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Utility of PET-CT to Evaluate Retroperitoneal Lymph Node Metastasis in Advanced Cervical Cancer: Results of ACRIN6671/GOG0233 Trial

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Abstract

Objective—To assess if FDG PET combined with diagnostic CT improves diagnostic CT accuracy to detect lymph node (LN) metastasis in advanced cervical cancer.

Methods—A prospective HIPAA compliant ACRIN/GOG multicenter trial was conducted. Patients underwent concurrent diagnostic contrast-enhanced CT (DCT) and PET and pelvic/

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abdominal lymphadenectomy. Seven independent blinded readers reviewed PET-DCT and DCT one-month apart. Reference standard was surgically removed LN pathology. Accuracy values were calculated at participant level, correlating abdominal (right and left para-aortic/common iliac) and pelvic (right and left external iliac/obturator) LN regions with pathology, respecting laterality.. Reader average sensitivities/specificities of PET-DCT vs. DCT were compared with generalized linear mixed models, and AUCs with Obuchowski's method.

Results—One hundred fifty-three patients had PET-DCT and pathology. Forty-three of 153 patients had metastasis to abdominal LNs. Sample size calculation required review of the first 40 abdominal positive and 40 randomly selected abdominal negative studies. Patients were 24 to 74 years (48.9 ± 10.6) old. Mean sensitivities of PET-DCT/DCT for detection of LN metastasis in abdomen were 0.50 (CI: 0.44, 0.56) and 0.42 (CI: 0.36, 0.48), ($p=0.052$) and in pelvis 0.83 (CI: 0.78, 0.87) and 0.79 (CI: 0.73, 0.83) ($p=0.15$). Corresponding specificities were 0.85 (CI: 0.80, 0.89) and 0.89 (CI: 0.84, 0.92) ($p=0.21$) and 0.63 (CI: 0.54, 0.70) and 0.62 (CI: 0.53, 0.69) ($p=0.83$). Mean AUC values were 0.70 (CI: 0.61, 0.79) and 0.68 (CI: 0.59, 0.77) ($p=0.43$) and 0.80 (CI: 0.71, 0.88) and 0.76 (CI: 0.67, 0.85) ($p=0.21$) respectively.

Conclusion—Addition of PET to DCT resulted in statistically borderline increase in sensitivity to detect LN metastasis in abdomen in advanced cervical cancer.

Keywords

Cervical cancer; Lymph node metastasis; PET-CT; CT

INTRODUCTION

Nonsurgical therapy fails to control loco-regional disease in 20%–85% of patients with locally advanced cervical carcinoma [1–6]. This may be due to clinical under-staging related to undiagnosed lymph node (LN) metastases in the abdomen in many instances [7, 8, 9]. Currently, the presence of LN metastasis is evaluated by CT and MRI. A recent meta-analysis does not show significant difference between CT and MRI with positive-predictive value of CT being 60% and the negative-predictive value being 91% for detection of retroperitoneal LN metastasis [10].

The 2008 annual report of the U.S. National Oncologic PET Registry (NOPR) indicated that out of 81,951 PET studies conducted at 1368 facilities, 8,362 studies (10.2%) were performed on gynecological tumors [11].

Several reports have shown that PET using [^{18}F]fluorodeoxyglucose (FDG) is useful for evaluation of LN metastasis [12–16]. In a meta-analysis for cervical cancer, pooled sensitivity and specificity of PET for para-aortic LN metastasis were 0.84 and 0.95 and for pelvic LN metastasis were 0.79 and 0.99, respectively [12]. A more recent meta-analysis of the literature that was published prior to 2007 showed that PET or PET-DCT had pooled sensitivity of 82% and specificity of 95%, while CT had 50% and 92%, and MRI had 56% and 91%, respectively for detection of pelvic LN metastasis on patient-based analysis [17].

There is no published multicenter trial on the accuracy of PET combined with contrast-enhanced diagnostic CT (DCT) to detect LN metastasis in the abdomen and pelvis, and its

correlation with a contrast-enhanced diagnostic CT, in a cohort of patients with uterine cervical cancer.

