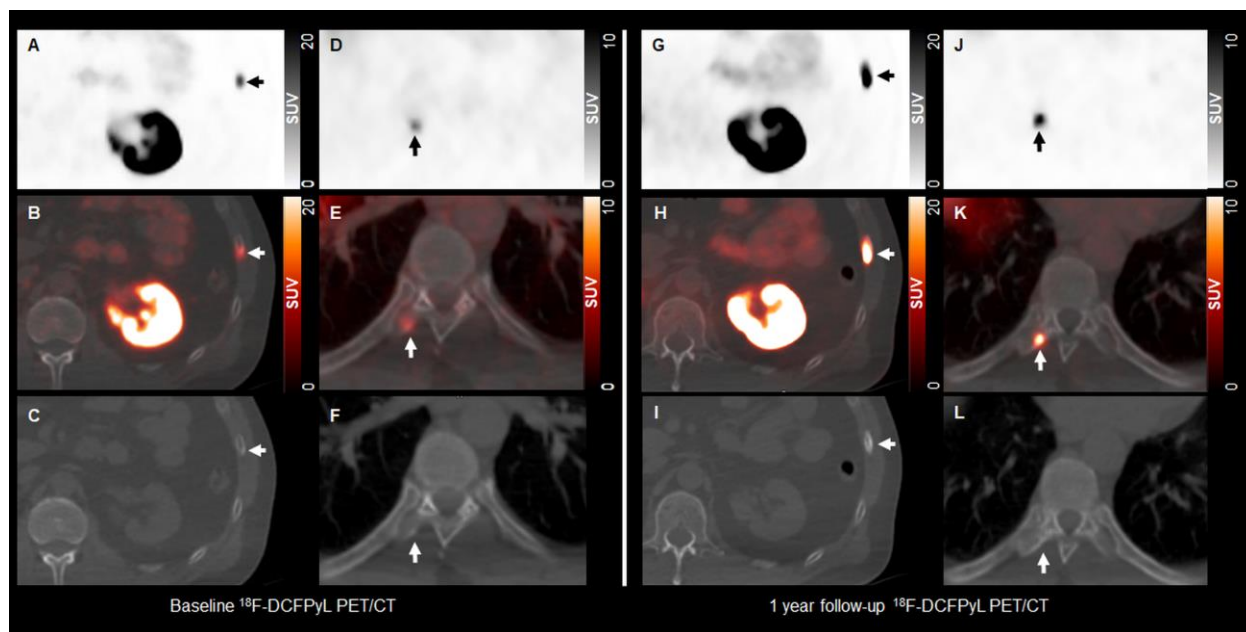


Supplemental Figure 1. Patient-level total follow-up duration in months from pre-PSMA (blue) to post-PSMA (red) for all 48 patients with at least one PSMA-positive IBL. Only the earliest and latest follow-up imaging or biopsy information are shown. (*)Bx = biopsy of the IBL; (●)PSMA = ^{18}F -DCFPyL PET/CT; (▽)BS = $^{99\text{m}}\text{Tc}$ -MDP SPECT bone scintigraphy scan; (Δ)CXR = chest x-ray; (○)MRI = magnetic resonance imaging; (□)CT+ = any non-PSMA imaging incorporating CT such as PET/CT, BS/CT, or CT only.

Supplemental Table 1. Detailed patient-level pre-PSMA and post-PSMA imaging and interventions for patients with at least one PSMA positive IBL. Imaging modalities that could follow a lesion's status are included and displayed in the order they occurred. All interventions for PCa management except prostate biopsy are included.

