

# Role of dynamic sentinel node biopsy in carcinoma penis with or without palpable nodes

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## ABSTRACT

**Introduction:** We aimed to evaluate the role of dynamic sentinel node biopsy (DSLNB) in patients diagnosed with carcinoma penis and clinically N0 disease using superficial inguinal dissection as the standard staging modality.

**Materials and Methods:** Twenty consecutive men (40 groins) with carcinoma penis having clinically N0 status were enrolled in the study. Patients underwent DSLNB if fine needle aspiration cytology from the groin nodes was negative, followed by injection of radiocolloid and blue dye. The sentinel lymph node(s) were harvested. The inguinal incision was then extended and a modified superficial inguinal dissection was performed and all nodes were labeled separately and sent for frozen section. A completion deep inguinal with pelvic dissection was performed if any of the nodes were reported positive for malignancy.

**Results:** The median age of the patients was 52.5 years. Ten patients were smokers. Phimosis was present in five patients. Lesions were present over the glans penis and shaft in 18 and two patients, respectively. Wide local excision, partial penectomy and total penectomy were performed in one, 15 and four patients, respectively. Clinically palpable nodes were found in 19 groins. Median follow-up was 26 months. Nodes were positive in 10 groins. DSLNB missed the sentinel node in one groin. The accuracy and false-negative rate of DSLNB was 97.5% and 10%, respectively.

**Conclusion:** DSLNB is a useful and reliable technique to identify the involved node(s) in patients diagnosed as having carcinoma penis with clinical N0 status (with or without palpable nodes). It helps to avoid the morbidity associated with a staging inguinal dissection in these patients.

**Key words:** Cancer of penis, metastasis, Methylene blue, scintigraphy, sentinel lymph node biopsy

## INTRODUCTION

Management of clinical N0 (cN0) nodes in patients with penile cancer has been an area of controversy for many years. Histological grade and T status are important prognostic factors of nodal involvement.<sup>[1,2]</sup> Evaluation of palpable inguinal nodes using fine needle aspiration cytology (FNAC) has showed a false negativity rate of 15% with or without use of ultrasonographic guidance.<sup>[3]</sup> Imaging modalities like computed tomography (CT) scan, magnetic resonance imaging, fluorodeoxyglucose

positron emission tomography-CT fusion imaging were used in different studies with varying results and were not accurate in detecting micro metastasis.<sup>[4,5]</sup>

Although the concept of sentinel node biopsy (SNB) was first introduced in penile cancer by Cabanas<sup>[5]</sup> in 1977, it has not gained widespread acceptance due to the high false-negativity rates. A large two-center trial on 323 patients by Horenblas *et al.*,<sup>[5,6]</sup> evaluating the role of dynamic sentinel node biopsy (DSLNB) in carcinoma penis, showed a low false-negative rate of 7%. Following the publication of this study, various guidelines have included DSLNB as an option in the management of cN0 groins in carcinoma penis.<sup>[7]</sup>

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All palpable nodes at diagnosis may not be malignant; in 30–50% of the patients, it may be inflammatory.<sup>[8]</sup> In addition, most patients with carcinoma penis in India are from poor socio-economic backgrounds and are barefoot walkers. This leads to an increased incidence of palpable inguinal nodes with a non-malignant inflammatory pathology. Accurate staging of the inguinal nodes avoiding the consequences of both under- and overtreatment in this unique subgroup of patients was a major reason that prompted us to study the feasibility of using DSLNB in our population.

We performed a superficial inguinal lymph node dissection that entails lymph node dissection superficial to the fascia lata as the reference standard staging tool after dissection of the sentinel nodes.<sup>[9,10]</sup>

## MATERIALS AND METHODS

This prospective study included 20 consecutive patients with carcinoma penis treated at our institution between February 2010 and July 2012. These patients underwent clinical evaluation and biopsy from the primary in the penis to confirm malignancy. Patients with palpable inguinal nodes had an initial FNAC; if negative, they also underwent an ultrasonography (USG)-guided FNAC to confirm the absence of inguinal nodal metastasis. The patients also underwent chest X-ray and USG of the abdomen and pelvis as part of the metastatic workup. In the absence of distant metastasis, these patients underwent surgery for the primary with DSLNB, followed by superficial inguinal dissection. All sentinel nodes and all significant superficial inguinal nodes were labeled separately and sent for frozen section. If any of these nodes were reported positive, an ipsilateral completion deep inguinal and pelvic dissection was performed. All DSLNB procedures were performed by the author. Our inclusion criteria was: Patients having non-metastatic carcinoma penis with a negative FNAC for metastasis from palpable or non-palpable inguinal nodes. Patients with unilateral or bilateral FNAC-proven inguinal node metastasis were excluded from the study.