There is some data suggesting therapeutic effect of lymphadenectomy in advanced cervical cancer management [18, 19, 20]. We conducted a prospective multicenter clinical trial sponsored by ACRIN (American College of Radiology Imaging Network) and GOG (Gynecology Oncology Group) to evaluate the efficacy of PET-DCT in the evaluation of LN metastasis in women with high-risk endometrial cancer and loco-regionally advanced cervical cancer. Here, we report the result from the loco-regionally advanced cervical cancer cohort; the high-risk endometrial cancer cohort will be reported separately. The primary objective of the study was to determine the accuracy of PET-DCT to detect retroperitoneal LN metastasis in abdomen in loco-regionally advanced cervical cancer patients.

MATERIALS & METHODS

Study Population

This is a HIPAA compliant non-randomized prospective multicenter study, which was approved by institutional review board (IRB) of each institution that participated in this trial and was conducted by ACRIN/GOG. All patients consented to participate in the study.

Patients with primary, histologically confirmed, untreated loco-regionally advanced (FIGO stages IB2, IIA2, IIB-IVA) invasive carcinoma of the cervix who had no contraindication to surgery were accrued. Patients underwent extra-peritoneal or laparoscopic pelvic and abdominal LN sampling within 2 weeks after PET-DCT. We excluded patients who had metastasis outside of the pelvis or abdominal LNs, prior pelvic radiation therapy or prior pelvic or abdominal lymphadenectomy, or other malignancies within the last 5 years. Figure 1 shows trial schema.

Imaging Protocol

All patients underwent FDG PET-DCT prior to surgery. Patients fasted for at least 4 hours and had a blood glucose level less than 200 mg/d prior to FDG injection.

PET imaging was scheduled to begin sixty minute (± 10 min) after 10–20 mCi (0.14–0.21 mCi/kg) of FDG administration. The region imaged extended from the base of the skull to the upper thighs. For DCT, patients received oral contrast and a nonionic intravenous contrast when there was adequate intravenous access and no contradictions to contrast agent. Of the entire cohort accrued, nine patients could not receive intravenous contrast and six oral contrasts. The difference of the trial and the standard of care was to mandate both examinations are done concurrently (more detailed description of the imaging protocol in Appendix S1).

Surgery

Patients underwent lymphadenectomy in eight nodal regions: right and left obturator, right and left external iliac, right and left common iliac, and right and left para-aortic LNs. Right para-aortic LNs included aorto-caval LNs. Upper extent of abdominal aortic region was inferior mesenteric artery. Common iliac extended from aortic bifurcation to common iliac

artery bifurcation. LNs posterior to the iliac vessels and anterior to the obturator nerve were considered obturator LN. LNs anterior or medial to the external iliac vessels were considered external iliac LNs. LNs at boundary region were considered belonging to the region above. PET-DCT results were compared with lymphadenectomy results at the region level. Surgeons were required to provide full lymphadenectomy for each of the eight regions. If malignant regional LNs were not resectable, surgeon was expected to perform intra-operative biopsy to confirm LN metastasis. For data analysis, abdominal region included combined para-aortic and common iliac sub-regions; pelvic region consisted of combined external iliac and obturator LN sub-regions. A patient was considered to have pelvic or abdominal malignant lymphadenopathy if there was at least one of the included 4 sub-regions in the pelvis or abdomen involved.

Surgeons had access to the imaging results. Protocol required discussion of the results of PET-DCT with the surgeons to encourage surgeons to remove positive LNs that could potentially be left behind such as nodes posterior to the common iliac vessels or high in the apex of obturator fossa. This was to prevent a potential false positive diagnosis for PET-DCT.

