PET in Cervical Cancer — Implications for ‘Staging,’ Treatment Planning, Assessment of Prognosis, and Prediction of Response

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Key Words
Cervical cancer, functional imaging, PET, PET-CT

Abstract
The use of functional imaging techniques such as fluorodeoxyglucose-positron emission tomography and positron emission tomography–computed tomography to manage patients with cervical cancer is constantly increasing. Current roles include pretreatment staging and diagnosis of recurrent disease. Reports have also shown its ability to predict survival based on pre- and posttherapy scans. These techniques are not fool-proof, however, and reports of both false-negative and false-positive scans document some limitations. Future studies must further elucidate their exact roles in the management of this disease process. (JNCCN 2008;6:37–45)

Cervical cancer spreads primarily through direct extension, although lymphatic and hematogenous spread can result in distant metastases. Traditionally, clinical examination and cross-projectional imaging have been used to stage cervical cancer but are accurate in only 60% of cases. A recent study by the American College of Radiology Imaging Network (ACRIN) and the Gynecologic Oncology Group (GOG) showed improved clinical staging of the extent of local disease with increasing use of cross-sectional imaging, such as CT and MRI. Clinical staging and cross-sectional imaging have significant limitations, however, in identifying lymphatic and distant spread. The sensitivity of CT has been calculated as only 24% to 34%, and 24% to 62% for MRI, perhaps because of the limited ability to detect small or microscopic metastases. In a more recent meta-analysis, the pooled sensitivities of CT and MRI for detecting retroperitoneal lymph node metastasis were found to be 47% and 54%, respectively. Detection of lymphatic metastases seems to be more successful with functional imaging techniques. Positron emission tomography (PET) most commonly uses the radiolabeled tracer 18F-fluorodeoxyglucose (FDG-PET), and may be fused with a conventional cross-sectional CT (PET-CT) to improve localization of abnormal FDG uptake compared with FDG-PET alone. Compared with normal cells, FDG is preferentially taken up by malignant cells, but is also accumulated in proliferating and inflammatory cells. Optimism has led to further use of these imaging modalities for surveillance and detection of recurrent disease and to predict recurrence and survival based on pre- and posttherapeutic scans.

Preoperative Lymph Node Staging
Between 15% and 30% of patients with locoregionally advanced cervical cancer are anticipated to have metastatic disease to the para-aortic lymph nodes (PALNs), which is strongly associated with disease stage. Identification through cross-sectional imaging has proven difficult. The role of FDG-PET and PET-CT in diagnosing metastases to pelvic and PALNs has been explored in several single-institution studies. A major limitation of many of these studies is the inclusion of patients with both newly diagnosed and recurrent cervical cancer. Furthermore, results are often difficult to compare...
because of differences in study inclusion criteria. Some studies have included only patients with cervical cancer with negative-appearing lymph nodes on cross-sectional imaging, whereas some include only positive-appearing lymph nodes, and some have included both. A final limitation of many studies evaluating FDG-PET and PET-CT is that metastases to lymph nodes are sometimes confirmed through clinical follow-up rather than pathology. These studies have been excluded from this review, except those involving a combination of pathologic and clinical follow-up.

Table 1 summarizes the results of the preoperative lymph node staging studies. Many reports have evaluated the usefulness of FDG-PET imaging for diagnosing lymph node metastases from cervical carcinoma. The most promising results are reported in studies evaluating patients with locoregionally advanced cervical carcinoma.11–15 For diagnosing para-aortic metastases, sensitivities range between 75% and 86%, with specificities between 92% and 97%. Similar results have been reported for detecting pelvic lymph nodes, with sensitivities and specificities reported as 80% to 100% and 92% to 100%, respectively. When evaluating patients with only early stage disease,16–19 reported sensitivities are lower (50% for para-aortic metastases and 10%–53% for pelvic lymph node metastases), bringing into question the value of FDG-PET in this patient

