

Intraoperative sentinel lymph node mapping in patients with colon cancer: Study of 38 cases

Yavuz ALBAYRAK¹, Durkaya ÖREN², Cemal GÜNDOĞDU³, Ali KURT⁴

Departments of ¹General Surgery Burn Unit and ⁴Pathology, Erzurum Region Education and Research Hospital, Erzurum
Departments of ²General Surgery and ³Pathology, Atatürk University, School of Medicine, Erzurum

Background/aims: Sentinel lymph node mapping has become a cornerstone of oncologic surgery because it is a proven method for identifying nodal disease in melanoma and breast cancer. In addition, it can ameliorate the surgical morbidity secondary to lymphadenectomy. However, experience with sentinel lymph node mapping for carcinoma of the colon and other visceral malignancies is limited. The purpose of this study was to evaluate the feasibility and reliability of in vivo sentinel lymph node mapping in patients with colon cancer. **Methods:** In the period March 2004 through June 2009, 38 patients underwent curative surgery for colon cancer. Thirty-eight patients with intraperitoneal colon tumors undergoing resection were studied prospectively. Sentinel lymph nodes were identified as the first blue-stained node(s) after in vivo peritumoral injection of Isosulfan blue dye. **Results:** Detection of sentinel lymph nodes was successful in 36 out of 38 colon cancer patients. In 94.7% of the patients with colon cancer, at least one sentinel lymph node was found. No patients had a false negative sentinel node. The sensitivity was 100%, with a negative predictive value of 100%. Aberrant lymphatic drainage was not identified in any patient. **Conclusion:** The technique of in vivo sentinel lymph node mapping is technically feasible with high sensitivity, high negative predictive value, and high accuracy. Although sentinel lymph node mapping did not alter the surgical management of colon cancer, it does make possible a more focused and cost-effective pathologic evaluation of nodal disease.

Key words: Sentinel lymph node, colon cancer, lymphadenectomy, aberrant lymphatic drainage

Kolon kanserli hastalarda intraoperatif sentinel lenf nodu haritalaması: 38 vakalık çalışma

Amaç: Sentinel lenf nodu haritalaması, melanom ve meme kanserinde nodal hastalığı göstermede kanıtlanmış bir metod olduğundan onkolojik cerrahide bir köşe taşı olmuştur. Ayrıca, lenfadenektomiye bağlı cerrahi morbiditeyi düzeltmiştir. Ancak, kolon kanserli ve diğer viseral malignansiler ile ilgili sentinel lenf nodu haritalaması hakkında deneyim sınırlıdır. Bu çalışmadaki amacımız, kolon kanserli hastalarda sentinel lenf nodu haritalamasının yapılabilirliği ve güvenilirliği araştırmaktır. **Yöntem:** Mart 2004 ile Haziran 2009 tarihleri arasında, küratif kolon kanser cerrahisi uygulanan 38 hasta prospektif olarak çalışmaya alındı. İzosülfan mavi boyasının in vivo peritümoral enjeksiyonu sonrası ilk boyanan lenf nodu veya nodları sentinel lenf nodu olarak tanımlandı. **Bulgular:** Kolon kanserli 38 hastanın 36'sında sentinel lenf nodu başarı ile belirlendi. Kolon kanserli hastaların %94.7'sinde en az bir sentinel lenf nodu tespit edildi. Hiçbir hastada yalancı lenf nodu yoktu. Sensitivite ve negatif prediktif değeri %100 olarak bulundu. Hiçbir hastada aberran lenf nodu drenajı tespit edilmedi. **Sonuç:** İn vivo sentinel lenf nodu haritalama tekniği, sensitivite, negatif prediktif değeri ve yüksek kesinliği ile yapılabilir bir yöntemdir. Sentinel lenf nodu haritalaması kolon kanserinde cerrahi yöntemini değiştirmemesine rağmen, nodal hastalıklarda lenf nodlarına odaklanarak ve maliyet-etkin şekilde değerlendirilmesini sağlayabilir.