Pathology Analysis

Pathology review was performed at the primary institution of the accrued patients and confirmed at the semiannual GOG meeting by a team of pathologist. Institutional pathologists were all gynecology oncology pathology experts. LNs smaller than 10mm in long axis were bisected into two halves. For nodes equal or longer than 10mm, they were sectioned at 5mm intervals parallel to their short axis, and one slide was prepared from each section. This was done to make sure slice section is not more than 5mm to prevent missing small volume disease. We collected the following data: total number of LNs per sub-region, presence/absence of LN metastasis, and size of the largest focus of involvement in each region was recorded. The latter information was collected since it is the size of focus of involvement that determines detectability on PET.

Central Reader Study Design and Power Analysis—The primary objective of the study was to evaluate the diagnostic sensitivity and specificity of preoperative FDG-PET-DCT imaging in identifying metastases to abdominal (common iliac, para-aortic, and paracaval) lymph nodes in participants with loco-regionally advanced cervical carcinoma. The secondary objectives were sensitivity/specificity values in the pelvis and abdomen and pelvis combined, and comparison of sensitivity and specificity values of FDG-PET-DCT and diagnostic CT. The analysis for the primary aim will utilize diagnostic scan interpretation data obtained via the central reader study, in which all radiologists will interpret all FDG-PET-DCT scans independently and blinded to pathology results. Readers were asked to score LNs of a region from 1 to 6 with 1 being definitely negative and 6 being definitely positive to allow us to create an ROC curve. Reader interpretations were dichotomized into negative (1, 2, 3) and positive (4, 5, 6) in order to compute estimates of reader sensitivity and specificity. Readers were informed about the threshold for positivity that would be used in the analysis. Individual reader's sensitivity or specificity, and the mean sensitivity or specificity across all readers were calculated.

A multi-reader design was used for the assessment of sensitivity and specificity of the FDG-PET-DCT for abdominal lymph node assessment. In this design, several readers interpreted all cases in the reading set. The multi-reader design reduces the number of cases needed when compared to a single reader study and also provides estimates of variability across readers. The number of truly positive and truly negative cases required to achieve appropriate precision in the estimates of mean sensitivity and specificity was calculated by an approach based on an adaptation of the commonly used formulas for multi-reader multi-case study design presented in [22]. Note that the precision of estimates and the statistical power depend on both the number of cases and the number of readers. Using equal number of positive and negative cases is the most efficient design. Our calculation determined that a multi-reader study with 30 positive cases and 30 negative cases, each case read by 7 central readers, will provide adequate precision for the estimates of mean sensitivity and specificity of the FDG-PET-DCT for abdominal lymph node assessment. Assuming an estimate of sensitivity or specificity of 0.7, such sample size will provide an expected half-length of 0.15 of the 95% CI for the sensitivity or specificity.

Assuming that approximately 20% of the enrolled women will have positive nodes in the abdomen and 8% of the accrued patients will not undergo lymphadenectomy, due to the finding of biopsy proven metastatic disease outside of the pelvis or abdominal lymph node regions, we calculated that a total of 165 patients with cervical cancer would be required to provide 30 patients with positive abdominal lymph node.

Readers were informed about the threshold for positivity that would be used in the analysis. Individual reader's sensitivity and specificity, and the mean sensitivity and specificity across all readers were calculated.

All 7 readers were experienced clinical PET readers with range of experience in reading gynecology PET being 10 to 27 years. Four of the seven had previous experience in review of PET-DCT trials and three underwent an initial didactic training for the trial as well as 3 test cases before reviewing study PET-DCTs to familiarize them with filling the forms. PET-DCT readers were blinded to the clinical information and final pathology results and reviews were performed independently. Reviewers were chosen from centers not involved in the accrual of patients. The central review was performed at the ACRIN headquarter PET lab using the same workstation. Review process was arranged in two steps; a) all DCT examinations were reviewed alone without knowledge of PET findings, b) after at least a one- month washout period, both PET and DCT images were reviewed together.

Imaging Review

Instructions on how to determine a LN as positive or negative are detailed in Appendix S2. Figure 2 is an example of a positive LN with mildly increased uptake relative to the uptake in comparable normal structures or surrounding tissues.

