Imaging Pancreatic Neuroendocrine Tumors (PNETs): CT, MRI, EUS, Nuclear

Eric Tamm, M.D.
Department of Diagnostic Radiology
Division of Diagnostic Imaging
MD Anderson Cancer Center
Houston, TX
Disclosure

- I have no relationships with commercial interests to disclose.
Overview and Core Points

- “At the [AFIP] we believe all non-microadenoma [nonfunctional, < 0.5cm] PETs have malignant potential”*
- Goal: identify all sites of disease to aid decision making
  - Both focused (CT/MR/EUS) & whole body.
  - Evaluate: Primary, vessels, nodes, poss. metastases
  - Imaging strategy driven by:
    - Suspected functional (and type) vs. nonfunctional
    - Well or poorly differentiated (octreo vs FDG PET)

*Lewis, Radiographics, 2010
Insulinoma

- Most common fxn islet: Incidence: 2-4/million
- Low fasting serum glucose with high serum insulin levels and serum C-peptide levels
- Majority are small, solitary, 40% < 1cm.*
  - Multiple in 2-10%, usually MEN I, and VHL
- 10% are malig: usu. >3cm, to peripanc nodes
- Imaging strategy:
  - Most in pancreas, and often octreotide negative
  - Workup: usually CT or MRI, intraoperative ultrasound and palpation**

Multiphasic MDCT

- For all functional PETs, sensitivity up to 96%. *
- By phase
  - Early arterial: sensitivity 83-88%.
  - Pancreatic parenchymal: study of just 13 patients, 100% sensitivity.
  - Portal venous: sensitivity 11-76%, some seen only on this phase.
    - Useful also to assess venous involvement, liver mets.
- For insulinoma, sensitivity 94-96%, similar to intraop US and palpation**
- Negative contrast useful to identify lesions in/near bowel.

*Jeung Radiographics, 2002, **Gouva AJR 2003
Dual Energy MDCT

Studies of 35 patients, with 39 proven lesions, who went to surgery:

- Dual energy, dual phase:
  - Detected 87% (20/23), (monochromatic or iodine map images).
  - 96% (22/23), (monochromatic plus iodine map images).
- Dual phase, single energy: detected 69% (11/16).

MRI:

- Many ways to find the tumor
  - Fat suppressed T1
  - Dynamic post contrast fat sat T1 weighted images.
  - Fat suppressed T2
  - Diffusion weighted imaging
    - Evolving role: detection, nodal sites, liver mets*, and unique biomarkers
- Overall sensitivity 74-100%; similar to MDCT
  - However, probably better for liver metastases than MDCT, especially when considering liver specific agents.

*d'Assignies, G. (2013). Radiology
Diffusion, ADC Maps

- Potential role in noninvasively grading PNET
  - Data is preliminary
  - 49 patients, ADC moderately correlated with WHO tumor grade*
- To differentiate solid appearing serous cystadenoma from PNET**
  - 15 solid appearing SCN vs 30 PNET
  - SCN- nonrestrictive, PNET restrictive

Endoscopic Ultrasound

- Sensitivity of approximately 94%, similar to intraoperative ultrasound*
  - Pro: Can biopsy real time, without contrast
  - Con: operator dependent, invasive
    - Limited evaluation of tail, nodal sites.
- When MDCT and EUS were both used, combined sensitivity was near 100%**
- Usually well-rounded, smooth, hypoechoic

*Zimmer Digestion 2000  **Gouja, AJR 2003
In-111 Octreotide Imaging

- Agent is an analog of somatostatin
  - Binds strongly to receptors 2 and 5, weakly to 3
  - Binds well to well differentiated non-insulinoma PNET, but not to poorly differentiated.
- Sensitivity: overall 60-90%
  - Glucagonomas 100%, VIPomas 88%, Gastrinomas 73%,
  - Insulinomas sensitivity only 50-70 % because they express predominantly SSTR-3.
- Imaging at our institution, 4 hour, and 24 hours, with SPECT and fusion with CT
- Future directions, PET agents, e.g. 68Ga-DOTA-NOC

*Gotthardt Endocrine Related Cancer, 2006*
Gastrinoma

- Incidence 1-2/million
- Hypersecretion of gastric acid,
  - Zollinger-Ellison syndrome.
  - H/o ulcers, often recurrent
- 70-80% sporadic, 20-25% MEN I
  - In MEN I more often multicentric, extrapancreatic, & benign
  - Is most common islet tumor in MEN I
- 60% are malignant- often liver/nodal mets
- Most outside of pancreas & octreotid(e)(+)
  - CT/MR, EUS, SPECT/CT octreotide*
Distal Duodenal/Jejunal Site of Gastrinoma and Liver Metastasis
Multifocal Gastrinoma: Fused Imaging

