

# The rational of Cloquet lymph node as a sentinel lymph node in iliac dissection in lower limb melanoma

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## Background and aims

Intraoperative lymphatic mapping and sentinel lymphadenectomy (LM/SL) is a growingly popular operating procedure for staging regional lymph nodes in early-stage melanoma. The groin is a promising area for this method since superficial groin dissection and iliac dissection have a significant risk of morbidity. There is currently no consensus on how best to treat cases with tumor-positive sentinel lymph nodes (SNs) during surgery involving these basins.

## Methods

A total of 182 cases were treated using the LM/SL method. There was consistent detection of sentinel lymph nodes. SN dissection was performed on patients who had tumor in their SN. A hematoxylin and eosin stain was used to analyze the sentinel lymph nodes. Patient selection for SN dissection was based only on the presence of tumor in that node. Computerized database containing log-rank tests and Cox regression models for statistical analysis.

## Results

61% of the 182 cases were female, with an average age of 50 (range, 15–89). Tumor-positive SNs were detected in 21% of cases. 67% of cases were identified to have sentinel full lymph node dissection and a single tumor-positive lymph node after LM/SL, whereas 27% had 2 tumor-positive lymph nodes and 6% had 3 or more tumor-positive lymph nodes. Recurrence in the dissected basin occurs in just 4% of individuals with tumor-negative SNs. Cases whose lymph nodes tested negative for tumors had a significantly greater 5-year overall survival (mean±SD, 94% 5%) compared with those whose lymph nodes tested positive for tumors (meanSD, 75% 4%;  $P=0.01$ ). Primary tumor thickness ( $P=0.03$ ), Tumor-positive SN ( $P=0.001$ ) and ulceration ( $P=0.001$ ) were revealed to be important indicators of survival in multivariate studies using a Cox regression model.

## Conclusions

This surgical treatment ought to become common for cases with early-stage melanoma of the lower extremities and trunk because the accuracy of LM/SL as judged by the infrequent recurrences implies that it should. When a tumor-positive SN is found in the groin, it is important to take a sample from the Cloquet node so that one may decide whether or not an iliac dissection is necessary.

## Keywords:

Cloquet node, iliac dissection, melanoma, recurrence, sentinel

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## Introduction

Melanoma is a fatal malignancy that typically affects the skin. Over the past 50 years, the worldwide prevalence of melanoma has elevated dramatically. It is prevalent among populations with fair complexion and in regions of lower latitude. Melanoma is one of the most prevalent cancers identified in adolescent and young adult populations. It is more prevalent in older populations, but it is also one of the most prevalent malignancies among young adults and adolescents. In reality, it is one of the malignancies with the highest average number of years of life lost per fatality. The rate of melanoma changes based on gender, which is correlated with disparities in anatomic sites [1].

Melanoma has become more prevalent over the past several decades. In many fair-skinned populations that

dominate regions such as North America, Northern Europe, and Australia, each year the prevalence has increased by as much as 4 to 6%. Even within populations, incidence rate increases vary by age and sex, as well as by ethnicity and geographic location. These distinctions must be taken into account to avoid obscuring true trends in melanoma incidence [2].

Three, four, or five deep inguinal lymph nodes are possible. Under the cribriform fascia, they reside medial to the femoral vein. The uppermost lymph node is known as Cloquet's node (which is

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additionally Rosenmüller's node) and is located in the groin. This node honors either the French surgeon Jules Germain Cloquet or the German anatomist Johann Christian Rosenmüller. Additionally, it is the lowest of the external iliac lymph nodes. Regarded as a potential sentinel lymph node is Cloquet's node. The deep inguinal lymph nodes discharge superiorly to the external iliac lymph nodes, followed by the pelvic lymph nodes, and finally the para aortic lymph nodes [3].

The surgical excision of melanoma lymph node metastases provides exceptional regional control, and five year survival rates of 25–42% have been documented following therapeutic pelvic dissection. In spite of these results, it remains uncertain which subset of cases would benefit most from pelvic dissection. Due to the fact that pelvic dissection could elevate the potential for consequences involving lymphedema and wound infections related to groin dissection alone, considerable morbidity rates contribute to the confusion that surrounds the usefulness of pelvic dissection [4].

The appropriate extent and usefulness of complete regional lymphadenectomy have been a source of debate ever since the first appearance of sentinel lymph node biopsy (SNB). SNB in melanoma reliably distinguishes regional nodal disease, advances staging and ultimately offers crucial prognostic information [5].