Anahtar kelimeler: Sentinel lenf nodu, kolon kanseri, lenfadenektomi, aberran lenfatik drenaj

INTRODUCTION

Colon cancer was the seventh most common cancer in Turkey in 2005. It constitutes the sixth most

common cancer in men and women (1). It is well known that the nodal status of colon cancer is a

Address for correspondence: Yavuz ALBAYRAK
Erzurum Region Education and Research Hospital,
Department of General Surgery and Burn Unit, Erzurum, Turkey
Phone: + 90 442 242 22 75
E-mail: yavuzalbayaakdr@gmail.com

Manuscript received: 25.05.2010 **Accepted:** 21.09.2010

Turk J Gastroenterol 2011; 22 (3): 286-292
doi: 10.4318/tjg.2011.0214

major survival determinant. The presence of lymph node involvement signifies stage III disease and a marked decrease in the survival rate compared to stage I and II disease. Thus, the ability to identify nodal involvement more accurately is an important challenge in colon cancer (2).

In addition to establishing the prognosis, lymph node staging determines the adjuvant treatment strategy. The presence of nodal metastasis is the primary indication for adjuvant systemic chemotherapy. Chemotherapy offers a significant survival benefit for those with colon cancer (2-4). Conventional methods for examining lymph nodes have specific limitations and are subject to sampling error, which increases the risk of understaging. Since up to 70% of tumor-involved lymph nodes are less than 0.5 cm in diameter, nodes that contain small metastases can be easily missed in the gross dissection or microscopic examination (5,6).

The sentinel lymph node (SLN) concept is based on the premise that lymphatic drainage of tumors initially occurs through a small number of lymph nodes prior to draining into the lymphatic basin. The SLN is therefore the one most likely to harbor metastatic cells (2). Mapping the SLN may therefore help to identify unusual patterns of lymphatic drainage from a primary tumor site, which could then designate areas for extended regional lymphadenectomy. Methods of identifying the SLN and the value of studying these nodes for evidence of micrometastases have been described for most solid gastrointestinal tumors. Large multicenter studies have now validated the use of intraoperative lymphatic mapping with SLN, in both melanoma and breast cancer, as a means of eliminating routine elective lymphadenectomy in patients with clinically normal lymph nodes (7,8). Work on other solid gastrointestinal tumors, such as esophageal, gastric and colon cancer, has also gained ground in the last decade. At present, however, no consensus has yet been reached on the usefulness of SLN for colon cancer. Nevertheless, it is of interest to explore the use of new prognostic markers to evaluate the progression of this disease (9). Currently, the mainstay of treatment for non-metastatic colorectal cancer is complete surgical resection of the tumor-bearing colon, together with en bloc regional lymphadenectomy (10). As there is minimal associated complexity or morbidity with lymphadenectomy for this indication, SLN mapping and biopsy for colon cancer do not appear to provide any additional information that

would alter the extent of the operation. Rather, the principal advantage of SLN mapping in colon cancer would appear to be the identification of nodes that can provide the detailed pathologic scrutiny necessary for optimizing staging accuracy and for the upstaging of node-negative patients to node positivity (11,12).

The established method of SLN mapping in colon cancer is to use just one dye to guide the surgeon to the sentinel node. Colon cancer sentinel node mapping has, so far, seen very good accuracy and identification rates by many authors using only the dye-guided method (12-15). The most commonly used dye is Isosulfan blue. SLN mapping is carried out through an open procedure by injection of 1-3 ml Isosulfan blue with a tuberculin syringe and a 29-gauge needle subserosally in four quadrants around the tumor. The subserosal injection is carried out before vascular ligation. Within 5-10 minutes (min) after the blue dye injection, the SLN can be identified by following the blue-stained lymphatic vessels leading to the blue-stained SLN. These lymph nodes are tagged with a long suture. SLNs are defined as the first 1 to 4 blue-stained lymph nodes seen within the regional basin. After marking of the SLNs, routine resection is performed.

The purpose of this study was to determine whether SLN mapping is applicable to patients with colon cancer by evaluating the accuracy and predictive value of the SLNs in the pathologic staging of these patients.