**Table 1.** FDG-PET and PET-CT for Preoperative Lymph Node Staging

<table>
<thead>
<tr>
<th>PET Study</th>
<th>N</th>
<th>Stage</th>
<th>Pelvic Lymph Nodes</th>
<th>Para-Aortic Lymph Nodes</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sensitivity</td>
<td>Specificity</td>
</tr>
<tr>
<td>Rose et al.11</td>
<td>32*</td>
<td>2B–4A</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Narayan et al.12</td>
<td>7</td>
<td>1B–4B</td>
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<td>92%</td>
</tr>
<tr>
<td>Reinhardt et al.13</td>
<td>35</td>
<td>1B–2</td>
<td>91%</td>
<td>100%</td>
</tr>
<tr>
<td>Kuhnel et al.14</td>
<td>15†</td>
<td>1B1–2A</td>
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<td>89%</td>
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<tr>
<td>Yeh et al.15</td>
<td>42</td>
<td>1B–4A</td>
<td>——</td>
<td>——</td>
</tr>
<tr>
<td>Lin et al.16</td>
<td>50</td>
<td>1B–4A</td>
<td>——</td>
<td>——</td>
</tr>
<tr>
<td>Yen et al.17</td>
<td>135</td>
<td>1B2–4B + recurrence</td>
<td>88%</td>
<td>100%</td>
</tr>
<tr>
<td>Wright et al.18</td>
<td>59§</td>
<td>1A2–2A</td>
<td>53%</td>
<td>90%</td>
</tr>
<tr>
<td>Park et al.19</td>
<td>36</td>
<td>1B1–2A</td>
<td>43%</td>
<td>100%</td>
</tr>
<tr>
<td>Chou et al.20</td>
<td>60</td>
<td>1A2–2A</td>
<td>10%</td>
<td>94%</td>
</tr>
<tr>
<td>Choi et al.21</td>
<td>22</td>
<td>1B–4A</td>
<td>76.9%</td>
<td>55.5%</td>
</tr>
<tr>
<td>Sironi et al.22</td>
<td>47</td>
<td>1A–1B</td>
<td>73%</td>
<td>97%</td>
</tr>
<tr>
<td>Amit et al.23</td>
<td>75</td>
<td>1–4 + recurrence</td>
<td>60%</td>
<td>94%</td>
</tr>
</tbody>
</table>

PET-CT Study

| Choi et al.24 | 19 | 1B–4A | 75% | 96% | 75% | 96% | 100% | 99% | 94% | 100% |

*Pelvic lymph node assessment based on 17 patients.
†Sensitivity, specificity, PPV, and NPV based on per-patient analysis of pelvic and para-aortic lymph nodes combined.
§Para-aortic assessment based on 7 patients.
¶Para-aortic assessment based on 45 patients.
*No metastases to para-aortic lymph nodes found in this patient population.
**Pelvic assessment based on 27 patients before radical surgery.

Abbreviations: CT, computed tomography; NPV, negative predictive value; PET, positron emission tomography; PPV, positive predictive value.
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population. An apparent exception to this finding is the series by Reinhardt et al.,\textsuperscript{20} which evaluated 35 patients with stage IB and II cervical cancer before radical hysterectomy and lymphadenectomy. The series included patients with stage IIB disease, however, among whom 6 of the 11 pelvic metastases occurred.

Several studies comparing FDG-PET with conventional cross-sectional imaging have shown its ability to identify lymph node metastases in the absence of abnormal CT or MRI findings.\textsuperscript{11,12,20–23} In some, inclusion criteria for the entire study included negative findings on cross-sectional imaging.\textsuperscript{11,14,19} Sugawara et al.\textsuperscript{24} correctly identified 6 of 7 (86%) patients with known lymph node metastases using FDG-PET, compared with only 4 using CT. Similarly, Lin et al.\textsuperscript{25} evaluated 50 patients with negative abdominal CT findings (PALNs < 10 mm in longest diameter) and found 12 patients with histologically confirmed PALN metastases using PET.

