



PET/CT in Gynaecological Cancers

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Outline of this talk

- Cervix cancer
 - Initial staging
 - Treatment monitoring/guidance (RTP)
 - Early detection of recurrence
- Ovarian cancer
 - DD adnexal mass
 - Initial staging
 - Detection of recurrence

Cervix Cancer

- Incidence EU 13/100.000 per year
 - Related to HPV infection
 - Decrease expected in future due to vaccination programs
- Important decrease in mortality rates due to screening programs (PAP smear): detection of early stage disease <-> situation in RSA

Cervical Cancer T-stage

- Based on FIGO classification
 - Stage I limited to cervix
 - Stage II extends beyond the cervix
 - Stage III extends to pelvic wall
 - Stage IV extends into adjacent organs
- ➔ MR = technique of choice
- No additional value for PET due to low anatomical resolution
- FDG uptake correlates with aggressiveness

Cervical Cancer T-stage

Baseline FDG uptake as a prognostic factor

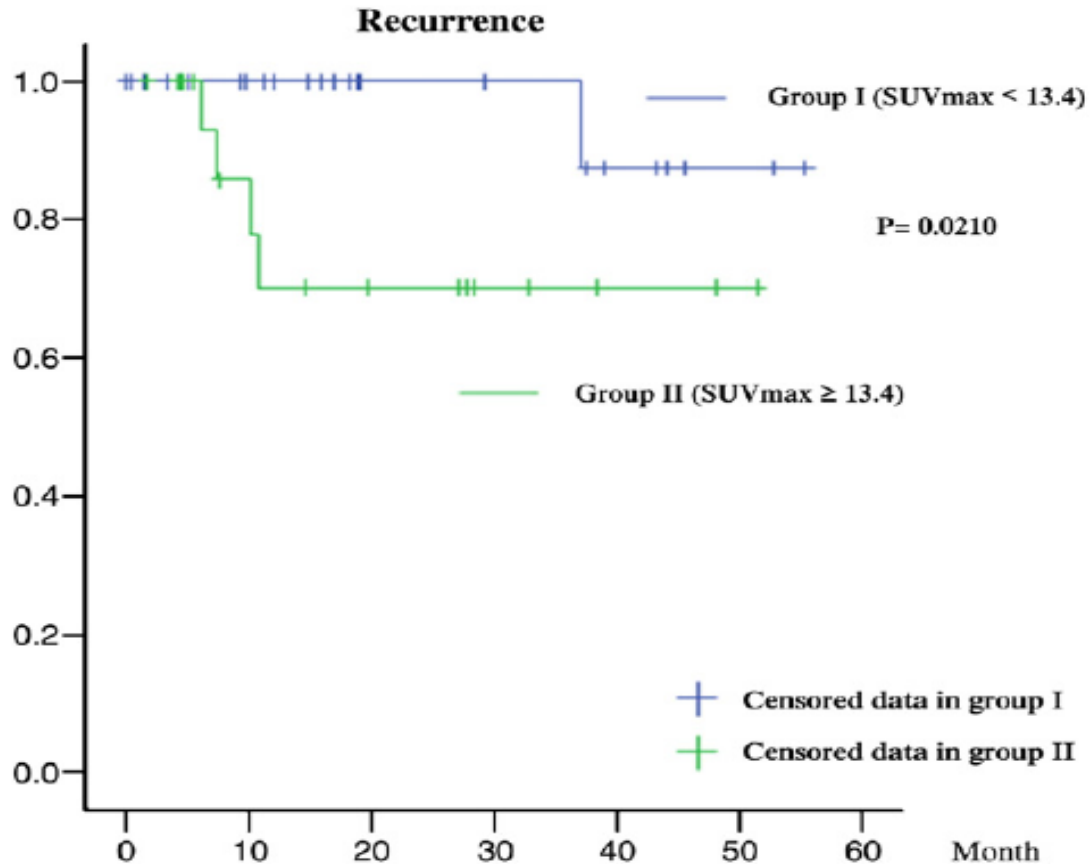


Fig. 1. Recurrence rate according to SUVmax of more than 13.4.

Cervical Cancer – N-stage

- Important prognostic factor for outcome (5y survival)
 - No LN ~ 90-95%
 - Pelvic Nodes + ~ 50%
 - Para-aortic LN ~ 30%
- Predictable pattern
 - Parametrial invasion -> pelvic LN -> PALN
 - Skip LN metastasis very rare (1%), microM+ are frequent
- Historically: surgical staging
- Imaging

PET and PET/CT for Nodal staging

Kitajima et al, Eur Radiol. 2009

- Prospective study in 45 patients with endometrial or cervical cancer with PET/CT prior to lymphadenectomy
- PET/CT on Biograph 16 with optimized protocol
 - Low dose CTAC→PET → diagnostic CT abdomen (IV contrast, 230 mAs, 140 kVp, 2 mm slice thickness)
- Analysis: any uptake > BG projecting in a LN = positive
LN > 1 cm but PET neg is regarded benign

PET and PET/CT for Nodal staging

Kitajima et al, Eur Radiol. 2009

Table 2 Overall patient- and node-based diagnostic accuracy of PET/CT

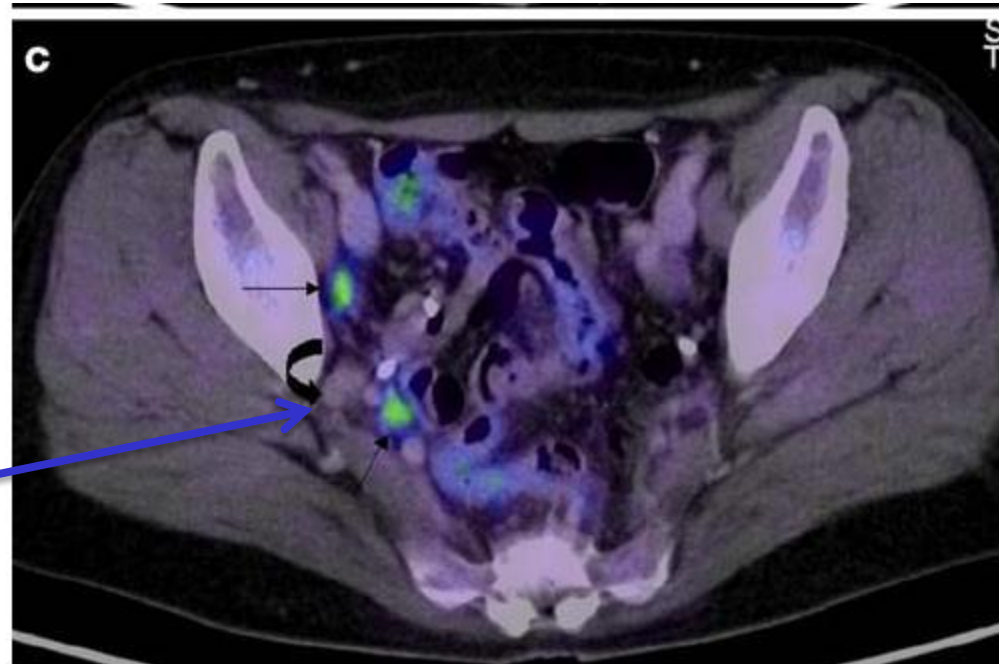
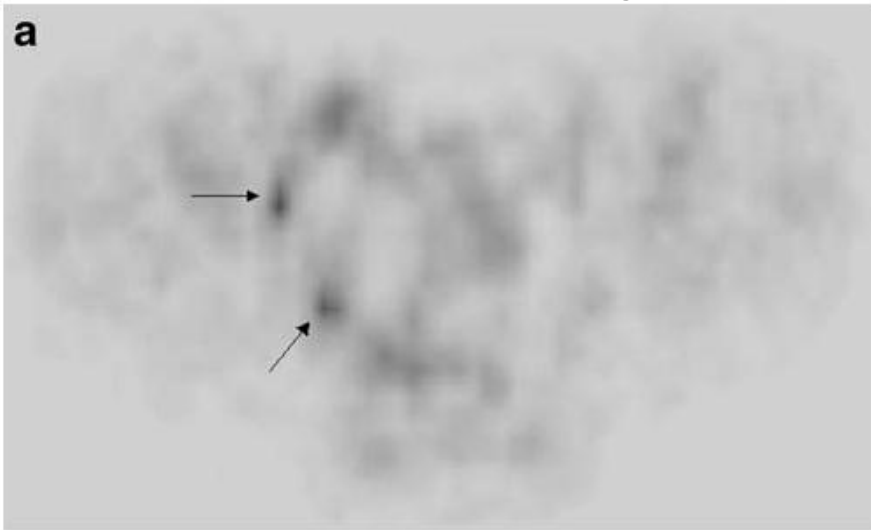
	Sensitivity	Specificity	PPV	NPV	Accuracy
All patients (<i>n</i> =45)	50.0% 6/12	90.9% 30/33	66.7% 6/9	83.3% 30/36	80.0% 36/45
All lymph nodes (<i>n</i> =1,976)	51.1% 23/45	99.8% 1,927/1,931	85.2% 23/27	98.9% 1,927/1,949	98.7% 1,950/1,976
Pelvic lymph nodes (<i>n</i> =1,223)	52.2% 12/23	99.8% 1,198/1,200	85.7% 12/14	99.1% 1,198/1,209	98.9% 1,210/1,223
Paraaortic lymph nodes (<i>n</i> =753)	50.0% 11/22	99.7% 729/731	84.6% 11/13	98.5% 729/740	98.3% 740/753

