Addition of an Iliac/Obturator Lymph Node Dissection Does Not Improve Nodal Recurrence or Survival in Melanoma

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BACKGROUND: Controversy exists regarding the value and indications for inguinal dissection alone or in combination with an iliac/obturator lymph node dissection for melanoma.

STUDY DESIGN: We reviewed patients from a multicenter prospective clinical trial and a single center who underwent inguinal dissection alone or combined with an iliac/obturator dissection for cutaneous melanoma. Analyses were stratified and compared by microscopic or macroscopic (palpable or detected by imaging) disease.

RESULTS: The study was composed of 134 patients with a median follow-up of 39 months. Indications for inguinal dissection were microscopic disease in 94 (70%) patients and macroscopic nodal disease in 40 (30%) patients. An iliac/obturator dissection yielded tumor-positive pelvic nodes in 25% vs 55% in the microscopic vs macroscopic groups, respectively (p = 0.10). No risk factors for positive pelvic nodes were identified. For both microscopic and macroscopic disease, addition of an iliac/obturator dissection to an inguinal dissection did not significantly reduce the risk of pelvic nodal recurrence. Five-year overall survival rates for 4 groups were compared: microscopic disease, inguinal dissection alone (72%); microscopic disease, iliac/obturator dissection (68%); macroscopic disease, inguinal dissection alone (51%); and macroscopic disease, iliac/obturator dissection (44%) (p = 0.0163). On survival analysis, addition of an iliac/obturator dissection in either microscopic or macroscopic disease did not affect disease-free survival or regional lymph node recurrence-free survival.

CONCLUSIONS: The addition of an iliac/obturator dissection to an inguinal dissection for both microscopic and macroscopic nodal disease did not significantly affect lymph node recurrence rates, disease-free survival, or overall survival. (J Am Coll Surg 2014;219:101–110. © 2014 by the American College of Surgeons)

In the era of sentinel lymph node (SLN) biopsy for cutaneous melanoma, patients with micrometastatic disease in the inguinal lymph nodes are usually offered a completion lymphadenectomy of the inguinal lymph node basin for locoregional disease control and potential cure. Likewise, patients with palpable nodal disease in the inguinal lymph nodes often undergo therapeutic lymphadenectomy of the involved nodal basin with the same goals of treatment. The extent of lymphadenectomy necessary to achieve optimal staging, locoregional disease control, and cure in patients with micrometastatic (SLN positive) or macrometastatic (palpable or radiologically evident) disease is not clear.

CME questions for this article available at http://jacscme.facs.org

Disclosure Information: Authors have nothing to disclose. Timothy J Eberlein, Editor-in-Chief, has nothing to disclose.

This is a review of data from the Sunbelt Melanoma Trial, which was an investigator-initiated clinical trial supported in part by a grant from Schering Oncology Biotech. All data management and subsequent analysis was performed independently at the University of Louisville. Schering Oncology Biotech was not directly involved in the conduct of the trial or in the production of this manuscript.

Presented at the Western Surgical Association 121st Scientific Session, Salt Lake City, UT, November 2013.

Received January 3, 2014; Revised February 24, 2014; Accepted February 24, 2014.

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Practice patterns for the extent of lymph node dissection offered to patients with inguinal lymph node metastases are mixed. In the case of clinically evident (palpable or radiologic) metastatic disease in the pelvic (iliac or obturator chain) lymph nodes, most surgeons would advocate for both an inguinal and iliac/obturator node dissection. The answer regarding the extent of dissection to perform in the absence of evidence of pelvic nodal disease is much less clear. In instances in which there is clinically evident macrometastatic disease in the inguinal lymph nodes, some authors advocate a combined inguinal lymph node dissection with an iliac/obturator dissection, citing high rates of pelvic node metastases, improved staging information, and improved locoregional disease control. Others have shown no improvement in locoregional disease control or survival when an iliac/obturator dissection is added to an inguinal dissection for palpable inguinal lymph node disease.

Recommendations regarding inguinal dissection vs combined inguinal and iliac/obturator dissection for micrometastatic, or tumor-positive SLN disease, also vary widely. Many authors advocate an inguinal dissection alone for SLN-positive inguinal disease, citing low rates of microscopically positive pelvic lymph nodes and acceptable survival outcomes. Practice patterns do vary, however. A recent international survey of melanoma surgeons found that for SLN-positive inguinal nodes, an approximately equal proportion of respondents advocated only an inguinal dissection, a combined inguinal and iliac/obturator dissection in all cases, or a selective use of an iliac/obturator dissection. Given the lack of consensus on the management of inguinal lymph node metastases in melanoma, this study was performed to evaluate whether a combined inguinal and iliac/obturator dissection improved locoregional disease control and survival compared with an inguinal dissection alone in the absence of clinical or radiologic evidence of pelvic lymph node metastases.

