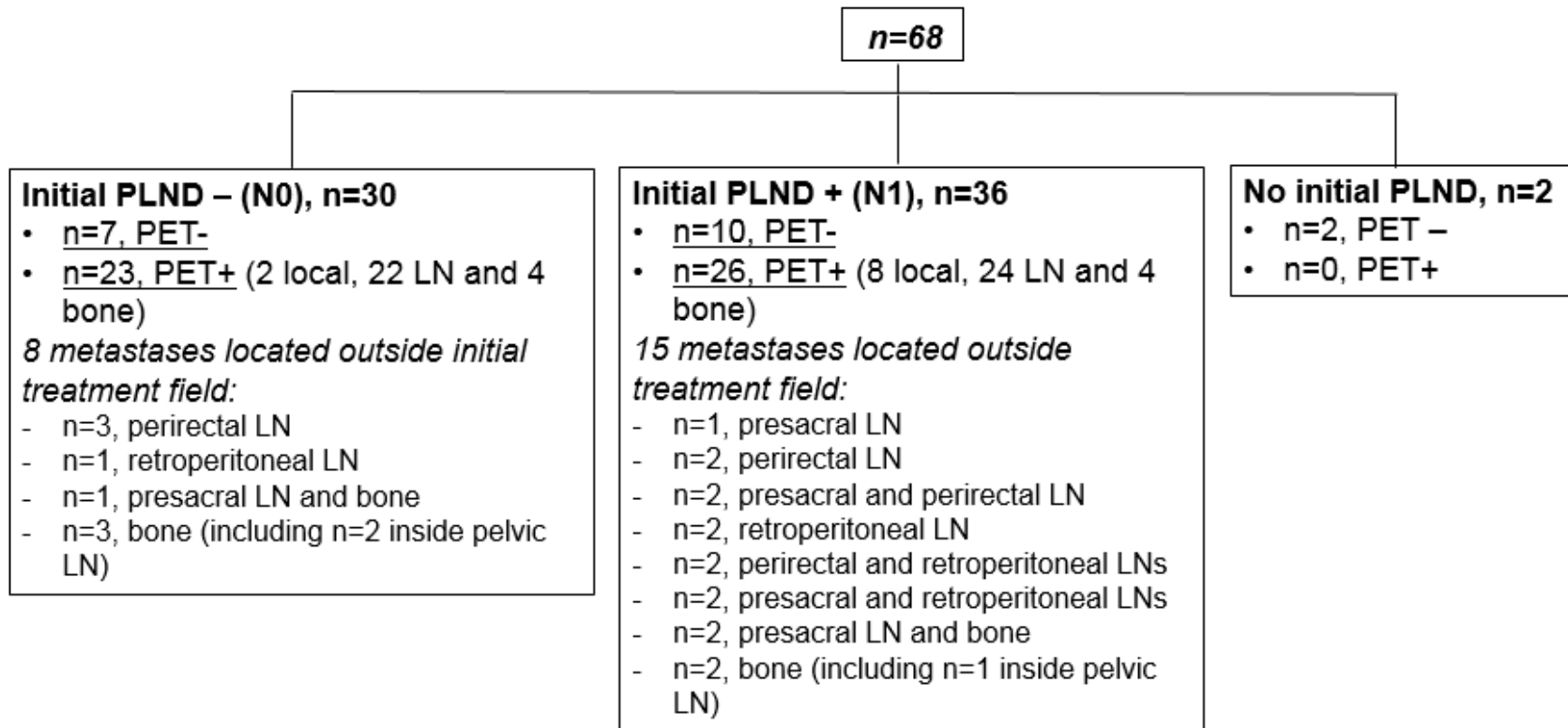
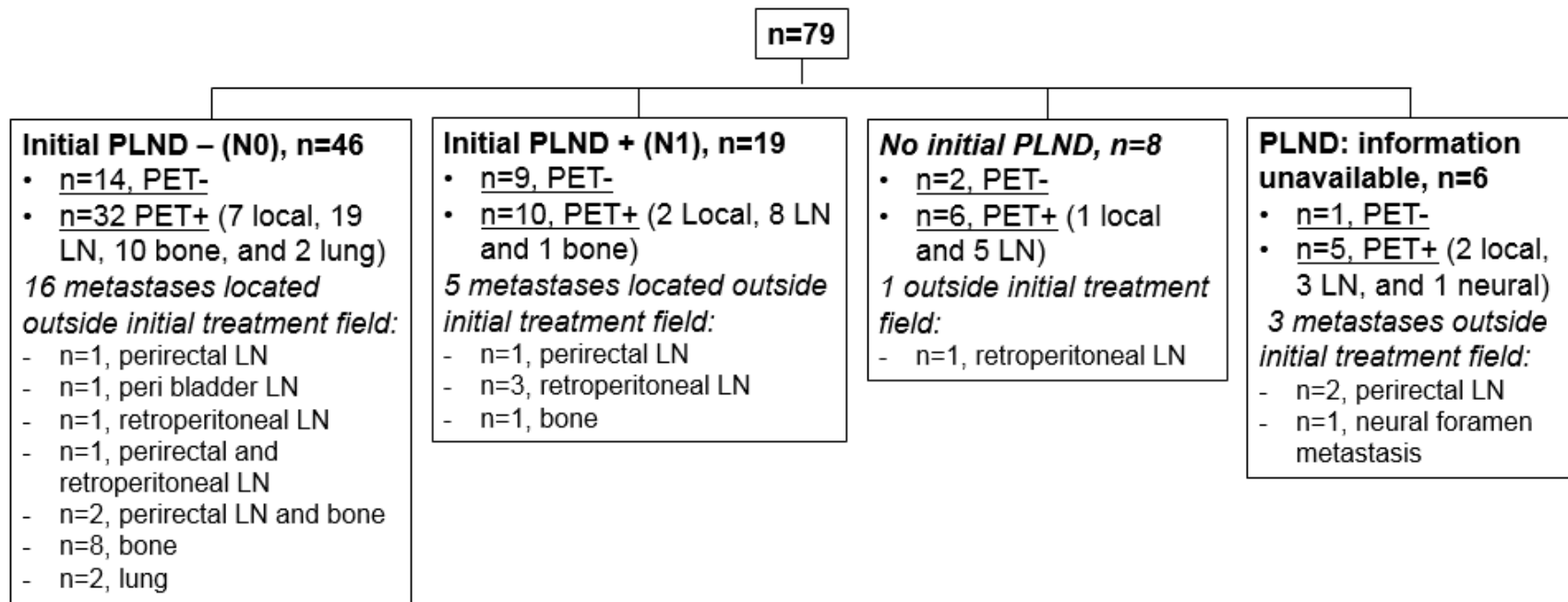


