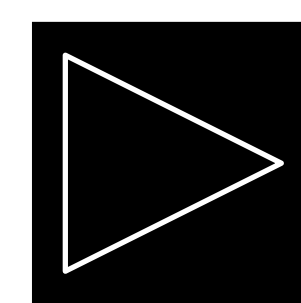




INTRODUCTION

Inclusion criteria for Peptide Receptor Radionuclide Therapy (PRRT) uses the qualitative Krenning score to determine adequate uptake, typically based on planar Octreoscan imaging, as was performed in the NETTER-1 trial. With the availability of DOTATATE PET, it is unclear if the Krenning score is equivalent between modalities.

MATERIALS AND METHODS

156 NET patients were imaged using both Octreoscan and DOTATATE PET at the NIH. These patients were imaged previously as part of a prospective clinical trial evaluating the use of DOTATATE PET compared to Octreoscan (1). Octreoscan (planar and SPECT) and DOTATATE PET were graded using the Krenning score (0 = no uptake, 1 = very low, 2 = equal to or less than liver, 3 = greater than liver, 4 = greater than spleen). The size and the number of lesions were recorded in a 5-score scale as following: 1 = 1-3 sub 2 cm, 2 = multiple sub 2 cm, 3 = 2-5 cm lesions, 4 = largest lesion > 5 cm and < 5 lesions, 5= Largest lesion > 5 cm and > 5 lesions. Each study was read by two nuclear medicine trained physicians and a Fleiss's Kappa was used to evaluate for inter-rater variability.

REFERENCES

Sadowski SM et al. Prospective Study of 68Ga-DOTATATE Positron Emission Tomography/Computed Tomography for Detecting Gastro-Entero-Pancreatic Neuroendocrine Tumors and Unknown Primary Sites. Clin Oncol. 2016 Feb 20;34(6):588-96.

TABLE 1: Breakdown of Krenning scores from 0-5 across all patients imaged, broken down by reader and imaging modality.

Krenning Score	Reader 1			Reader 2		
	Planar	SPECT	SSTR PET	Planar	SPECT	SSTR PET
0-1	106	84	43	120	103	45
2	14	16	3	4	5	3
3	18	33	18	14	25	15
4	13	21	92	13	20	91

TABLE 2: Breakdown of Krenning scores from 0-5 in patients with evidence of SSTR-positive disease on any imaging modality, broken down by reader and modality.

Krenning Score	Reader 1			Reader 2		
	Planar	SPECT	SSTR PET	Planar	SPECT	SSTR PET
0-1	60%	39%	0%	72%	54%	0%
2	13%	14%	3%	4%	5%	3%
3	16%	29%	16%	13%	23%	14%
4	11%	18%	82%	12%	18%	83%

TABLE 3: Percent of Octreoscans that are positive (planar and SPECT), in cases that were read as DOTATATE+, broken down by size criteria.

	Reader 1				Reader 2			
	Size ≥ 3		Size < 3		Size ≥ 3		Size < 3	
	Planar	SPECT	Planar	SPECT	Planar	SPECT	Planar	SPECT
#	21	31	10	24	12	12	18	34
%	70%	100%	13%	30%	86%	86%	20%	37%