### Technique of DSLNB

All patients who fulfilled the inclusion criteria had peri-tumoral, intra-dermal injection of radiocolloid (Tc99m-labeled sulfur colloid-TCK-5, BRIT, Mumbai, India) the previous day of the procedure. Static images in supine position were acquired the day after injection (Gamma View-i, RC1500I, Hitachi, Japan) [Figure 1]. The static images were used to mark the location of the nodes on the skin and the patient was then sent to the operation theater. Intra-operatively, 1 mL of methylene blue was injected using an insulin syringe peri-tumorally, intradermally 5 min before the skin incision. The activity over the skin markings was confirmed using a hand-held Gamma probe (Neo2000 Gamma Detection System, Neoprobe Corporation, Dublin, OH, USA) and skin incisions were made. Nodes showing activity with

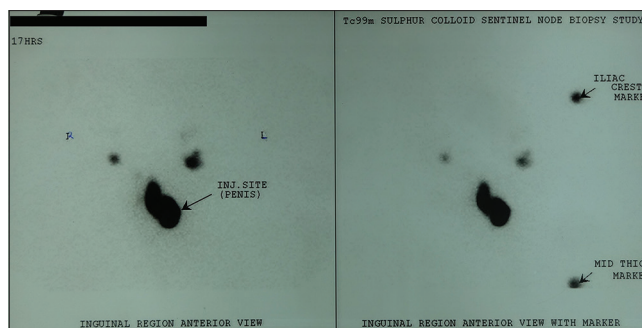


Figure 1: Pre-operative scintigraphy showing nodal uptake

the gamma probe or nodes with blue dye, or both, were identified and dissected [Figure 2]. These nodes were labeled separately and sent for frozen section. A completion deep inguinal and pelvic dissection was completed if any of these nodes was reported positive for metastasis. The patients were followed-up with 2-monthly physical examination and yearly USG for the inguinal and pelvic nodes for the first year, 3-monthly for the next 2 years, 6-monthly for the 4<sup>th</sup> and 5<sup>th</sup> years and annually thereafter. Data were analyzed using SPSS 17 software.

## RESULTS

A total of 20 patients, with 40 groins, were included in the study. Patient characteristics are displayed in Table 1. Histopathologically positive nodes (either on frozen or permanent section) were found in 10 (25%) groins. Of these, DSLNB could identify the positive node(s) in nine groins. The groin in which the node could not be identified was the first patient of the study.

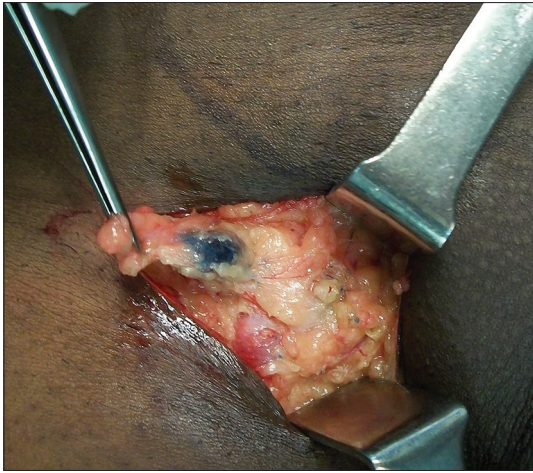
Sentinel node(s) as the only positive node(s) (after complete dissection) was seen in seven (17.5%) groins. Of these, four (10%) groins had a single positive sentinel node and three (7.5%) groins had two positive sentinel nodes.

The average number of sentinel nodes identified was 2.3 nodes (range 0–4 nodes) per groin and the average number of nodes dissected during superficial dissection was 11.9 nodes (range 4–35 nodes) per groin. No regional recurrences have been noted after the superficial dissection. The median follow-up period was 26 months (range 7–42 months).

Visualization and identification data are given in Table 2. The sensitivity, specificity and accuracy were 90%, 100% and 97.5% respectively. The false-negative rate was 10%.

