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Utility of Frozen Section Analysis of Sentinel Lymph Node Biopsy for Melanoma in Surgical Decision-Making

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Abstract

Background—Debate exists whether frozen section analysis of sentinel lymph nodes (SLN) for melanoma is an accurate method to detect metastatic disease to the lymph nodes. The purpose of this study is to evaluate the utility of intra-operative frozen section for SLN's in melanoma.

Methods—We reviewed 133 patients (271 nodes) who underwent a SLN biopsy with frozen section for melanoma between April 2003 and September 2007. Frozen section diagnosis was compared to final diagnosis to determine concordance between intra-operative and postoperative diagnosis.

Results—A total of 11 nodes (8% of patients) were found to have metastatic disease. All patients underwent lymph node dissections at the time of SLN biopsy. No false positive SLN's were found on frozen section. False negative rate for SLN biopsy frozen section was 1/133 patients (0.8%).

Conclusion—Intra-operative frozen section can be an accurate and reliable tool in the right setting for analysis of sentinel nodes in cutaneous melanoma and deserves further study.

Keywords

Sentinel lymph nodes; melanoma; frozen section; completion nodal dissection

INTRODUCTION

A report from the American Cancer Society estimates that nearly 60,000 Americans will develop melanoma in 2008. In men, melanomas most often arise in the head, neck or trunk, while in women lesions typically appear on the extremities. The pattern of dissemination for these tumors, however, is the same. Cutaneous melanomas first spread to the sentinel node, the lymph node preferentially draining a particular area of skin, and from there to other regional nodes and finally the systemic circulatory system. This was first recognized by William Sampson Handley who stated in 1907 that surgical excision with regional lymph node dissection should be performed in the treatment of patients with melanoma. Handley's recommendations formed the basis of treatment of malignant melanoma for the next 60 years[1].

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Melanoma is highly curable with surgical resection when localized to the primary site, but after melanomas spread to the regional lymph nodes the 5-year survival rate is only 29% and once disease has disseminated to major organs the rate falls to 7%[2, 3, 4]. Although wide local excision is still the standard of care for the primary tumor site, the treatment of the regional lymph node basin has evolved over the last twenty years. Our current therapy for patients with clinical regional lymph node involvement includes appropriate wide local excision of the primary tumor and removal of regional lymph nodes[5, 6]. Lymphadenectomy can be beneficial to patient health and can serve an important palliative role in distant disease[6], however removal of uninvolved lymph nodes can have long-term consequences such as reduced immunological capability, tissue morbidity, and lymphedema, i.e. swelling due to poor drainage, which may outweigh survival benefits[2, 7]. Since a majority of patients with clinically negative regional lymph nodes will not have nodal involvement with tumor by histology, treatment of the regional lymph node basin has evolved to the sampling of sentinel lymph nodes (SLN) with removal of regional lymph nodes only if the SLN is positive for tumor[8, 9]. This procedure is performed for primary skin tumors greater than 1mm in thikcness[10]. Success rates identifying the sentinel node have been reported as 99.5% with a false-negative rate on frozen section ranging from 5–12%[11–13].

Debate exists regarding whether frozen section analysis of SLN's for melanoma is accurate enough to guide intra-operative surgical decision-making leading to completion lymph node dissection (CLND) at the time of SLN biopsy. Due to this high false negative rate up to 12%, many centers argue against intra-operative frozen sections and favor a second procedure upon the final result of the SLN biopsy[12, 14, 15]. However, other centers feel that frozen section is useful in that it allows for completion lymph node dissection (CLND) to be performed in the same procedure as the sentinel node biopsy using one anesthetic, which is highly preferred by patients who don't have to return for a second procedure which potentially subjects them to additional risks. In fact, one study even reports that survival of patients with false-negative results of SLN biopsy is not statistically significant from that of patients undergoing completion lymph node dissection (CLND)[16]. The purpose of this study is to evaluate the accuracy of intra-operative frozen section for melanoma sentinel lymph nodes in our institution and its utility in the surgical decision-making process to avoid the morbidity of a second operation for a completion lymph node dissection.

