Assessing the Quality of Colorectal Cancer Staging

Documenting the Process in Improving the Staging of Node-Negative Colorectal Cancer

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Hypothesis: Examination of 14 or more nodes is the optimal criterion to accurately stage node-negative colorectal cancer and predict outcome.

Design: Case series.

Setting: Three university-affiliated community medical centers.

Patients: A total of 2149 individuals with apparently localized, invasive colorectal cancer examined between January 1, 1990, and December 31, 2002.

Intervention: Study of tumor registry data.

Main Outcome Measures: Nodal status and disease-specific survival.

Results: The number of nodes examined ranged from 0 to 97 (mean ± SD, 18 ± 15 nodes). The mean number of nodes examined in node-positive individuals was 21.0 vs 16.6 in node-negative individuals (P < .001). The mean number of nodes examined at medical center A was 22.3; center B, 17.9; and center C, 14.0. The mean number of nodes examined for T3 and T4 tumors at center A was 26; center B, 20; and center C, 16 (P < .001). The node-positive rate for all T3 and T4 lesions was 49.7% at center A, 57.8% at center B, and 50.0% at center C (P < .001). Despite significant differences in the mean number of nodes examined between medical centers, the overall survival in patients with node-negative colorectal cancer in the 3 medical centers was not statistically different (P = .79). The criterion of examining 14 or more nodes distinguished between individuals at low risk for recurrence and those at increased risk.

Conclusions: Variability exists between medical centers in the pathological analysis of colorectal cancer specimens. However, within an institution, examining a mean of 14 or more nodes accurately stages apparently node-negative colorectal cancer and accurately predicts outcome.

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The presence or absence of nodal metastases is the single most important pathological determinant of prognosis in apparently localized carcinoma of the colon and rectum and currently represents the most important factor in determining whether an individual is a candidate for adjuvant systemic therapy. There is an increasing consensus that insufficient harvesting and/or examination of regional lymph nodes in individuals with colorectal cancer can have an impact on the outcome in apparently node-negative individuals, presumably because of understaging of the disease in these individuals. For this reason, appropriate measures to ensure that adequate numbers of lymph nodes are being harvested and/or examined are critical.

The outcome of patients with colorectal cancer with apparently localized disease is dependent on the quality of care received throughout a multidisciplinary treatment process delivered by numerous health care professionals. Much of the quality of the care is determined by the initial surgical outcome and accurate staging of the tumor at the time of diagnosis. Because individual surgical skills and other factors that impact surgical outcome are difficult to measure and evaluate, we have focused on the pathological processing of colorectal cancer specimens in an effort to improve the accuracy of staging in these specimens.

Our group previously reported that a minimum of 14 nodes need to be examined to accurately stage individuals with colorectal cancer. However, the recommended minimum number of nodes that need to be examined to accurately stage...
the regional lymph node basin has varied from 6 to 17 nodes. Still, others have suggested that considerably more nodes need to be examined to have a high probability of accurately staging these individuals and that most patients with colorectal cancer may be routinely understaged. Insufficient examination of the regional node basin can result in poorer outcomes. For this reason, establishing explicit criteria to measure the accuracy of staging in colorectal cancer is critical in assessing the quality of care delivered within a healthcare system.

It remains unclear whether explicit criteria developed in specialized centers are applicable to community medical centers. Anecdotal observations have suggested that these institutions are infrequently harvesting or examining the minimum of 14 nodes. However, the validity of these anecdotal observations has not been established. This report examines whether explicit criteria, previously reported to accurately stage patients with colorectal cancer, are being met and whether the outcomes observed in patients with node-negative colorectal cancer are predicted by explicit a priori criteria (a minimum of 14 nodes examined) in community medical centers.