MATERIALS AND METHODS

This study was performed between March 2004 and June 2009 in one regional hospital (Erzurum Region Education and Research Hospital) and in one university hospital (Atatürk University, Faculty of Medicine Hospital). Although the operating teams in these cases were different, the dyeing process and SLN marking were carried out by the same surgeon in all cases. The study was approved by the local scientific ethics committee (Ataturk University, Faculty of Medicine ethical committee decision no. 11, dated 2 April 2004), and all patients gave informed consent. Only patients with histologically proven primary colon carcinoma were included in the study. Exclusion criteria included stage IV recognized preoperatively and massive lymph node involvement, including spreading to the lumboaortic area. Prior gastrointestinal surgery and/or the presence of more than

one tumor were additional exclusion criteria. Since preoperative radiotherapy can cause sclerosis in regional lymph canals, resulting in a reduction in SLN mapping, patients who had undergone radiotherapy prior to the operation were also excluded from the study (10,16,17). The presence of rectal cancer was a further exclusion criterion.

Preoperatively, all patients underwent clinical evaluation, colonoscopy with biopsy and computerized tomography of the thorax and abdomen. An exploratory laparotomy was performed to find the extent of the primary tumor and any distant metastases. During initial mobilization of the bowel, attempts were made to minimize dissection of the mesenteric peritoneum. Once isolation of the primary lesion was performed, 1 ml of Lymphazurin (Lymphazurin 1% in aqueous solution; Ege University Faculty of Pharmacy, İzmir, Turkey) was injected subserosally by a tuberculin syringe around the primary tumor in a circumferential manner. Occasionally, slightly more than 1 ml of the dye was needed, i.e., in the case of a large primary tumor (5 cm). Care was used to ensure that there was no injection into the lumen of the bowel. In the technique, lymphatics stained blue within a few minutes, and the first 1 to 4 blue lymph nodes were categorized as sentinel nodes. They were removed en bloc with the specimen by a standard oncological resection of the primary tumor along with the draining of regional lymph nodes.

Histopathologic Protocol

Specimens were sectioned and processed within 4 hours of receipt in the laboratory to minimize postoperative movement of blue dye to nonsentinel nodes. Standard processing of the tumor included reporting the tumor size and grade, T stage and surgical margin status. Suture-tagged sentinel nodes were measured, described and embedded in a separate cassette. Pathologic review entailed routine microscopic analysis of the tumor, margins and all lymph nodes via hematoxylin and eosin (H&E) staining. Lymph nodes were manually dissected from the mesenteric fat. Routinely, no chemical fat clearance methods were used. All identified lymph nodes were bisected, and a single section was examined via H&E staining. If results were negative, each marked sentinel node was examined by a focused technique originally developed for the examination of SLNs draining colon carcinomas (5). The pathologist bisected or sectioned each sentinel node into slices no thicker than 2-3 mm. Paraffin sections, each approximately 4 µm

thick, were cut at two levels separated by 200 µm. One section from each level was stained with H&E. A false-negative SLN was defined as a sentinel node that contained no tumor cells when one or more nonsentinel nodes in the specimen were positive for tumor. Pathological examination was performed by two of the authors.

RESULTS

Thirty-eight patients with carcinoma of the colon were studied. Characteristics of the patients and primary tumors are detailed in Table 1. The mean patient age was 62.6 years (SD=15.4); the median age was 54.0 years (range: 32 to 78 years). Male gender was predominant, at 52.6%. In terms of TNM staging, the group encompassed 16 stage-II-I patients (42.1%), 20 stage-II patients (52.6%), and 2 stage-I patients (5.3%). The average tumor size was 5.2 cm (SD=4.8), with a median of 5 cm (range: 2.5-9.5 cm).

The total number of lymph nodes examined by the routine pathological method was 684, with a mean of 18 nodes retrieved per patient (684/38). SLNs totaled 115, with an average of 3.2 nodes per patient (115/36). At least one SLN (median 3 SLNs) was found in 36 of the 38 patients (94.7%); no SLN could be detected in 2 patients. One of the two failed procedures was in a patient with a carcinoma in the sigmoid colon surrounded by a concurrent multiple polyposis. The other patient had extended lymph node metastases with angio-invasion on pathological examination. All of the 684 nodes, including 115 SLNs and 569 non-SLNs, underwent a complete workup using stepwise sections. The false-negative rate, calculated as the number of patients with false-negative sentinel nodes (no patient) divided by the total number of patients

Table 1. Patients and primary tumor characteristics

Sex	
Male	20
Female	18
Age	
Mean	62.6 years
Histology	
Poorly differentiated	4
Moderately differentiated	18
Mildly differentiated	16
Anatomic site	
Ascending	13
Transverse	6
Descending	19

with lymph-node metastases (15 patients), was 0.0%. The accuracy of the SLN procedure in this study was 94.7%, as the pathological status of the SLN corresponded with the definitive lymph node status in 36 of the 38 patients. The sensitivity was 100%, with a negative predictive value of 100%. Table 2 summarizes the lymph node analysis. No metastases were found in the SLNs of 21 (55.2%) patients. Of these 21 cases, all other non-SLNs were also negative for metastatic involvement (0% false-negative rate). Therefore, we found no evidence of skip metastases to other nodes.

