Technical aspects

- Localisation:
  - Requires < 1cm between lumen and cys
  - Access through closest bowel wall
- Plastic stents vs SEMS: NS
- Single vs multiple stents: NS in liquid PFC
- Nasocystic drainage: + stent when viscous
- Pancreatic duct stenting / transpapillary drainage:
  - May be 1st step in small communicating head or body PFC
  - Best results if < 6cm and > 6 mo
  - At 2 weeks if ductal leak on MRI?



Van Brunschot, Clin Gastro Hep 2012;10:1190-1201
Siddiqui. Gastrointest Endosc. 2013;78:589-95
Shen. Pancreatology. 2014 Mar-Apr;14(2):87-90
Bang. Clin Endosc. 2014 Sep; 47(5): 429–431
Bang. Surg Endosc. 2014 Oct;28(10):2877-83
Dhir. Gastrointest Endosc. 2015 Oct;82(4):650-7

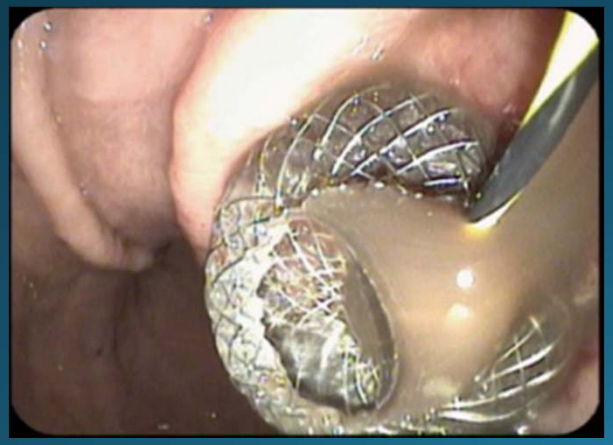
PFC drainage: Sequence

- Access with 19G vs cystotome vs needle-knife
- Insert 1 or two 0.035 guide wires into PFC with 2-3 loops
- Place stents:
  - PFC: double pigtail stent
  - PFC with debris: stent + nasocystic tube with irrigation
  - If metal stent: LAMS or 10 x 60mm + double pigtail stent

Seewald. Gastrointest Endosc. 2006 Nov; 64(5):805-8
Talreja, Gastrointest Endosc. 2008 Dec; 68(6):1199-203
Vilmann. World J Gastroenterol. 2015 Nov 7; 21(41): 11842–11853
Safteiu. Endosc Ultrasound. 2015 Oct-Dec; 4(4): 319-325

EUS-guided WOPN treatment

- Agressive irrigation may prevent necrosectomy
  - Endoscopic + percutaneous if >12cm and extending to paracolic gutters
  - Multiple gateway technique: 92% clinical success
- LAMS: 81% success with Axios stent
- 10% secondary infections



Seifert. Gut. 2009 Sep; 58(9):1260-6
van Santvoort. N Engl J Med. 2010 Apr 22;362(16
Varadarajulu. Gastrointest Endosc. 2011 Jul;74(1
Ross. Gastrointest Endosc. 2014 Jun; 79(6):929-3
Bang. Clin Endosc. 2014 Sep; 47(5): 429–431
Bhutani, Endosc Ultrasound. 2015 Oct-Dec; 4(4)

Necrosectomy

- Necrosectomy comes with worse outcomes
  - 28% adverse events (2.1% mortality, 5.3% perforation, 14% bleeding, air embolism)
  - 88% clinical resolution with median of 4 sessions
- EUS vs surgical : less adverse effects with EUS, less expensive, shorter hospital stay

Seifert. Gut. 2009 Sep; 58(9):1260-6
Fabbri, World J Gastroenterol 2014 July 14; 20(26): 8424-8448

PFC drainage: Stent removal

- Never is better?
- 3 weeks after metal stenting if no ductal leak or disconnection?
- Not before complete resolution on imaging
- Up to 38% recurrence after removal