METHODS
This study reviewed patients from both the Sunbelt Melanoma Trial and the University of Louisville melanoma database. The details of the Sunbelt Melanoma Trial have been described previously. Briefly, all patients in the Sunbelt Melanoma Trial had a primary melanoma of ≥1.0 mm Breslow thickness and no clinical evidence of lymph node metastases. All patients underwent SLN biopsy and subsequent lymphadenectomy of the involved nodal basin if the SLN was positive. An inguinal dissection was defined as removal of all fatty and lymphatic tissue in the space defined by 5 cm above and parallel to the inguinal ligament, inferior to the level of the femoral triangle, medially along the border of the adductor magnus muscle, and laterally to the sartorius muscle. An iliac/obturator dissection was defined as any dissection in which iliac or obturator lymph nodes were removed, no matter the number of lymph nodes removed. The addition of an iliac/obturator dissection to an inguinal dissection in instances of a tumor-positive inguinal SLN was left to the discretion of the operating surgeon. Likewise, for patients treated at the University of Louisville, performance of an inguinal dissection alone or a combined inguinal and iliac/obturator dissection was at the discretion of the surgeon. Patients who underwent an inguinal dissection or a combined inguinal and iliac/obturator dissection for a tumor-positive SLN were categorized as having microscopic disease. Similarly, patients who presented with palpable or radiologically evident inguinal lymph node disease or who suffered a palpable recurrence in the inguinal lymph node basin were categorized as having macroscopic disease. Patients with any clinical or radiologic evidence of pelvic (iliac/obturator) lymph node metastases at the time of the performance of the inguinal dissection or iliac/obturator dissection were excluded from this study.

Clinicopathologic factors were compared using chi-square tests or ANOVA, as appropriate. Survival between groups was compared using Kaplan-Meier curves and the log-rank test. Survival times were calculated from the time of initial inguinal or iliac/obturator lymph node dissection. Overall survival was time to death from any cause. Disease-free survival, inguinal lymph node survival, and pelvic lymph node survival events were any type of recurrence, a recurrence in the inguinal lymph node basin, or a recurrence in the iliac/obturator lymph node basin, respectively. Routine follow-up was not specified. Nodal recurrences were diagnosed by either cross-sectional imaging or physical examination and confirmed with PET scan or biopsy. Differences were considered statistically significant if p < 0.05. All analyses were conducted with JMP software, version 10 (SAS, Inc). All participating centers had institutional approval for participation in the Sunbelt Melanoma Trial, and the University of Louisville Institutional Review Board approved review and analysis of these databases.

RESULTS
We identified 134 patients from 31 centers who met the inclusion criteria of having either an inguinal dissection alone or combined inguinal and iliac/obturator dissection without clinical or radiologic evidence of metastatic disease in the iliac/obturator lymph nodes; median follow-up was 39 months. Inguinal dissection alone was performed in 100
patients (75%); 34 combined inguinal and iliac/obturator dissections were performed (25%). Clinicopathologic data are summarized in Table 1, stratified by both indication and type of dissection. These findings are presented without statistical comparison, due to the limited sample sizes in each of the 4 groups.

The median number of inguinal lymph nodes removed was 11 (range 2 to 37). When an iliac/obturator dissection was performed, the median number of pelvic lymph nodes removed was 11 (range 3 to 33). When a combined inguinal and iliac/obturator dissection was performed, the median number of total lymph nodes removed was 22 (range 10 to 51).

The majority of patients in this study underwent an inguinal dissection for microscopic (SLN positive) disease (94 of 134, 70%); 12 of these patients underwent a combined inguinal and iliac/obturator dissection at the discretion of the operating surgeon (13% of microscopic disease patients). The rate of tumor-positive pelvic lymph nodes when a combined inguinal and iliac/obturator dissection was performed for microscopic disease was 25% (3 of 12). Recurrence rates in the pelvic lymph nodes were not statistically different between inguinal dissection alone (11%) and combined inguinal and iliac/obturator dissection (5%), but this may have been due to small sample size and there may very well be a trend toward increased pelvic node recurrence rates when an iliac/obturator dissection is omitted. Larger studies would be needed to confirm this trend. Complication rates were similar between inguinal dissection alone and combined inguinal and iliac/obturator dissection, 33% vs 32%, respectively (p = 0.92). Reported rates of lymphedema were 16.7% for inguinal dissection and 9.1% for combined inguinal and iliac/obturator dissection (p = 0.47).