## DISCUSSION

SNB was accepted as an option in patients with clinically node-negative penile cancer after the publication of the two-center study by Horenblas *et al.*,<sup>[5]</sup> and was recommended for use in patients with non-palpable nodes. Reservations



**Figure 2:** Node identification with blue dye

about the use of SNB include the fact that most of the current results are from one institution and that no other study has reported such low false-negative rates.

We could identify the sentinel node during surgery (either with the blue dye or the radiocolloid, or both) in 39 of 40 groins, with an identification rate of 97.5%, which is comparable with that reported in the literature.<sup>[6,11]</sup> The node-positive rate was 25% (10 of 40 groins). The only groin in which DSLNB could not identify the metastatic node was in the first patient of the current study. The sensitivity was 90%.

The study of SNB for carcinoma penis so far has yielded conflicting results. The false-negative rates in different studies have varied from 7% to 42.5%.<sup>[6,11]</sup> Hornables *et al.*, using DSLNB, achieved a low false-negative rate of 7%.<sup>[5]</sup> Perdona *et al.* had a false-negative rate of 11%.<sup>[12]</sup> Gonzanga-Silva *et al.*, using the isolated gamma probe technique, reported a sensitivity of 25% with a false-negative rate of 42.8%.<sup>[13]</sup> Pettaway *et al.* performed extended sentinel node dissection in 20 patients, which were all negative for metastasis, but five patients developed inguinal metastasis at a median of 10 months with a false-negative rate of 25%.<sup>[14]</sup> Roshan<sup>[11]</sup> reported a false-negative rate of 66% and concluded that lymphatic mapping with the methylene blue method alone is not a reliable method of detecting the sentinel node. Spiess *et al.* compared SNB by isosulfan blue with combined techniques and found the sensitivity be 55% and 71%, respectively.<sup>[15]</sup> In most of these studies, a single technique was used and had high false-negative rates. The false-negative rate in this study (10%) is comparable with that reported by Horenblas *et al.*<sup>[5]</sup>

The study by Heyns<sup>[16]</sup> showed a false-negative rate of 13% with the use of DSLNB in patients with palpable nodes. Nodes positive on FNAC were not excluded from the study, which may have contributed to the high false-negative rates.

**Table 1: Patient characteristics**

Median age	52.5 (23-75) years (%)
Smokers	10 (50)
Alcoholics	4 (20)
Phimosis	5 (25)
Location of primary	
Glans penis	18 (90)
Skin over the penile shaft	2 (10)
Grade of the tumor	
1	2 (10)
2	14 (70)
3	4 (20)
Type of surgery	
Wide local excision	1 (5)
Partial penectomy	15 (75)
Total penectomy	4 (20)
pT status	
Tx	1 (5)
T1	2 (10)
T2	14 (70)
T3	3 (15)
Clinically nodes were palpable	19 groins (47.5)
Clinically non-palpable nodes	21 groins (52.5)

**Table 2: Visualization and identification of nodes**

	HPE-positive groins	HPE-negative groins	Total
SLN-positive groins	9 (true positive)	0 (false positive)	9
SLN-negative groins	1 (false negative)	30 (true negative)	31
Total	10	30	40

HPE= Histopathological examination, SLN= Sentinel lymphnode

In the present study, palpable nodes were identified in 19 groins (47.5%). The average size of the palpable node was 1.12 cm (largest node was 2 cm).

Most of the nodal recurrences in carcinoma penis occurs within 2 years.<sup>[17]</sup> The median follow-up in this study is 27 months, which is good enough to assess the effectiveness of both DSLNB and modified inguinal dissection performed.

Better standardization of the technique by (a) proper selection of cases with the use of pre-operative USG-guided FNAC to exclude patients with metastatic nodes, (b) use of DSLNB (using both radiocolloid and blue dye), (c) use of pre-operative scintigraphy to localize the nodes and (d) injection of the dye/radiocolloid in the correct plane (intradermally) and preferably if done in a high-volume center will help to reduce the false-negative rate.

## CONCLUSION

DSLNB is a relatively accurate and safe technique to identify the involved nodes in patients with cN0 groins in carcinoma penis and helps to reduce the morbidity involved in staging inguinal dissection without compromising oncological outcomes. Careful selection of patients and better standardization of the technique will help reduce the false-negative rates.

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### *Conflicts of interest*

There are no conflicts of interest.

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