RESULTS

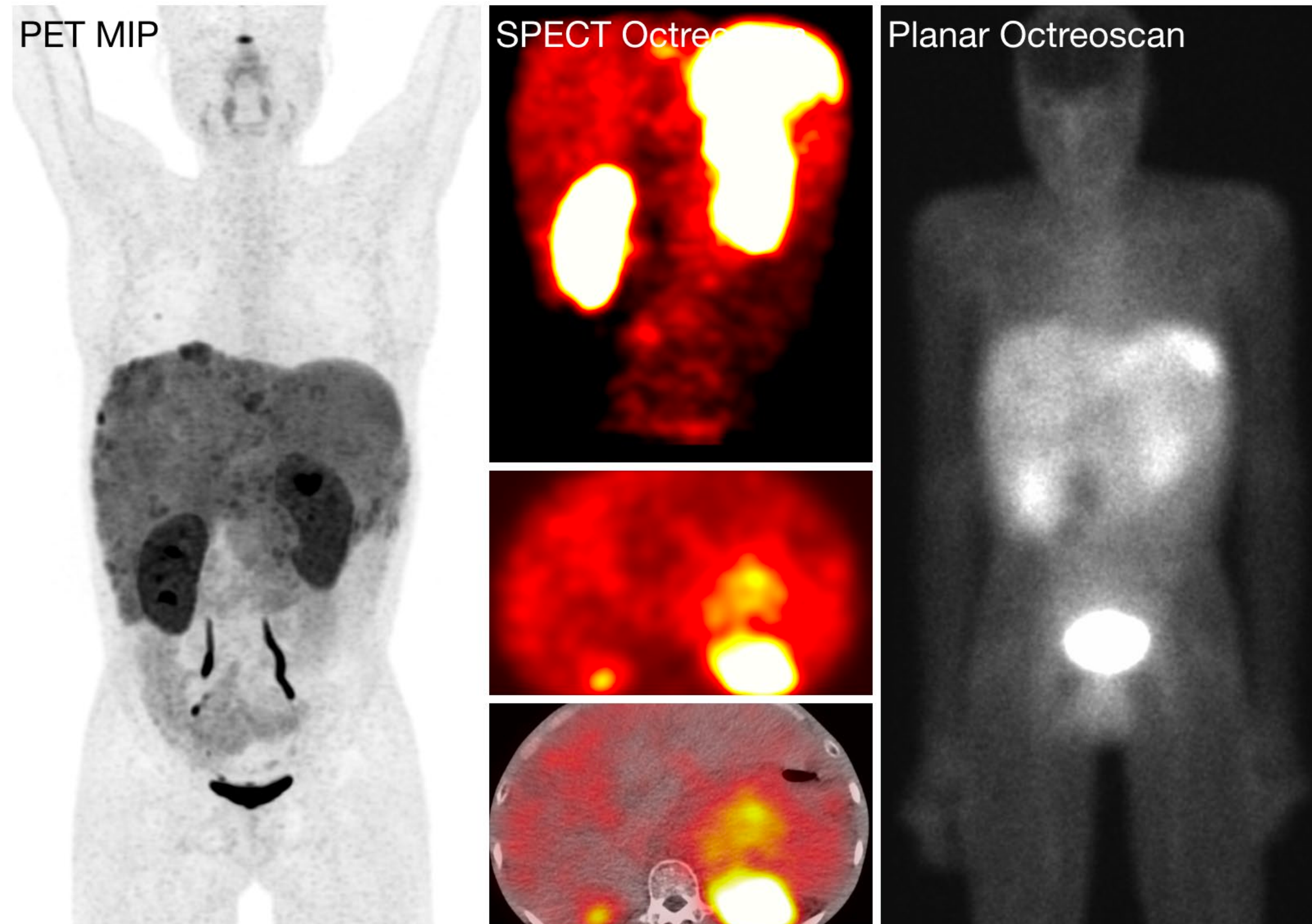
SSTR PET demonstrated a much higher percentage of patients with Krenning 4 disease compared to Planar and SPECT imaging using Octreoscan (Table 1). 27% of patients had no evidence of disease, and of patients with positive disease, 82-83% were Krenning 4 on DOTATATE PET, while only 18% were Krenning 4 on SPECT imaging and 11-12% on planar imaging (Table 2). Stratified by size and number of lesions, planar and SPECT visualized 70-100% of DOTATATE avid score 3/4/5 lesions while visualized 13% and 37% of size 1/2 lesions (Table 3). Interrater variability for planar images, SPECT imaging, DOTATATE imaging and lesion size were: 0.68, 0.56, 0.84, and 0.70. Cases demonstrating the imaging of the three modalities are provided.

DISCUSSION

Krenning scoring using DOTATATE PET results in a markedly higher rate of Krenning 4 patients compared to Octreoscan imaging, which is primarily due to small lesions not being detected on Octreoscan. 90% of patients on the NETTER-1 trial had Krenning 3/4 disease on planar Octreoscan imaging. In patients with low volume disease, the majority of patients with Krenning 3/4 disease on DOTATATE PET would not have qualified for the NETTER-1 trial, and caution must be taken to apply criteria used in the NETTER-1 trial to DOTATATE PET results. When using SSTR-PET for inclusion criteria into PRRT, size and extent of disease should be taken into account in addition to the uptake seen on SSTR-PET.