Clinicopathologic risk factors for a tumor-positive pelvic lymph node were evaluated in all patients who underwent combined inguinal and iliac/obturator dissection (n = 34) (Table 2). The overall rate of positive pelvic lymph nodes in all patients undergoing combined inguinal and iliac/obturator dissection was 44.1%. There was a trend toward an increasing number of positive inguinal nodes being associated with positive pelvic nodes, but this was not statistically significant. When there were 4 or more positive inguinal nodes, the risk of positive pelvic nodes was 66.7% vs 39.3% with less than 4 positive inguinal nodes (p = 0.22). No statistically significant risk factors for a tumor-positive pelvic lymph node were identified that could identify patients at high risk for pelvic lymph node metastases in patients without a priori clinical or radiologic evidence of metastases.

The 5-year lymph node recurrence-free survival rate was 77%. Pelvic node recurrence rates were not statistically

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### Table 1. Clinicopathologic Factors in Patients Undergoing Inguinal Dissection or Combined Inguinal and Iliac/Obturator Dissection

<table>
<thead>
<tr>
<th>Factor</th>
<th>Microscopic Inguinal dissection</th>
<th>Combined inguinal + iliac/obturator dissection</th>
<th>Macroscopic Inguinal dissection</th>
<th>Combined inguinal + iliac/obturator dissection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y, mean (95% CI)</td>
<td>46 (43, 49)</td>
<td>47 (40, 55)</td>
<td>62 (56, 69)</td>
<td>53 (47, 59)</td>
</tr>
<tr>
<td>Breslow thickness, mm, mean (95% CI)</td>
<td>3.3 (2.7, 3.8)</td>
<td>2.5 (1.1, 3.9)</td>
<td>1.9 (0.5, 3.2)</td>
<td>3.5 (2.3, 4.7)</td>
</tr>
<tr>
<td>Male sex</td>
<td>37 (46.8)</td>
<td>4 (33.3)</td>
<td>6 (40.0)</td>
<td>7 (36.8)</td>
</tr>
<tr>
<td>Clark level &gt;3</td>
<td>50 (83.3)</td>
<td>7 (100.0)</td>
<td>6 (85.7)</td>
<td>6 (85.7)</td>
</tr>
<tr>
<td>Ulceration</td>
<td>39 (48.2)</td>
<td>4 (33.3)</td>
<td>7 (53.8)</td>
<td>10 (58.8)</td>
</tr>
<tr>
<td>Regression</td>
<td>7 (10.5)</td>
<td>1 (8.3)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Extremity primary site</td>
<td>46 (56.1)</td>
<td>8 (66.7)</td>
<td>6 (33.3)</td>
<td>6 (27.3)</td>
</tr>
<tr>
<td>Lymphovascular invasion</td>
<td>9 (14.5)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Number of inguinal lymph nodes removed, median (range)</td>
<td>11 (2, 26)</td>
<td>11 (5, 29)</td>
<td>11.5 (5, 29)</td>
<td>12 (3, 37)</td>
</tr>
</tbody>
</table>

Unless otherwise noted, data are expressed as n (%).
different between all inguinal dissections compared with combined inguinal and iliac/obturator dissections (12% vs 8.9% respectively, p = 0.61). In the 3 patients who suffered a pelvic node recurrence after a combined inguinal and iliac/obturator dissection, the total numbers of pelvic nodes removed were 9, 13, and 16. These numbers are comparable to the total number of pelvic nodes removed in the remaining patients who did not suffer a pelvic node recurrence after a combined inguinal and iliac/obturator dissection (median total number pelvic nodes removed, 10.5, range 3 to 33). This would suggest that an adequate iliac/obturator lymph node dissection was performed in patients suffering a pelvic recurrence. Inguinal or pelvic node recurrences after inguinal dissection or combined inguinal and iliac/obturator dissection were often associated with systemic recurrences; 60% of patients with a nodal recurrence also suffered a systemic recurrence. For both inguinal dissection and combined inguinal and iliac/obturator dissection, the most common type of recurrence was a systemic recurrence (43% and 48%, respectively). Systemic recurrences were higher in the macroscopic group compared with the microscopic group (40% and 31%, respectively). When stratified by indication (microscopic vs macroscopic nodal disease),

