Correlation of ^{68}Ga-DOTATOC Uptake and Pathologic Grade in Neuroendocrine Tumors

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Introduction

^{68}Ga-DOTATOC is a somatostatin analog used to detect neuroendocrine tumors (NETs). The Ki-67 protein (Ki-67) is a marker of cell proliferation and has been established as both a diagnostic and prognostic factor in the treatment of NETs. In general, tracer uptake in somatostatin receptor (SSTR) PET is higher in lower grade NETs (1). Past studies have studied the correlation between Ki-67 proliferation index (Ki-67 PI) and DOTATATE maximum standard uptake values (SUV_{max}) and yielded mixed results (2).

We aimed to match the lesions biopsied to the lesions observed on ^{68}Ga-DOTATOC to establish a correlation between Ki-67 PI and SUV_{max} in the same lesion.

Methods

We retrospectively reviewed 238 consecutive DOTATOC PET scans performed at UCSF during 2014-2016. Patients were excluded if:

- No pathology was available;
- Tumors were fully resected prior to imaging;
- A correlate lesion between pathology and imaging could not be identified; or
- DOTATOC PET scan was >365 days from date of biopsy.

A total of 90 patients had pathology available, and 54 patients had Ki-67 PI available. SUV_{max} from biopsied lesions was correlated with Ki-67 PI using the Pearson correlation coefficient.

Results

For 110 lesions from 90 patients with pathology available, DOTATOC PET had 92.7% sensitivity and 100% specificity (102 true positives; 8 false negatives) for detection of NETs. In 54 patients, we were able to obtain Ki-67 PI values for 63 lesions for which we had corresponding SUV_{max} information. There was no correlation between Ki-67 PI and SSTR-PET uptake (r=-0.169, p = 0.252). There were 26 grade 1 lesions (mean Ki-67 PI 1.1%; mean SUV_{max} 40.6), 31 grade 2 lesions (mean Ki-67 PI 8.0%; mean SUV_{max} 34.4), and 6 grade 3 lesions (mean Ki-67 PI 32.9%; mean SUV_{max} 13.8).

Table 1. Ki-67 proliferation index and SUV_{max} according to tumor grade (n = 63).

Grade	Total n (%)	Ki-67 PI Mean ± SD	SUV_{max} Mean ± SD
1	26 (41%)	1.1% ± 0.70	40.6 ± 43.6
2	31 (49%)	8.0% ± 4.41	34.4 ± 33.3
3	6 (10%)	32.9% ± 12.2	13.8 ± 15.3

Figure 1. Relationship between Ki-67 PI and DOTATOC SUV_{max}.

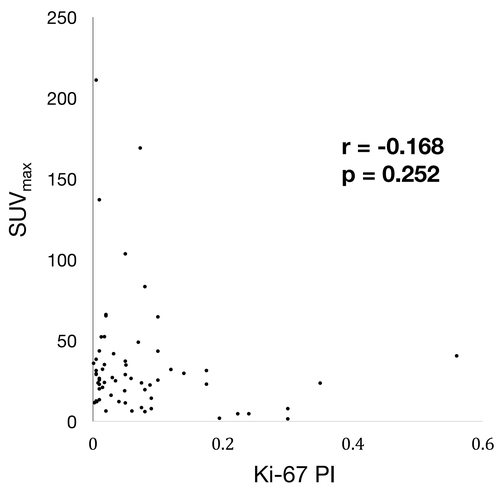

Table 2. Location of primary tumors and biopsy sites in 54 patients.

Location	Primary Tumor (n = 54)	Biopsy Site (n = 63)
Pancreas	18 (33%)	13 (21%)
Small Bowel	12 (22%)	5 (8%)
Lung	4 (7%)	5 (8%)
Kidney	2 (4%)	2 (3%)
Rectum	2 (4%)	-
Peritoneum	1 (2%)	-
Presacrum	1 (2%)	-
Stomach	1 (2%)	2 (3%)
Liver	-	23 (36%)
Lymph Node	-	4 (6%)
Pelvis	-	4 (6%)
Ovary	-	2 (3%)
Breast	-	1 (2%)
Femur	-	1 (2%)
Skull Base	-	1 (2%)
Unknown	13 (24%)	-

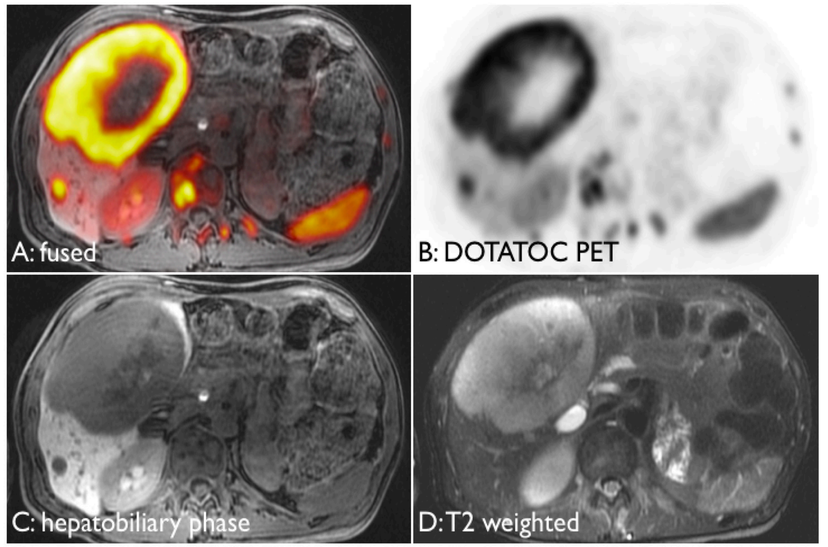

Figure 2. In a 51-year-old man with metastatic NET, there is a 10 cm hepatic mass. On pathology, the lesion demonstrated a Ki-67 PI <1% and was found to be consistent with a WHO grade 1 NET. On DOTATOC imaging (A-D), variable uptake was seen within the lesion (A and B), ranging from SUV of 2.4 in the center to SUV of 29 on the periphery. Depending on where the lesion was sampled, the measured SUV_{max} of the lesion may not correspond with the Ki-67 PI of the biopsy site due to extensive intra-lesional heterogeneity.

Conclusion

Our analysis demonstrates high sensitivity and specificity in DOTATOC PET imaging for detection of NETs and lack of correlation between Ki-67 PI and SUV_{max} in NETs. In Grade 1 and 2 lesions SSTR-PET provides independent information from Ki-67 PI that can help guide clinical management and treatment.

References

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