In a recent analysis of 15 published FDG-PET studies on cervical cancer, Havrilesky et al.\textsuperscript{26} showed that the pooled specificity and sensitivity of FDG-PET for detecting pelvic lymph node metastases were 79% (95% CI, 65%–90%) and 99% (96%–99%), respectively, compared with 72% (53%–87%) and 96% (92%–98%), respectively, for MRI and 47% (21%–73%) for CT (pooled specificity for CT not available). In this review, the pooled sensitivity and specificity of FDG-PET for detecting PALNs were 84% (95%, CI 68%–94%) and 95% (89%–98%), respectively (pooled sensitivity and specificity for CT or MRI were unavailable).

Data on the usefulness of PET-CT for lymph node evaluation in cervical cancer are more limited. Using MRI and PET-CT, Choi et al.\textsuperscript{27} evaluated 22 patients who underwent regional lymphadenectomy. PET-CT detected metastatic disease in 19 of 33 lymph node groups compared with only 10 using MRI (P = .026). On a per-patient basis, PET-CT correctly predicted 10 of 13 patients with metastatic disease compared with only 4 using MRI (P = .047). Many of the false-negative PET-CT scans were caused by micrometastases. Sironi et al.\textsuperscript{28} confirmed the limited ability to detect small metastases. All correctly identified lymph nodes had short-axis diameters greater than 0.5 cm, whereas the 5 false-negative lymph nodes on PET-CT in this series all had short-axis diameters of 0.5 cm or less and contained micrometastases.

Only one study in cervical cancer has compared FDG-PET with PET-CT. In a study by Amit et al.,\textsuperscript{29} 75 patients underwent PET-CT either before radical surgery or pelvic radiation, or secondary to a suspected recurrence. Imaging of only 33 patients was compared with histopathology, with the remainder compared with clinical follow-up only. The authors report that, compared with FDG-PET and CT individually, combined PET-CT yielded an improved diagnosis in 32 patients (43%) and resulted in change to management in 10 patients.

Finally, FDG-PET and PET-CT have been shown to be useful in detecting patients with disease outside of the pelvic and para-aortic region. Disease sites include supraclavicular lymph nodes (SCLNs), mediastinal lymph nodes, lung, bone, peritoneum, omentum, adrenal gland, and liver.\textsuperscript{11,14,19,29–31}

The GOG, in partnership with ACRIN, recently initiated a joint study comparing PET-CT findings with lymph node biopsy or lymphadenectomy in previously untreated patients with cervical carcinoma stages IB2 through IVA (GOG 233/ACRIN 6671). All patients will undergo histopathologic evaluation of their pelvic and PALNs unless distant disease is identified through PET-CT. Patients will also undergo a preoperative MRI using an ultrasmall particle iron oxide, preferentially taken up by the lymphatics, for comparison. One objective of this large, multi-institutional prospective trial is to directly compare PET-CT with CT and FDG-PET imaging alone for identifying PALN metastases.

Assessing Prognosis Using Pretreatment PET

Functional imaging with FDG-PET and PET-CT has also been used to predict progression-free (PFS) and overall survival (OS) in patients with cervical cancer. Grigsby et al.\textsuperscript{32} reported on 101 patients with stage IA through IVB cervical cancer who underwent CT for lymph node staging and a whole-body FDG-PET scan before treatment initiation. CT showed abnormally enlarged pelvic lymph nodes in 20% of patients and PALNs in 7%. FDG-PET showed uptake in pelvic lymph nodes in 67%, PALNs in 21%, and SCLN in 8%. The 2-year PFS based solely on pelvic lymph node status for patients who had CT(+/PET(−), CT(−)/PET(+), and CT(+/PET(+) results was 73%, 49%, and 39%, respectively (P = .001). The 2-year PFS based solely on PALN status for patients who had CT(−)/PET(−), CT(−)/PET(+), and CT(+/PET(+) results was 64%, 18%, and 14%, respectively (P = .0001).
Multivariate analysis for PFS showed lymph node status determined through FDG-PET to be the only significant prognostic variable. In a subsequent report of a subset of 47 patients with stage IIB disease, the cause-specific 3-year survival rate was 73% for those without lymph node metastases as determined by FDG-PET, 58% for those with only pelvic lymph node metastases, 29% for those with pelvic and PALN metastases, and 0% (P = .0005) for those with pelvic, PALN, and SCLN metastases. Similar findings have also been reported for patients with stage IB disease when stratified by pelvic, PALN, or SCLN metastases identified through FDG-PET.