The SNB procedure has the advantage of identifying early stage III disease, which might make use of systemic therapy and quick completion node dissection, while sparing patients with no proof of microscopic nodal disease from additional operations and systemic therapy. The likelihood of finding additional non SN illness in the final dissection material following a positive SNB is nearly 20% [6,7].

It appears that the risk of detecting concealed pelvic illness is low in individuals with SNB-recognized disease, but high in those with medically confirmed nodal load in the groin (i.e., by radiographic staging or physical examination) [8]. To this day, even in the face of commonplace pelvic dissections, efforts are made to determine which cases would gain the most from the procedure. According to 19th-century surgeon-anatomist Jules Germain Cloquet, the superior naso-inguinal artery (SNB CN) is located medially to the femoral vein and above the inguinal ligament near the apex of the femoral triangle [9,10].

Involvement of the CN in Melanoma has been thought to be possibly indicative of the disease state of pelvic nodes and a reason for pelvic dissection since it follows successive anatomic lymphatic drainage patterns which additionally function as the basis of SNB. Throughout elective lymphadenectomy for clinical indications of nodal illness, the rate of metastasis to CN was anywhere from 24 to 49 percent before to the use of SNB. Too far, nevertheless, there have been almost no investigations assessing the prevalence of CN in the context of SNB [11]. The purpose of this research was to evaluate Cloquet LN for its potential as a sentinel LN in iliac dissection for melanoma of the lower extremities.

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### Patients and methods

Lower limb melanoma patients presenting to hospitals affiliated with Menoufia University among 2019 and 2022 were gathered for this study. Following SN positivity, patients who had complete node dissection were chosen for analysis of surgery and pathological reports. Participants who underwent a complete groin dissection with or without a pelvic dissection and had CN diagnosed and submitted were additionally involved in the analysis. Individuals who were identified by the surgeon for CN but in whom CN was not found at pathology were not included in the study. Cases were regularly examined with a full set of preoperative tests, involving a history and physical, a chest radiography and a blood profile that included lactate dehydrogenase levels. Imaging techniques such as computed tomography (CT) of the abdomen, chest, and pelvis, magnetic resonance imaging, and positron emission tomography were sometimes employed to confirm or rule out distant metastases after clinical suspicion. Cases were not allowed to participate in LM/SL if they were found to have metastases. Factors and treatments were recorded, together with demographic and clinicopathologic information. Primary tumor factors included location (lower extremities vs. trunk), Breslow thickness, Clark's level, histologic type (superficial spreading vs. acral lentiginous vs. nodular vs. desmoplastic vs. unknown), mitotic rate, the existence of regression, ulceration and lymphovascular invasion. This study analyzed the efficacy of SNB and following lymphadenectomies. The frequency of metastatic disease involvement in the CN was determined by analyzing findings from a complete lymph node dissection. We observed and recorded cyclical patterns. Surgical diagnosis and management of CN In cases of positive inguinal SNB, completion node

dissection was done. There is clinical indication of regional lymph node disease (palpable node or preoperative radiological evidence of regional illness) necessitating dissection was a contraindication. The decision of whether to do a groin dissection alone or a combined groin and pelvic node dissection, in addition to other factors such as the patient's and surgeon's preferences, was determined on a case-by-case basis based on clinical data at presentation. Surgeons have different definitions and procedures for obtaining CN. If (1) the surgeon describes dissecting the apical node at the level of the femoral ring inside the medial portion of the femoral canal (medial to the femoral vein since it goes beneath the inguinal ligament), then the CN has been detected during dissection. and submitting the specimen separately as 'CN', Surgery in which the highest inguinal node is removed from the femoral canal and a separate submission is made is referred to as the 'highest inguinal node.', (3) the surgeon acquires the groin dissection specimen as a whole, identifying the most apical node by suture labeling it as 'CN'. To ensure proper submission, labeling, and CN analysis, pathology reports were reviewed. Pathology Lymph node dissection histological findings were ascertained by examining related surgical pathology reports.

During surgery, hematoxylin and eosin were always used to examine tissue samples from the groin and pelvic dissections. Patients who experienced a delayed pelvic recurrence following complete lymph node dissection underwent a pathologic examination to confirm a diagnosis of CN.

#### Statistical analysis

SPSS (statistical program for social science) version 20.0 was utilized to gather and analyze the data on an IBM compatible computer (SPSS Inc., Chicago, IL, USA). The chi-square test was employed to evaluate the qualitative data, while the mean, standard deviation, median, and range were determined for the quantitative data. The statistical method known as regression analysis was utilized to estimate the individual risk of melanoma advancement; a *P* value of less than 0.05 was deemed statistically significant.