**METHODS**

**PATIENTS**

Urban Honolulu, Hawaii, is served by 5 community medical centers. Under institutional review board approval, tumor registry data between January 1, 1990, and December 31, 2002, for individuals with the diagnosis of colon or rectal cancer from 3 of these community medical centers were reviewed. These 3 medical centers (designated A, B, and C in this report) represent the core teaching institutions for a community-based residency training program in both general surgery and pathology. A total of 2793 patients were identified. Individuals with in situ disease (256 patients) and those with nonregional metastatic disease at the time of diagnosis (stage IV) (371 patients) were excluded from the analysis because of the possibility that they had less than a recommended lymphadenectomy as part of their surgical management. Individuals who had a lymph node dissection performed but in whom the number of nodes examined was unknown were excluded from the analysis (17 patients). A total of 2149 patients composed the study population.

**TREATMENT APPROACH**

Resection of carcinoma of the colon and rectum was presumed to be performed by means of standard anatomic guidelines. No specialized surgical approaches, such as extended lymphadenectomies or no-touch techniques, were routinely used. Total mesorectal resection of the rectum has become increasingly a part of the surgical approach to carcinoma of the rectum. Radiation therapy for T3 and/or node-positive rectal cancer is routine, as is adjuvant systemic therapy for all patients with node-positive colorectal cancer. The use of preoperative radiation therapy in rectal cancer became increasingly common during the period of this study.

**PATHOLOGICAL ANALYSIS**

Specimens were routinely delivered to pathology in the fresh state and grossly examined by pathology assistants and pathology residents under the supervision of the attending pathologist. All laboratories in the study medical centers are staffed by general pathologists who interpret cases as assigned. Pathological interpretation by an organ subspecialty pathologist is not routinely performed. A gross examination protocol was used at all 3 study institutions, and the results were reported in a standard synoptic gross description format. Briefly, the colectomy specimen was oriented and the external surface was examined and inked over the palpable tumor. The specimen was then opened on the antimesenteric border, weighed, and measured. The tumor was identified and sectioned, and the distance from the proximal, distal, and radial margins was recorded. The mesenteric and adventitial fat was carefully displaced by manual pressure, visually inspected for lymph nodes, and palpated for the presence of firm tissue that was indicative of a lymph node. No specialized techniques such as fat clearance were used. The following standard sections were submitted for microscopic examination: proximal, distal, and closest radial margins; tumor including the area of deepest invasion and junction with adjacent normal mucosa; and representative uninvolved mucosa and lymph nodes. Representative sections were examined in all grossly involved lymph nodes; grossly uninvolved lymph nodes smaller than 3 mm were submitted whole, and those 3 mm or larger were bivalved and submitted for routine hematoxylin-eosin examination.

The T status of the tumor was determined after pathological examination of the resected specimen and defined according to the American Joint Committee on Cancer Staging criteria. Tumor grading was determined according to the degree of differentiation of the glands, the degree of nuclear and cellular pleomorphism, and the mitotic activity and reported in a standard synoptic format for colorectal carcinoma in accordance with recommendations from the College of American Pathologists.

**STATISTICAL ANALYSIS**

All statistical analyses were performed with NCSS statistical systems for Windows (NCSS, Kaysville, Utah). Survival was determined by the method of Kaplan-Meier, and statistical differences were compared by means of a log-rank test. The paired t test and χ² test were used where appropriate.

