Abstract #125: The role of octreotide imaging in detecting neuroendocrine tumors (NETS) in 2010: Do we still need it?

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Introduction

- The goal of the presentation is to understand the relative utility of CT or MRI (morphologic imaging) and octreotide scan (functional imaging) to detect disease in patients with neuroendocrine tumors.
- Many patients in the preoperative/postoperative metastatic setting are actually getting both of these imaging modalities and it is unclear if there is an incremental benefit of using both modalities in detecting neuroendocrine tumors.

Background – Neuroendocrine Tumors and Octreotide

- Neuroendocrine tumors (NETs) are uncommon tumors that express the neuroendocrine markers synaptophysin and chromogranin.
- Per SEER data presented by Dr. Yao the *incidence* of NETs is increasing. Their *prevalence* is also increasing as patients live longer with the disease.
- Well differentiated NETs typically express somatostatin receptors.
- Octreotide is an eight amino analogue of the 14-amino acid regulatory hormone somatostatin. It binds to tumor cells that have predominantly type 2, 3, 5 somatostatin receptors (SSRT).

Octreotide Scan (aka OctreoScan™) – Background

- A diagnostic nuclear medicine imaging modality utilizing an octreotide molecule linked via a chelator to Indium.
- Injected and binds to predominantly SSRT 2, 3, 5 when delivered to the cell surface.
- Radioactivity is internalized into the cell via endocytosis and a gamma camera takes pictures of tumors to evaluate extent of disease.

Comparison of Radiation Exposure and Cost

- An Octreotide scan's radiation exposure is similar to that of a CT scan.
- Estimate approximately 10 mSv (millisieverts) for CT abdomen/pelvis (range 6-27.4) and 11.98 for an octreotide scan.
    - Millisieverts is a measurement used to assess the *biological* amount of radiation as opposed to *physical* amount which is characterized by the absorbed dose measured in gray (Gy).
- Medicare Reimbursement (2009)
    - Octreotide Scan (SPECT) - $1500
    - CT Chest/Abdomen/Pelvis - $300 per study (total $900)
    - MRI Chest/Abdomen/Pelvis - $400 per study (total $1200)

Octreotide Scan – Historical Perspective

- Dr. Reidy-Lagunes explained that prior to octreotide scanning, conventional imaging too often failed to detect primary and metastatic lesions.
- Early prospective trials in gastrinomas (N=80) report that octreotide detected 58% of primaries and 70% of metastases. (Gibril et. al., *Annals of Internal Med*, 1996)

  - CT detected 30% of primaries and 38% of metastases
  - MRI detected 31% of primaries and 45% of metastases
- Similar results are seen in other pancreatic islet cell carcinomas as well as with metastatic disease.
- Technology has greatly improved across the board so these vast differences would not necessarily be seen today. CT and MRI resolution has substantially improved over the past two decades achieving more sophisticated resolution, and finer cuts.
- Octreotide scans have also improved. Most institutions now use SPECT (single photon emission computerized tomography) imaging which allows 2-dimensional planar images and transforms them into three dimensional SPECT-CT.
- Dr. Reidy-Lagunes showed examples of the vast improvement of CT scans from 1980 to today pointing out that there has been significant improvement in capturing the architectural anatomy of the organs.
- Octreotide scan rate of false positives is ~20%. It can pick up infections, other tumors (other than neuroendocrine) and some healthy organs can be octreotide positive.

Other Potential use of Octreotide Scans

- Disease staging
  - Use octreotide to further evaluate the extent of disease in patients with metastatic disease already determined on CT/MRI.
  - Search for metastases in a setting where CT/MRI was negative.
  - Evaluate the extent of disease as the only imaging modality (no CT or MRI)
- Determine the somatostatin-receptor status (may be important for treatment implications)

Study Purpose

- To evaluate if modern octreotide scan use in conjunction with modern CT or MRI increased sensitivity in disease detection.

Methods

- MSKCC electronic medical records identified all patients between January 2003 and June 2008 who underwent BOTH an octreotide scan and either a CT or MRI within 30 days of each other.
- The reports of the octreotide scan and CT or MRI were reviewed by a medical oncologist and a senior radiologist.
- Reports were chosen to see what information was given to the clinician and how that information was interpreted. Scans were not reexamined by the speaker or colleagues.

Methods – Octreotide Scan Reports

- Consistent with the majority of octreotide scan reports. Positive findings were noted by organ not by the number of lesions within that organ.
  - E.g. If a lesion was seen in the liver and lung, this was recorded as “positive in the liver and lung.”

Methods – CT or MRI Reports

- A lesion was considered positive if by report the MSKCC radiologist referred to the findings as:
  - “Increased in size”
  - “Enlarged”
  - “Masses or lesions consistent with tumor”

  - "Hypervascular"
- If a concerning or suspicious finding was recorded, prior scans and follow-up scans were used to confirm if they changed. Only if the lesion or abnormality changed was it considered positive.