Arvanitakis. Gastrites Endosc. 2007;65:609-19
Dhir. Gastrointest Endosc. 2015 Oct;82(4):650-7
Bhutani, Endosc Ultrasound. 2015 Oct-Dec; 4(4): 304–311

When to consider surgery

- **Multidisciplinary decision**
- Patients who do not satisfy the criteria for endoscopic or percutaneous drainage
- Perforation
- Disease recurrence following a successful endoscopic drainage
- Previous endoscopic failures
- The *minimally invasive step-up approach* lowers

van Santvoort. N Engl J Med. 2010 Apr 22; 362(16):1491-502
Seewald. Dig Endosc. 2012 Jan; 24(1):36-41

Case

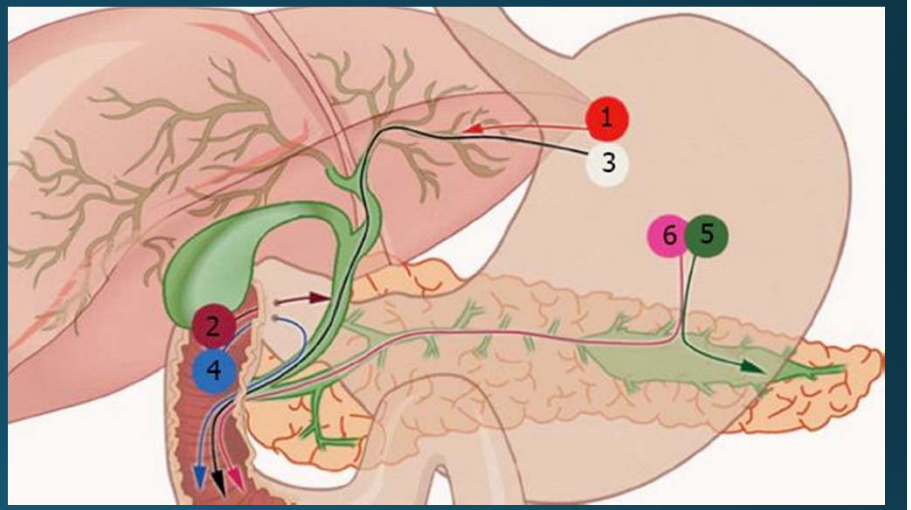
- Three months later…
- Patient returns with obstructive jaundice. His pancreatitis and pseudocyst have completely resolved.
- ERCP was attempted by an experienced endoscopist. Biliary access was not achieved due to tumor infiltration of the duodenum.
- What are your options?

EUS-guided biliary drainage

- Indications
  - Obscured ampulla by cancer / stent
  - Surgically altered anatomy
  - ERCP failure
  - Contraindication to percutaneous access (PTBD)

EUS-guided biliary drainage

- Approaches
  - Transpapillary 3-4-6
    - Rendez-vous procedure (RV)
    - Antegrade transpapillary (AT)
  - Transmural
    - Choledochoduodenostomy (CD) 2



Park. Gastrointest Endosc. 2011 Dec;74(6):1276-84
Kahaleh, World J Gastroenterol. 2013 Mar 7; 19(9): 1372-9
Ogura. World J Gastroenterol. 2015 Jan 21; 21(3): 820–828
Kahaleh, World J Gastroenterol. 2015 Jan 21; 21(3): 726–741
Bhutani, Endosc Ultrasound. 2015 Oct-Dec; 4(4): 304–311