#### Results

In all, 86% of patients had primary tumors on their lower limbs; 61% of patients were female; 53% of patients were 50 or younger (range, 15–89 y). The thickness of the primary tumors varied from 0.30 to

**Table 1 Comparison of 182 Patients with Tumor-Negative and Tumor-Positive Sentinel Lymph Nodes**

Factor	Patients With Tumor-Negative Sentinel Lymph Nodes, N (%)	Patients With Tumor-Positive Sentinel Lymph Nodes, N (%)	<i>P</i> value
Sex			
Men	51 (31)	21 (9)	0.92
Women	79 (47)	31 (13)	
Age, y			
≤50	71 (38)	13 (12)	0.38
>50	89 (40)	9 (9)	
Primary tumor site			
Trunk	41 (11)	11 (3)	0.47
Lower extremity	99(67)	31 (19)	
Clark level*			
I/II	10 (8)	2 (<1)	0.004
III	40 (30)	5 (2)	
IV	45 (36)	40 (15)	
V	2 (3)	5 (2)	
Unknown	5 (18)	30 (30)	
Histologic abnormality†			
Superficial spread	80 (35)	32 (9)	0.90
Other	30 (26)	20 (8)	
Unknown	10 (17)	10 (4)	
Ulceration status‡			
Without ulceration	75 (35)	65 (31)	0.004
With ulceration	10 (9)	2 (3)	
Unknown	15 (11)	15 (11)	
Thickness (continuous)			
≤2.0 mm	80 (43)	10 (4)	<0.001
>2.0 mm	60(33)	32 (20)	

\*Fourteen primary cancers did not reach the Clark threshold. †Ninety-one primary cancers lacked histological analysis data. ‡Ninety-seven primary tumors lacked information about ulceration.

14.00 mm (the average was 1.89 mm). 54% of primary tumors were classified as Clark level IV or V, and 15% were ulcerated. The primary tumors in 44% of cases were histologic abnormalities that spread just superficially. Compared with individuals with tumor-negative SNs, those with tumor-positive SNs had primary tumors that were thicker and had a greater Clark level (Table 1).

LM/SL was performed on 182 people, and SN was found in every single one of them.

Table 2 displays the percentage of patients whose SNs were tumor-free and the percentage who subsequently experienced nodal recurrence. Tumor-positive SNs were found in 21%. In all but four of the tumor-positive SN patients, full sentinel lymph node dissection (LND) was done. 67% of cases had a single positive lymph node for tumor cells, 27% had two positive lymph nodes and 6% had three or more positive lymph nodes. A total of 40 out of 93 cases (40%) with tumor-positive dissections had experienced a recurrence. Cases have a high mortality rate (11%). Cases with tumor-positive inguinal SNs had either superficial (inguinal) basin removal (SGD) ( $n=20$ ), SCLND ( $n=31$ ) with Cloquet lymph node sample to assess the necessity for ilioinguinal dissection, or Ilioinguinal dissection (ILND) ( $n=38$ ) as normal therapy. The decision not to perform SCLND on four cases with tumor-positive SNs was made by either the patient or the treating physician.

Cases with tumor-positive SNs tended to have primary tumors in the trunk (17%). One case who had tumor-positive inguinal lymph nodes on both sides opted out of SCLND. It was only an SGD for one case. The Cloquet lymph node was sampled during SGD in 10 individuals. The Cloquet node's tumor status was unknown in 4 instances that required dissection of both the inguinal and iliac lymph nodes.

From primary melanoma of the lower limbs, 76 individuals exhibited tumor-positive SNs. Three tumor-positive SN patients declined SCLND. SGDs were done in 19 cases. To ascertain whether

or not a deep groin dissection was necessary, the Cloquet node was sampled during an SGD in 21 cases. SGD and deep groin dissection were combined in 33 of these cases.

Patients with tumor-positive dissections had a substantially lower mean SD 5-year disease-free survival ( $52\pm 9\%$ ) compared with those with tumor-negative dissections ( $82\pm 7\%$ ) ( $P < 0.001$ ). Overall 5-year survival was lower ( $75\% 4\%$  vs.  $94\% 5\%$ , respectively;  $P < 0.001$ ) due to the disparity in disease-free survival. There was an increased risk for individuals with tumor-positive lymph nodes only when the Clark level and thickness were high.

Among those whose SNs were negative for tumors, 16% had seen a recurrence. Twenty-two out of the fifty first-site recurrences occurred at transit nodes. Four percent experienced recurrences in the dissected basin, and 13% in other locations. Lymph node recurrence occurred between 28 and 132 months following tumor-negative LM/SL in the median case.