METHODS

A retrospective review was completed on 133 patients who underwent a wide local excision for melanoma by with SLN biopsy by three different surgeons at our institution (a tertiary care academic medical center) between April 2003 and September 2007. All patients underwent preoperative injection in the nuclear medicine department with 1 millicurie of ^{99m}Tc sulfur colloid solution. The solution was injected subdermally at the site of the cutaneous melanoma primary lesion.

Prior to resection of the cancer, 0.5 to1.0 ml of lymphazurin blue-dye was injected under the melanoma lesion and massaged into the tissue for a period of five minutes. Prior to patient positioning, the sentinel node was first grossly localized with a handheld gamma counter. The operation then proceeded with wide excision of the primary cutaneous tumor using approved margin recommendations. After resection of the primary melanoma, the lymph node basin was assessed by sentinel node biopsy. The SLN was found using the combination of blue dye technique and gamma radiation counts. Nodes having dye-uptake and or increased gamma counts were removed as "sentinel nodes" and sent for frozen section analysis. The procedure was completed once all background tissue was less than 10% of the gamma count value of the sentinel nodes[17].

All sentinel lymph nodes (N = 271) were examined via frozen section by board-certified pathologists at the time of operation. The lymph nodes received during surgical operation in the pathology laboratory were examined macroscopically and bisected. One part was frozen and sectioned, the other part was analyzed for final permanent section by fixation in formalin. Frozen sections were all performed in duplicate and the slides were stained routinely with hematoxylin and eosin (H&E), cover-slipped, and examined microscopically. Permanent sections are embedded in paraffin and routinely sectioned and stained with hematoxylin and eosin for microscopic examination. Duplicate sections are then stained immunohistochemically with antibodies to S-100 and a melanoma cocktail containing antibodies to HMB-45 and Melan-1. Positive and negative controls are run in parallel in each case.

Frozen section diagnosis was compared to final diagnosis to determine concordance between intra-operative and post-operative diagnosis. Final pathology was verified in 3–5 days and patients were called back into our clinic for completion nodal dissection if discordance was found. Statistical analysis was performed on table variables using the chi-squared test in SAS to compare tumor type and Clark's thickness in both men and women. Fisher exact test was used to analyze tumor stages and student t-test was used to analyze age and the Breslow depth of the tumor in both men and women. Significance for all statistical analyses was defined as a p-value <0.05.

RESULTS

From April 1 2003 through September 1 2007, a total of 133 patients underwent SLN biopsy procedures for cutaneous melanoma, yielding a total of 271 sentinel nodes (average of 2.04 nodes per patient). Of these, 8% of patients (4% of all sentinel nodes) were found to be positive for malignancy on frozen section. Table 1 summarizes the data with regards to patient and tumor characteristics. The data was broken down to evaluate the tumor stage, pathologic type, Breslow thickness, and Clark's level for both men and women. Sentinel node characteristics are summarized in Table 2, including a comparison of the false negative rate of the SLN in relation to the total number of patients and total number of SLN that were evaluated.

The average overall age of patients in our study was 57 years. Men were significantly older at presentation (average age of 60 years) than women (average age of 54 years) with a p-value of 0.04 (Table I). Complete pathological staging data was available on 88 patients. As expected, the majority of patients in this study were found to have either stage I (N = 40) or stage II (N = 37) melanomas. Eleven patients (8% of 133 total patients) had stage III disease with positive sentinel nodes. There were no patients with stage IV disease. Women were significantly more likely than men to have earlier stage disease (61% stage I vs. 43% in men) whereas men were more likely to have advanced disease (65% stage II vs. 29% in women; $p = 0.02$). Little difference was found between men and women in stage III disease (18% vs. 11%; $p = 0.31$).