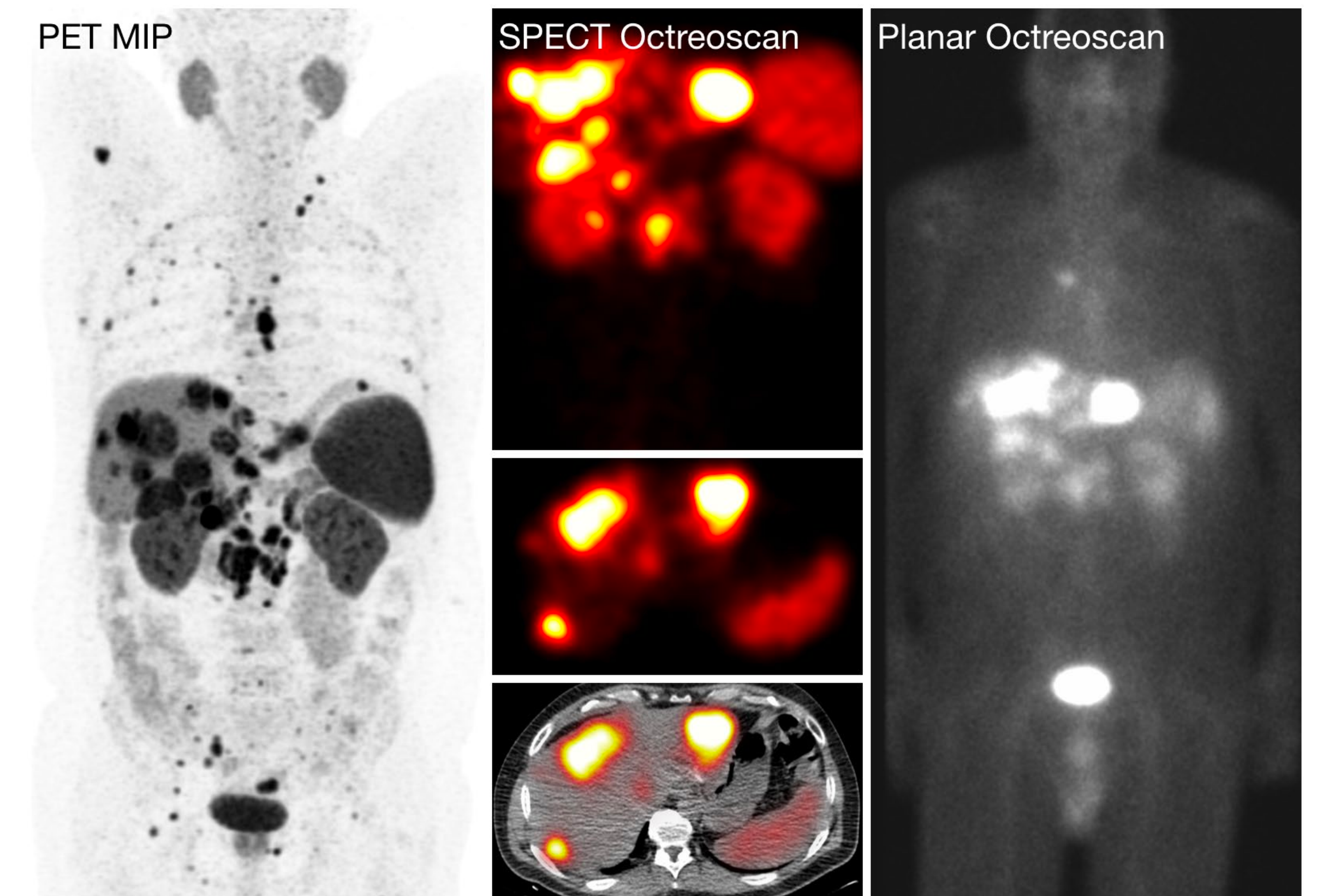
EXAMPLE CASE 1

Example case of disagreement. One reader read the PET/CT as a Krenning 2 and another read it as a Krenning 3. In this case the difficulty is in the volume of disease in the liver (which is nearly replaced), and without conventional imaging with contrast it is difficult to determine what the uptake is in the background liver. One important interpretative point is that the uptake in the spleen is nearly identical to that of the liver, suggesting liver replacement.