Table 2. Clinicopathologic Factors Associated with Tumor-Positive Pelvic Nodes in Patients Undergoing Combined Inguinal and Iliac/Obturator Dissections

<table>
<thead>
<tr>
<th>Factor</th>
<th>Negative pelvic nodes (n = 19 [55.9%])</th>
<th>Positive pelvic nodes (n = 15 [44.1%])</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>6 (35.3)</td>
<td>5 (35.7)</td>
<td>0.98</td>
</tr>
<tr>
<td>Breslow thickness, mm, mean (95% CI)</td>
<td>3.7 (2.0, 5.5)</td>
<td>2.5 (0.7, 4.2)</td>
<td>0.31</td>
</tr>
<tr>
<td>Age, y, mean (95% CI)</td>
<td>53.6 (46.0, 61.2)</td>
<td>47.4 (38.8, 56.0)</td>
<td>0.28</td>
</tr>
<tr>
<td>Ulceration</td>
<td>6 (42.9)</td>
<td>8 (53.3)</td>
<td>0.57</td>
</tr>
<tr>
<td>Regression</td>
<td>1 (14.3)</td>
<td>0 (0.0)</td>
<td>0.22</td>
</tr>
<tr>
<td>Extremity primary tumor site</td>
<td>7 (36.8)</td>
<td>7 (46.7)</td>
<td>0.56</td>
</tr>
<tr>
<td>Lymphovascular invasion</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1.0</td>
</tr>
<tr>
<td>Positive inguinal lymph nodes, n, mean (95% CI)</td>
<td>1.74 (0.52, 2.95)</td>
<td>2.05 (0.89, 3.20)</td>
<td>0.71</td>
</tr>
<tr>
<td>Number of positive inguinal lymph nodes</td>
<td></td>
<td></td>
<td>0.58</td>
</tr>
<tr>
<td>0</td>
<td>7 (36.8)</td>
<td>5 (23.8)</td>
<td></td>
</tr>
<tr>
<td>1−3</td>
<td>10 (52.6)</td>
<td>12 (57.1)</td>
<td></td>
</tr>
<tr>
<td>≥4</td>
<td>2 (10.5)</td>
<td>4 (66.7)</td>
<td></td>
</tr>
</tbody>
</table>

Unless otherwise specified, data are shown as n (%).
Number of positive inguinal nodes reflects positive lymph nodes in the inguinal dissection performed after the sentinel lymph node biopsy, so a positive sentinel lymph node would not be counted in this number.

Figure 1. Pelvic node recurrence-free survival in microscopic (A) and macroscopic (B) disease for patients with inguinal lymph node metastases undergoing either inguinal lymph node dissection alone (Inguinal) or combined inguinal and iliac/obturator dissections (Inguinal + Iliac/Obturator).
there was no difference in pelvic node recurrence-free survival or disease-free survival for inguinal dissection alone compared with combined inguinal and iliac/obturator dissection (Figs. 1 and 2). Disease-free survival was greater for microscopic compared with macroscopic disease ($p = 0.0002$, Kaplan-Meier curve not shown). Five-year overall survival rates for the 4 groups were compared: microscopic disease, inguinal dissection alone (72%); microscopic disease, combined inguinal and iliac/obturator dissection (68%); macroscopic disease, inguinal dissection alone (51%); and macroscopic disease, combined inguinal and iliac/obturator dissection (44%) ($p = 0.0163$). There was no difference in overall survival for inguinal dissection alone compared with combined inguinal and iliac/obturator dissection when stratified by indication (Fig. 3). As seen previously, overall survival was worse in macroscopic inguinal node disease compared with microscopic disease.

**DISCUSSION**

The most important finding in this work is that there was no difference in disease-free or overall survival between patients who underwent an inguinal dissection alone compared with a combined inguinal and iliac/obturator dissection for metastatic melanoma to the inguinal nodes. Patients who underwent a combined inguinal and iliac/obturator dissection did not have improved pelvic lymph node recurrence rates compared with patients having inguinal dissection alone. These findings were in patients without clinical or radiologic evidence of pelvic lymph node involvement before dissection and were similar for patients with microscopic and macroscopic metastases.