Table 3 Node-based sensitivity of PET/CT according to the node size

Node size (mm)	Sensitivity (%)
2–4	12.5 (2/16)
5–9	66.7 (16/24)
10–12	100 (5/5)
Total	51.1 (23/45)

PET and PET/CT for Nodal staging

Kitajima et al, Eur Radiol. 2009



False negative lymph node of 9 mm

Cervical Cancer – Nodal Staging

Meta-analysis Choi et al. Cancer Science, June 2010

Table 4. Summary sensitivity and specificity of CT, MRI, and PET or PET/CT

Category	No. of studies	Summary sensitivity, % (95% CI)	Summary specificity, % (95% CI)
Patient-based comparison			
CT	16	50 (43–57)	92 (90–94)
MRI	21	56 (51–62)	91 (90–93)
PET or PET/CT	12	82 (75–87)	95 (93–97)
Region/node-based comparison			
CT	4	52 (42–62)	92 (90–94)
MRI	9	38 (32–43)	97 (97–98)
PET or PET/CT	8	54 (46–61)	97 (96–98)

Table 5. Pair-wise comparisons between modalities for sensitivity, specificity, AU

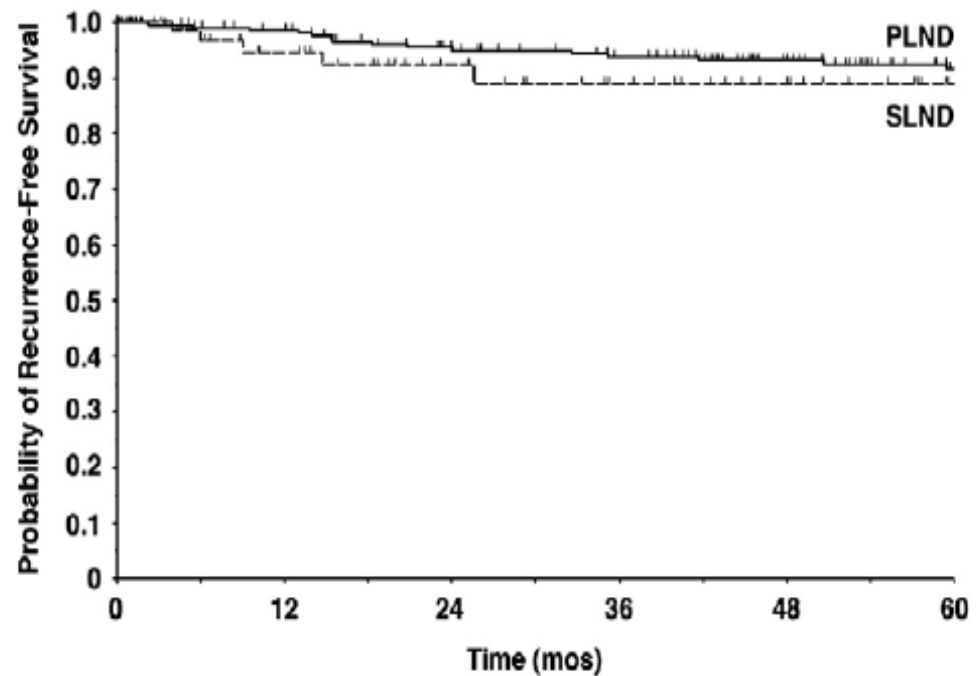
Category	Sensitivity	Specificity
Patient-based comparison		
CT vs MRI	50% vs 56% (0.19)	92% vs 91% (0.43)
CT vs PET or PET/CT	50% vs 82% (<0.001†)	92% vs 95% (0.04†)
MRI vs PET or PET/CT	56% vs 82% (<0.001†)	91% vs 95% (<0.001†)
Region/node-based comparison		
CT vs MRI	52% vs 38% (0.02†)	92% vs 97% (<0.001†)
CT vs PET or PET/CT	52% vs 54% (0.75)	92% vs 97% (<0.001†)
MRI vs PET or PET/CT	38% vs 54% (<0.001†)	97% vs 97% (1.00)

Sentinel Node Imaging in Cervical Cancer

L. Gortzak-Uzan et al. Gynecologic Oncology 116 (2010) 28–32

Prospective study 3:1 randomisation of SLND vs Pelvic lymphadectomy

	SLN (n = 81)	Control
Mean age (years)	38.2	41.4
Mean tumour size (mm)	6.6	4.7
Histology (%)		
Squamous cell carcinoma	42	47
Adenocarcinoma	42	42
AdenoSquamous carcinoma	16	11
Mean depth of invasion (mm)	6.8	6.4
Positive CLS (%)	43.2	41.7
Stage (%)		
IA	39	9
IB	61	91
LN+	14 (17%)	15 (7%)



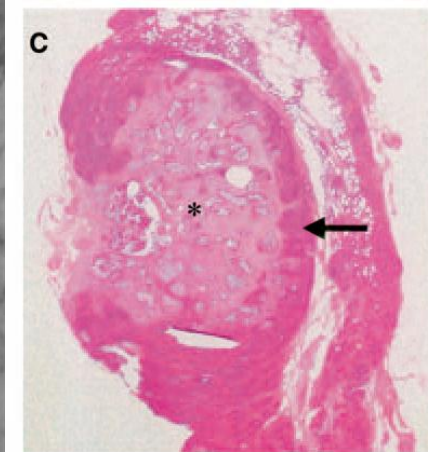
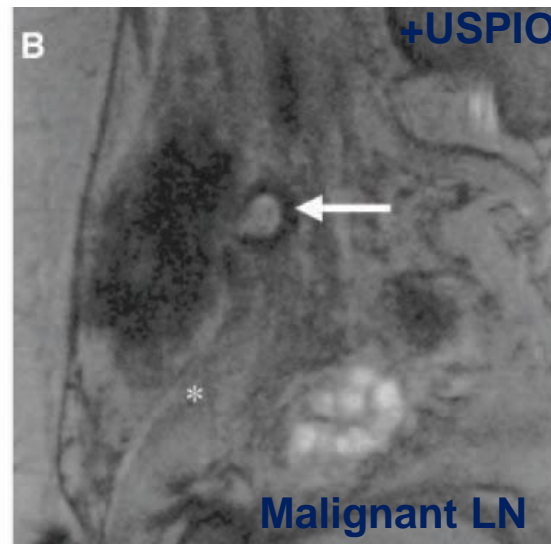
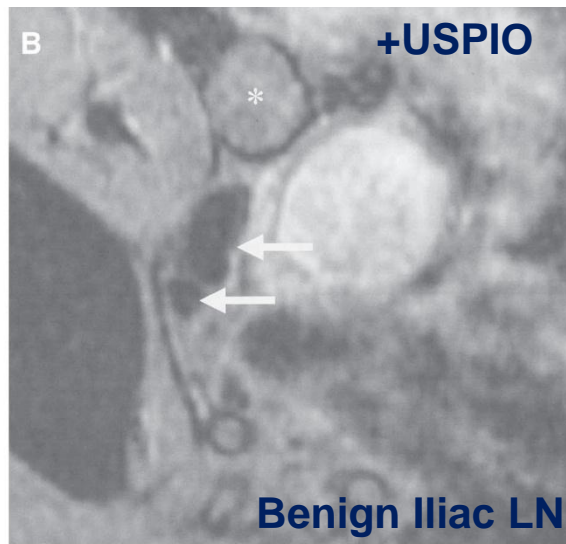
Site	Number of hemipelvises identified 162
Obturator	127 (78%)
External iliac	36 (22%)
Common iliac	18 (11%)
Internal iliac	7 (4%)
Paraaortic	1 (1%)