Patient	Treatment Status at PSMA Imaging	Pre-PSMA Imaging	Post-PSMA Imaging	Pre-PSMA Intervention	Post-PSMA Intervention
1	BCR	BS/CT, CXR, NaF PET/CT, BS/CT x2	BS/CT x3, NaF PET/CT, DCFPyL PET/CT, BS/CT x2, NaF PET/CT, DCFPyL PET/CT	ADT, Brachytherapy, SRP	Trial (18-C-0005)
2	BCR	BS/CT, NaF PET/CT, BS/CT x2, CT x2	BS/CT	RP, ADT x2, RT	ADT
3	BCR	CT x2, Axumin PET/CT, MRI x2	None	RP, SRT	None
4	BCR	MRI x3, Axumin PET/CT, BS/CT, MRI, NaF PET/CT, CXR	MRI, BS/CT, DCFPyL PET/CT	ADT, Brachytherapy	Trial (18-C-0005)
5	High-risk	FDG PET/CT x2, CT x3, MRI, BS/CT	CT, FDG PET/CT, CT	None	ADT, Docetaxel, Abiraterone, IMRT
6	BCR	MRI, CT, MRI	NaF PET/CT, BS/CT x6, FDG PET/CT, DCFPyL PET/CT, NaF PET/CT	ADT, RT, LDR Brachytherapy, ADT	Trial (16-C-0048)
7	BCR	NaF PET/CT, MRI x2, CXR, MRI	BS/CT x 2	RP, ADT, RT	ADT
8	High-risk	MRI x2, BS/CT, BS, CT, MRI, BS/CT, NaF PET/CT, BS/CT, MRI	CT x2	None	RP
9	BCR	CT, MRI, CXR, MR, CT, MRI	biopsy	ADT, Enzalutamide, RP	None
10	BCR	BS/CT, MRI	BS/CT x2, NaF PET/CT, BS/CT x2, FDG PET/CT, NaF PET/CT, DCFPyL PET/CT	RP, SRT, ADT, Trial (16-C-0035)	ADT, Enzalutamide
11	BCR	MRI x2, BS/CT, MRI	NaF PET/CT, MRI x2	RP, RT, ADT	Trial (16-C-0048)
12	BCR	BS/CT x4	BS/CT, DCFPyL PET/CT, NaF PET/CT	RT, ADT, Trial (16-C-0035), RCT (15-C-0075)	RP, SBRT, ADT, Enzalutamide
13	BCR	CXR, CT x2, MRI	None	ADT, RT	None
14	BCR	BS/CT x2, MRI	MRI	RP	Trial (18-C-0028), ADT
15	BCR	BS/CT x3, NaF PET/CT	NaF PET/CT	RP, ADT, SRT, Ra-223	None
16	BCR	CT, CXR, BS/CT, CXR, MRI	None	RP	RT
17	High-risk	MRI, MRI, CXR, BS/CT, CXR	NaF PET/CT, BS/CT, MRI	RCT (15-C-0205)	Biopsy, RT, ADT

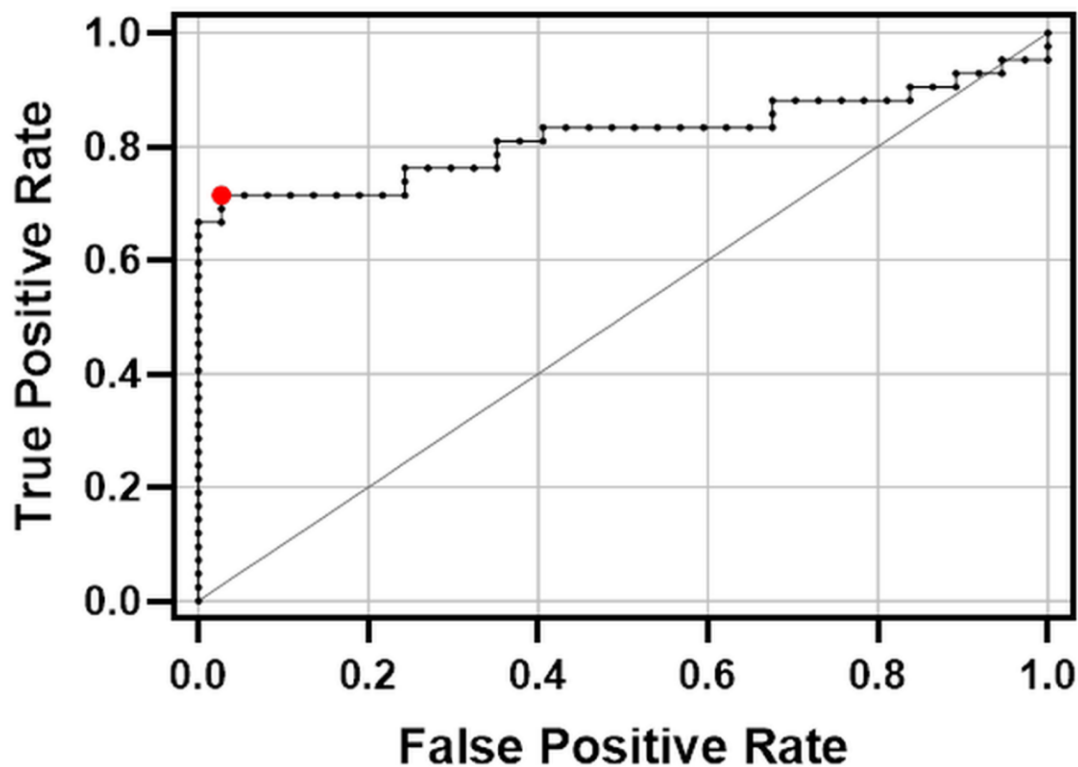
18	BCR	CT, BS	BS/CT x2, NaF PET/CT, DCFPyL PET/CT, FDG PET/CT	EBRT, ADT	Trial (18-C-0076), ADT, Abiraterone, Denosumab
19	BCR	BS, CXR, NaF PET/CT, BS/CT	NaF PET/CT x2	RP, RT	Trial (18-C-0005)
20	BCR	FDG PET/CT, BS/CT	None	RP	None
21	BCR	BS/CT, FDG PET/CT, CT	CXR, BS/CT, CT	RP	Biopsy, ADT
22	BCR	BS/CT, NaF PET/CT, DCFPyL, NaF PET/CT	BS/CT, NaF PET/CT, BS/CT	RP, SRT, ADT, Ra-223	Trial (18-C-0005)
23	BCR	BS/CT, MRI, BS/CT, MRI	None	EBRT	None
24	BCR	MRI	None	RP, ADT, SRT, ADT	Biopsy
25	High-risk	BS/CT	CXR, CT, BS/CT, MRI	TURP x4	RP
26	BCR	BS/CT, CT, Axumin PET/CT	None	RP, RT, ADT	None
27	BCR	BS/CT	None	RP, RT	None
28	BCR	CT, MRI	None	RP, SRT	ADT, Sipuleucel-T
29	BCR	BS/CT, MRI	None	ADT, RT, Abiraterone	Biopsy, ADT x2
30	High-risk	BS/CT, NaF PET/CT	CXR x2	None	Biopsy, EBRT, ADT
31	High-risk	NaF PET/CT	None	None	Biopsy, LRP, ADT
32	BCR	BS/CT, MRI	None	RP, RT	ADT, Abiraterone
33	High-risk	MRI, BS/CT, MRI	CT, BS/CT	RT	RP, ADT, Enzalutamide
34	BCR	CT, MRI	None	RP, SRT	Biopsy, ADT, Docetaxel
35	BCR	BS/CT, Axumin PET/CT, NaF PET/CT, MRI, BS/CT	MRI	LDR Brachytherapy	RT
36	BCR	MRI	NaF PET/CT	RP	None
37	High-risk	MRI, BS/CT, MRI	NaF PET/CT, CT x2	None	Trial (16-C-0048), RT
38	BCR	BS/CT	CXR	RT, SRP, ADT x2	Biopsy, ADT, RT
39	BCR	CT, NaF PET/CT	None	RP, RT	None
40	BCR	BS/CT	CXR	RP	Biopsy
41	BCR	CT	None	Brachytherapy, SBRT	None
42	High-risk	BS/CT	None	None	EBRT, Brachytherapy, ADT
43	High-risk	BS/CT	None	None	RP
44	High-risk	BS/CT	None	None	None
45	High-risk	BS/CT	FDG PET/CT	None	ADT, IMRT
46	BCR	BS/CT	None	RP, ADT, SRT, Enzalutamide	None
47	BCR	MRI, NaF PET/CT	None	LRP, SRT, ADT	None
48	High-risk	MRI	None	None	None