The subsets of patients who would stand to benefit from the addition of an iliac/obturator dissection are those with metastatic disease in the pelvic lymph nodes. When there is either radiologic or biopsy-based evidence that the
pelvic lymph nodes contain metastatic melanoma, an iliac/obturator dissection is an appropriate consideration for locoregional disease control. We excluded any patients with preoperative evidence of pelvic lymph node metastases in order to investigate the more common clinical scenario of known inguinal lymph node disease in which the disease status of the pelvic lymph nodes is unknown. We were unable to identify any a priori risk factors for micrometastatic melanoma in the pelvic lymph nodes. Extracapsular extension in the inguinal lymph nodes and the presence of metastasis in Cloquet’s lymph node are commonly used criteria to perform an iliac/obturator dissection. These findings were inconsistently reported in our series of patients, so an analysis of the significance of these factors could not be performed. Other authors have identified risk factors for pelvic node metastases, including inguinal metastatic tumor burden, age, and Breslow thickness.7,11-14 These risk factors are inconsistently identified in the literature, so currently there is no reliable set of parameters by which one can estimate the risk of pelvic lymph node metastases.

The appropriate outcomes measure to determine the efficacy of an iliac/obturator dissection in addition to an inguinal dissection for local disease control is the nodal recurrence rate, and more specifically, the pelvic node recurrence rate. Pelvic node recurrences were relatively low and not statistically different between inguinal dissection alone (12%) and combined inguinal and iliac/obturator dissection (8.9%) in all types, and in each subtype (microscopic and macroscopic) in this study. These findings are consistent with previous reports in the literature of nodal recurrence rates ranging from 2% to 10%, suggesting that lymph node recurrence rates are relatively low and are not improved by more extensive lymph node dissections.4,15 Low lymph node recurrence rates and no additional improvement with the addition of an iliac/obturator dissection have been reported for both microscopic and macroscopic inguinal lymph node disease.15 Recurrence rates in the pelvic lymph nodes are not improved with addition of an iliac/obturator dissection.

Interestingly, in this study, the rates of pelvic node recurrences for macroscopic disease (11% and 5%) were slightly less than those for microscop ic disease (12% and 17%); these rates were not statistically significantly different (p = 0.70). Given the limited number of patients in these subgroups, statistical comparisons between them should be interpreted with caution. Reported rates of pelvic node recurrences after inguinal dissection or combined inguinal and iliac/obturator dissection for macroscopic nodal disease range from 8% to 33%, so our rates of pelvic node recurrences for macroscopic disease are consistent with the low range of those reported in the literature.2,5,15-17 Sabel and coworkers18 also reported nonsignificant differences in the rates of nodal recurrences after inguinal lymphadenectomy for microscopic (9%) compared with macroscopic (13%) inguinal metastases, and these rates were similar to what we report. They suggested the nonsignificant differences in nodal recurrence between the macro- and microscopic groups were due to increased rates of distant recurrences and death in the macroscopic group; this reasoning is consistent with our results as well.

Consistent with the findings of no improvement in locoregional disease control, there was no improvement in disease-free survival with the addition of an iliac/obturator dissection. Differences in survival were driven by the presentation classification of disease: microscopic vs macroscopic. Within each type of disease presentation, there was no difference in disease-free or overall survival. These findings suggest that locoregional disease control may not improve overall survival in patients with either microscopic or macroscopic inguinal lymph node metastases and are consistent with previous reports.4,5,18 Patients with stage III melanoma most often recur with systemic metastases.19 Even in patients with microscopic inguinal lymph node metastases, the most common site of first recurrence is systemic metastases.13 Any hope of improving overall survival in patients with stage III melanoma in the inguinal lymph nodes relies on the ability to reduce recurrences, specifically systemic metastases. Based on these data, addition of an iliac/obturator dissection to an inguinal dissection for either microscopic or macroscopic inguinal lymph node disease was not associated with a survival benefit.

One argument for an extensive lymph node dissection that includes the iliac/obturator chain is the sampling of more lymph nodes that allows for improved accuracy in staging. There may be a prognostic benefit to identifying pelvic lymph node metastases. We found no statistically significant difference in disease-free survival or overall survival in patients who underwent an iliac/obturator dissection between patients with tumor-positive and -negative pelvic lymph nodes (data not shown). Several authors have shown that in patients undergoing an iliac/obturator dissection, the presence or absence of tumor-positive pelvic lymph nodes has prognostic significance.3,5,12,14 Therefore, a potential benefit to an iliac/obturator dissection, in the absence of a survival benefit or improved locoregional control, is improved risk stratification of patients, which may be used to guide decision making regarding adjuvant therapy and appropriateness for enrollment in clinical trials.

