



# Neuroendocrine Tumors: A Single-Center Retrospective Analysis

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## Introduction

- Previous analyses have demonstrated that neuroendocrine (NE) tumor grade correlates well with OctreoScan positivity, SST2 and Chromogranin A IHC staining. Historically lower grade tumors are more likely to have a higher amplification of STT2 receptors and OctreoScan positivity. There have however, been reports of pancreatic neuroendocrine tumors expressing a high degree of SST2 receptors.
- We hypothesized that tumor origin, Chromogranin A and SST2 IHC staining, would correlate with OctreoScan positivity and Wick's tumor grade.

## Purpose

Assess for a correlation of NE tumor location, Chromogranin A and SST2 immunohistochemical staining with OctreoScan positivity and Wick's tumor grade.

## Methods/Patients

- We retrospectively analyzed 38 paraffin embedded tumor specimens based on tumor histological origin as being of small bowel or pancreatic origin, Wick's tumor grade, SST2 receptor and Chromogranin A IHC staining.
- Evidence of stage IV disease by CT scan was corroborated with OctreoScan imaging.
- OctreoScan imaging was graded as positive or negative.
- Wick's grading system:
  - 1 = Well differentiated
  - 2 = Moderately differentiated
  - 3 = Poorly differentiated
- SST2 and Chromogranin A IHC stains were performed and graded 1+, 2+ or 3+.

## Results\*

- There were a total of 40 tumor specimens from 40 patients, but only 38 tumor specimens were available for complete analysis by Wick's grade 1, 2, 3: 11/38, 11/38 and 16/38 respectively.
- Wick's grade 1:
  - Primary tumor status revealed 73% (8/11) samples were of small bowel neuroendocrine origin. The remaining tumor primaries were two pulmonary neuroendocrine and one rectal carcinoid.
- Wick's grade 2:
  - Primary tumor status revealed 18% (2/11) and 18% (2/11) were of small bowel and pancreatic neuroendocrine origin respectively. The remaining NE primaries consisted of 2 rectal, 2 gastric, 1 thymic, 1 pulmonary and 1 unknown NE primary.
- Wick's grade 3:
  - Primary tumor status revealed 31% (5/16) of small bowel and 50% (8/16) being of pancreatic neuroendocrine origin. The remaining three NE primaries were of 1 thymic, 1 pulmonary, and 1 cerebral pontine origin.
- SST2 immunohistochemical staining:
  - Small bowel NE tumors: 27% (4/15) were 1+, 33% (5/15) were 2+, 33% (5/15) were 3+ and 7% (1/15) were SST2 negative.
  - Pancreatic NE tumors: 20% (2/10) were 1+, 20% (2/10) were 2+, 50% (5/10) were 3+ and 10% (1/10) were SST2 negative.
- Chromogranin A immunohistochemical staining:
  - Small bowel NE tumors: 7% (1/15) were 1+, 20% (3/15) were 2+, and 73% (11/15) were 3+.
  - Pancreatic NE tumors: 10% (1/10) were 1+, 20% (2/10) were 2+ and 70% were 3+.
- \*\*Over 90% of patients with pancreatic neuroendocrine tumors had a positive OctreoScan.

\*All stains and grading read by Barry De Young

Primary Tumor (NETs)	WICK GRADE 1	WICK GRADE 2	WICK GRADE 3
Small Bowel	53% (8/15)	13% (2/15)	33%(5/15)
Pancreatic	0% (0/10)	20%(2/10)	80%(8/10)

Wick Grade	ChrgA 1+	ChrgA 2+	ChrgA 3+	SST2 1+	SST2 2+	SST2 3+	SST2 Neg.
1	(0/11) 0%	(1/11) 9%	(10/11) 91%	(2/11) 18%	(4/11) 36%	(4/11) 36%	(1/11) 9%
2	(1/11) 9%	(2/11) 18%	(8/11) 73%	(1/11) 9%	(4/11) 36%	(5/11) 45%	(1/11) 9%
3	(2/16) 13%	(3/16) 19%	(11/16) 68%	(8/16) 50%	(2/16) 12.5%	(4/16) 25%	(2/16) 12.5%

Chromogranin A IHC STAIN	Pancreatic tumors	Small bowel tumors
1+	10% (1/10)	7% (1/15)
2+	20% (2/10)	20% (3/15)
3+	70% (7/10)	73% (11/15)

SST2 IHC STAIN	Small bowel tumors	Pancreatic tumors
1+	27% (4/15)	20% (2/10)
2+	33% (5/15)	20% (2/10)
3+	33% (5/15)	50% (5/10)
Negative	7% (1/15)	10% (1/10)

\*\*OctreoScan results were not available for all patients preoperatively and thus only radiographic images of patients with unresectable pancreatic NE and small bowel NE tumors with stage IV disease were captured in our imaging results.

## Conclusion

- Our results demonstrate that pancreatic neuroendocrine tumors were most often of a higher grade (Wick's grade 3) and consistently OctreoScan positive.
- Small bowel tumors were more likely to be Wick's grade 1-2.
- Chromogranin A and SST2 IHC staining of 2-3+ appeared to correlate with Wick grade in carcinoid tumors of the small bowel, but were neither sensitive nor specific in those of pancreatic neuroendocrine origin.

## Summary

- Almost all specimens from patients with radiographic evidence of metastases on CT scan demonstrated OctreoScan positivity.
- The vast majority of the neuroendocrine tumors of small bowel origin were a Wick's grade 1-2 with 66-70% being SST2/ChrgA 2-3+ on IHC staining, which correlated with their Wick grade.
- Pancreatic neuroendocrine tumors were more likely to have a SST2/ChrgA 2-3+ IHC staining despite 80% being of a higher Wick's grade 3.
- Although published reports have demonstrated a correlation with OctreoScan positivity with lower grade neuroendocrine tumors, our results demonstrate that pancreatic neuroendocrine tumors were most often of a higher grade and consistently OctreoScan positive.