USPIO-MR for Nodal staging

Rockall et al, JCO 2005

Table 3. Diagnostic Performance of Size Criteria* and USPIO Criteria,† Pelvic Side Wall and Para-Aort

Criteria	No. of Nodes	Histology Negative		Histology Positive		Sensitivity		Specificity		
		TN	FP	TP	FN	Mean	95% CI	Mean	95% CI	
Size, mm										
> 5	335	252	66	10	7	0.59	0.33 to 0.82	0.79	0.72 to 0.86‡§	
> 8	335	311	7	6	11	0.35	0.14 to 0.62‡	0.98	0.95 to 1.00	
> 9	335	316	2	5	12	0.29	0.10 to 0.56‡§	0.99	0.98 to 1.00	
> 10	335	316	2	4	13	0.24	0.07 to 0.50‡§	0.99	0.98 to 1.00	
Size ratio	335	314	4	5	12	0.29	0.10 to 0.56‡§	0.99	0.97 to 1.00	
USPIO										
Reader 1	317	294	9	13	1	0.93	0.66 to 1.00‡	0.97	0.92 to 1.00‡	
Reader 2	316	293	9	14	3	0.82	0.57 to 0.96§	0.97	0.94 to 0.98§	



Nodal PET stage = Important Prognostic factor

Kidd, .. And Grigsby, J Clin Oncology 2010

Evaluation of the prognostic effect of nodal stage on PET in a prospective cohort of 560 patients with newly diagnosed cervix cancer

Table 2. Comparison of Pelvic and Para-Aortic Lymph Node Metastasis by Stage From Combined Historical Data^{3,16-19} and Data From This Study With FDG-PET Lymph Node Staging

FIGO Stage	Pelvic Nodal Metastasis (%)		Para-Aortic Metastasis (%)	
	Historical Data	Current Study	Historical Data	Current Study
I	12-38	9-51	0-5	0-9
IIA	10-45	50	0-12	21
IIB	26-62	54	10-21	17
IIIA	39-59	50	21-33	25
IIIB/IV	39-88	55-85	13-38	27-60

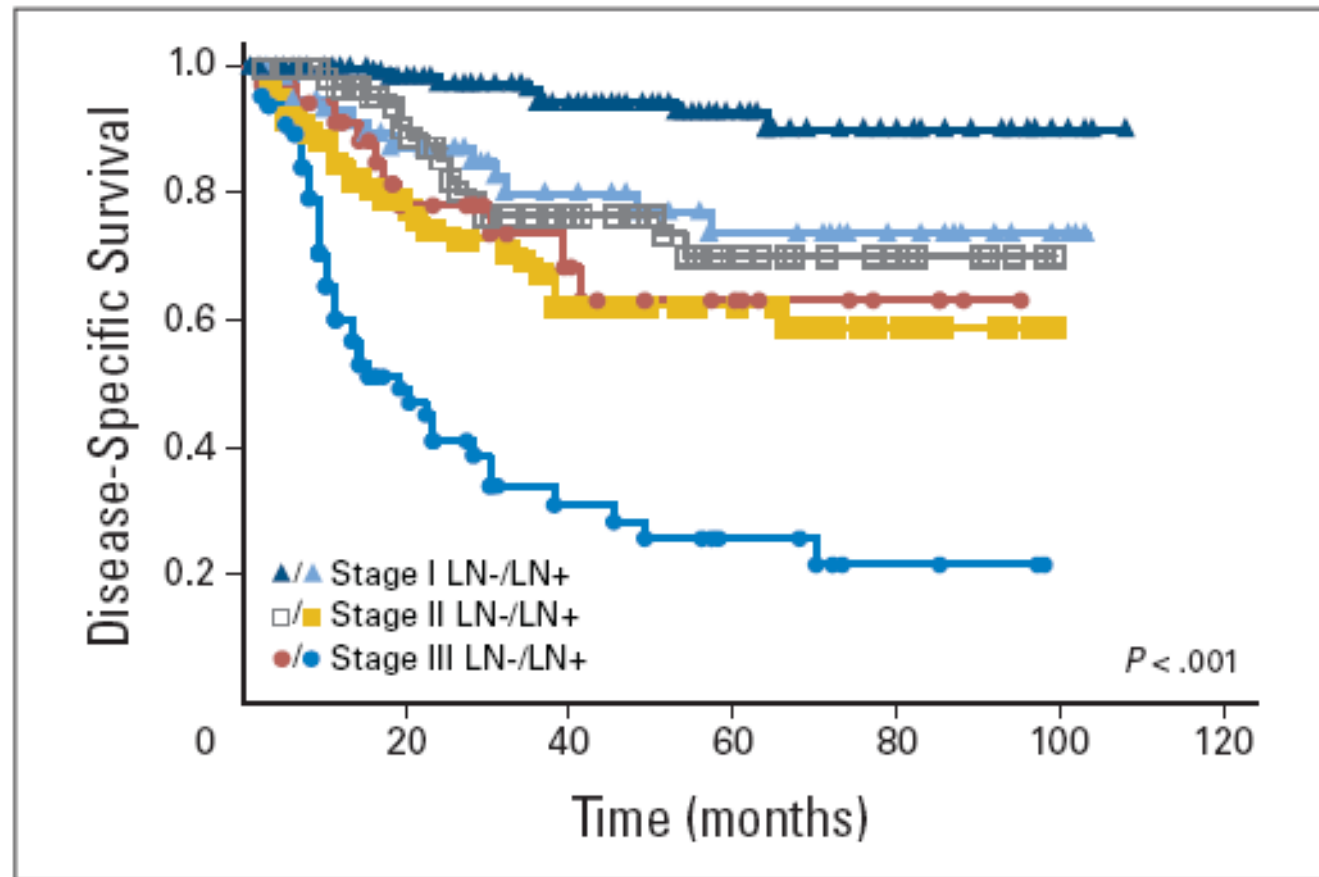
Abbreviations: FDG-PET, positron emission tomography with [¹⁸F]fluorodeoxyglucose; FIGO, International Federation of Gynecology and Obstetrics.