Patient Characteristics

- Total of 91 NET patients
  - 81 had metastatic disease
  - 10 had local or local regional disease only
  - Of metastatic patients, 15 had functional tumors:
    - Carcinoid =7
    - VIPOMA= 2
    - Gastrinoma=3
    - ACTHoma=1
    - Insulinoma=2
- In terms of histology, 19 patients considered high grade, 7 intermediate grade, and 56 low grade. Nine were unspecified due to insufficient material.

Results - Imaging Modalities Utilized

- 70% of CT scans were triphasic (triple phase).
- All MRIs and CT scans were with contrast.
- All octreotide scans were done with SPECT.
- SPECT-CT was used after April 2006 so there were 40 patients with SPECT-CT in this study.

Results: Local or Local Regional Only (N=10)

- As mentioned earlier, 10 patients had local or local regional disease only
  - 7 pre-operative scans of which all were pancreatic lesions. All 7 have CT scans prior to surgery
  - 6 of 7 had positive octreotide scans. 1 of 7 had negative octreotide scan despite the pancreas lesion seen on CT.
  - All were low grade tumors
  - 3 had post-operative scans – CT and octreotide scans were negative

Results - Metastatic Disease (N=81)

- 18 of 81 (22%) patients with metastases on CT/MRI had a <u>negative</u> octreotide scan (assume they did not have the receptor).
  - 12 high grade
  - 1 intermediate grade
  - 3 low grade
  - 2 unspecified
- 53 of 56 (95%) of *low* grade NETs had positive imaging on octreotide scan.
- 7 of 19 (37%) of *high* grade NETs had positive imaging on octreotide scan.
  - Dr. Reidy-Lagunes thought 37% was higher than expected as most high grade NETs are carcinomas or thought to not have the somatostatin receptor.

Difference in Lesion Detection Between CT/MRI and Octreotide scan in Patients whose Tumors were Octreotide Scan Positive

- N=63 (18/81 metastatic patients had negative octreotide scans)

Patients with positive (+) octreotide scan AND positive (+) CT/MRI

- 16 of 63 (25%) with metastases on CT/MRI had one or more areas of metastatic disease not reported on octreotide scan
  - 4 high grade
  - 4 intermediate grade
  - 8 low grade
- The speaker chose to only review the low grade patients (N=8) since traditionally scanning is used in low grade NETs.
  - 8 of 53 low grade NETs with metastases on CT/MRI had one or more lesion suspicious for metastases NOT reported on octreotide scan.
  - A review of these scans with a MSKCC radiologist suggested that 5 of these patients had lesions on CT/MRI not seen on octreoscan that were consistent with NETs.

Low grade NETs patients with positive (+) octreotide scan AND positive (+) CT/MRI

	CT/MRI	Octreotide scan
Patient 1	Liver/pancreas	Liver
Patient 2	Liver/pancreas	Liver
Patient 3	Pelvic mass, LN, mesentery	Pelvic mass
Patient 4	Mesenteric mass, liver	Mesenteric mass
Patient 5	Liver, bone, pancreas	Liver, bone

Of these 5 patients, 2 were on octreotide and 1 on chemotherapy

Did Octreotide Scan Pick up any Lesions NOT Seen on CT/MRI?

- 4 of 63 patients (2 of 53 low grade) have positive octreotide scan findings not reported on CT/MRI.
- All of these lesions were bone metastases (no soft tissue findings) and all of the patients had extensive soft tissue metastatic disease.

Serial Octreotide and CT/MRI Imaging

- 6 patients underwent serial octreotide scanning and CT/MRI.
- Found octreotide scanning did not detect any additional metastatic sites of disease.

Are There Other Studies That Support these Findings?

- A French team reported in *JCO* in 2005 a prospective study of the detection of liver metastases from endocrine tumors. Studied 40 patients with NETs and liver metastases who prospectively underwent MRI, CT and octreotide imaging confirmed by pathology (biopsy or surgery).
- Number of metastases was counted by independent and blinded radiologists.
- Found the number of liver metastases detected was significantly higher with MRI, followed by CT and then octreotide scan. Biopsy proven.

Potential Limitations of the Current MSKCC Study

- Retrospective study.

- Lesions suspicious on CT/MRI were not biopsied to confirm NETs.
- This was a review of reports.
- Some patients were on treatment.
    - Most studies show however that somatostatin analog treatment modifies the biodistribution of octreotide scanning increasing tumor to background ratio.

Conclusions

- CT and MRI have substantially improved sensitivity over the past few decades.
- Octreotide scanning has also undergone improvements (SPECT and SPECT-CT).
- In this review, reports from octreotide scans did *not* demonstrate increased sensitivity over those of CT/MRI for detection of soft tissue lesions.
- In 2 of 56 (4%) of patients with low grade NETs, octreotide scans identified bone metastases not seen on CT/MRI.
- Further prospective trials comparing contemporary CT/MRI with octreotide scanning and/or new radiolabeled tracers are warranted.