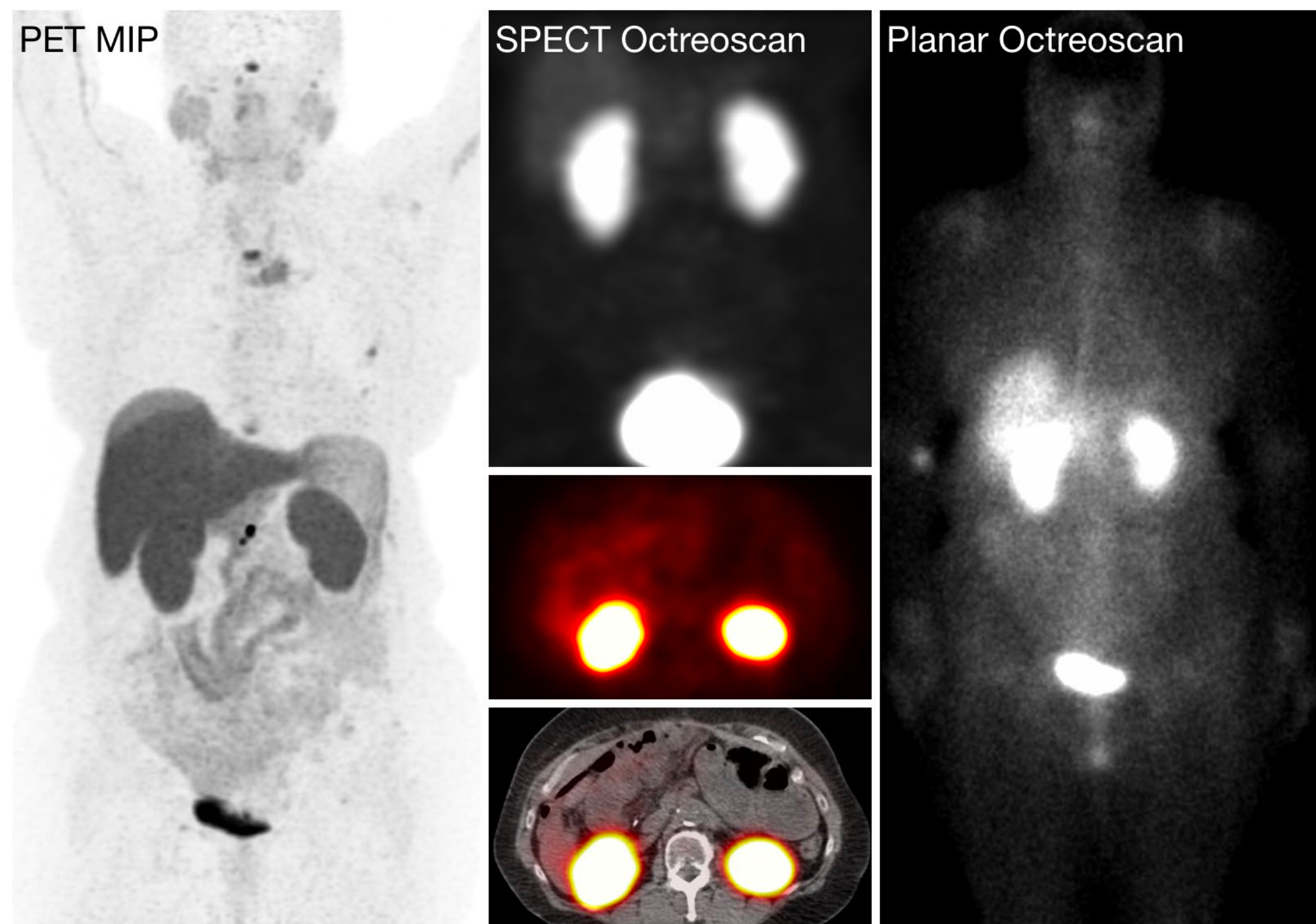
EXAMPLE CASE 2

Example case of agreement. This patient was graded as having Volume 5 disease (ie at least one lesion greater than 5 cm and more than 5 lesions). All imaging studies were read by both readers as having Krenning 5 disease. Note that the SSTR-PET demonstrates more lesions, particularly in the bones compared to the SPECT/CT and the planar imaging study.



EXAMPLE CASE 3

Example case of SSTR PET demonstrating higher Krenning score than Octreoscan in low volume disease. This patient was graded as Krenning 3 and 4 on SSTR PET (by the two readers respectively), but as Krenning 0 on planar and SPECT Octreoscan. The extent of disease was graded as 1 by the two readers (ie 1-3 sub-2 cm lesions).



EXAMPLE CASE 4

Unusual case where single sub-2cm hepatic metastases is seen on all three imaging modalities as a Krenning 3 lesion. Both readers agreed on grading across all imaging modalities. This was one of three cases with disease rated as size Grade 1, that had uptake greater than or equal to 3 on planar Octreoscan.