Incidence of PET+ LN is comparable with historical data after surgical staging

Lymph Node Staging by Positron Emission Tomography in Cervical Cancer: Relationship to Prognosis

Elizabeth A. Kidd, Barry A. Siegel, Farrokh Dehdashti, Janet S. Rader, David G. Mutch, Matthew A. Powell, and Perry W. Grigsby

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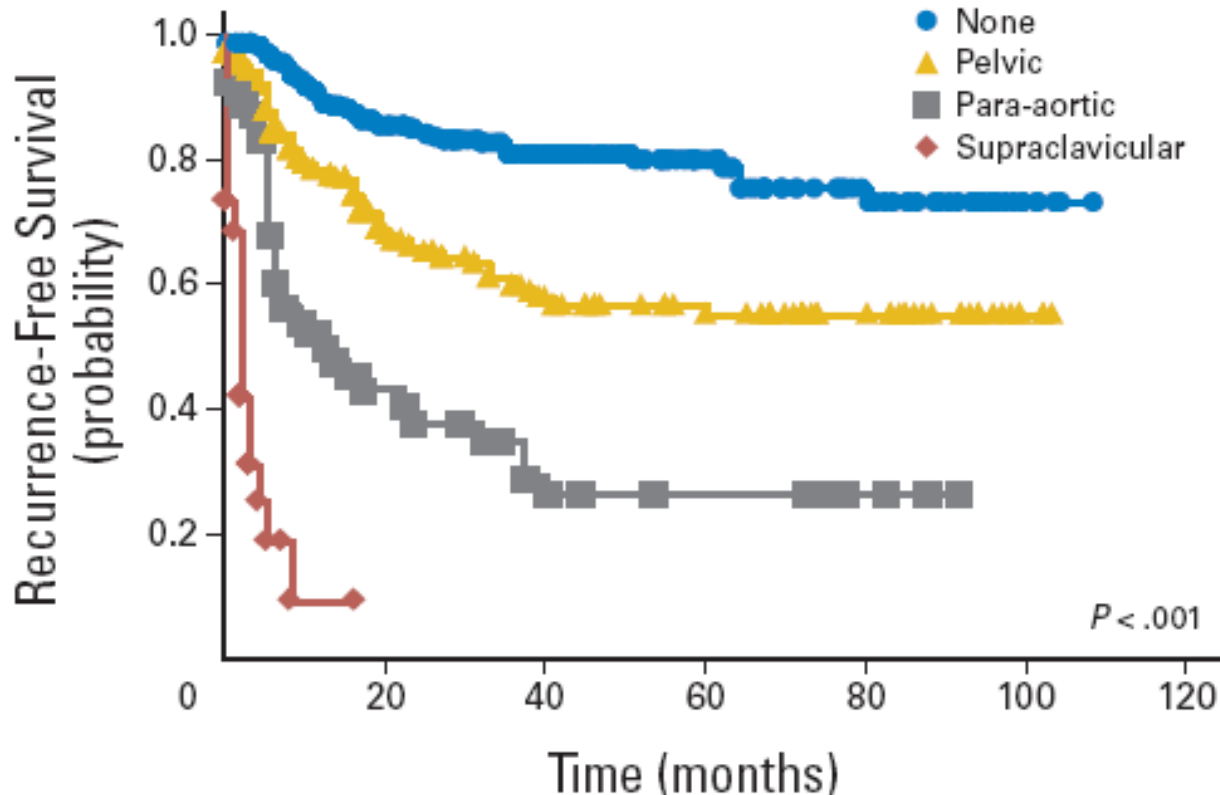


Prognostic effect in every FIGO stage

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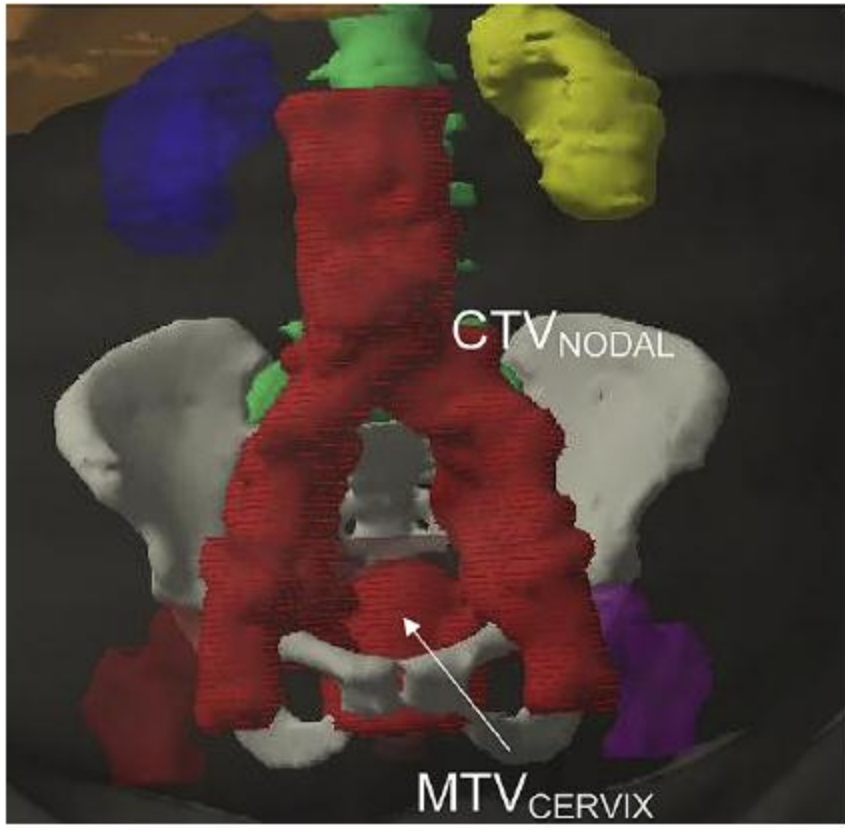


Prognostic effect of highest level of LN involvement independent from FIGO stage

PET/CT guided IMRT for advanced CC

Kidd, ...Grigsby. Int. J. Radiation Oncology Biol. Phys, 1085–1091, 2010

- Clinical outcome of PET/CT based IMRT compared to standard RT in a prospective cohort of 452 patients



Before 2005 (n=317)

Whole pelvis and split-field RT (step-wedge technique) + brachytherapy + Cisplatin (83% of patients)

After march 2005

IMRT + brachy + Cisplatin (89%)

Tumor delineation

Primary T : isocontour 40% SUVmax

LN vessel contouring until highest positive LN level + 7mm margin for CTV LN + 7 mm margin

PTV nodal

Table 1. Patient and tumor characteristics for the IMRT, non-IMRT, and total groups

Characteristic	IMRT	Non-IMRT	Total	<i>p</i> Value
Mean age at diagnosis (y)	52	52	52	
Chemotherapy	120 (89%)	262 (83%)	449	0.2238
Stage				0.7003
Ia2	0 (0%)	2 (0.7%)	2	
Ib1	20 (14.8%)	33 (10.4%)	53	
Ib2	21 (15.6%)	56 (17.7%)	77	
IIa	3 (2.2%)	7 (2.2%)	10	
IIb	58 (43.0%)	126 (39.7%)	184	
IIIa	2 (1.5%)	2 (0.6%)	4	
IIIb	29 (21.5%)	82 (25.9%)	111	
IVa	2 (1.5%)	7 (2.2%)	9	
IVb	0 (0%)	2 (0.6%)	2	
Histology				0.3710
Adenocarcinoma	13 (9.6%)	17 (5.4%)	30	
Adenosquamous	2 (1.5%)	9 (2.8%)	11	
Squamous	117 (86.7%)	286 (90.2%)	403	
Other	3 (2.2%)	5 (1.6%)	8	
Lymph nodes				0.0309
None	68 (50.4%)	131 (41.3%)	199	
Pelvic only	41 (30.4%)	140 (44.2%)	181	
Para-aortic	23 (17.0%)	36 (11.4%)	59	
Supraclavicular	3 (2.2%)	10 (3.2%)	13	