**RESULTS**

Fifty-six percent of patients were male. The patients ranged in age from 23 to 98 years (mean, 68.7 years). **Table 1** summarizes the anatomic distribution of the primary tumors in the study population. The majority of lesions occurred in the ascending colon, including the cecum and hepatic flexure, or the sigmoid or rectosigmoid colon. Eighteen percent of patients were treated for rectal cancers. The mean number of nodes varied between anatomic sites and by medical center (**Table 2**). The ascending colon had a mean of 22.9 nodes. In contrast, the anatomic site with the fewest nodes harvested was the rectosigmoid colon, with a mean of only 15.2 nodes (P < .001). There was a significant difference in the distribution of anatomic location between medical centers, with center A having more rectal cancers and less frequently lesions involving the transverse colon than the other study institutions (P = .006). The majority of patients (1333 [62%]) presented with T3 primary tumors; 281 (13%) had T1, 421 (20%) had T2, and 114 (5%) had T4. The number of nodes examined ranged from 0 to 97 (mean ± SD, 18 ± 15 nodes). Fifty-nine percent of pa-
tients (1261 patients) were node negative in the population. The median follow-up was 51 months (range, 0-164 months) for the entire study population. Node-positive individuals had significantly more lymph nodes examined than node-negative individuals (21.0 vs 16.6; \( P < .001 \)). Individuals who were node positive had a significantly worse survival than individuals who were node negative (median survival, 59 months vs 123 months; \( P < .001 \)).

Statistically significant differences were observed between the 3 study medical centers (Table 3). Patients treated at center C were older and tended to have more moderately differentiated tumors than the other study institutions and had significantly more early T-stage lesions. In addition, there were significant differences between the numbers of nodes examined at the 3 medical centers. However, all medical centers met the explicit criteria previously established. The mean number of nodes examined at center A was 22.3; at center B, 17.9; and at center C, 14.0 (\( P < .001 \)). This did result in a significant difference between the node-positive rates at the 3 study institutions. Because of the significant number of early

### Table 1. Anatomic Site of Primary Tumor

<table>
<thead>
<tr>
<th>Primary Site</th>
<th>Total (N = 2149)</th>
<th>A (n = 922)</th>
<th>B (n = 481)</th>
<th>C (n = 746)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascending*</td>
<td>603 (28.1)</td>
<td>259 (28.1)</td>
<td>132 (27.4)</td>
<td>212 (28.4)</td>
</tr>
<tr>
<td>Transverse</td>
<td>237 (11.0)</td>
<td>80 (8.7)</td>
<td>63 (13.1)</td>
<td>94 (12.6)</td>
</tr>
<tr>
<td>Descending</td>
<td>126 (5.9)</td>
<td>51 (5.5)</td>
<td>35 (7.3)</td>
<td>40 (5.4)</td>
</tr>
<tr>
<td>Sigmoid/rectosigmoid</td>
<td>779 (36.2)</td>
<td>325 (35.2)</td>
<td>178 (37.0)</td>
<td>276 (37.0)</td>
</tr>
<tr>
<td>Rectum</td>
<td>394 (18.3)</td>
<td>201 (21.8)</td>
<td>70 (14.6)</td>
<td>123 (16.5)</td>
</tr>
<tr>
<td>NOS</td>
<td>10 (0.5)</td>
<td>6 (0.7)</td>
<td>3 (0.6)</td>
<td>1 (0.1)</td>
</tr>
</tbody>
</table>

Abbreviation: NOS, not otherwise specified.
*Appendix, cecum, ascending colon, hepatic flexure.

### Table 2. Number of Nodes Harvested by Anatomic Site of Primary Tumor

<table>
<thead>
<tr>
<th>Primary Site</th>
<th>Total</th>
<th>A</th>
<th>B</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascending*</td>
<td>22.9</td>
<td>27.7</td>
<td>22.8</td>
<td>17.1</td>
</tr>
<tr>
<td>Transverse</td>
<td>19.9</td>
<td>29.3</td>
<td>16.2</td>
<td>14.4</td>
</tr>
<tr>
<td>Descending</td>
<td>20.4</td>
<td>26.2</td>
<td>19.2</td>
<td>14.0</td>
</tr>
<tr>
<td>Sigmoid/rectosigmoid</td>
<td>15.2</td>
<td>18.2</td>
<td>15.7</td>
<td>13.2</td>
</tr>
<tr>
<td>Rectum</td>
<td>16.3</td>
<td>18.4</td>
<td>15.7</td>
<td>13.2</td>
</tr>
<tr>
<td>NOS</td>
<td>17.6</td>
<td>18.5</td>
<td>16.3</td>
<td>16.0</td>
</tr>
</tbody>
</table>

Abbreviation: NOS, not otherwise specified.
*Appendix, cecum, ascending colon, hepatic flexure.