Supplemental Figure 2. 58-year-old patient with BCR PCa and PSA of 2.0 ng/mL. Axial ^{18}F -DCFPyL PET (A, D, G, J), ^{18}F -DCFPyL PET/CT (B, E, H, K), and CT (C, F, I, L) images demonstrate multifocal PSMA-avid uptake. A-F: Baseline ^{18}F -DCFPyL PET/CT shows PSMA-avid uptake with SUV_{max} of 12.1 in the left 9th rib and subtle sclerotic CT features (A-C, left arrows) and another subtle PSMA-avid uptake with SUV_{max} of 3.8 in the right T8 transverse process with subtle sclerotic CT features (D-F, up arrows). G-L: A 15-month follow-up ^{18}F -DCFPyL PET/CT scan showed that both lesions had intense PSMA uptake and sclerotic morphological changes (arrows), and additional PSMA-avid lesions were present (not shown). Thus, the IBLs in A-F were determined to be malignant.

Supplemental Table 2. ^{18}F -DCFPyL PET/CT based lesion and scan variables that do not predict IBL interpretation. Statistical significance is evaluated based on 3-way interpretation (M vs. B vs. E). IBL=indeterminate bone lesion; mets=metastases; B=benign; E=equivocal; M=malignant.

Non-predictive Variables		Interpretation of IBLs (n=98)			Statistical Significance
		Malignant (n=42)	Benign (n=37)	Equivocal (n=19)	P-value (n=98)
SUV _{max} , Median (range)		10.6 (1.0–35.9)	2.9 (1.2–8.8)	2.1 (1.2–6.4)	M vs. B: $P=0.288$ M vs. E: $P=0.525$ B vs. E: $P=0.688$
CT feature	sclerotic	7	8	7	$P=0.608$
	lytic	4	0	0	
	mixed	2	4	1	
	negative	29	24	12	
PSMA-avid lymph nodes	negative	15	31	5	$P=0.113$
	positive	27	6	14	
PSMA-avid bone lesions	one IBL	4	17	9	$P=0.299$
	≥ 2 IBLs	27	18	8	
	other mets	11	2	2	



Supplemental Figure 3. ROC curve evaluating the SUV_{max} of IBLs interpreted as benign or malignant (n=79). The red point indicates the selected threshold of SUV_{max} equal to 5 based on the maximized Youden index which had the highest true positive rate (sensitivity, y-axis) and the least false positive rate (1-specificity, x-axis).