Presence/absence of metastatic LNs was recorded during the review of each of the 8 regions. Reviewers were asked to identify the location of involved LN in the abdomen or pelvis if it was outside the 8 regions. A pelvic LN was considered outside the 4 pelvic regions if it was

located in the internal iliac or pre-sacral region. A para-aortic or para-caval LN above IMA was considered an abdominal LN outside the 4 abdominal LN regions.

Statistical Analysis

For the purpose of sensitivity and specificity calculation, 1–3 was considered negative and 4–6 was considered positive. Analysis was made at the patient level considering LN region comparison. PET-DCT results were compared to pathology data. The abdomen and pelvic regions were analyzed separately. The abdomen or pelvis region was considered positive on pathology if at least one of the corresponding four sub-regions had a malignant LN, and negative if all 4 regions were negative. Therefore, data from abdominal or pelvic region was considered analyzable if all 4 regions in the abdomen or pelvis underwent lymphadenectomy unless there was a positive LN removed from one of the four regions.

In order for the reader to get credit for making a correct diagnosis of positive LN, the positive node identified by the imaging should be on the same side as on pathology. Ipsilateral para-aortic/paracaval and common iliac LNs were combined on both PET-DCT and pathology for data analysis. We did the same for external iliac and obturator LNs. The reason being, in spite of anatomical instructions for regional placement of LNs provided to the surgeons, there is a possibility of placing overlapping LNs in the wrong region, i.e. para-aortic or paracaval vs. common iliac and external iliac vs. obturator LNs.

For the calculation of sensitivity, specificity, and AUC, the individual reader scores were used. Seven readers average was used for calculation of test accuracy values.

For each reader, 95% confidence intervals (CIs) for the estimates of sensitivity, specificity were presented as the exact confidence intervals (Clopper-Pearson). Ninety-five percent CIs for the differences in sensitivity and specificity were calculated using the method by Fleiss et al. [23]. P-values for the sensitivity and specificity comparisons were based on McNemar's test statistic. Estimates of 95% CIs and P-values related to AUC were derived by using the DeLong & DeLong method [24] for empirical ROC curve. A p-value of <0.05 was considered significant.

Comparison of the average sensitivity/specificity between DCT alone and PET-DCT of the seven readers was done with a generalized linear mixed model when the reader is treated as random effect. The comparison of average empirical AUCs between DCT and PET-DCT results, from all seven readers, were computed using Obuchowski's method [22]. PET-DCT diagnoses of LN metastasis (yes/no) from the seven readers were compared with Fleiss' Kappa statistics, assuming all observations are independent, for DCT and all PET-DCT scan, and for abdominal, pelvic, and combined abdominal and pelvic regions. The sensitivities or specificities between the seven readers were compared with generalized estimating equation methodology.

RESULTS

Patient Characteristics

One hundred sixty- nine women were accrued to the trial between September 2007 and June 2013 at 22 accruing institutions. Sixty patients were excluded because of PET-DCT poor quality (N=2), PET-DCT not done (N=3), pathology not submitted (N=11), incomplete pathology (N=44) (figure 3). In the 44 patients with incomplete pathology, lymphadenectomy had not been performed in one or more regions in the abdomen with the other regions being negative resulting in incomplete reference standard. Incomplete lymphadenectomy was generally due to technical reasons. Therefore, one hundred and nine patients had complete reference standard available for abdominal LNs (43 positive and 66 negative) and 120 had analyzable reference standard available for pelvis LNs. The prevalence of LN metastasis was 39.4% (43/109) in the abdomen and 57.5% (69/120) in the pelvis. Although the design of the central reader study called for 30 abdominal positive and 30 abdominal negative cases, we included the first 40 positive (out of 43) and 40 (out of 66) randomly selected negative cases to increase the study power. All 80 patients had complete pathology results in the abdomen. Seventy-seven of these 80 patients had complete pathology results in pelvis: 51 were positive and 26 were negative. Of the 80 patients selected for the central reader study, 3 did not have IV contrast because of high serum creatinine.