### Table 3. Patient Characteristics by Study Institution

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y (mean)</td>
<td>66.8</td>
<td>69.7</td>
<td>70.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Grade, % moderately differentiated</td>
<td>77.5</td>
<td>83.1</td>
<td>84.0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>T stage, No.</td>
<td></td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>1</td>
<td>116</td>
<td>48</td>
<td>117</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>159</td>
<td>115</td>
<td>147</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>604</td>
<td>266</td>
<td>463</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>43</td>
<td>52</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>No. of nodes (mean)</td>
<td>22.3</td>
<td>17.9</td>
<td>14.0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Positive nodes, %</td>
<td>42.0</td>
<td>46.4</td>
<td>25.5</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>T3-4</td>
<td>49.7</td>
<td>57.8</td>
<td>50.0</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>
T-stage lesions treated at center C, we examined nodal staging for T3 and T4 tumors at the 3 institutions. The node-positive rate for all T3 and T4 lesions was 49.7% at center A, 57.8% at center B, and 50.0% at center C (P < .001). Center B had the highest node-positive rate despite having only the second highest mean number of nodes harvested.

Despite statistically significant differences in the number of nodes examined, node-negative individuals from the 3 study institutions, when stratified by T stage, had no statistically significant difference in overall survival (P = .79). To determine whether the criterion of 14 or more nodes examined predicted outcome, we compared T3 or T4 node-negative individuals who had 13 or fewer nodes examined with those who had 14 or more negative nodes examined in the resected specimens (Figure). The 5-year actuarial survival for 13 or fewer nodes was 75.7%, and that for 14 or more nodes, 84.8% (P = .02) (Table 4). An absolute actuarial survival advantage of 25.7% was observed when node-negative individuals had 7 or fewer nodes identified and examined (P < .001) when compared with those with 8 or more nodes and diminished to 9.1% when 13 or fewer nodes were examined. However, between patients with 14 or fewer nodes examined and 15 or more nodes examined, there was no statistically significant difference in 5-year actuarial disease-specific survival.

Substantial evidence now supports the concept that the number of nodes examined affects the accuracy of staging of colorectal cancer and prognosis in node-negative individuals. However, the minimum number to most accurately stage colorectal cancer remains controversial. This report examines whether exclusion of individuals with 14 or more nodes examined in the resected specimens (Figure) can vary between surgeons and can affect outcome in colorectal cancer. Although well-established guidelines exist to standardize the conduct of colorectal surgery, substantial variations in performing the procedure may still be present, making it difficult to evaluate. Variations include discrepancies in anatomic definitions used, distal and proximal margins, extent of radial margins, adequacy of lymphadenectomy, and documentation of inadvertent perforation, all of which could have significant prognostic and therapeutic importance.

In our study we believed it was not unreasonable to presume that these variations are minimized in a community in which the majority of surgeons performing curative surgery for carcinoma of the colon and rectum were trained in the general surgery residency program that uses these 3 medical centers as core teaching institutions. For the foregoing reasons, as well as the complexity of assessing the surgical skills of individual practitioners, the structural aspects of the system were not examined in this report. However, we caution that potential surgical issues should not routinely be ignored. Our initial approach to quality assessment in the staging of colorectal cancer was to develop explicit process criteria that are easily measured and broadly applicable. Determining the number of nodes after curative resection meets this goal.

Anecdotal comments and observations from surgeons at the study institutions had raised the possibility...
that demonstrable differences might exist within our community medical centers and led us to examine whether previously established criteria were being met and whether they predicted outcome within each of the health systems. These anecdotal observations, in fact, were supported by our analysis. However, despite significant differences in the mean number of nodes examined, all institutions met the criteria previously established as indicating that an adequate nodal harvesting and/or examination had been performed.