Aberrant lymphatic drainage was not identified in any patient. Additionally, none of the patients experienced an adverse reaction associated with intraoperative Isosulfan blue dye injection.

DISCUSSION

Determining the status of regional lymph nodes and minimizing the number of false negatives is of great importance for correct prognosis and choice of treatment regimen. Approximately 55% of patients with colorectal cancer present initially with disease confined to the wall of the bowel and no evidence of nodal metastases (stage I or II per the American Joint Committee on Cancer [AJCC]) (18,19). The necessity for improved staging is reflected by the fact that 20-30% of patients with stage II colon cancer will eventually die from a local tumor relapse or distant metastases (13). It is reasonable to assume that a considerable percentage of these patients represent a subset of patients with occult nodal metastases not detected by conventional histopathological analysis. It is important to recognize that lymphatic micrometastasis is one potential facet of an individual patient's multiple prognostic anatomic/pathologic parameters that could be used to determine the risk of recurrence. The current standard examination is histopathological evaluation of H&E-stained lymph node sections, sometimes supplemented by immunohistochemistry. These methods are time-

consuming, dependent on the supply of skilled pathologists, and micrometastases might escape detection since only a few sections of the lymph node are routinely analyzed. The concept of the sentinel node has proven useful in the context of identifying patients with lymphatic metastases since it can be regarded as being representative of the whole regional nodal basin, and thus allows for focused examination of a specific lymph node. Clearly, accurate staging of patients with colon cancer is important not only for prognostic purposes but also to identify those patients who can truly benefit from adjuvant chemotherapy (20).

Pathological sampling and evaluation of lymph nodes is controversial and its adoption varies from hospital to hospital. The optimal number of lymph nodes necessary for a definitive staging based on lymph nodes must be at least 12 to 16 (21-23). However, in a metaanalysis carried out in England, Johnson et al. (24) reported that fewer than 12 lymph node dissections were done in 33.2% of the cases operated for colon cancer. Thus, insufficient numbers of lymph node dissections are carried out in approximately one-third of colon cancer cases. This indicates a need for new methods that can facilitate the identification of lymph node metastasis in colon cancer patients.

The SLN concept is based on an orderly, stepwise progression of tumor cells from the primary site, through organized lymphatic channels, into the regional lymph nodes. Once the SLN has been identified, a dedicated and cost-effective evaluation of the SLN can be performed. When accurate SLN mapping is combined with a well-performed oncologic surgery, focused pathological analysis of the SLN(s) can add to the staging accuracy by identification of micrometastasis.

The first study in the literature on SLN mapping in colorectal cancers is the one conducted by Joosten et al. (25) in 1999 with patented blue V dye. Later, many other studies on this subject were added. In the SLN mapping Joosten et al. carried out

Table 2. Analysis of lymph nodes

	Number of patients	Percentage
Total number of patients (M/F)	38 (20/18)	100
Patients with identified SLN	36	94.7
Patients with positive lymph nodes with H&E	15	39.4
Patients with SLN and non-SLN metastasis	21	60.6
Patients with negative SLN and positive non-SLN (false negatives)	0	0

M: Male - F: Female. H&E: Hematoxylin and eosin.