Recurrence has occurred in 40% of cases with tumor-positive SNs. The vast majority (84%) of these recurrences have occurred at distant places, rather than locally (in regional lymph nodes, at sites of metastasis, or at the site of the extensive excision). For dissections that turned up tumors, the median duration to distant recurrence was 7.6 months.

The predictive value of a wide range of clinicopathologic characteristics was investigated. The only statistically significant factors ( $P < 0.05$ ) were tumor thickness, SN tumor status, and ulceration (Table 3).

Following LM/SL, the regional lymph nodes were treated with a wide range of surgical options (Table 4). The surgical procedure was decided upon at the discretion of the physician and, in certain cases, the case. Cloquet node tumor status was found to have a 66% positive predictive value in determining the status of the deep groin lymph nodes, with a 97% negative predictive value.

**Table 2 Distribution of First-Site Recurrences for 182 Patients With Primary Melanoma of the Lower Extremities and Trunk\***

Sentinel Lymph Node Status	Local Recurrence, No. (%)	In-transit Recurrence With or Without Lymph Node Tumor Recurrence, No. (%)	Recurrence in Lymph Nodes, No. (%)	Distant Recurrence, No. (%)
Tumor negative ( $n=338$ )	3 (0.7)	33 (10.1)	11 (3.5)	42 (12.6)
Tumor positive ( $n=93$ )	3 (2.3)	12 (14.0)	4 (3.3)	32 (33.4)

\*Fifty-five cases with tumor-negative sentinel lymph nodes and thirty-seven cases with tumor-positive nodes made up the total number of cases with first-site recurrences.

## Discussion

With the advent of LM/SL, the treatment of cases with early-stage melanoma has been transformed. In addition to providing a foundation for SN removal and a targeted pathologic evaluation of the material, this procedure also helps surgeons determine the pattern of lymphatic outflow from the main site to the regional lymph node basin. Staging the lymph nodes in this way has resulted in a more uniform staging in these individuals than was previously anticipated. Five-year survival rates for cases with lymph node metastases (American Joint Committee on Cancer stage III) have been reported to vary from 15% to 70% in several retrospective investigations [12–15] conducted before the discovery of LM/SL. The historical variability of cases presenting with American Joint Committee on Cancer stage III illness, reflected in the vast range of outcomes. Patients, primary tumors, and lymph nodes are all considered when determining prognosis in stage III illness [9,15]. Thick primary tumors of the trunk (>4 mm) are the only exception [16], survival rates after the onset of nodal illness are most strongly associated with factors pertaining to the lymph nodes. The number of lymph nodes containing tumors, the percentage of lymph nodes positive for tumors, the existence of extracapsular extension, macroscopic versus microscopic evidence of disease,

ulceration of the primary tumor, clinically tumor-positive lymph nodes, and the highest level of tumor-involved nodes are all significant prognostic factors [9]. It has been claimed that between 70 and 90% of patients will survive if their lymph nodes test negative for tumors [15–17]

However, these results raise questions about the importance of SCLND because most cases with tumor-positive SNs would have just a single lymph node with metastases, leading to a highly consistent prognosis for most cases with lymph node metastases. Having nodes in the superficial part of the groin confirmed by a pathologist increases the 5-year survival rate from 30 to 75% [4,6,18]. Our 75% 5-year survival rate is better than that found by other researchers [15–17,19]. The clinical and pathologic state of the superficial inguinal nodes is the only determinant of whether or not a deep groin dissection should be done. In 15% to 100% of instances, the existence of tumor in the iliac nodes may be predicted from the presence of tumor in the inguinal nodes [2,4,18]. Clinical nodal involvement to some extent is a strong predictor of iliac node tumor positive, as determined by Sterne *et al.* [18]. One mobile superficial groin lymph node was related with pathologically tumor-positive iliac nodes in 8% (36%), while numerous mobile nodes or fixed nodes were consistently related to positive iliac nodes in their group of 25 patients who underwent ILND. Pathologically tumor-positive inguinal nodes correlate directly with the prevalence of iliac node tumor positivity. Once 1 inguinal node is pathologically tumor positive, the likelihood of tumor-positive iliac nodes increasing to 4 or more nodes is 50%, as indicated by research by Finck *et al.* [7] When three or more inguinal nodes contain metastatic disease, other researchers [20] have found a 100% rate of iliac node tumor positive. However, after finding a tumor-positive SN, the number of nodes carrying tumor is not easily

**Table 3** There were 182 patients who had lymphatic mapping and sentinel lymphadenectomy for primary tumors in the lower trunk and extremities

Factor	Univariate Analysis	Multivariate Analysis
Age <50 y	0.612	NA
Sex	0.271	NA
Primary tumor site	0.911	NA
Clark level (II/III vs. IV/V)	0.187	NA
Thickness,mm	0.0005	0.002
Ulceration status	0.014	0.0034
SN status	0.0001	0.044

There were univariate and multivariate analyses of the factors that predicted overall survival for these cases. NA, not applicable.