It is well recognized that the number of lymph nodes harvested may vary between anatomic sites of the colon and rectum. Our results are consistent with these findings. Patients with tumors arising in the ascending colon have significantly more nodes examined than patients with tumors arising in the rectum, rectosigmoid, or sigmoid colon. The reasons for this are not apparent but might reflect a more extensive resection at some sites. Our analysis, however, did not allow us to compare the gross anatomic measurements of these specimens, which might provide some insight into these differences. Although differences exist in the distribution of primary sites between institutions, these differences are not likely to explain the differences between the mean numbers of nodes examined between medical centers, as the institution with the highest mean number of nodes examined also had the highest percentage of rectal cancers.

Evidence indicates that neoadjuvant therapy can impact nodal staging in rectal cancer. Baxter and coworkers, in a population-based study, demonstrated a significant difference in the number of lymph nodes examined in patients receiving preoperative radiotherapy when compared with those who underwent resection alone. Wichmann and associates demonstrated that preoperative radiochemotherapy in advanced rectal cancer resulted in a significant decrease in the mean number of lymph nodes examined and an increase in the number of patients having inadequate lymph node harvesting and/or examination. However, Tepper et al noted that the number of nodes in rectal cancer specimens that are examined and/or harvested can substantially impact outcome, and they suggested that a minimum of 14 nodes be examined to ensure adequate nodal staging.

Despite possible variations in treatment of patients with rectal cancer, the mean number of nodes harvested in the patients in this study was 16.3, well above the 14-node minimum hypothesized to accurately stage these individuals. However, medical center C barely achieved this minimum mean node examination, possibly because of differences in practice patterns with an increasing use of neoadjuvant therapy or the older age of the population. Recognition of the impact of neoadjuvant therapy on nodal staging requires increased diligence in both the resection and harvesting of the regional lymph nodes. This information should be considered part of the historical data when a rectal specimen is submitted to pathology and might warrant establishing separate nodal criteria for this anatomic site.

Outcome analysis for these node-negative individuals supports that the 14-node minimum was an appropriate criterion to indicate that patients in different medical centers, despite the significant differences in the mean number of nodes being examined, can anticipate similar outcomes. Node-negative individuals who have fewer than 14 nodes examined are at an increased risk of an adverse outcome (Table 4). These results are similar to those of Swanson and coworkers, who examined the relationship between the number of lymph nodes examined and prognosis in data from the National Cancer Data Base and observed significantly different 5-year survival rates for T3 N0 colon cancer when 14 or more nodes were examined. Prandi and coworkers demonstrated that the relative risk of recurrence increased when only 8 to 12 nodes were examined when compared with 13 to 17 nodes being examined. Le Voyer et al performed an analysis of Intergroup Trial INT-0089, a mature trial of adjuvant chemotherapy for high-risk patients with stage II and stage III colon cancer, to determine the relationship between survival and number of nodes analyzed from surgical specimens. They concluded that the number of lymph nodes analyzed is itself a prognostic variable on outcome. They suggested that examination of more than 20 nodes helped define patients with high-risk and lower-risk node-negative colon cancer. The reason for the differences in these recommendations is unclear but may represent differences in other, as yet undefined, primary tumor risk factors.

Our previous work suggested that the more nodes examined, the more likely nodal metastases will be detected, if they are present. In this report, medical center B, which had the second-highest mean number of nodes examined, had a significantly higher node-positive rate than the other 2 centers. This might be explained, in part, by the significant differences in the T stage at diagnosis between institutions, with center C having significantly more early-stage tumors. However, when only T3 and T4 lesions were examined, the statistical differences in the node-positive rate persisted between center B and the remaining institutions, although the node-positive rates for centers A and C were almost identical. The reasons for this remain unclear, although it may represent a function of the substantially different ethnic groups treated at each institution, the age of the individuals, and the higher number of T4 tumors at center B, or as yet poorly characterized primary tumor characteristics.