The most common pathologic tumor type (Table I) was superficial spreading melanoma (57%), followed by nodular sclerosing (22%), lentigo (13%), and then acral lentiginous (9%). This trend was consistent for both men and women as we did not observe any statistical differences between genders.

Of the 133 melanoma patients evaluated for SLN biopsy, Breslow thickness data were reported on 77 patients (58%). Thirteen patients had T_1 primary tumors (Breslow <0.75mm), 30 had T_2 tumors (Breslow 0.76–1.5mm), 27 had T_3 tumors (Breslow 1.51–4.0mm), and 7 patients had T_4 tumors (Breslow >4.0mm). This correlated to overall percentages of 17, 39, 35, and 9%, respectively (Table I). In comparing the Breslow thickness in both men and women, we found that women have a higher percentage of T_2 tumors (54% vs. 26%) while men had more

T_3 disease (43% vs. 26%) but neither differences were found to be statistically significant with a p = 0.54 for T_2 tumors and 0.82 for T_3 tumors. Minimal difference was found between the genders in T_1 and T_4 disease with a p-value of 0.82 for T_1 and 0.22 for T_4 tumors. Clark's Level data were available on 50 patients (38%) with a majority of patients having Clark's level IV tumors. Men, however, were significantly more likely to have Clark's level IV tumors (66% vs. 33%) while women tended to have level III tumors (43% vs. 10%; p= 0.01 using fisher exact test).

In this study, of the 133 patients and 271 SLN's evaluated, 8% of patients and 4% of nodes were found to have tumor spread based on frozen section (Table II). Overall, 10 SLN's were positive on frozen section and 11 were positive on permanent evaluation. This led to a single false negative SLN, or 0.8% of all patients and 0.4% of all SLN's, respectively. We did not have any false positive nodes. The overall sensitivity of intra-operative frozen section was 91% with a negative predictive value of 99.6% and a specificity of 100%.

DISCUSSION

Accurate staging of melanoma is important to assess patient prognosis and determine which patients would benefit from adjuvant therapy. The staging process currently includes evaluation of the patients' regional nodal status, performed by lymphatic mapping with SLNB and subsequent completion nodal lymphadenectomy if the SLN is positive for malignant cells. This model for nodal analysis has led to a drop in the performance of CLND and its complications such as lymphedema, wound infection, and nerve injury[18]. There remains a debate as to whether SLN frozen section is accurate enough to direct when CLND should be performed. The addition of an accurate intra-operative frozen section of the SLN can help guide management of the nodal basin, allowing either termination of the procedure or continuing with a CLND during the same operation. This could obviate the necessity of a secondary procedure, which carries the potential morbidity of a second incision and anesthetic, additional recovery time as well as time lost from work to schedule the operation.

Controversy exists over the use of frozen section to determine the malignant status of a melanoma SLN due to the high false negative rates and low sensitivities (as low as 47 to 59%) reported[12, 14]. Studies have suggested drawbacks to intra-operative frozen sectioning, such as the risk of missing micrometastatic disease or a small cluster of isolated melanoma cells due to frozen section sampling errors. Additionally, some authors note that diagnostic tissue can be lost during the method of facing the block for frozen section[19]. Tanis et. al. found that frozen section is well utilized in breast cancer with a 74% sensitivity but did not endorse frozen section in melanoma as they found a 47% overall sensitivitiy[14].

While some studies have not endorsed the use of frozen section analysis for the detection of metastatic disease[12, 15], others have accepted the use of frozen section in the evaluation of SLN in melanoma. Gipponi et. al. evaluated a total of 169 patients and found only 9 false negatives, a rate of 5.3%. Of those, only two (1.1%) were macrometastasis and the rest were micrometastasis discovered by permanent evaluation[20]. Similarly, Ariyan et. al. looked at 263 patients and found a false negative rate of only 7% (2/28)[13].