In addition to lymph node uptake, several other findings on FDG-PET have been correlated with survival. Miller and Grigsby reported that the 3-dimensional volume of the primary tumor by FDG-PET predicted both PFS (P = .005) and OS (P = .003). In a subsequent analysis, Miller et al. reported that visual analysis of FDG-PET findings in the primary tumor (size, shape, heterogeneity of uptake) and presence of lymph nodes could be scored and used to reproducibly predict PFS (P < .0001) and OS (P < .0001), and was superior to evaluation of lymph nodes alone. Xue et al. compared the semiquantitative standardized uptake value (SUV) in the primary cervical tumor with survival. Using a cutoff of less than 10.2 or 10.2 or greater, the 5-year PFS was 71% and 52%, respectively (P = .029); OS (72% vs. 69%) was not significantly different between groups. On multivariate analysis, SUV was only of borderline significance (P = .055), whereas FDG uptake in lymph node regions was strongly significant (P < .0001).

Finally, Hope et al. showed that endometrial extension of the primary tumor as determined by FDG-PET was associated with decreased 2-year PFS (78% vs. 58%, P = .046) and OS (92% vs. 65%, P = .047). Endometrial extension also accurately predicted FDG uptake in pelvic (70% vs. 23%, P < .001) and para-aortic (30% vs. 0%, P = .006) lymph nodes. On multivariate analysis, however, only FDG-PET lymph node status was predictive of OS. Narayan et al. reported similar findings using MRI. Finally, Grigsby et al. evaluated the benefits of concurrent chemotherapy in patients with cervical cancer and negative lymph nodes as determined by FDG-PET. Among 65 patients with stage IB2 through IIB disease, no differences were seen in 5-year OS or patterns of failure, leading the authors to conclude that adding chemotherapy to whole pelvic radiation therapy in this population added no benefit.

### Radiation Therapy Treatment Planning Using PET

Functional imaging using FDG-PET can also provide 3-dimensional conformational images to aid in radiotherapy treatment planning. In patients with cervical cancer, FDG-PET can more accurately estimate the cervical cancer volume and the 3-dimensional spatial relationship of the cervical tumor to the brachytherapy applicator, bladder, and rectum. In a preliminary report, Malyapa et al. evaluated 11 patients undergoing curative radiotherapy. Patients underwent conventional orthogonal radiographs for 2-dimensional treatment planning and an FDG-PET scan of the pelvis with the brachytherapy applicator in situ. Tumor volumes determined with FDG-PET were greater than those estimated clinically and, although not statistically significant, the maximal bladder and rectal doses predicted with FDG-PET were greater than those predicted using conventional 2-dimensional planning. In a subsequent report, Lin et al. described the use of sequential FDG-PET imaging to plan brachytherapy in 24 patients. Once again, the maximal bladder and rectal doses predicted using FDG-PET were significantly greater than those predicted with 2-dimensional treatment planning.