In this study, there were no significant differences in the complication rates between inguinal dissection alone and combined iliac/obturator dissection. The
complication rates for both inguinal dissection alone and combined iliac/obturator dissection in both microscopic and macroscopic diseases were approximately one-third. These complication rates are consistent with previous reports.\textsuperscript{11,16,18,19} However, lymphedema was not objectively measured in this study; reporting of lymphedema was based on patient symptoms and physical examination during follow-up. Wound infection was not graded in severity. Complications rates were not strictly defined within a 30-day period; rather, any patient with a complication recorded in their follow-up period in the records was considered in this study. Nevertheless, based on our findings (with the inherent limitations discussed above) and those reported in the literature, addition of an iliac/obturator dissection does not appear to significantly increase the morbidity associated with an inguinal dissection alone.

This study has several limitations that must be considered when interpreting the results. The study is retrospective in nature and subject to the limitations inherent in such studies. Survival time was measured from time of lymph node dissection rather than the time of melanoma diagnosis, so there may be some lead time bias. This bias is likely minimal because all patients underwent SLN biopsy within 90 days of diagnosis in the Sunbelt Melanoma Trial and there is no reason to believe that the lead times before dissection would be different in the different dissection groups. We use overall survival rather than melanoma-specific survival, because this is the metric captured in our database, so there may be some nonmelanoma-related deaths that are counted in the overall survival analysis and likely account for the small discrepancy in 5-year overall survival in the macroscopic group (44% to 51%) and the systemic recurrence rate (41%). The decision to perform an iliac/obturator dissection in addition to an inguinal dissection was at the discretion of the operating surgeon in both the Sunbelt data and the University of Louisville data. There is certainly some degree of selection bias involved in the decision to perform an iliac/obturator dissection in situations in which the operating surgeon has a high degree of suspicion that the pelvic lymph nodes harbor metastases. There is some suggestion from the data that for patients with macroscopic disease, surgeons were more likely to offer a combined inguinal and iliac/obturator dissection in younger patients or with thicker primary tumors, but larger studies would be needed to confirm these trends in this small subgroup analysis. Furthermore, the extent or quality of the iliac/obturator dissection performed by the different surgeons participating in Sunbelt is difficult to measure, and we do not suggest that all such dissections were carried out in a standard fashion because the iliac/obturator dissection was not specifically defined in the Sunbelt protocol. However, we would propose that all centers participating in the Sunbelt Melanoma Trial were high-volume melanoma centers and would suggest that the dissections were performed adequately by appropriately experienced surgeons. Cloquet’s node is often used as a “sentinel” node for pelvic node metastases, but this node was often not identified in the pathologic specimen and was used inconsistently as a criterion for an additional iliac/obturator dissection. Approximately half of the patients in the Sunbelt protocol in this study underwent adjuvant interferon therapy. We do not have reliable data on other adjuvant therapies or use of radiation therapy, so we cannot comment on the relative differences in adjuvant therapy use that may be confounding our findings.