Kidd, ...Grigsby. Int. J. Radiation Oncology Biol. Phys, 1085–1091, 2010

PET/CT guided IMRT for advanced CC

Kidd, ...Grigsby. Int. J. Radiation Oncology Biol. Phys, 1085–1091, 2010

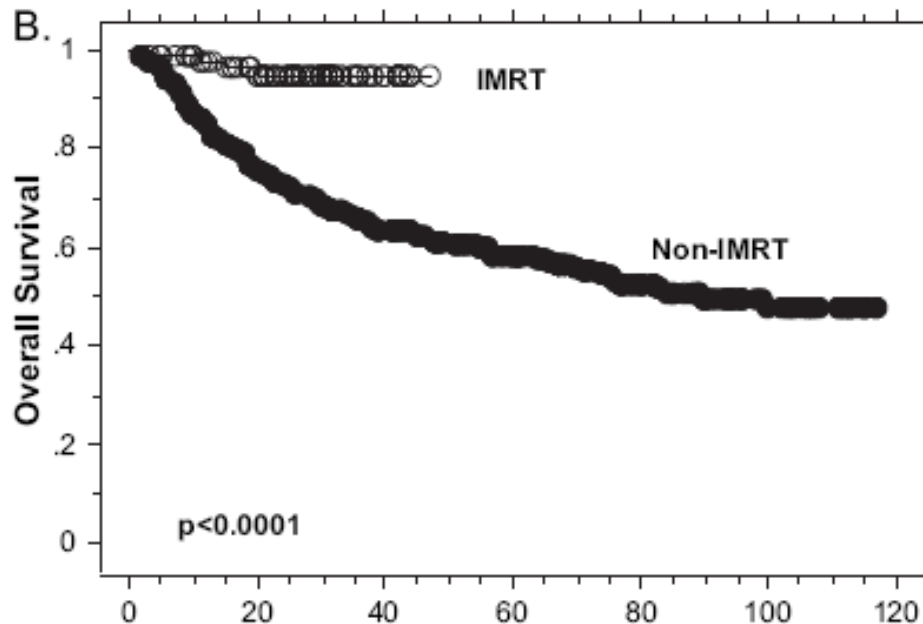


Table 4. Grade 3 or greater gastrointestinal and genitourinary complications in study group

Complication	IMRT group	Non-IMRT group	Total
Rectovaginal fistula	2	12	14
Vesicovaginal fistula	0	11	11
Small bowel obstruction	2	7	9
Large bowel obstruction	2	5	7
Cystitis, Grade 4	1	5	6
Rectal ulcer	1	5	6
Ureteral stricture	0	4	4
Rectal stricture	0	2	2
Proctitis, Grade 4	0	2	2
Ischemic colitis	0	1	1

Table 2. Distribution of recurrences for the IMRT, non-IMRT, and total groups

Recurrence	IMRT	Non-IMRT	Total	<i>p</i> Value
Overall	39 (28.9%)	139 (43.8%)	178	0.036
Pelvic	11 (8.1%)	33 (10.4%)	44	
Distant	21 (15.6%)	78 (24.6%)	99	
Both	7 (5.2%)	28 (8.8%)	35	

Detection of recurrence

- Most patients relapse within first 2 year
- Early detection essential for salvage therapy
- How?
 - No reliable tumor marker
 - PAP smear can be FP after RT
 - CT/MR difficult post RT/surgery
- Indication for PET/CT?

Detection of recurrence

Table 3 FDG–PET for posttherapy surveillance and recurrence

	<i>n</i>	Study	Imaging modality	Symptom?	Site of relapse	Se	Sp	Recurrence confirmation
Lai et al. ⁴⁸	45	P	PET vs MRI	Yes	Overall	0.91	0.98	Histo/follow-up
Yen et al. ¹⁰¹	55	R	PET vs CT/MRI	Yes	Overall	0.89	0.98	Histo/follow-up
Chang et al. ⁹⁵	27	P	PET vs CT	Yes	Overall	0.94	0.78	Histo/follow-up
Havrilesky et al. ⁹²	50	R	PET	Yes	Overall	0.86	0.87	Histo/follow-up
Unger et al. ⁷¹	47	R	PET	No (<i>n</i> = 21)	Overall	0.8	1.00	Histo/follow-up
			PET	Yes (<i>l</i> = 26)	Overall	1.00	0.86	
Sun et al. ⁹⁰	20	R	PET	Yes	CPR	0.86	0.92	LND/follow-up
					PELN	1.0	0.94	
					PALN	1.0	1.0	
Park et al. ¹⁷	36	R	PET	No	CPR	1.00	0.94	Histo/follow-up
Husain et al. ⁹⁷	20	P	PET	Yes	Extra-pelvic	1.00	0.73	Histo/follow-up
Wong et al. ¹⁵	41	R	PET	Yes	CPR	0.82	0.97	Histo/follow-up
					Distant	1.00	0.90	
Chung et al. ⁹⁵	121	R	PET	Yes	Overall	0.96	0.84	Histo/follow-up
Chung et al. ⁹⁴	52	R	PET–CT	Yes	Overall	0.90	0.81	Histo/follow-up
Chang et al. ⁹⁶	20	P	PET	Serum SCC elevation	Overall	0.97	–	Histo/follow-up
Sakurai et al. ⁸²	25	R	PET	Yes	Overall	0.91	0.57	Histo/follow-up
Ryu et al. ⁹⁹	249	R	PET	No	Overall	0.90	0.73	Histo/follow-up

Se: sensitivity, Sp: specificity, R: retrospective, P: prospective, SLN: sentinel lymph node, CPR: centropelvic relapse, PELN: pelvic lymph node, PALN: para-aortic lymph node, histo: histological examination.

Can PET with diagnostic CT do beter?

Kitajima, EJNMM 2009

Table 1 Patient and tumour characteristics

Characteristic	Uterine cervical cancer	Endometrial cancer	Total
Number	50	40	90
Age (years)			
Median	58	60	59
Range	37–82	38–78	37–82
Stage ^a			
I	14	8	22
II	13	12	25
III	19	16	35
IV	4	4	8
Original histology			
Squamous cell carcinoma	43	–	43
Adenocarcinoma	5	–	5
Adenosquamous cell carcinoma	2	4	6
Endometrioid adenocarcinoma	–	33	33
Clear-cell carcinoma	–	2	2
Serous papillary adenocarcinoma	–	1	1
Primary treatment			
Surgery	10	12	22
Surgery + chemotherapy	10	17	27
Surgery + chemoradiotherapy	20	9	29
Chemoradiotherapy	10	2	12
Time from last treatment to PET/CT study (months)			
Median	19	18	17
Range	6–70	6–61	6–70

^a International Federation of Gynecology and Obstetrics (FIGO) stage.

Detection of recurrence

Kitajima, EJNMM 2009

A. Patient – based Analysis (N=90)

Table 2 Patient-based diagnostic results of PET alone, CT alone, and PET/CT

Modality	True-positive	False-negative	True-negative	False-positive	Sensitivity (95% CI)	Specificity (95% CI)	Accuracy (95% CI)
PET	35	9	34	12	79.5 (67.6–91.4)	73.9 (61.2–86.6)	76.7 (68.0–85.4)
CT	30	14	40	6	68.2 (54.4–81.9)	87.0 (77.2–96.7)	77.8 (69.2–86.4)
PET/CT	40	4	43	3	90.9 (82.4–99.4)	93.5 (86.4–100)	92.2 (86.7–97.8)