Although it is reasonable to presume that the observed differences in outcome in node-negative patients with fewer nodes examined can be attributed solely to stage migration, the possibility that fewer nodes are the result of an inadequate lymphadenectomy should not be ignored. A more extensive lymphadenectomy that selects unrecognized disease might contribute to improved outcome. In addition, aberrant lymphatic drainage has been observed during mapping of the lymphatics in carcinoma of the colon, and this might explain, at least in part, poorer outcomes in specimens with fewer nodes due to unresected disease in these nodes. This issue might be resolved by examining the site of first failure, but identifying a regional failure, in contrast to breast cancer or melanoma, is problematic. It is unlikely that any differences in outcome observed in node-negative individuals resulted from the benefits of adjuvant systemic therapy, as this has not been the standard of care in this community. To minimize the possibility that
surgical variation contributes to these outcomes, we emphasize that adherence to principles of cancer surgery remains essential.

Although our data support that identifying all nodes in a regional lymphadenectomy specimen is critical to accurate staging, identifying metastatic disease in these nodes represents a second potential problem. Techniques to improve the nodal harvesting, including fat clearance, are costly and time intensive and appear not to have improved on the standard approach that has been used in our pathology laboratories. Other options that might be considered include sentinel node identification, which has the potential to allow the pathologist to concentrate on hematoxylin-eosin–negative nodes that may harbor micrometastatic disease, although the approach remains controversial.

This report demonstrates the importance of documenting the quality of care in colorectal cancer by meeting explicit criteria. Despite numerous anecdotal reports about the absence of nodes in colorectal specimens, we have documented that institutions in our community meet previously reported criteria for accurate node-negative staging and that the 14–node minimum distinguishes node-negative individuals, who have a better prognosis than those with 13 or fewer nodes in the specimen. However, approximately half of patients in these study institutions were designated node negative on the basis of 13 or fewer nodes. This suggests that continued efforts to maximize lymph node harvesting and/or examination in these centers are warranted.

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REFERENCES


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nal evaluation and surgical treatment to prognosticate and stratify for further multidisciplinary management. Wong et al are to be lauded for further advancing the criteria for correct staging. In review of 2149 patients with colorectal carcinoma from 3 separate hospitals in Honolulu, 14 nodes examined have been validated again as a simple criterion to determine adequacy of staging T3 and T4 N0 disease. Patients with fewer than 7 nodes examined actually fared significantly worse and should be considered candidates for adjuvant chemotherapy.

In T3 and T4 N0 stage, the survival rates improve incrementally with greater numbers of lymph nodes examined, reaching a plateau at 14 lymph nodes recovered. This phenomenon can be explained by 3 main factors: (1) stage migration, (2) wider surgical margins encompassing potential sites of occult regional disease, and (3) postoperative adjuvant chemotherapy. Adjuvant chemotherapy most likely plays a minor role, since John Spratt indicated similar findings in 1967, when adjuvant chemotherapy was not used. In addition, the number of lymph nodes in pathological specimens was analyzed in a large phase 3 adjuvant chemotherapy study, the Intergroup 0089 Trial, in which all patients received chemotherapy, showing similar results with regard to number of nodes examined. Whether good pathology or good surgery or both are responsible, we will have to await results of prospective studies with predetermined surgical endpoints.

New methodologies currently under development, such as sentinel lymph node (SLN) mapping and molecular probes, including immunohistochemical tissue stains and polymerase chain reaction, have the potential to change the staging parameters. I would like to ask the authors, what is the impact of number of nodes examined in node-positive disease in their study? In terms of novel methodologies, are the authors presently using SLN mapping and any molecular probes, and what is their role in the staging process?