SPECT/CT Octreotide
Somatostatin Receptor Imaging with 68Ga-DOTA-NOC (PET Agent)

Study of 2100 patients, Sens 93% spec 95%*, given orphan drug status

*Hofman, Radiographics 2015
MEN 1, Multiple Gastrinomas Seen on Diffusion

Diffusion may aid detection*, evaluating tumor grade, ** and differential diagnosis ***

Non-Functioning PNET

- Account for 50 to 70% PNET
- Most are sporadic, solitary, large
  - But can be mult. in MEN I/VHL
  - Symptoms from mass effect
  - Often secrete hormones such as pancreatic polypeptide but no syndrome
- More likely to be metastatic at presentation (liver, nodes)
- Can invade ducts, 33% have venous thrombus
- Well differentiated are octreotide positive
Size: Evolving Role of Imaging for <2cm Incidental Non-Functioning PNET

- More ≤ 2cm non-fxn PNET being found incidentally because of proliferation of cross-sectional imaging(1)
- Controversy regarding management (<2cm)
  - Some studies have shown no growth, no evidence of nodal or distant spread for these small lesions(2)
  - Other studies: in up to 8% late mets or recurrence(3)
- ENETS (Eur Neuroend Tumor Soc)- lesions “≤ 15mm can be safely managed with non-operative treatment.”(4)
- NCCN (2015): resection (including enucleation), with observation in selected cases (5)

(4)Falconi Neuroendoc(rinology 2016 (Consensus Guidelines); (5) Kulke JNCCN 2015 NCCN Guidelines
Non-functioning PNET: 18F-FDG PET CT

- Sensitivity of 18F-FDG PET CT is approximately 58% (complementary to octreotide)
  - More likely to show uptake when poorly differentiated
  - Biopsy results useful for choosing whole body assessment
- SUV predicts overall survival and progression free survival exceeding that of Ki67, liver metastases and chromogranin A levels

Poorly Differentiated PNET

- Are poorly visualized on octreotide, much better seen on FDG-PET/CT
- May show atypical enhancement
  - Hypovascular or PV>Art Ph enhance
  - Lower ADC values than well differ.
- Poor prognosis
- Higher incidence of liver metastases, lymph node metastases, necrosis

*Worhunsky DJ et.al. HPB 2013, Rodallec JCAT 2002*
Nodal Disease

- Usually, CT, MRI, octreotide/PET
- Limited information on modalities
  - CT: sensitivity 35%, specificity 91%*
    - Predictors Nodal mets: Primary >4cm, radiological detectable nodes*
    - Appearance of nodes variable, can mimic vessels
- Fused octreotide:SPECT/CT, improves specificity
- All techniques perform poorly for micrometastases

Nodal Disease: MRI- T2, Diffusion and Black Blood Vessels
Octreotide for Nodal Disease: High Specificity

Retroperitoneal adenopathy

Mediastinal adenopathy
Liver Metastases: Multiphasic Imaging

- While classically hyper/hypo (art/pv), lesions can be very varied in same patient and between studies
- Comparison of 64 pts, Octreo/CT/MRI
  - Sensitivity: MRI > CT > octreotide*
- MRI: Study with 41 pts with liver mets, 18 control**
  - Sensitivity: Diff: 72%, T2: 57%, Dyn: 48%
  - Only limited information for gadoxetate disodium

*Dromain, J Clin Onc 2005 ** d’Assignies Radiology 2013
Liver Metastases DECT and Octreotide

70 kev  Iodine(-water) MDI  Oct SPECT CT
MRI: Comparison of Sequences, PNET Liver Metastases

Art Dyn  PV Dyn  20 min Del Gadox Disodium  T2  Diffusion
Conclusion

- Goal is to identify all sites of disease, to determine management, and to maximize survival.

- Imaging approach varies with nature of tumor:
  - Insulinoma: CT/MRI, intraop ultrasound/palpation
    - Often octreotide negative, primary almost always within pancreas.
  - Gastrinoma: EUS, CT/MRI, octreotide
    - Octreotide positive, often metastatic, frequently primary outside of pancreas.
  - Nonfunctioning: well differentiated- octreotide, CT/MRI
  - Poorly differentiated tumors: CT/MRI, FDG-PET/CT
Thank you!