B. Region based Analysis (N=900)

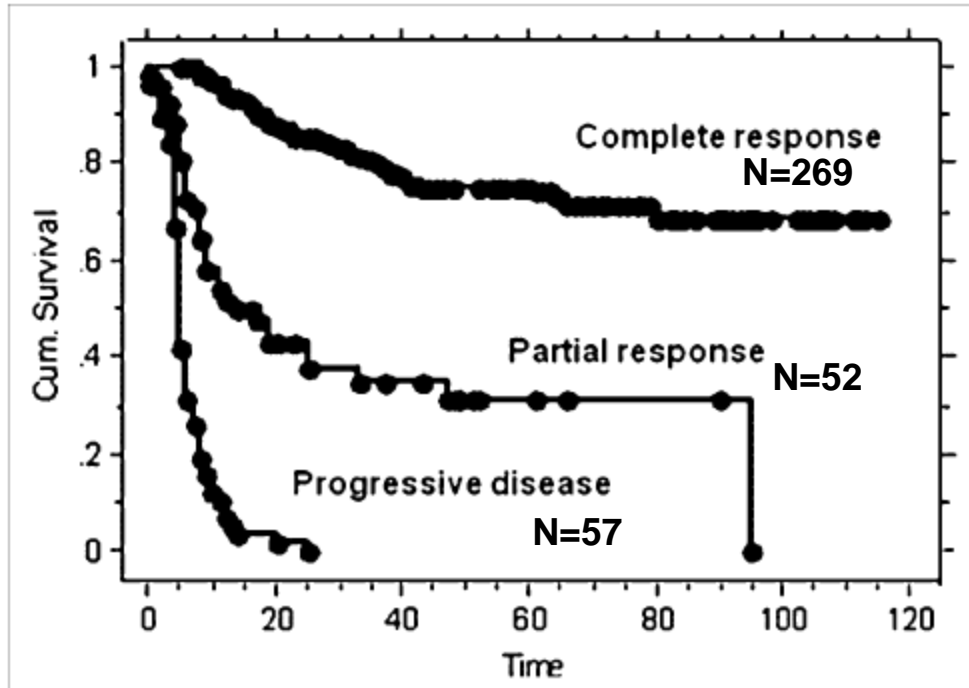
	Sens (%)	# FN	Spec (%)	# FP	Acc (%)
PET	71,4	18	97,7	19	95,9
CT	60,3	25	99	8	96,3
PET/CT	90,5	6	99,5	4	98,9

PET/CT FN = submm lesions; FP = bowel uptake, sarcoidosis, degenerative bone disease
PETonly FP mostly due to bowel and ureter uptake mimicking disease

Change in patient management in 38/90 patients (42%)

PET for Response evaluation

- Identify patients with residual disease early to allow salvage surgery
- Schwarz et al. JAMA 2007
 - Retrospective analysis in 378 patients, PET before and 3 m after CRT



Pilot Study in 36 pts of PET during therapy

After 4 weeks,: 4,SD, 26 PR and 6 CR

3m post CRT : 3 PD, 1 PR and 29 CR

Optimal Timing and threshold?

If confirmed adapt therapy early

- boost

- other chemo

Use of PET/CT in Uterine Cervical Cancer

Conclusions

Early stage Cervical Cancer

- no indication for PET/CT
- Sentinel Node biopsy?

Locally advanced cervical cancer

- recommended PET/CT for staging (N+/M+)
 - include all PET+ LN in PTV
- Early response assessment (3 m post R/) to guide additional therapy
- Investigational: PET during therapy

Detection of recurrence

- PET/CT is technique of choice

PET-CT in Ovarian Cancer

- Characterization of ovarian lesions
- Initial Staging
- Recurrence

Asymptomatic Adnexal Masses: Correlation of FDG PET and Histology

Fenchel et al Radiology, 2002

- 99 pts asymptomatic mass on abdominal US underwent PET, MR and transvaginal US

TABLE 4
Statistical Results

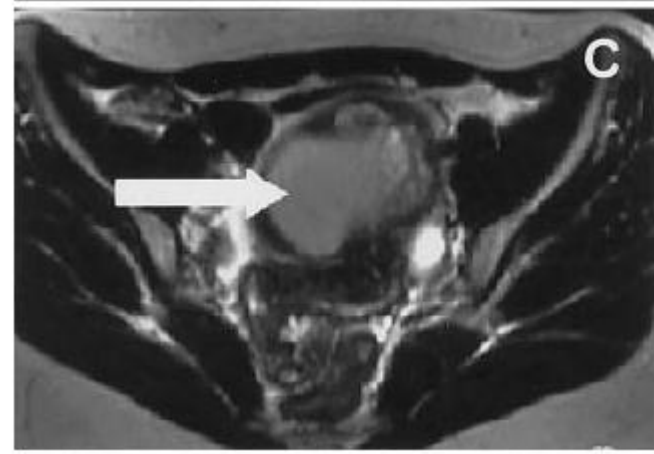
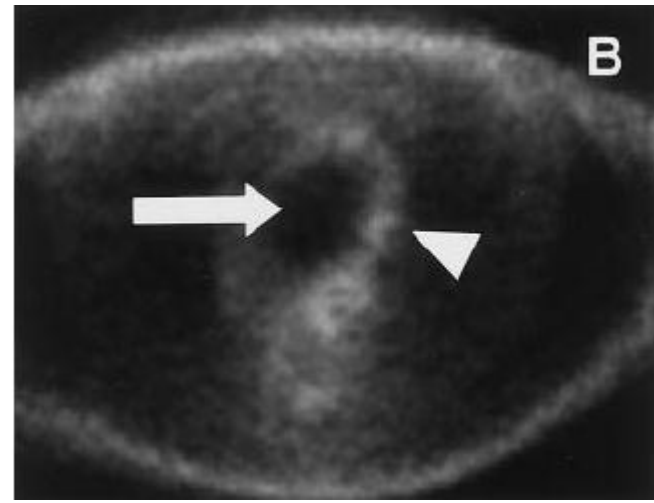
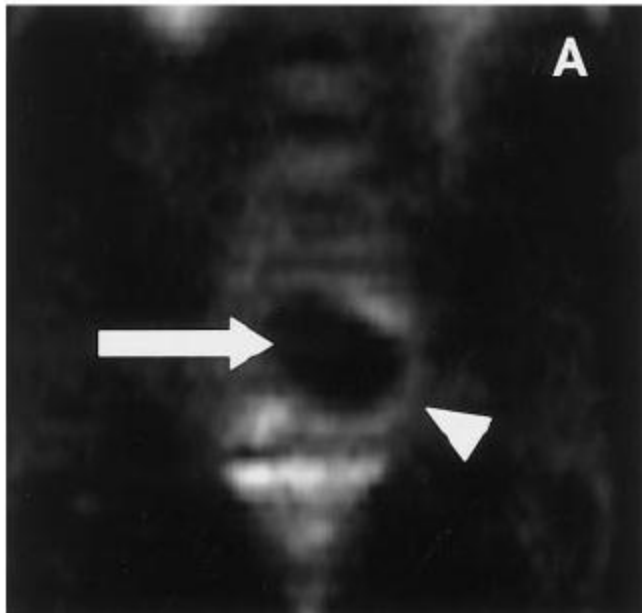
Modality	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Accuracy
FDG PET	58 (27.7, 84.8)	76 (65.5, 84.4)	25 (10.7, 44.9)	93 (84.3, 97.9)	74 (63.9, 82.1)
Transvaginal US	92 (61.5, 99.8)	60 (48.7, 70.1)	24 (12.6, 38.8)	98 (89.9, 100)	64 (53.4, 73.1)
MR imaging	83 (51.6, 97.9)	84 (74.5, 90.9)	42 (24.4, 65.1)	97 (90.7, 99.7)	84 (75.1, 90.5)
Combination of FDG PET, US, and MR imaging	92 (61.5, 99.8)	85 (75.8, 91.8)	46 (25.5, 67.2)	99 (92.8, 100)	86 (77.4, 92.0)

Note.—Data are expressed as percentages. Data in parentheses are 95% CIs.