Muito et al. reported on the use of FDG-PET images to guide intensity-modulated radiotherapy (IMRT) for cervical cancer with PALN involvement. Dose escalation to the PALNs was feasible with FDG-PET-guided IMRT. Acceptable doses to surrounding critical structures (colon, stomach, liver, and spinal cord) were obtained. An improvement on this technique was reported by Esthappan et al. and involved treatment planning using PET-CT. Treatment plans were developed that successfully delivered 59.4 Gy to the FDG-PET-positive PALNs and 50.4 Gy to the remainder of the PALNs, and spared surrounding critical structures.

The Washington University group also used a combination of FDG-PET and CT to modulate radiation dose to involved lymph nodes. Increasing doses of radiation were administered to patients with increasing-diameter PET-positive lymph nodes. Among 208 patients with lymph nodes ranging from negative nodes up to 1 cm to positive nodes 4 cm or larger, risk for an isolated lymph node failure was less than 2%. On multivariate analysis, lymph node size was not a significant predictor of failure.
Monitoring Response to Chemotherapy Using PET

Tumor response to chemotherapy has traditionally been measured in terms of bidimensional or unidimensional measurements obtained with cross-sectional imaging. More recently, FDG-PET has been used to monitor tumor response to chemotherapy. The first report evaluated 2 patients with recurrent cervical cancer undergoing chemotherapy. PET imaging was used to diagnose recurrences and monitor response to chemotherapy, which, in one case, occurred earlier than could be seen with MRI. Dose et al. reported using FDG-PET to identify recurrent cervical cancer not seen with CT and also to document complete response after combination chemotherapy. Finally, Yoshida et al. used FDG-PET to monitor response to neoadjuvant chemotherapy. In 3 patients, decrease in SUV by FDG-PET was better correlated to histopathologic response than MRI-evaluated Response Evaluation Criteria in Solid Tumors.

Predicting Recurrence After Radiation or Chemoradiation Using PET

Most recently, FDG-PET findings at completion of radiation therapy have been used to predict recurrence and survival. In the study by Nakamoto et al., 20 patients underwent FDG-PET evaluation 3 to 7 months after completing curative radiotherapy. Visual interpretation of FDG uptake was correlated with recurrence. If the scan was believed to be “probably abnormal” or “definitely abnormal,” 3 of 7 (43%) and 2 of 4 (50%) recurred, respectively. The sensitivity was therefore 100%. The relatively low specificity of 60% was believed to be caused by the lack of anatomic correlation obtained with FDG-PET alone.

In a study comparing posttherapy FDG-PET with survival, Grigsby et al. compared preradiation FDG-PET studies with postradiation studies performed 2.4 to 10.4 months after therapy on 76 patients with cervical cancer. The 2-year PFS was 86% for 53 patients with no abnormal FDG uptake, 40% for 12 patients with persistent abnormal uptake, and no survivors were seen at 2 years among 11 patients with new sites of abnormal FDG uptake (P < .0001). The authors updated this series in 2004 and reported on 152 patients. The 5-year cause-specific survival was 80% among 114 patients with no posttherapy FDG uptake, 32% among 20 patients with persistent FDG uptake, and no 5-year survivors were seen among 18 patients with new areas of FDG uptake (P < .001). On multivariate analysis, posttherapy FDG uptake was the most significant predictor of death from cervical cancer. In another series from the same group, Lin et al. evaluated residual FDG uptake in the cervix alone. Reporting on 32 patients undergoing radiation with curative intent, these investigators performed FDG-PET scans 3 months after completion of therapy and compared them with pretreatment scans. Patients with no residual FDG uptake in the cervix had a 5-year disease-free survival of 83% compared with 0% for patients with residual cervical FDG uptake (P = .005).

Diagnosis of Recurrence

Approximately one third of all patients with cervical carcinoma will experience recurrence. One limitation of cross-sectional imaging in diagnosing recurrence is the inability to differentiate recurrent disease from postoperative scar tissue, radiation fibrosis, or necrosis. Case reports have shown the ability of FDG-PET to diagnose cervical cancer recurrence in the pelvis, abdomen, and extra-abdominal sites, including inguinal lymph nodes, PALNs, peritoneum, liver, spleen, transposed ovaries, mediastinal lymph nodes, SCLNs, the myocardium, intercostal muscle, bone, pleura, and lung. Adding CT can help localize the site of abnormal FDG uptake and allow biopsy of distant metastases.