Data from this study echoes previously reported series suggesting that SLN evaluation with frozen section indeed has a high concordance rate with the permanent pathologic evaluation[13, 20]. In our cohort, only one patient was noted to have a false negative SLN on final pathologic evaluation (0.8% or 1/133) using H&E and immunohistochemistry and this patient was felt to have micrometastatic disease. Using the total number of sentinel nodes studied, the false negative rate drops to 0.4% (1/271). No false positive nodes were discovered in our study. All the nodes discovered to have metastatic melanoma on frozen section were

verified on our permanent evaluation. The overall sensitivity of intra-operative frozen section is 91% while the NPV is 99.6% and the specificity is 100% as we did not have any false positive nodes. These numbers again closely resemble Gipponi et. al. who reported a sensitivity of 76.3% for T_1/T_2 tumors, 90% for T_3/T_4 tumors, and a specificity of 100%[20]. Although not reported, their data shows an overall sensitivity of 82% for all tumors. Unlike Gipponi, who advocated frozen section use only in T_3 and T_4 tumors, we found the use of frozen sections to be accurate and valid in all T stage categories.

The lone subject with the negative concordance between the frozen and final pathology was a 59 year-old male with a 1.2mm thick, Clark's level IV melanoma. This patient had a micrometastasis discovered on final S-100, HMB-45, and Melan-1 immunohistochemistry staining. The concern about missing a micrometastasis on frozen section has been posed in various other studies[15, 19]. These concerns include tissue loss during "facing-up" of the SLN and tissue distortion after thawing the node for formalin-fixing at room temperature[15]. This issue of missing micrometastatic disease could lead to delayed diagnosis and recurrence of the tumor at an advanced stage. While this potential concern exists, this study only noted one patient out of 133 with micrometastatic disease found on permanent evaluation which led to a prompt CLND. Gipponi et. al. had only 9 false negatives, however, only 2 two (1.1%) were macrometastasis and the rest were micrometastasis discovered by permanent evaluation.

Definitive examination of the SLN's with serial sectioning and IHC or molecular biology techniques detected 16–30% of SLN's that had been classified as negative by routine H&E staining[20]. Ariyan et. al. raised the question of how often small foci of metastatic cells are not identified on permanent sections. Their final pathologic evaluation included S-100 and HMB-45 stains which were able to pick up an additional 3 patients with micrometastatic disease[13]. Nodes evaluated in permanent section were subjected to not only standard H&E staining, but also detailed immunohistochemistry staining with S-100, HMB-45 sand Melan-1, which should be sufficient for the detection of micrometastatic disease.

Of the 133 consecutive patients, 8.3% of our overall population demonstrated stage III disease with spread to the lymphatics. This rate is less than those reported in other studies which average between 15 – 24%[9, 21, 22]. Part of this reflects the larger percentage of patients in lesions having wide local excision with SLN biopsy. Our study population this study with T_1 contained 13 patients with tumor depths less than 0.75mm with an average depth of 0.57mm ± 0.18. Since the rate of metastatic spread in tumors of < 1mm is less than 4%[23], this would suggest that many of the patients in our study were low risk for metastatic spread, lowering the overall percentage of patients with nodal disease. The low percentage (8.3%) of positive SLN based on final pathologic evaluation does decrease the overall power of our study as we hoped to find more patients with positive lymph nodes. In this group of patients with lesions less than 1mm Breslow thickness, SLN was performed due to either patient risk factors (high risk patient, family history of melanoma or personal history of skin cancer) or positive deep margin on initial biopsy prior to referral indicating a likely deeper lesion.

The significance of metastatic detection in frozen section of melanoma lymph nodes remains controversial. Although current recommendations are against the use of this approach, our data show that the frozen section can be useful for the evaluation of low risk patients. We cannot fully explain why metastases was discovered in only 8.3% of patients, other than to suggest our patients had a low risk for metastatic disease. However, we would like to argue that only these 8.3% of patients had metastases large enough to be clinically significant. Future research on the detection of melanoma metastases by means of molecular biology will show whether those metastases invisible microscopically are of clinical significance, or like tumor cells circulating in the blood are of no clinical significance at all.