The rates of tumor-positive pelvic lymph nodes were relatively high for both microscopic (25%) and macroscopic (55%) indications, suggesting that the surgeons were performing combined inguinal and iliac/obturator dissections in patients who were at an increased risk of pelvic lymph node metastases without any radiologic evidence of such disease. Surgeons were very good at selecting patients for iliac/obturator dissection. In the macroscopic group, based on the rates of positive pelvic nodes in 55% of patients and only an 11% pelvic node recurrence rate in patients undergoing only an inguinal dissection, surgeons were “correct” 55% and 89% of the time when they chose to either perform or omit an iliac/obturator dissection. Similarly, for microscopic disease, the surgeon was correct 25% and 88% of the time, respectively. Clearly, we are not capturing surgeon judgment adequately in this analysis. In an unselected group of patients who underwent iliac/obturator dissections for all microscopic SLN-positive inguinal metastases, the rate of pelvic node metastases was 12%, which is essentially half of our rate in a group in which iliac/obturator dissection was added at the discretion of the operating surgeon.\textsuperscript{11} Even with a high proportion of patients with pelvic lymph node metastases who would be expected to benefit from an iliac/obturator dissection, we found no improvement in pelvic lymph node recurrence rates, disease-free survival, or overall survival. The study is relatively small and is likely underpowered to detect more subtle survival benefits that may exist for patients undergoing an iliac/obturator dissection. Some of the subgroups analyzed have very few patients (eg, only 12 patients with microscopic disease underwent a combined dissection), so we have limited our statistical comparison of subgroups and would caution readers to interpret our findings with these limitations in mind. Only a randomized, prospective trial could provide level I evidence on the effect of the addition of an iliac/obturator dissection to an inguinal dissection.
CONCLUSIONS
In conclusion, we found that for patients with microscopic (SLN-positive) inguinal lymph node disease, addition of an iliaco-obturator dissection to an inguinal dissection did not improve locoregional disease control. In this small series, there was no survival benefit to the addition of an iliaco-obturator dissection in the microscopic or macroscopic group. These findings must be considered in light of the limited sample size in this study that may have been unable to detect small improvements in survival with an additional iliaco-obturator dissection. There was a trend toward improved pelvic nodal disease control in macroscopic disease with the addition of an iliaco-obturator dissection (5% vs 11%). Additionally, the rate of tumor-positive pelvic nodes when an iliaco-obturator dissection was added for macroscopic disease was quite high (55%). The addition of an iliaco-obturator dissection for macroscopic inguinal lymph node metastases is likely to clear additional microscopic disease in the pelvic lymph nodes and may be considered in addition to an inguinal dissection; the survival benefit to this approach is not clear.

Author Contributions
Study conception and design: Egger, Brown, Quillo, Martin, Scoggins, McMasters
Acquisition of data: Egger, Brown, Roach, McMasters
Analysis and interpretation of data: Egger, Brown, Quillo, Martin, Scoggins, Stromberg, McMasters
Drafting of manuscript: Egger, Stromberg, McMasters
Critical revision: Egger, Brown, Roach, Quillo, Martin, Scoggins, Stromberg, McMasters

REFERENCES

Discussion
INVITED DISCUSSANT: DR JEFFREY LEE (Houston, TX):
Dr Egger and his group have provided a retrospective analysis of patients who underwent inguinal lymph node dissection for melanoma lymph node metastasis. They compared outcomes measures in those who underwent superficial dissection alone with those who underwent combined superficial and deep inguinal lymph node dissection. They found no evidence for benefit from the addition
of deep dissection; complications rates were similar. They concluded that deep dissection is not indicated in patients with microscopic inguinal nodal metastasis; they suggested that deep dissection can be considered in patients with clinically apparent inguinal nodal metastasis.

In putting these findings in context, it is important to recognize that care for patients with advanced melanoma is changing rapidly. Within a few years, the data presented here will likely need to be re-evaluated as we incorporate new and dramatically more effective systemic therapies (including BRAF and MEK inhibitors, and immune checkpoint inhibitors) into our adjuvant treatment strategies. The ongoing MSLT-II phase III randomized trial of completion lymph node dissection vs observation in patients with microscopic regional lymph node metastasis is relevant because it may provide more definitive information on whether any completion lymph node dissection (superficial or combined) is likely to provide survival benefit to this group of patients.

I have 2 questions: First, the authors report a relatively high rate (55%) of involved deep nodes in the macroscopic group, and a surprisingly high rate (25%) in the microscopic group. Could the application of Cloquet’s lymph node biopsy in some patients account for unmeasured selection, and the relatively high rates of deep nodal metastasis? How many patients underwent Cloquet’s lymph node biopsy, how many Cloquet’s lymph nodes were subjected to frozen section, how many frozen sections were positive, and how many of the frozen section results influenced the operative plan?

Second, although this report includes a relatively large number of patients who underwent deep dissection, as the authors point out, the study is in some ways underpowered; it contains some very small subgroups (for example, there are only 3 patients in the subgroup with microscopic disease and involved deep nodes). With this in mind, are there any subgroups of patients with microscopic inguinal nodal disease perhaps more likely to have deep metastasis (that is, more likely to be in the 25%) to whom the authors would offer deep node dissection?

**DR KELLY McMASTERS:** On the extent and quality of the pelvic lymph node dissection, the median number of pelvic lymph nodes was 11, mean of 13.4, with a range of 3 to 33. I don’t think there were too many who just had 3. So it looks like pretty reasonable iliac/obturator lymph node dissections in most of the cases.