For diagnosing recurrence, the sensitivity of FDG-PET varies from 75% to 100% and the specificity from 57% to 100%. When used in posttreatment surveillance (i.e., without clinical suspicion of recurrence), the sensitivity ranges from 80% to 90% and the specificity from 76% to 100%. In a series of 26 patients with recurrent cervical cancer, Lin et al. showed improved sensitivity of FDG-PET for detecting nodal (77.3% vs. 45.5%; P = .043) and distant soft tissue (66.7% vs. 26.7%; P = .028) metastases compared with CT or MRI, but not for local lesion detection (100% vs. 71.4%; P = .462). Ryu et al. reported similar findings, with 100% sensitivity of FDG-PET for detecting hilar, SCLN, mediastinal,
liver, spine, and chest wall recurrences, but only 75% for detecting retrovesical lymph nodes. Interestingly, the reported sensitivity was only 85% for lung recurrences and 75% for para-aortic recurrences. No comparison to cross-sectional imaging was made. In the review of 15 published articles, Havrilesky et al. showed that the pooled sensitivity and specificity of FDG-PET for diagnosing recurrence when clinical suspicion was present were 96% and 81%, respectively.

Finally, FDG-PET imaging has been used to further evaluate patients with recurrent cervical cancer before undergoing planned curative therapy. The obvious benefit of a whole-body scan is the ability to detect distant, and therefore noncurative, metastases. In Lai et al., 40 patients with recurrent cervical cancer were evaluated for curability with FDG-PET and CT or MRI. PET was more sensitive than cross-sectional imaging at documenting recurrent disease, and better identified distant metastases, leading to treatment alteration in 22 (55%) patients. Similarly, Yen et al., 46 reported that, compared with CT or MRI imaging, FDG-PET led to altered treatment in 31% of patients. In Chang et al., 47 FDG-PET identified distant metastases in 11 of 20 patients (55%) and avoided unnecessary curative surgery for localized recurrences in 14 of 20 (70%) patients found to have distant disease. Yen et al., 46 reported that, among 55 patients considered curable with salvage therapy before imaging, 36 (65.5%) experienced treatment plan modifications based on FDG-PET findings, including 27 who underwent palliative therapy only. Others have reported similar findings, showing the usefulness of FDG-PET or PET-CT in detecting metastatic disease before pelvic exenteration. 56

### False-Negative and False-Positive FDG-PET Findings

False-negative FDG-PET scans predominantly occur because of the presence of only microscopic disease. 4,11,13,14,16,20,27,9,72 In a study by Narayan et al., 11 false-negative FDG-PET findings were seen in 2 patients with 9-mm deposits in mildly enlarged lymph nodes. In the Kuhnel series, 16 of the 3 false-negative FDG-PET scans of the pelvis, 2 were associated with micrometastases 2 mm or smaller. This was also true with the

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Table 2: FDG-PET and PET-CT for Diagnosing Recurrence