Fifty-three of 80 (66%) were white, 7 (9%) black, 11 (14%) Asian, and the status of 9 (11%) was unknown. Ages ranged from 24 to 74 years (mean; 48.9 ± 10.6). Stages of the primary were: IB=25, IIA=6, IIB=38 and III=1. Sixty-nine primaries were squamous cell carcinomas, 4 adenocarcinoma, 2 adenosquamous, and 5 others. Tumor grades were: grade 1=3, grade 2=47, grade 3=26, and 4 were unknown. The mean primary tumor size was 6.3 ± 1.4 cm (median; 6.1cm, range 3.7 to 10.9cm based on CT measurement).

Sensitivity, Specificity and AUC of PET-DCT in the Abdomen

The reader average sensitivity, specificity and AUC of PET-DCT for abdominal LNs are shown in Table 1. The sensitivities of PET-DCT ranged from 0.45 to 0.55 for the 7 individual readers. The specificities of PET-DCT ranged from 0.75 to 0.90 for the 7 individual readers... The difference between PET-DCT and DCT sensitivity to detect LN metastasis in the abdomen reached borderline significance ($p=0.052$). The average specificity of PET-DCT was not significantly different from diagnostic CT in the abdomen ($p=0.21$) (Table 1).

Sensitivity, Specificity and AUC of PET-DCT in the Pelvis and Combination of Abdomen and Pelvis

The corresponding values for pelvis and combination of abdomen and pelvis are outlined in Table 2. Although PET-DCT sensitivity to detect LN metastasis in the pelvis was higher than DCT, it did not reach statistical significance ($p=0.15$). Both DCT and PET-DCT had low specificity in the pelvis (62–69% on average). Reader average AUC of combined abdomen and pelvis PET-DCT was statistically significantly higher than DCT ($p=0.03$).

Lymph Nodes Outside of Eight Lymphadenectomy Regions

Amongst 80 cases selected for central review, there were 7 cases that were read by 4 or more reviewers as positive LN above IMA on PET-DCT. They all had positive abdominal LNs below IMA on pathology, which were correctly identified on PET-DCT by 4 or more reviewers. The corresponding numbers for pelvic LNs outside the 4 pelvic lymphadenectomy regions were 9, 8/9 cases had positive LNs in the pelvic lymphadenectomy regions on pathology, all 8 were correctly called by 4 or more of the reviewers but were not removed because they were outside standard lymphadenectomy regions.

Inter-reader variability

Kappa statistics between the seven readers for PET-DCT and DCT review are seen in Table 3. The agreements between the readers are substantial, with kappa statistics ranging between 0.61 and 0.77.

Pathology results of the removed lymph nodes

Each participant had 24.8 ± 12.7 LNs (6.0 ± 6.7 positive and 20.4 ± 11.9 negative) removed. The average number of positive lymph node in abdomen was 1.8 ± 3.7 and 2.6 ± 3.2 in pelvis on pathology. Considering the 7 reader average, the number of positive lymph node identified on PET-DCT was 1.3 ± 2.4 in the abdomen and 1.8 ± 1.5 in the pelvis, all of which were significantly fewer than what was identified on the pathology in abdomen, pelvis, and abdomen and pelvis combined ($p=0.015$, 0.0018 , and 0.0007 respectively).

The size of the largest positive focus was 17.9 ± 13.8 mm in the abdomen (median 15mm) and 22.7 ± 12.8 mm in the pelvis (median 20mm). The sizes of the largest focus was significantly higher in the pelvis ($p=0.001$ by paired t-test).

Sensitivity of PET-DCT in the subset of patients with small positive focus of disease

After dichotomizing the positive LNs identified on pathology by their respective median value of the largest positive focus, PET-DCT had significantly better sensitivity than that of DCT in the pelvis; 81% vs. 71%, $p=0.036$ and in the abdomen and pelvis combined; 81% vs. 71%, $p=0.019$ in the lymph nodes with the largest focus less than the median value. The difference was not significant ($p>0.05$) for the largest positive focus more than the median size.