on 50 consecutive patients with colorectal cancer, they determined the recognition rate of lymph nodes to be 70% and the sensitivity to be 45%. Fifteen patients whose SLN dyeing was negative were further subjected to immunohistochemical dyeing, and metastasis was discovered in 2 of the patients. With these results, Joosten *et al.* reported that SLN mapping was not an effective method for colorectal cancers (25). In a recently published compilation by Cahill *et al.* (26) of 52 studies conducted between 2000 and 2008 involving 3,390 patients, only 5 showed a sensitivity below 50%, whereas in 20 studies, this rate was observed to be over 90%. Of the 38 patients in our study, SLN mapping was successful in 36. In our study, the success rates of SLN mapping were seen to be 100% in the right and transverse colons, and 90% in the left colon. The reason for the high rate of success in SLN mapping in our study may be that the application of dyeing was carried out by the same physician and that rectal cancers were not included in the study. Due to the low success rate of SLN mapping in rectal cancers, Paramo *et al.* (19), Waters *et al.* (27), and Bendavid *et al.* (28) also excluded rectal tumors from their studies. Differing results were reported on the determination rate of false-negative results with SLN mapping. While very low rates of false-negativity were established in most of the studies, a higher rate (0-75%) was observed in a very small number (2,9,13-19,22,25,27-35). Bilchik *et al.* (33), in their study of 100 cases, reported identifying false-negativity in 5 of the 40 patients diagnosed with lymph node metastasis. Of these patients, 3 were stage III-IV patients. They noted that in 4 of these 5 patients, there was a technical error regarding the dyeing process, and 3 of them were among the first 30 patients of the study. Wood *et al.* (14), similar to Bilchik *et al.*, also established false-negativity in 5 of 44 patients, and reported that in 4 of these 5 cases, a technical error occurred. They also noted that these 5 cases were among the first 30 of the study, and were stage III-IV patients. Tsioulis *et al.* (34), in their study in which they applied dye injections through colonoscopy to 14 patients who had undergone laparoscopic colectomy, obtained a false-negative result in 1 patient. In the literature, it has been reported that in studies where false-negative rates were relatively high in SLN mapping of colorectal cancers, the reasons were mostly technical errors, lack of experience in SLN mapping, and patients in advanced stages such as stage III-IV (2,9,13-19,22,25,27-35). While false-

negative rates were reported as 0-75% in the compilation prepared by Cahill *et al.* (26), it is observed that in only 10 of the studies, the false-negative rate is over 30%. In our study, in conformance with many studies in the literature, there were no false-negative cases. The injection of the dye into the tumor or into the colon lumen, starting colon resection before or immediately after the dye is injected, damage to the lymphatic canals due to pre-operative radiotherapy, the primary tumor area being in the colon or rectum, or insufficient dye injection may be considered to be technical errors causing false-negative results in the SLN mapping of colorectal cancers (10). However, since the dye used for marking is lipophilic, the false-negative rate could be high, especially in overweight patients, and therefore the use of this method in overweight patients is precluded (35). Cahill *et al.* (26) reported that SLN mapping could also cause particular false-negativity in T3, T4, and larger-volume tumors and, therefore, should only be applied to specially selected patients.

In the compilation of Cahill *et al.* (26), although the success rates are given as ranging between 20-100% in the studies carried out thus far, they reported that the success rate was below 90% in only 11 of the 52 studies they researched. It has been observed that in SLN definition, the success rate increases after the first 5 cases. A study carried out by Paramo *et al.* (19) has shown that the learning curve of 7 surgeons in recognizing lymph nodes is relative to the consecutive operations they carry out. They have reported that after the first 5 operations, the lymph node recognition rate is over 98%. Bilchik *et al.* (33) reported that in the SLN mapping they carried out on 100 patients, technical insufficiencies were observed in the first 50 patients, and of the 5 false-negative results, 3 were among the first 30 cases. In our study, although the operating teams were different, the dyeing process and SLN marking were carried out by the same physician in all cases. We believe the 95% success rate in SLN marking was due to the same physician recognizing and marking the lymph nodes in all cases.

The unforeseen and irregular lymphatic spread in colon cancer from the submucosal lymphatic canals to the epicolic, paracolic, intermediate, and paraaortic lymph nodes is called aberrant lymphatic spread (10). In studies that have used SLN mapping, aberrant lymphatic drainage was reported in 0-10% of the patients (2,9,13-19,22,25,27-

36). In our present study, we had no patients with aberrant lymphatic drainage. Therefore, no changes were made in the lymphadenectomy limits in any of our cases as a consequence of SLN mapping. Although probable aberrant lymphatic spread may be detected by SLN mapping in colorectal cancer patients, the primary role of lymphatic mapping in colorectal cancer should be upstaging of node-negative patients to node positivity and a more accurate ultrastaging of patients (12,23). This would allow more exact establishment of the limits of the lymphadenectomy during the operation, thereby raising the success rate of surgical resection.