**Table 4** Additional Lymph Nodes detected as Tumor-Positive After Undergoing Four Surgical Methods and Observing Recurrence Patterns \*

Type	Patients, N	Recurrence in Superficial Groin, N (%)	Recurrence in Deep Groin, N (%)	Recurrence in Cloquet Node, N (%)
SGD	22	7 (29)	3 (15)	NA
SGD and deep (iliac and obturator) groin dissection	34	8 (19)	3 (9)	NA
SGD with intraoperative analysis of Cloquet lymph node	29	11 (33)	1 (0)	1 (3)
LM/SL only for tumor-positive SN s	2	2 (50)	2 (50)	NA
LM/SL for tumor-negative SN s	91	11 (4)	2 (<1)	NA

LM, lymphatic mapping; NA, not applicable; SGD, superficial groin dissection; SL, sentinel lymphadenectomy.

measured following operation and is not relevant for deciding whether or not to undertake ILND.

The Cloquet node status has been shown to be 79 percent predictive of occult iliac node metastases by Coit *et al.* [9] According to our findings, the Cloquet lymph node may be used as a positive and negative predictor when assessing the deep groin basin. SGD is the go-to for removing metastatic nodes in the groin, however the value of ilioinguinal dissection is debated. In cases when occult metastatic illness is found in the inguinal nodes, a further deep node dissection may not be necessary, according to the findings of certain researchers [21]. But this has not been the conclusion reached by others [5,6]. In the case of clinically apparent iliac metastases, deep node dissections are typically undertaken. Deep node positive is only a sign of disseminated disease, according to those who oppose deep node dissection and think the potential morbidity exceeds any survival advantage. Previous research has shown a wide range of 5-year survival rates (from 0% to 34%) in individuals with pathologically confirmed deep node metastases [2,3]. Even with 2–4 tumor-positive lymph nodes, 5-year survival rates for LM/SL patients have improved to 40–50% in recent years [15].

The efficacy of our therapy strategy for deep groin nodes was evaluated by analyzing data from 294 cases with American Joint Committee on Cancer grade III melanoma. Cases selected for minimal risk had greater success with superficial groin dissections. While systemic disease is typically found in cases with deep node metastases, a 29% 5-year survival rate after deep groin dissections in cases with histologically tumor-positive deep nodes suggests that SGD plus deep groin lymph node dissection may be helpful for certain individuals. The feminine gender, younger age, and lower tumor load were all found to be positive prognostic variables in multivariate analyses of survival. Occult iliac node metastases were more reliably predicted by the Cloquet node's pathologic condition than by the superficial groin nodes' clinical status.

Through this study, we show that LM/SL is useful for regional lymph node staging in early-stage melanoma. Several other studies have shown similar results, demonstrating the reliability of this minimally invasive surgical method, thus these findings are not surprising. When compared with standard groin dissections (with or without deep groin dissections), LM/SL decreases morbidity and expenses associated with lymph node staging. Recurrence in the lymph

node basin following tumor-negative LM/SL occurred in only 3% of patients, however due to the great prevalence of synchronous in-transit illness, this complication can have a major impact on patients' lives [21]. In a similar vein, individuals who have had a tumor removed from their superficial groin may have in-transit discomfort and an increased likelihood of developing persistent lower extremities pain or lymphedema as a side effect of their therapy if they experience a recurrence. Our observations imply that tumor status of the Cloquet node may be the most helpful technique to evaluate the tumor status of the deep groin lymph nodes after LM/SL, even if the therapeutic efficacy of SCLND is uncertain and is being studied (in the Multi-center Selective Lymphadenectomy Trial II) [22].

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## Conclusion

Our findings show that LM/SL is prognostically relevant for groin-draining melanoma in its early stages. The low rate of recurrence after LM/SL surgery implies it should be routine for individuals with early-stage melanoma of the lower limbs and trunk. When a tumor-positive SN is found in the groin, a sample from the Cloquet node should be taken to establish whether or not an iliac dissection is necessary.

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### Declarations

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#### Conflicts of interest

There are no conflicts of interest.

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