Supplemental Figure 1. Patients with persistently elevated PSA after initial RP and with PET/CT-positive recurrence outside initial treatment field.



Supplemental Figure 2. Patients after initial RP followed by salvage RT with PET/CT-positive recurrence outside initial treatment field.



Supplemental Figure 3. Patients after initial RT with PET/CT-positive recurrence outside initial treatment field.

n= 30

- n=3, PET-
- n=27, PET+ (19 local, 15 LN, 5 bone, mediastinal LN and 1 lung)

13 metastases located outside treatment field:

- n=3, perirectal LN
- n=3, retroperitoneal LN
- n=5, bone (including n=1 inside pelvic LN)
- n=1, lung
- n=1, mediastinal LN

Supplemental Table 1. ¹¹C-choline PET/CT reading concordance: blinded reading by R1 vs. unblinded reading by R1 and unblinded reading by R1 vs. consensus reading

Unblinded Score	Blinded			Consensus			Total
	0	1	2	0	1	2	
0	83	4	0	80	4	3	87
1	4	33	10	15	23	9	47
2	3	3	147	3	7	143	153
Total	90	40	157	98	34	155	287

The unblinded reading by R1 positivity agreed with the blinded one in 91.6% of cases overall and in 93.8%, 75.9%, and 94.8% for scores 0, 1, and 2, respectively. The *kappa* coefficient was 0.86, while the weighted *kappa* was 0.93.