Michael J. Hart, MD, Seattle, Wash: Just one quick quibble with some of your statistics. You said that all of your institutions are meeting a 14-node minimum requirement. If hospital C only has a mean of 14.0 nodes, that means that almost 50% of their patients are below 14 nodes per patient. I don’t think that you can say that they are meeting the minimum.

Sherry M. Wren, MD, Palo Alto, Calif: Do your pathologists use any size criteria for cutoff of examination of a node? My institution’s pathologists do not want to examine nodes unless they reach a minimum of 7 mm. I find it so difficult to get a consistent number of nodes from the same operations because every month we have a change of pathology residents. How have you been able to standardize your protocols or techniques to get consistent high numbers of nodes?

Theodore X. O’Connell, MD, Los Angeles, Calif: My question is, even though the surgeons were trained at the same center and therefore that aspect is consistent, where were the pathologists trained? Obviously, the pathologists are a very important factor in this and they will almost always find as many lymph nodes as the surgeons want them to find. How is that controlled for in this study?

Dr Wong: Thank you, Dr O’Connell. Thank you, Dr Chu, for your discussion and provocative questions and to all of the other discussants as well for their questions. We have had considerable interest over the years in quality controlling the conduct of our colorectal cancer care. As Dr Johnson noted in his outstanding presentation, when we have presented these data in our community, the issue has arisen whether we actually are achieving the criteria that we are publishing for staging accuracy. The purpose of this paper was to examine whether our 3 main teaching hospitals were in fact achieving the minimum established criteria for staging accuracy in colorectal cancer. As the data indicate, we are.

Let me address questions that were asked. Dr Chu asked us, what is the impact of the number of nodes on node-positive individuals? We haven’t formally analyzed this at this point in time, but in our initial examination of these data, it again appears that we can establish criteria that suggest that the number of nodes being harvested in node-positive individuals actually does impact outcome. This is an ongoing analysis that we will report at a later date.

Dr Chu asked, were there roles for other types of pathological analyses, such as sentinel lymph node mapping or perhaps very sensitive molecular probes? We and others have investigated the role of sentinel lymph node mapping in colorectal cancer. Although we believe there may be a role for this approach in apparently node-negative colorectal cancer patients, the results of these studies remain somewhat controversial and probably need to be subjected to prospective randomized trials. However, I believe that sentinel node staging may provide an avenue that might allow us to obviate some of the difficulties that we discussed in terms of number of nodes.

Dr Hart correctly surmised that about 50% of our patients are not actually achieving the 14-node minimum. Because our analysis was to determine whether a mean of 14 nodes were being harvested, approximately 50% of this entire population is in fact not having 14 nodes examined. However, we were not asking the specific question, were all patients actually achieving the 14-node minimum, but rather, in our health care system, was the average of 14 nodes being achieved. This in fact was proven to be the case. However, it does indicate that more work needs to be done on these particular individuals in whom we potentially are not achieving that level of staging accuracy.

Dr Wren, a 3-mm lymph node in our view is the same as a 3-mm lymph node or a 10-mm lymph node. How do we determine whether it is a lymph node? Anything that is considered palpably consistent with a lymph node is put into a cassette and examined microscopically. On occasion the tissue submitted proves not to be lymphoid tissue, but we believe that these small fragments of tissue do need to be examined to determine their nature. Can small lymph nodes have metastatic disease? The answer is absolutely, and there are substantial data that would support that.

Dr O’Connell, do we have pathological controls? Similar to our surgical training program in which many of the graduating chief residents enter practice in the community, much of the pathology that is done in Honolulu is performed by graduates of the Pathology Residency Training Program. Is that reasonable control, or might there still be considerable pathology variability? I am unsure. I will mention that the most frequent comment I get with regard to these data by surgeons is, “We need your pathologist.” I want to emphasize that we as surgeons, as well as our colleagues in pathology, need to optimally perform what we are trained to do. It may be that a better operation is necessary in addition to good pathology.