Our institution has a dedicated group of pathologist who review all of the frozen and permanent pathologic results of melanoma sentinel lymph nodes. We believe this has helped improve the accuracy of frozen section results at our hospital. Although variability is certain between different pathologists, a standardized method for evaluation of the frozen SLN's exists. We recommend that each institution assign a set of pathologists to consistently evaluate melanoma SLN's. If random pathologists are evaluating the SLN frozen section, the accuracy of the frozen section results may decrease and render this intra-operative method for assessing melanoma SLN's inaccurate.

We used the older AJCC classification for Breslow thickness instead of the newer classification introduced in 2002. The older method was chosen as it allowed us to compare results with previous papers published using the older AJCC Breslow classification. However, using the older AJCC classification did not change the overall results and we feel had little impact on the false negative rates of our frozen section sentinel lymph nodes. Also, regarding table 1, not all of the pathologic data for each patient was complete in the database. We were unable to attain complete staging, tumor type, Breslow, Clark's level thickness for all 131 patients. Therefore, some of the data may seem incomplete. However, we did discuss trends that were noted with the available data.

In this series, men presented with thicker lesions than women which is consistent with historic data. Since most patients had follow-up for less than 2 years, disease-free survival data was not reported and is currently being tracked at our institution. For future studies it will be important to evaluate the local failure rate and rate of recurrence in the regional lymph node basin as well as this effect on overall survival. Gershenwald et. al. looked at 243 histologically negative SLN's and found 27 or 11% with nodal recurrence. Only 4.1% developed nodal metastasis in the previously mapped basin[23]. A similar study out of Massachusetts General Hospital reported similar findings with only an 8% regional lymph node recurrence[24]. Another group from Poland reported that survival of patients with false negative results of SLN biopsy does not differ statistically significantly from that of patients undergoing CLND[16]. Due to the high correlative rate of a negative SLN indicating a negative regional lymph node basin, we expect this limitation should not diminish the utility of intra-operative frozen section in assisting the surgeon in identifying patients appropriate for concurrent CLND.

While there are several potential benefits to performing intraoperative frozen section on the SLN, including ability to perform a CLND under the same anesthetic without subjecting the patient to an additional procedure days to weeks later, we did not perform a detailed cost-analysis comparing intra-operative frozen section, operative time and the cost of a second operation on a different day. Future studies evaluating long-term follow-up and outcomes in these patients will also attempt to evaluate cost comparison; however results from a retrospective study comparing results performed by three different surgeons at a tertiary-care facility will need to be carefully analyzed to account for surgeon-dependent variability in operative time and technique.

CONCLUSION

At our institution, intra-operative frozen section is a highly accurate test that can be utilized in melanoma patients undergoing SLN biopsies. The low false negative rate (0.4 to 0.8%), high sensitivity (91%), NPV (99.6%) and specificity (100%) demonstrate the accuracy and reliability of this technique among all melanoma T stages. Having an accurate staging assessment of draining lymph nodal basins allows completion lymph node dissections to be performed at the time of SLN biopsy, avoiding the potential morbidity and cost of a second procedure and anesthetic. For these reasons, we believe this technique is promising and deserves further study.