- 7/12 cancers were detected. FN in 5 pT1a cystadenocarcinomas
- 66/87 benign masses were TN. FP uptake in inflammation, schwannoma, corpus luteum cysts)

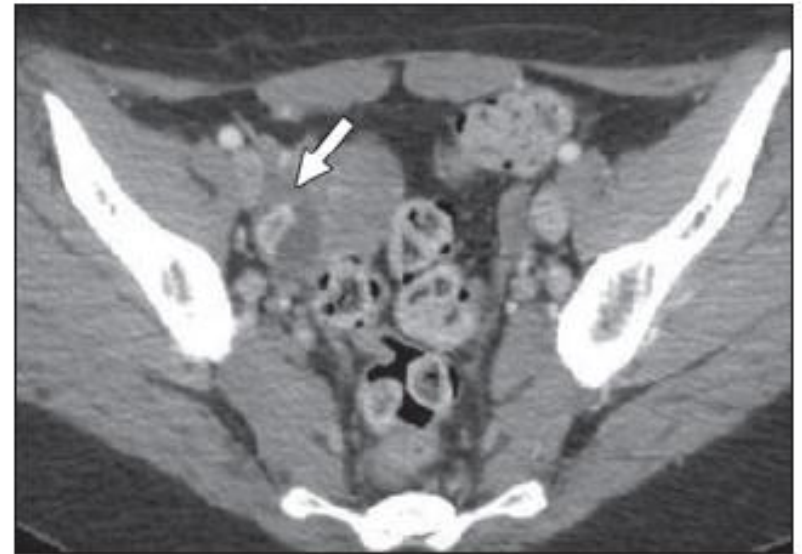
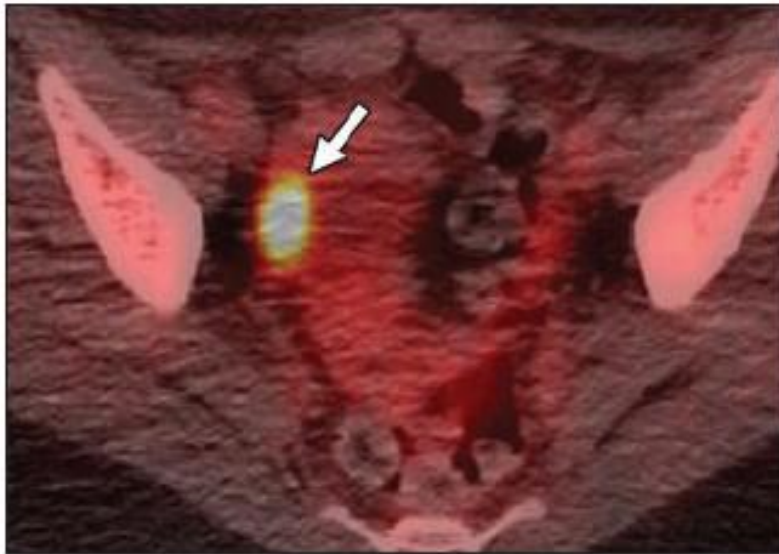
Asymptomatic Adnexal Masses

Fenchel et al Radiology, 2002



Cystic endometrioma presents as a photopenic defect without elevated FDG uptake. The tumor is surrounded by gastrointestinal activity

Luteal cyste



PET for initial Staging of Ovarian Cancer

- Patients often present with already advanced stage disease at diagnosis due to lack of specific symptoms.
 - linked to a poor prognosis (5y survival)
 - 20–40% for stage III
 - 10% for stage IV
- Accurate staging important to define optimal treatment strategy (debulking)
 - Presence and location of peritoneal spread
 - Nodal involvement
 - Extra-abdominal or liverinvolvement

PET for detection of Peritoneal Carcinomatosis

Pfannenbergh et al, Annals of Surg Oncol 2009

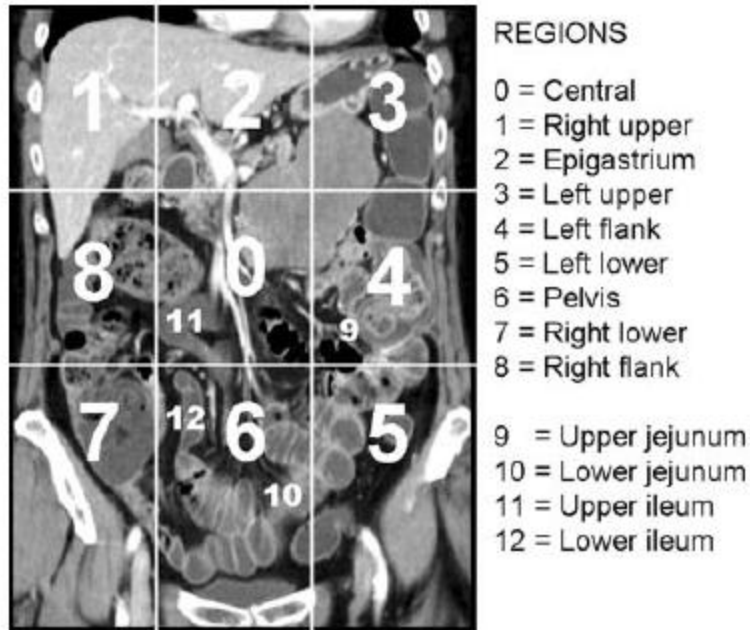
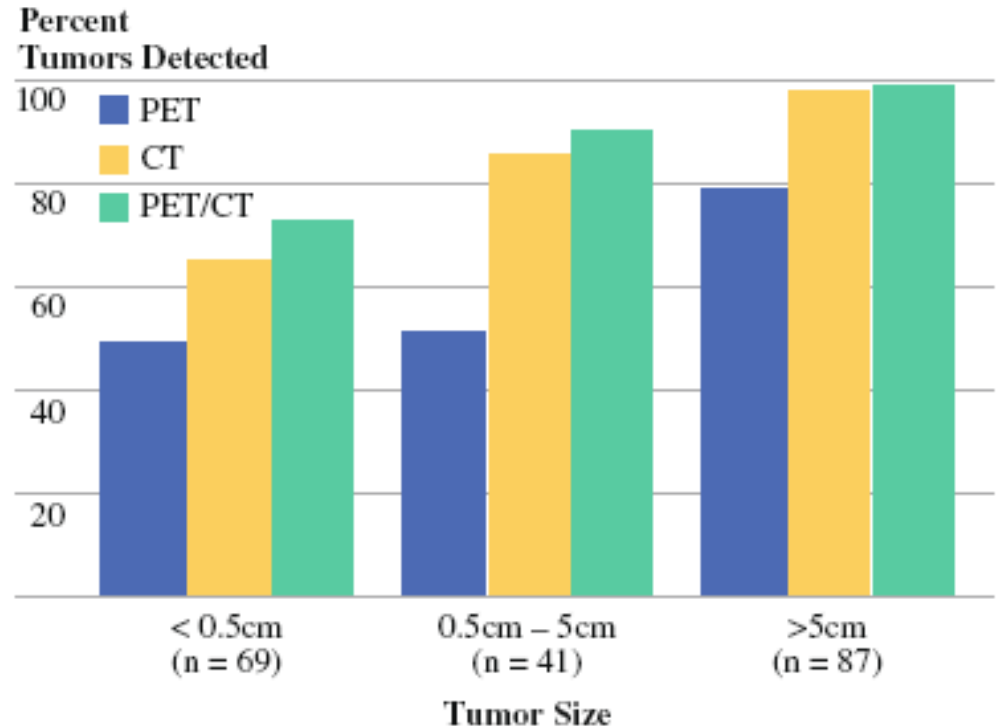


FIG. 1 Abdominopelvic regions 0–12 according to the Peritoneal Cancer Index (PCI)



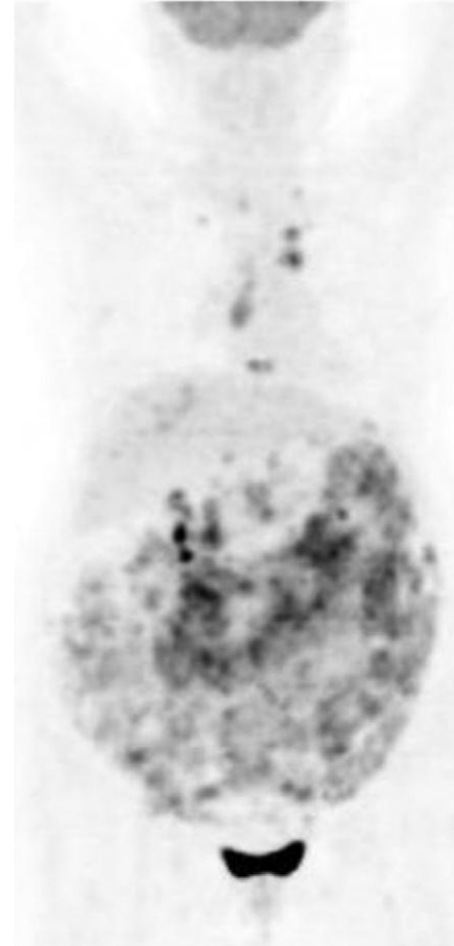
higher amount of PET/CT false negatives with nodules smaller than 0.5 cm. This is particularly true in upper abdomen quadrants including the hepatic dome (Q1), epigastrium (Q2) and left upper abdomen (Q3).