The consensus reading positivity agreed with the unblinded reading by R1 one in 85.7% of cases overall and in 86.5%, 56.8%, and 92.9% for scores of 0, 1, and 2, respectively. The *kappa* coefficient was 0.76, while the weighted *kappa* was 0.87.

Supplemental Table 2. Patients classified as negative in the blinded reading and equivocal or positive by the unblinded or consensus reading.

age	Gleason	TNM	N	category	delay	PSA level	PSA dt	B	UB	C	Comments	Treatment and follow up
63	9 (4+5)	pT3bN0	III	PSA still high after RP	0.44	0.25	-	0	0	2	Faint uptake in small pelvic LNs not seen by the first reader	Salvage RT, after PSA<0.05ng/mL
66	8 (4+4)	pT3bN1	IV	PSA still high after RP	0.41	2.7	-	0	1	1	After unblinded, small right int iliac LN with faint uptake doubtful because of PSA level and N1	Salvage RT+HT, PSA decreased after therapy
62	7 (4+3)	pT3aN0M0	III	RP+RT	2.20	3.6	0.8	0	0	1	Consensus: doubtful faint pelvic uptake (PSA level)	HT, PSA continue to increase, 4 months after PSA=23.5, new imaging: bone metastasis. Treatment: Olaparib
55	7 (3+4)	pT3aN0	III	RP+RT	5.04	0.25	10.5	0	0	1	Small LN left ext iliac with faint uptake consider inflammatory by the first reader and doubtful after consensus	Observation. 5 months after PSA=0.43ng/mL. New choline PET: unchanged. Continue observation
68	8 (4+4)	pT3bN1	IV	RP	1.22	0.3	1.7	0	0	1	After consensus, doubtful local recurrence	Salvage RT, after PSA<0.05ng/mL
71	7 (3+4)	pT2bN0	IIA	RP	2.33	0.22	8.67	0	0	1	B and UB: T12 right mild uptake without CT correlation, negative in NAC images, seems unspecific. After consensus T12 bone lesion consider as doubtful	Salvage RT pelvic only (T12 not included), after PSA<0.05ng/mL → False positive consensus reading
75	7 (3+4)	pT3aN0	III	RP	11.44	0.6	29.7	0	0	2	B and UB: Iliac distal LNs most likely inflammatory: bilat, fat center and uptake decrease between dynamic, static and final images. After consensus, LNs considered positive because of the PSA level	Salvage RT, after PSA<0.05ng/mL

70	6 (3+3)	pT2bR0N0	IIA	RP	16.98	0.5	6	0	2	2	After unblinded (PSA level and dt): left pararectal LN with mild uptake SUV 1.5 suspicious	biopsy LN para rectal left: positive. Treatment: RT+HT, after PSA< 0.05
75	7 (3+4)	pT2cN0	IIB	RP+RT	17.11	0.6	16.6	0	1	2	After unblinded: mild doubtful local uptake corresponding to the local equivocal nodule described on MRI. After consensus, local uptake considered as suspicious	Follow up because of co-morbidities
68	9 (4+5)	pT2bN0	IIB	RP	0.66	0.3	1.9	0	2	2	After unblinded (Gleason, delay between surgery and rising PSA and PSA dt) suspicious LNs right ext iliac SUVmax 2.3 and right common iliac	Salvage RT+HT, after PSA< 0.05
69	10 (5+5)	pT3bN1	IV	RP+RT	7.80	2.2	4.4	0	1	1	After unblinded (initial Gleason, N1 and PSA level and dt): right ext iliac LN initially considered as inflammatory considered as doubtful	HT
76	7 (3+4)	?	?	RP+RT	15.72	10.4	11	0	1	0	After unblinded (high PSA level) small LNs left obturator and ext iliac SUVmax 1.1 initially considered as inflammatory considered as doubtful. Finally considered inflammatory after consensus	HT
70	7 (4+3)	pT3aN0	III	RP	4.56	0.7	1.4	0	0	2	B and UB: reactive inguinal and ext iliac distal LNs After consensus: ext iliac and RP LNs suspicious because PSA level	Salvage RT+HT, after PSA< 0.05
82	7 (4+3)	maxT2b	IIA	RT	4.76	10.7	9.4	0	2	2	B: pulmonary nodule linked with other disease After unblinded: mild avid lung nodule suspicious in the context (PSA high and no other avidity)	HT

N= NCCN grade; delay= time between initial treatment and PET (years); PSA level ng/mL; PSA_{dt}= PSA doubling time in months; Scores for B= blinded reading, UB= unblinded reading, C=consensus reading; LN= lymph node.