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Appendix

Discussion

Dr. Edward Nelson (Salt Lake City, UT): Whether to do an intraoperative sentinel node evaluation in staging melanoma patients is a question of ongoing debate, since the accuracy of immediate evaluation of sentinel lymph nodes determines the need for full nodal dissection or a later second operation for these patients. I have several comments regarding this report. First, although the patients included in this study underwent surgery between April of 03 and September of 07, they were evaluated using the older AJCC staging system and not the newer staging system introduced the year before in 2002. In addition, I found the characteristics of the patient population a little difficult to follow and interpret based on the data presented. To be more specific, the total number of patients was 133, yet only 88 individuals were staged; only 23 had tumor type described, and only 77 reported breast node thickness measurements. A more thorough description of this information for the total patient population would have made interpretation of your data more meaningful and perhaps a little less confusing. Given these concerns about the data, the point of this manuscript is to evaluate the accuracy of intraoperative sentinel lymph node evaluation with frozen section which at your institution is apparently very accurate, with a false negative rate of only 0.8%. I have three questions: First, since frozen section evaluation which involves bisection of the sentinel nodes has been criticized as a technique which may miss small metastasis, can you tell us more about the technique at your institution – whether serial sections were performed? Do you have a dedicated group of pathologists or do you have other special techniques. My next question is related to my first and that is why is your false negative rate of 0.8% is approximately one tenth that reported in the literature? Is this somehow related to the population you studied? How the nodes were evaluated intraoperatively and on final pathology? And finally, just a hypothetical case – can you tell us how you would handle a low risk patient with a thin melanoma if on sentinel node frozen section evaluation, the nodes are negative, but on permanent evaluation the so-called nanometastases or passenger cells are found on more sophisticated staining. I appreciate the opportunity to have read this manuscript in advance. I enjoyed your presentation and look forward to your answers.

Dr. Weesam Alkhatib (Kansas City, KS): Thank you Dr. Nelson. I will go ahead and first start with the comment about the staging of the tumors. Now, what we had initially looked at is that the reason we had used the older staging is there is previous studies that had used the older staging and had suggested that frozen section should be used for T1 and T2 lesions using just their older staging methods which was 0.75 and then 0.75 to 1. So what we wanted to do was correlate our data with their data, so that is why we used the older staging to see that they would correlate with one another. The second thing is talking about the patient population with respect to – there is confusion with respect on the first slide that I had because I didn't have full staging information, full breast node thickness information. The pathologic evaluations over the last four years not every path report had a both Clarks level and a breast node level. Not every report looked at – some of the reports came from outside institutions so they did not give us the thickness – the University of Kansas did not give us the thickness because the initial

biopsy was done at an outside institution. However, with that said, that doesn't affect the overall results that we found with respect to frozen section because the biopsies were done and we did do our frozen sections and then evaluate them with permanent sections using immunohistochemistry staining. Looking at the three questions that you had: We do have a dedicated group of pathologists looking at melanoma. What they do is they take a node and bivalve it – just put it in half. One is used for permanent, the other is used for frozen. They will then section the half that is frozen until they get to a cross-section where they believe gives them adequate representation of the node. They will then cross-section this which I believe is between 1–2 mm in thickness, cross section that, and place it on a slide. They will make a duplicate placed on a slide. They will perform four different cross sections. So they will have four slides with a duplicate on their frozen side. Until they get to near the end of the half where there is a frozen section and the remaining portion will be sent for permanent evaluation. There is a possibility that you could lose micrometastatic disease. The other question looking at the reason we had such a low rate of 0.8% and what it relates that to our patient population. Again, we do have aggressive dermatologists. They gave us a lot of patients with T1 T2 lesions and we did look at a significant portion of patients with T1 lesions. So, possibly based on that, it would lower the overall false negative rate. However, it doesn't change the overall results that we found. There is still one out of 132 patients who did have a false negative node. And I think finally there is a question of a hypothetical patient. If they did have micrometastatic disease, the question is would you perform complete lymph node dissection. At this moment, with no other data, if there is positive micrometastatic disease, a complete lymph node dissection from our suggestion should be completed. But this study is being looked at by the MSL T2 study, looking at whether metastatic disease should lean to complete lymph node dissections.