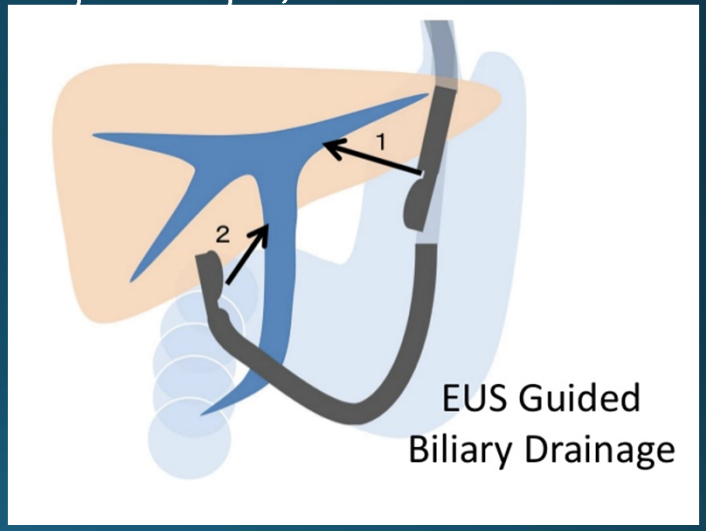
EUS-BD versus PTBD

- In comparative controlled studies:
  - Comparable success rates 88%
  - More adverse effects with PTBD 31 vs 9%
  - Comparable stent patency
- External tubing (50%) but same QOL
- More repeated interventions (2-3X)
- Longer hospital stay

Park. Gastrointest Endosc. 2011 Dec;74(6):1276-84
Bhutani, Endosc Ultrasound. 2015 Oct-Dec; 4(4): 304–311
Lee. Clin Gastroenterol and Hepatol. 2015 Dec; epub

Efficacy and safety

- Success rates: 76-96% (extrahepatic 96%, intrahepatic 84%)
- Stent patency: 130-689 days
- Adverse effects: 11-44%
  - Bile leak (more with intrahepatic route)
  - Peritonitis
  - Subcapsular hematoma
  - Pancreatitis (with AT)
  - Cholangitis (early and late complication)
  - Cholecystitis (early and late complication)
  - Stent migration (7%)



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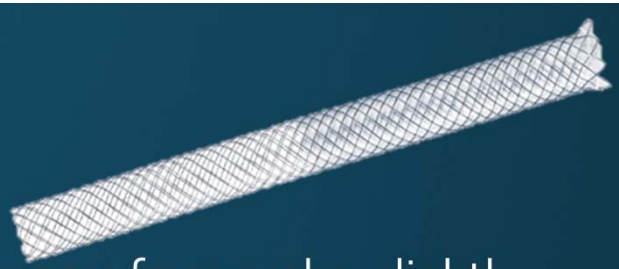
Bhutani, Endosc Ultrasound. 2015 Oct-Dec; 4(4): 304–311.

Technical tips



- Access: 19G needle or cystotome (vs needle-knife); 1-2cm from probe, slightly tangential
- Guidewire insertion: 0.025 stiff, angulated tip easier, watch for shearing (do not pull)
- Try rendez-vous when duodenoscope can reach papilla
- Use rotatable bending cannula if available for transpapillary
- Fistula tract creation and dilation:
  - cystotome /needle-knife or Soehendra dilators 8.5 Fr/ retreivers 7 Fr and dilating balloon 4-6mm (less bile leak and bleeding with non-cauterinzing and smaller caliber)
  - Never larger than stent introducer size

Sarkaria. Gut Liver. 2013 Mar; 7(2): 129–136
Ogura. World J Gastroenterol. 2015 Jan 21; 21(3): 820–828
Prachayakul, World J Gastroenterol. 2016 Jan 16; 7(1):37-44

Limitations to EUS-BD

- Intolerance to endoscopy
- Uncorrected coagulopathy
- Poor angle / position for endosonography access
- Qualified endoscopists
- Dedicated training

Ogura. World J Gastroenterol. 2015 Jan 21; 21(3): 820–828
Lee. Clin Gastroenterol and Hepatol. 2015 Dec; ePub

Dedicated Lumen Apposing Stents: Uses

- PFC / WOPN access
- Drainage bile duct / gallbladder
- Gastro-gastrostomies
- Gastro-jejunostomies
- EDGE procedures