PET/CT for detection of Peritoneal carcinomatosis

Pfannenbergh et al, Annals of Surg Oncol 2009



PET/CT for detection of Peritoneal carcinomatosis



PET for initial staging Ovarian cancer

E.J. Nam et al / Gynecologic Oncology 116 (2010) 389–394

Table 2

Sensitivity, specificity, positive predictive value (PPV), and negative predictive values (NPV) in PET/CT, Doppler US, and CT or MRI in evaluating ovarian and adnexa, extra-ovarian pelvis, and abdomen and beyond lesions.

Anatomical region	Validity parameters	PET/CT (%)	CT or MRI (%) ^a	P value	Doppler US (%)	P value
Ovaries and adnexa	Sensitivity	97.9	95.2	0.391	89.7	0.045
	Specificity	73.7	45.5	0.050	53.3	0.125
	PPV	90.2	83.3	0.247	83.3	0.191
	NPV	93.3	66.7	0.153	66.7	0.016
Extra-ovarian pelvis and abdomen	Sensitivity	94.6	94.1 ^a	0.604		
	Specificity	82.8	71.4 ^a	0.900		
	PPV	87.5	94.1 ^a	0.144		
	NPV	92.3	71.4 ^a	0.505		
Lymph nodes	Sensitivity	83.8	62.5	0.074		
	Specificity	92.6	83.6	0.113		
	PPV	81.6	60.0	0.083		
	NPV	93.6	85.0	0.097		

^a MR imaging was adequate for analyzing pelvis and retroperitoneal lesion, not for abdominal implants. Therefore, comparison of extra-ovarian pelvis and abdomen lesion was made between PET/CT and CT.

Detection of recurrence – Ovarian Cancer

- High likelihood of relapse after initial therapy especially in locally advanced stages (\geq IIB)
 - 75% of the clinical responders
 - 50% of pCR
- Cure rates after salvage therapy limited
 - Clinical FU and CA-125
 - Imaging on indication
 - Detection of recurrent disease eligible for secondary cytoreductive surgery

Detection of recurrence – Ovarian Cancer PET results

Table 5. Diagnostic reliability of FDG-PET in the detection of recurrent disease in patients with epithelial ovarian cancer

Author	Patients (n)	SE (%)	SP (%)	PPV (%)	NPV (%)
Kubik-Huch <i>et al.</i> ⁽⁸⁵⁾	10	100	50	89	100
Yen <i>et al.</i> ⁽¹¹⁷⁾	24	91	92		
Chang <i>et al.</i> ⁽¹¹⁸⁾	28	95	87		
Torizuka <i>et al.</i> ⁽¹¹⁹⁾	25	80	100	100	55
Takekuma <i>et al.</i> ⁽¹²⁰⁾	29	85	100	100	43
Nakamoto <i>et al.</i> ⁽¹²¹⁾	12	80	50	89	33

Table 3. Diagnostic reliability of CT in the detection of persistent disease in patients with epithelial ovarian cancer undergoing second-look surgery

Author	Patients (n)	SE (%)	SP (%)	PPV (%)	NPV (%)
Clarke-Pearson <i>et al.</i> ⁽⁷⁷⁾	46	32	77	79	30
Silverman <i>et al.</i> ⁽⁷⁸⁾	48	40	99	96	87
Reuter <i>et al.</i> ⁽⁷⁹⁾	35	84	88	89	83
De Rosa <i>et al.</i> ⁽⁸⁰⁾	58	47	87	84	53
Topuz <i>et al.</i> ⁽⁸¹⁾	52	50	100	100	76
Cho <i>et al.</i> ⁽⁸²⁾	21	54	99	97	91
Picchio <i>et al.</i> ⁽⁸³⁾	25	70	83	89	59

Detection of recurrence – Ovarian Cancer

PET/CT results

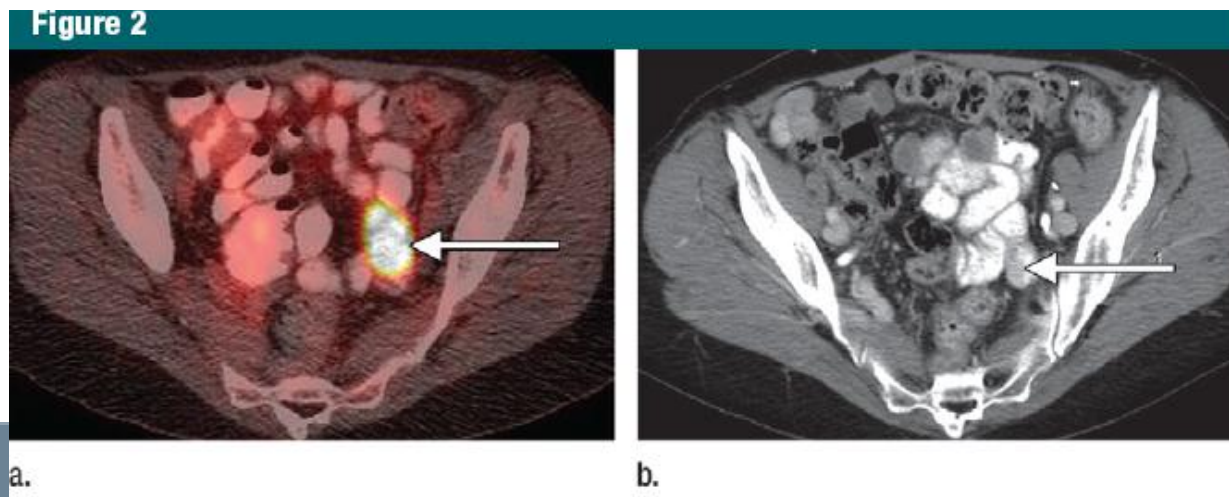
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Table 3 FDG PET/CT results in the detection of recurrent ovarian cancer in relation to indications for the FDG PET/CT scan

Indication	No. (%) of patients	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	Median CA-125 level (U/ml)	Median follow-up (months)
Elevated CA-125 level and negative or indeterminate CT scan	21(35)	95	NA	95	NA	90.4	208	30.6
Elevated CA-125 level and abnormal CT scan	17(28.3)	94.1	NA	100	NA	94.1	137.6	24.4
Clinical symptoms and normal CA-125 level with abnormal CT scan	18(30)	100	100	100	100	100	13.4	26.9



PET/CT in Ovarian Cancer

Conclusions

- DD diagnosis of ovarian masses
 - Limited value
- Primary staging
 - Sensitivity for peritoneal carcinomatosis too low
 - Only in equivocal CT cases, exclusion LN involvement of stage IV disease
- Detection of recurrence
 - Technique of Choice in in case of clinical symptoms or rising CA-125 levels with normal or equivocal CT findings.