Dr. Kelly McMasters (Louisville, KY): I appreciate the care with which you have done your analysis and presented in your results, but I don't really want anybody going away from this presentation thinking that frozen section for sentinel nodes for melanoma is a good idea. The College of American Pathology recommends against it and a recent international consensus conference of the International Sentinel Node Society with a group of expert melanoma pathologists from around the world has unanimously recommended against doing sentinel node frozen sections for . That report will be published in the near future. The problem is that even the best experts in melanoma pathology in the world don't feel they can accurately find micrometastatic disease on frozen section and that the tissue wasted can help miss some micrometastasis. In your own series you have an 8% rate of positive sentinel nodes; every other study published is somewhere between 15% and 20%. So, either you have missed half of the positive sentinel nodes or you have done sentinel node biopsy on a series of patients with a really low risk – some of them probably didn't need to have it done. So, I would like your comments on that.

Barbara Pockaj (Phoenix, AZ): I kind of echo some of Kelly McMasters' comments. I have just two questions for you to help get a better understanding of your data. 1. How many patients were truly T1 lesions based on the new staging system in your sample, and then of those patients that were sentinel lymph node positive, what were the size of the metastasis found on frozen section?

Dr. Weesam Alkhatib (Kansas City, KS): Thank you for your questions. I will go ahead and address the first question. Going back to that 8% number that we looked at, the reason for that is we did have a significant portion of patients who were T1 lesions. Now, we found and we actually looked at those patients, in that T1 lesions, the average depth of the tumor seemed to be 0.57 mm. Now, because I think those people were added to our study, it decreases the overall percentage of patients who did have positive sentinel lymph node on both frozen and final pathologic evaluation. So, I think that was the main reason why we had a lower number of positive sentinel lymph nodes. Now, I agree that many studies have shown between a 15 and

24% positive sentinel lymph node biopsy rate, but still, with that said, even looking at our other T2 T3 T4 lesions, we didn't find that doing a frozen section with our data affected the overall false negative rate. The second question how many are truly T1 lesions based on the newer staging? And also the third question, what was the size of the metastasis? We did not look at both of those. We don't have any data regarding this so I cannot adequately answer your question with respect to the second and third question.

Table 1

Patient and Tumor Characteristics for Subjects Having SLN Procedures

		Males	**%**	**Females**	**%**	**Overall**	**%**	**p-value**
Number of Patients		74	56	59	44	133		
Average Age		60		54		57		0.04
Stage		N=50		N=38		N=88		
	I	17	34	23	61	40	45	0.02
	II	26	52	11	29	37	42	
	III	7	15	4	11	11	13	
	IV	0	0	0	0	0	0	
Tumor Type		N=12		N=11		N=23		
	Lentigo	2	17	1	9	3	13	NS
	Superficial	6	50	7	64	13	57	
	Spreading							
	Nodular	3	25	2	18	5	23	
	Acral	1	8	1	9	2	9	
	Lentiginous							
Breslow Thickness		N=42		N=35		N=77		
T_1	<0.75	8	19	5	14	13	17	0.82
T_2	0.76 – 1.5	11	26	19	54	30	35	0.54
T_3	1.51 – 4	18	43	9	26	27	39	0.82
T_4	>4	5	12	2	6	7	9	0.22
Clarks Level		N=29		N=21		N=50		
	I	1	3	1	5	2	4	
	II	3	10	3	14	6	12	
	III	3	10	9	43	12	24	
	IV	19	66	7	33	26	52	0.01
	V	3	10	1	5	4	8	

*NS = Not Significant

Table 2

Results of Frozen Section analysis of SLN Biopsy

Total # of Patients	133
Total # of Sentinel Nodes	271
Overall % positive SLN	8%
Positive SLN via frozen	10
Positive SLN via permanent	11
# False negative nodes	1
% False negative SLN (all patients, N = 133)	0.8%
% False negative SLN (all nodes, N = 271)	0.4%
Sensitivity of Sentinel Node Frozen Section:	91%
Specificity of Sentinel Node Frozen Section:	100%
PPV for Sentinel Node Frozen Section:	100%
NPV for Sentinel Node Frozen Section:	99.6%