In conclusion, our study showed that the SLN mapping technique is technically simple, highly accurate, has a short learning curve, and has no apparent side effects. For colorectal cancers, SLN mapping carried out by an experienced surgeon with the proper dyeing technique results in a low rate of false-negative results, and thus a high rate of sensitivity. It allows the pathologist to focus at-

tention on a limited number of nodes for detailed analysis, thereby upstaging some patients with micrometastases that might otherwise have been missed by routine histological examination. The correct staging of colorectal cancer will facilitate the right decision for adjuvant chemotherapy for that patient, which in turn will improve the patient's survival.

In general, SLN mapping in colorectal cancers will not change the surgical treatment method or lymphadenectomy. The potential value of node mapping and SLN biopsy in colorectal cancer is the upstaging of node-negative patients to node positivity. However, this method does allow detection of probable aberrant lymphatic pathways. As a result, the limits of the lymphadenectomy during operation may be determined more precisely, thus increasing the success rate of surgical resection. The full impact of SLN mapping and the prognostic effect of micrometastases continue to be evaluated in prospective multicenter trials.

REFERENCES

1. <http://www.saglik.gov.tr/KSDB/BelgeGoster.aspx?F6E10F8892433CFF6407999D5EC50F896A5A2497543C96C6>
2. Baton O, Lasser P, Sabourin JC, et al. Ex vivo sentinel lymph node study for rectal adenocarcinoma: preliminary study. *World J Surg* 2005; 29: 1166-70.
3. International Pooled Analysis of Colon Cancer Trials (IMPACT) Investigators. Efficacy of adjuvant fluorouracil and folinic acid in colon cancer. *Lancet* 1995; 345: 939-44.
4. O'Connell MJ, Mailliard JA, Kahn MJ, et al. Controlled trial of fluorouracil and low dose Leucovorin given six months as postoperative adjuvant therapy for colon cancer. *J Clin Oncol* 1997; 15: 246-50.
5. Rodriguez-Bigas MA, Maamoun S, Weber TK, et al. Clinical significance of colorectal cancer: metastases in lymph nodes ≤ 5 mm in size. *Ann Surg Oncol* 1996; 3: 124-30.
6. Bilchik AJ, DiNome M, Saha S, et al. Prospective multicenter trial of staging adequacy in colon cancer: preliminary results. *Arch Surg* 2006; 141: 527-34.
7. Posther KE, McCall LM, Blumencranz PW, et al. Sentinel node skills verification and surgeon performance: data from multicenter clinical trial for early-stage breast cancer. *Ann Surg* 2005; 242: 593-9.
8. Morton DL, Thompson JF, Cochran AJ, et al. Sentinel-node biopsy or nodal observation in melanoma. *N Engl J Med* 2006; 355: 1307-17.
9. Des Guetz G, Uzzan B, Nicolas P, et al. Is sentinel lymph node mapping in colorectal cancer a future prognostic factor? A meta-analysis. *World J Surg* 2007; 31: 1304-12.
10. Stojadinovic A, Allen PJ, Protic M, et al. Colon sentinel lymph node mapping: practical surgical applications. *J Am Coll Surg* 2005; 201: 297-313.
11. Stojadinovic A, Nissan A, Protic M, et al. Prospective randomized study comparing sentinel lymph node evaluation with standard pathologic evaluation for the staging of colon carcinoma: results from the United States Military Cancer Institute Clinical Trials Group Study GI-01. *Ann Surg* 2007; 245: 846-57.
12. Ota DM. Is intraoperative lymph node mapping and sentinel lymph node biopsy for colorectal carcinoma necessary? *Ann Surg Oncol* 2000; 7: 82-4.
13. Saha S, Wiese D, Badin J, et al. Technical details of sentinel lymph node mapping in colorectal cancer and its impact on staging. *Ann Surg Oncol* 2000; 7: 120-4.
14. Wood TF, Nora DT, Morton DL, et al. One hundred consecutive cases of sentinel lymph node mapping in early colorectal carcinoma: detection of missed micrometastases. *J Gastrointest Surg* 2002; 6: 322-9.
15. Chan SH, Ng C, Looi LM. Intraoperative methylene blue sentinel lymph node mapping in colorectal cancer. *ANZ J Surg* 2008; 78: 775-9.
16. Prabhudesai AG, Kumar D. The sentinel lymph node in colorectal cancer – of clinical value? *Colorectal Dis* 2002; 4: 162-6.
17. Mulsow J, Winter DC, O'Keane JC, et al. Sentinel lymph node mapping in colorectal cancer. *Br J Surg* 2003; 90: 659-67.
18. Saha S, Nora D, Wong JH, et al. Sentinel lymph node mapping in colorectal cancer - a review. *Surg Clin North Am* 2000; 80: 1811-9.
19. Paramo JC, Summerall J, Poppiti R, et al. Validation of sentinel lymph node mapping in patients with colon cancer. *Ann Surg Oncol* 2002; 9: 550-4.
20. de Haas RJ, Wicherts DA, Hobbink MG, et al. Sentinel lymph node mapping in colon cancer: current status. *Ann Surg Oncol* 2007; 14: 1070-80.
21. Tepper JE, O'Connell MJ, Niedzwiecki D, et al. Impact of number of nodes retrieved on outcome in patients with rectal cancer. *J Clin Oncol* 2001; 19: 157-63.
22. Bilchik AJ, Nora DT, Sobin LH, et al. Effect of lymphatic mapping on the new tumor-node-metastasis classification for colorectal cancer. *J Clin Oncol* 2003; 21: 668-72.
23. Wiese D, Sirop S, Yestrepsky B, et al. Ultrastaging of sentinel lymph nodes (SLNs) vs. non-SLNs in colorectal cancer--do we need both? *Am J Surg* 2010; 199: 354-8.