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>N</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Park et al.</td>
<td>36</td>
<td>100%</td>
<td>94.4%</td>
<td>—</td>
<td>—</td>
<td>97.2%</td>
</tr>
<tr>
<td>Sun et al.</td>
<td>20</td>
<td>90%</td>
<td>100%</td>
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<tr>
<td>Havrilesky et al.</td>
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<td>86.7%</td>
<td>85.7%</td>
<td>86.7%</td>
<td>—</td>
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<tr>
<td>Yen et al.</td>
<td>135</td>
<td>90%</td>
<td>—</td>
<td>95%</td>
<td>98%</td>
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<tr>
<td>Lai et al.</td>
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<td>Wong et al.</td>
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</tr>
<tr>
<td>Unger et al.</td>
<td>21</td>
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<td>85.7%</td>
<td>93.3%</td>
<td>100%</td>
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</tr>
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<td>Chang et al.</td>
<td>27</td>
<td>94%</td>
<td>78%</td>
<td>89%</td>
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<td>Chang et al.</td>
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<td>97.5%</td>
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<td>94%</td>
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<td>Sakurai et al.</td>
<td>25</td>
<td>91.5%</td>
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<td>—</td>
<td>—</td>
<td>91.7%</td>
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<td>Husain et al.</td>
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<tr>
<td>Chung et al.</td>
<td>52</td>
<td>90.3%</td>
<td>81%</td>
<td>—</td>
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<td>86.5%</td>
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<tr>
<td>Surveillance</td>
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<td>Unger et al.</td>
<td>26</td>
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<td>100%</td>
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<td>Ryu et al.</td>
<td>249</td>
<td>90.3%</td>
<td>76.1%</td>
<td>35%</td>
<td>98.2%</td>
<td>—</td>
</tr>
</tbody>
</table>

*Detection of recurrence in symptomatic patients.
†Evaluation for PET-CT.
‡Detection of recurrence in asymptomatic patients.

Abbreviations: NPV, negative predictive value; PPV, positive predictive value.

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single false-negative FDG-PET scan of the para-aortic region. Wright et al.\(^{17}\) compared the size of the metastatic focus of tumor in PET-positive and PET-negative pelvic lymph nodes. Although the sizes of the lymph nodes were not different (16.7 mm vs. 15.4 mm; \(P = .66\)), the average size of the tumor implant in PET-positive pelvic lymph nodes was 15.2 mm compared with 7.3 mm in PET-negative pelvic lymph node metastases (\(P = .0017\)). The sizes of the metastatic implant in PET-negative lymph nodes ranged from 0.3 to 20 mm. Park et al.\(^{18}\) did not comment on the false-negative lymph nodes, but 5 of the true-positive lymph nodes were less than 1 cm in diameter, documenting the ability of PET to detect small metastases in at least some lymph nodes.

False-positive FDG uptake usually occurs in the presence of infection or inflammation. Cases of false-positive FDG uptake have been seen with tuberculosis, anthracosis,\(^{6,21}\) abscess,\(^{10}\) pneumonitis,\(^{40}\) and benign bone fracture,\(^{60}\) and have preceded the diagnosis of a rectovaginal fistula.\(^{44}\) In one report, a false-positive occurred in one patient with an infected intrauterine device, septicemia, and lymphadenopathy.\(^{12}\) Inflammation caused by radiation changes can have high metabolic activity and result in focally intense FDG uptake. False-positives have been seen with radiation colitis,\(^{49}\) radiation proctitis,\(^{46}\) and radiation fibrosis.\(^{47}\) Ovaries containing functional cysts, whether transposed or not, have been reported as another source of false-positive FDG uptake.\(^{64,26}\) Finally, FDG uptake is known to occur in the endometrium of menstruating women, and therefore may present as a false-positive for endometrial extension of cervical cancer.\(^{76}\) In many instances, however, “false-positive lymph nodes” are seen in patients who ultimately develop nodal recurrence.\(^{11,12}\)

Conclusions

Since the first reports of FDG-PET in patients with cervical cancer were published 10 years ago, the role for functional imaging in this disease has rapidly expanded. Investigators have documented its usefulness in identifying lymphatic and distant metastases in primary and recurrent cases in addition to predicting survival by findings on both pre- and posttherapy scans. The fusion of an FDG-PET scan with a cross-sectional CT has allowed better localization of abnormal FDG uptake and perhaps reduced the number of false-positive scans associated with small recurrences. Future trials, such as GOG 233/ACRIN 6671, may answer many of the remaining questions and clarify the role for PET-CT in the evaluation of patients with primary cervical carcinoma.

References


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