DISCUSSION

Knowledge of the extent of LN metastasis is important to predict prognosis and determine the radiation field in patients who undergo primary chemo-radiotherapy for loco-regionally advanced cervical cancer. Patients with loco-regionally advanced cervical cancer undergo pelvic radiation in most institutions. The decision for radiation of abdomen is currently based on the use of CT or MRI in most centers around the world [10, 25, 26].

We conducted a multicenter prospective study including patients with loco-regionally advanced cervical cancer. It should be emphasized that our study design required a

diagnostic CT including oral and IV contrast if possible. We planned to determine the sensitivity/specificity of PET-DCT including a diagnostic CT to detect LN metastasis in patients with loco-regionally advanced cervical cancer. The sample size calculation was chosen because of multi-reader multi-case study design (22) in which the study power is dependent on both the number of cases and the number of readers.

The median number of LNs removed in this cohort was 9 in the abdomen and 13 in the pelvis. The reader average sensitivity of PET-DCT was 50%, which was higher than 42% of DCT alone at borderline significance ($p=0.052$). Although this is lower than pooled results in the literature, it is close to the lower end of confidence interval of the most recent meta-analysis of para-aortic LN involvement in a cohort of patients with disease prevalence more than 15%; that was 73% (95%: CI 53%,87%) [27]. That study also showed a heterogeneous sensitivity results ranging from 10% to 72% [26]. We believe the results of this study better reflect performance of PET-DCT considering multicenter design of this study. PET-DCT sensitivity was 83% in the pelvis, which is similar to the available literature but was not statistically significantly higher than 79% of DCT alone. Lower sensitivity in the abdomen is likely due to smaller size of malignant LNs in the abdomen as compared to the pelvis because of sequential pattern of metastasis to the abdomen after pelvis in cervical cancer. Our results show that the sensitivity of PET-DCT was significantly lower when the largest positive focus in the region was less than the median value of the largest positive focus in this study. Specificity of PET-DCT in the abdomen was 85%, similar to the literature but not significantly different from DCT alone ($p=0.21$). Specificity of PET-DCT and DCT in the pelvis was similar ($p=0.83$). This is lower than reported in the literature. We speculate that this may be due to more advanced disease with larger size of the primaries resulting in large reactive LNs presumably secondary to tumor inflammation or infection. There was no significant difference in AUC values of PET-DCT and DCT ($p=0.21$ and 0.43).

Fifteen of 16 cases that had positive LN on PET-DCT outside 8-lymphadenectomy regions, by the majority reviewers, had positive LN in the corresponding abdominal/pelvic lymphadenectomy regions.

Inter-observer agreement for interpretation of PET-DCT was 0.65 in the pelvis and 0.77, which is in the substantial agreement range (0.6 to 0.8).

We would like to emphasize that PET-DCTs in this study included a DCT that was performed concurrently with PET. We recommend use of a DCT along with PET to increase the diagnostic value of PET and eliminate the need for a separate DCT as is suggested in a previous report [28]. However, low sensitivity of detection of LN metastasis in the abdomen does not justify utilization of PET-DCT to determine the upper extent of LN metastasis in a patient population with loco-regionally advanced cervical cancer.

One study limitation is lack of reference standard in all regions in all patients, but this should not affect our results because of the study design. Missing reference standard occurred when some LN regions were not surgically evaluated. This was considered a protocol violation, and occurred for a number of reasons. In some patients, LN dissection was not performed in all regions due to technical reasons, such as problems with

laparoscopic equipment or poor visualization, and in other patients due to retroperitoneal fibrosis. In the absence of all-regions lymphadenectomy, if one region in the abdomen or pelvis was positive, abdomen or pelvis was considered positive. However, to consider abdomen or pelvis negative, all four regions needed to be negative, otherwise, abdomen or pelvis was counted as incomplete reference standard in that patient. The added value of PET-DCT based on detection of disease outside LNs is not reported in this manuscript. This is the subject of another study since it requires review and reporting of the entire cohort.