The second question involved selection bias in that there was a very high rate of pelvic lymph node involvement, and how did the surgeons possibly figure out which patients needed a deep lymph node dissection when none of the data that we have showed anything that predicts the presence of positive deep lymph nodes? Did we use Cloquet’s lymph node? We don’t have the data on Cloquet’s lymph node. Forty percent of the data are from the University of Louisville, 60% from the Sunbelt Melanoma Trial. I know for at least the 40%, we didn’t use Cloquet’s lymph node and frozen sections to determine the need for a deep resection. I can’t tell you for sure that that didn’t happen, and it probably did happen, in fact, in some of the Sunbelt patients and may explain the high rate of deep nodal involvement. We don’t know if the extent of micrometastatic disease in the sentinel nodes was used as a criterion, and we excluded patients who actually had pelvic sentinel nodes positive from this analysis.

Finally, you asked if there are some ways that we could identify subgroups of patients with microscopic inguinal nodal disease more likely to have deep nodal metastases. Again, our statistical analysis doesn’t identify any predictors of deep nodal involvement, but if you were to ask me, I would have thought that we would have found that patients with truncal primary melanomas that were thick, ulcerated, with lymphovascular invasion in younger patients would be those with microscopically positive or sentinel node positive disease more likely to have positive deep nodes. Our study doesn’t show that. Is that a bias that I have and reasons that I might do an iliac/obturator lymph node dissection? Yes, I think our data overall suggest that we do very little good by doing deep lymph node dissections, but there may be patients who are at very high risk of recurrence who could achieve better locoregional disease control. However, we certainly didn’t show that with the data.

**DR JAMES JAKUB** (Rochester, MN): This is something that I struggle with, and it always seems like I guess wrong. When I choose not to do a deep pelvic node dissection, they come back years later with a positive CT scan. And when I choose to do one, the nodes are all negative. So I appreciate this presentation. The 44% 5-year survival for deep pelvic nodes positive is pretty impressive. It’s better than in most studies.

What do you do with mapping when you have primary drainage to both the pelvic and the inguinal sentinel nodes? And how does that affect your decision if you have a positive inguinal node later? I would be cautious about saying patients with more aggressive disease who had more aggressive treatment did just as well as patients with less aggressive disease who had less aggressive treatment. That if we did less aggressive surgery on everyone, they would have done just as well. In other words, you were more aggressive with patients with deep pelvic nodes positive. You selectively somehow chose that group to be more surgically aggressive. And your survival and local recurrence rate were just as good as those with the patients who just had inguinal nodes dissected. But I think if you backed up and didn’t do those pelvic dissections on those 50% of patients with positive nodes, it would be hard to say they wouldn’t have had recurrence.

**DR KELLY McMASTERS:** To your second point, I agree with you. To your first point, I don’t know how, throughout this study, the presence of concomitant inguinal and iliac/obturator sentinel nodes were dealt with. I think, as you suggest, if you demonstrate concomitant drainage to sentinel nodes both in the superficial and the deep nodes, and you have a positive superficial inguinal lymph node, that might persuade one to do a deep dissection.

I think all of us who do melanoma surgery recognize that when you see patients who have uncontrolled regional disease, especially bulky, palpable iliac and obturator nodal disease that has grown where you can’t palpate it and where you don’t want to do PET/CT scans every 2 months. Obese patients often develop bulky disease, which, by the time you need to address it surgically, is out of control. You no longer can achieve regional disease control. They have large nodes invading and encasing iliac vessels growing into the pelvic sidewall, etc.
That does happen to us and it's something to be avoided. I'm afraid, however, that we can't define very well when to perform a deep dissection by looking at the actual data.

**DR DAVID WINCHESTER** (Evanston, IL): You mentioned that most recurrences are systemic. I'm curious if inclusion of a deep dissection affected the location of a regional recurrence. Did a deep dissection lead to a prolonged disease-free interval or did the patients recur preferentially in deep nodes or superficial nodes?

**DR KELLY McMASTERS**: I'm not sure that I have the numbers to answer your question directly. I know that 60% of the patients who recurred with deep positive lymph nodes had systemic disease. And the reason that rate of recurrence in the deep nodes was lower in the macroscopic nodal disease group is unclear, but may be related to the fact that some of them died of systemic disease before they developed deep nodal disease that became evident, or we didn’t capture some of those deep nodal recurrences after the patients had their first systemic recurrence.

**DR DAVID WINCHESTER** (Evanston, IL): What about a difference in the disease-free interval? Was there any difference if you did a deep node dissection in terms of time of recurrence in the nodal basin?

**DR KELLY McMASTERS**: Time to recurrence was the same.