24. Johnson A, Rees JR, Schwenn M, et al. Oncology care in rural northern New England. *J Oncol Pract* 2010; 6: 81-9.
25. Joosten JJ, Strobbe LJ, Wauters CA, et al. Intraoperative lymphatic mapping and the sentinel node concept in colorectal carcinoma. *Br J Surg* 1999; 86: 482-6.
26. Cahill RA, Leroy J, Marescaux J. Could lymphatic mapping and sentinel node biopsy provide oncological providence for local resectional techniques for colon cancer? A review of the literature. *BMC Surg* 2008; 8: 17.
27. Waters GS, Geisinger KR, Garske DD, et al. Sentinel lymph node mapping for carcinoma of the colon: a pilot study. *Am Surg* 2000; 66: 943-5.
28. Bendavid Y, Latulippe JF, Younan RJ, et al. Phase I study on sentinel lymph node mapping in colon cancer: a preliminary report. *J Surg Oncol* 2002; 79: 81-4.
29. Read TE, Fleshman JW, Caushaj PF. Sentinel lymph node mapping for adenocarcinoma of the colon does not improve staging accuracy. *Dis Colon Rectum* 2005; 48: 80-5.
30. Thomas KA, Lechner J, Shen P, et al. Use of sentinel node mapping for cancer of the colon: 'to map or not to map'. *Am Surg* 2006; 72: 606-11.
31. Lim SJ, Feig BW, Wang H, et al. Sentinel lymph node evaluation does not improve staging accuracy in colon cancer. *Ann Surg Oncol* 2008; 15: 46-51.
32. Saha S, Seghal R, Patel M, et al. A multicenter trial of sentinel lymph node mapping in colorectal cancer: prognostic implications for nodal staging and recurrence. *Am J Surg* 2006; 191: 305-10.
33. Bilchik AJ, Nora D, Tollenaar RAEM, et al. Ultrastaging of early colon cancer using lymphatic mapping and molecular analysis. *Eur J Canc* 2002; 38: 977-85.
34. Tsioulis GJ, Wood TF, Spirt M, et al. A novel lymphatic mapping technique to improve localization and staging of early colon cancer during laparoscopic colectomy. *Am Surg* 2002; 68: 561-5.
35. Retter SM, Herrmann G, Schiedeck TH. Clinical value of sentinel node mapping in carcinoma of the colon. *Colorectal Dis* 2010 (Epub ahead of print).
36. Demirbaş S, Ince M, Baloglu H, Celenk T. Should sentinel lymph node mapping be performed for colorectal cancer? *Turk J Gastroenterol* 2004; 15: 39-44.