In conclusion, our results show borderline increase in sensitivity of PET-DCT over DCT alone in the detection of LN metastasis in the abdomen, which suggests no justification in the utilization of PET-DCT to determine the upper extent of LN metastasis in a patient population with loco-regionally advanced cervical cancer, unless statistically significant increase in sensitivity is confirmed in a larger clinical trial.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- 1.** PET combined with contrast-enhanced diagnostic CT (DCT) increases the sensitivity of diagnostic CT to detect LN metastasis in abdomen (0.05)
- 2.** PET-DCT sensitivity is higher than diagnostic CT in the pelvis but the difference does not reach statistical significance
- 3.** Specificity of PET-DCT and diagnostic CT to detect LN metastasis is comparable

Figure 1.
Study Schema

a

b

c

Figure 2.

PET-DCT of a patient with loco-regionally advanced cervical cancer. a) 6 mm short-axis right common iliac LN (arrow) called negative on DCT by the 7 reviewers. b) PET shows high FDG uptake in the node (arrow). c) PET fused with DCT confirming FDG avid LN (arrow).

Figure 3.
Patient Flow Chart

Table 1

Accuracy values with 95% CI of PET-DCT and diagnostic CT in the abdomen.

ABDOMEN	PET-DCT	CT	P value
Sensitivity	0.50 (CI:0.44,0.56) 0.45–0.55	0.42 (CI:0.36,0.48) 0.33–0.48	0.052
Specificity	0.85 (CI:0.80,0.89) 0.75–0.90	0.89 (CI:0.84,0.92) 0.83–0.95	0.21
AUC	0.70 (CI:0.61,0.79) 0.65–0.73	0.68 (CI:0.59,0.77) 0.61–0.70	0.43

AUC: Area Under Curve.

Table 2

Accuracy values with 95% CI of PET-DCT and diagnostic CT in the pelvis and abdomen/pelvis combined.

	PET-DCT	CT	P value
PELVIS			
Sensitivity	0.83 (CI: 0.78,0.87) 0.65 – 0.90	0.79 (CI: 0.73,0.83) 0.71 – 0.84	0.15
Specificity	0.63 (CI: 0.54,0.70) 0.54 – 0.73	0.62 (CI: 0.53,0.69) 0.38 – 0.73	0.83
AUC	0.80 (CI: 0.71,0.88) 0.65 – 0.84	0.76 (CI: 0.67,0.85) 0.67 – 0.83	0.21
COMBINED ABDOMEN/PELVIS			
Sensitivity	0.81 (CI: 0.77,0.85) 0.69 – 0.86	0.77 (CI: 0.73,0.81) 0.71 – 0.81	0.17
Specificity	0.69 (CI: 0.59,0.77) 0.57 – 0.86	0.63 (CI: 0.54,0.72) 0.48 – 0.81	0.32
AUC	0.83 (CI: 0.75,0.91) 0.72 – 0.90	0.77 (CI: 0.69,0.85) 0.72 – 0.86	0.03

AUC: Area Under Curve.

Table 3

Inter-observer agreement between seven readers for PET-DCT and diagnostic CT

	KAPPA		
	ABDOMEN	PELVIS	COMBINED
PET-DCT 7 READERS	0.77	0.65	0.71
CT 7 READERS	0.65	0.61	0.67

Table 4

Number of lymph nodes removed during lymphadenectomy

		RANGE	MEAN (SD)	MEDIAN
NUMBER OF LNS	ABDOMEN (N=80)	1–33	10.7±7.6	9
	PELVIS (N=80)	0–35	14.1±7.5	13
NUMBER OF POSITIVE LNS	ABDOMEN (N=40)	1–24	3.6±4.5	2
	PELVIS (N=51)	1–14	4.0±3.2	3