Supplemental Table 3. Correlation between ¹¹C-choline PET/CT positivity and clinical findings (scores 1 and 2 considered positive)

Factors	N	OR	95% CI	Univariate p-value
Gleason score	285			0.24
6-7		Ref.		
8		1.48	0.74, 3.10	
9-10		1.62	0.86, 3.16	
NCCN	272			0.78
I-II		Ref.		
III		0.98	0.53, 1.81	
IV		0.82	0.43, 1.53	
Log(PSA)	287	2.21	1.73, 2.90	<0.001
Log(PSA DT)	209	1.27	0.93, 1.75	0.13
Log(PSA velocity)	209	1.54	1.24, 1.94	<0.001
Log(Time) *	286	0.81	0.59, 1.08	0.17
Log(Time)²*	286	1.16	0.98, 1.37	0.08
Initial treatment	208			<0.001
RP		Ref.		
RT		12.5	3.52, 80.0	
Persistently elevated PSA		2.40	1.27, 4.67	

* LogTime and LogTime squared are analyzed together in the same model. In univariate analysis, increasing log(PSA) value, increasing log(velocity), as well as RT treatment and persistently elevated PSA are associated with a higher risk of scan positivity.

Variables with a p-value <0.20 in univariate analysis were entered in the multivariate model.

When adjusted for the other variables, only the value of log(PSA) was associated with the risk of having a positive scan: OR = 2.21 (95% CI 1.73, 2.90; p<0.001).

Supplemental Table 4. Examples of patients for whom ¹¹C-choline PET had an impact on management

age	Gleason	TNM	N	category	delay	PSA level	PSA dt	B	UB	C	¹¹ C-Choline findings	Other prior imaging findings	Treatment and follow up
63	9 (4+5)	pT3bR0N0M0	III	PSA still high after RP	0.38	2.23	-	2	2	2	LN metastases left pre-sacral (SUVmax 6.7) and 4 th rib uptake (SUVmax 8.5) highly suspicious of bone metastasis	Pelvic MRI and bone scintigraphy negative	Rib biopsy: positive for PCa metastasis Treatment: HT
73	7 (4+3)	pT3aN1M0	IV	PSA still high after RP	0.26	0.35	-	2	2	2	Small LN right para rectal (SUVmax 1.3), positive on NAC images, suspicious of metastasis	Pelvic MRI: no recurrence	Modification of the RT field including pararectal area. Treatment: RT (prostatic bed and nodes), then PSA<0.05
70	9(4+5)	pT3aN1M0	IV	RP+RT	1.88	1.11	0.6	2	2	2	T5 bone metastasis left anterior (SUVmax 6.6)	CT and bone scintigraphy: negative	Bone MRI: T5 suspicious T5 biopsy: positive for PCa metastasis Treatment: T5 RT and HT, after PSA<0.05
58	7 (3+4)	pT3bN0M0	III	RP	7.80	0.2	11.62	2	2	2	LN metastatic right internal iliac (SUVmax 2.4)	Pelvic MRI and bone scintigraphy negative	Right int iliac LN dissection: positive.
59	7(4+3)	?	?	RT	3.31	47.32	4.1	2	2	2	Local recurrence (SUVmax 4.8) and LN metastasis: obturator, external iliac, common iliac (left: SUVmax 15), peri aortic and infra mediastinal posterior	Chest-abdomen-pelvis CT: no evidence of metastatic disease	Treatment: HT

N= NCCN grade; delay= time between initial treatment and PET (years); PSA level ng/mL; PSA dt = PSA doubling time in months; Scores for

B= blinded reading, UB= unblinded reading, C=consensus reading, LN= lymph node, ?=unknown.