New anatomical classification of the axilla with implications for sentinel node biopsy

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Background: The exact anatomical location of the sentinel lymph node (SLN) in the axilla has not ascertained clinically, but could be useful both for teaching purposes and to reduce the morbidity of SLN biopsy. The aim of the study was to determine the position of the SLN in the axilla and to demonstrate that this location is not random.

Methods: A consecutive series of 242 patients with stage I breast cancer (T1/T2 N0) or ductal carcinoma in situ who underwent SLN localization by peritumoral injection were included in a prospective study to map the location of the SLN in the axilla. A new anatomical classification of the lower part of the axilla based on the intersection of two anatomical landmarks, the lateral thoracic vein (LTV) and the second intercostobrachial nerve (ICBN), is described. These two constant elements form the basis of four axillary zones (A, B, C and D).

Results: In 98.2% of patients the axillary SLN was located medially, alongside the LTV, either below the second ICBN (zone A, 86.8% per cent) or above it (zone B, 11.5% per cent). In only four patients (1.8% per cent) was the SLN located laterally in the axilla.

Conclusion: Regardless of the site of the tumour in the breast, 98.2% of SLNs were found in the medial part of the axilla, alongside the LTV. This information should help to avoid unnecessary lateral dissections.

Introduction

Sentinel lymph node (SLN) biopsy has gradually replaced axillary dissection for small invasive carcinomas, and indications for this procedure are increasing. Although SLN biopsy has reduced the rate of complications associated with axillary dissection, some patients still present with chronic arm pain or even lymphoedema. Clinical trials have shown that lymphoedema occurs in 5–7 per cent of patients after SLN biopsy, and chronic postoperative pain and sensory loss in up to 11 per cent. Knowledge of the precise anatomical location of the SLN in the axilla would be useful not only in reducing the morbidity associated with the technique but also for teaching purposes.

The primary aim of this study was to determine the position of the SLN in the axilla and to demonstrate that the location is not random, as the flow of lymph from the breast follows a predetermined route. To achieve this aim, a new anatomical classification of the lower part of the axilla (Berg’s level I and II, below and behind the pectoralis minor muscle) is described. The anatomical classification is based on the intersection of two constant anatomical landmarks in the middle of Berg’s level I: vertically, the lateral thoracic tributary of the axillary vein (LTV) and, horizontally, the second intercostobrachial nerve (ICBN). These two structures form the basis of four different axillary zones. A secondary aim was to identify, using the same classification, the association, if any, between the location of the tumour in the breast and that of the SLN in the axilla.
surgery to the same breast were excluded. All patients with clinically palpable nodes underwent preoperative fine-needle aspiration cytology; only patients with negative findings were included in the study.

Using anatomical landmarks, the lower part of the axilla (Berg’s level I and the lower part of Berg’s level II) was divided into four anatomical zones to localize the SLN. The intersection between the LTV (vertically) and the second ICBN (horizontally) is a constant anatomical landmark in the centre of Berg’s level \[16-21\] (Fig. 1). These two structures form a cross that creates four zones. Zone A is the area adjacent to the LTV, extending from the lower border of the axilla to the second ICBN. Zone B is the area adjacent to the LTV, extending from the second ICBN to the axillary vein; it extends medially under the pectoralis minor muscle (lower part of Berg’s level II). Zone C is the lateral axillary area outside zone A. Zone D is the lateral axillary area outside zone B. Fig. 2 is a schematic representation of these four axillary zones with the arm in a 90° abduction position; the base of the axillary pyramid is positioned laterally with its apex at Berg’s level III. Zones A and B are adjacent to the LTV.

To determine the association between the location of the SLN in the axilla and the site of the tumour, the breast was divided into nine sectors: retroareolar (RA), upper outer quadrant (UOQ), lower outer quadrant (LOQ), lower inner quadrant (LIQ), upper inner quadrant (UIQ), the junction of the upper quadrants (JUQ), the junction of the outer quadrants (JOQ), the junction of the lower quadrants (JLQ) and the junction of the inner quadrants (JIQ).

SLN localization was performed using either patent blue dye, technetium-99m nanocolloid tracer, or both, injected into the peritumoral area. The technetium-99m-labelled rhenium sulphide tracer (Nanocis®; CIS Bio International, Saclay, France) was administered the day before the procedure. Two syringes, each containing 60 MBq (0.2 ml) tracer, were injected under ultrasonographic guidance, one at the superficial and the other at the deep pole of the tumour. Lymphoscintigraphy was performed 2 h later. A handheld γ probe was used for counts at the breast injection site, the SLN and the axillary background. The blue dye (2 ml bleu patenté V sodique® 2.5 per cent; Laboratoires Guerbet, Villepinte, France) was injected immediately before the procedure, as soon as the patient had been anaesthetized. Rigorous massaging was performed after injecting the blue dye\[22-28\].

A transverse incision was made at the hairline of the axilla, or on the hotspot in patients who received the radiotracer. Blunt dissection was carried out to identify the blue-stained lymphatic channel, and was initially followed retrogradely towards the breast to ensure that no medial nodes were missed, then distally until the first SLN was located. In patients who received only the nanocolloid tracer, the γ probe was used to guide the dissection straight to the SLN without disturbing the surrounding tissues. The probe was used to check the identified nodes before and after excision (in situ and ex vivo). All blue and/or

Fig. 1 Intraoperative photograph of the axilla demonstrating the constant intersection of the lateral thoracic vein and the second intercostobrachial nerve, landmarks for the anatomical classification

Fig. 2 Schematic representation of the lower axilla. Zones A and B, and zones C and D form the medial and lateral parts of the axilla respectively
radioactive axillary nodes were sampled to reduce the rate of false-negative interventions. The axillary background was then mapped to ensure no remaining hot nodes had been left behind. Any other clinically suspicious non-SLNs were excised. According to the authors’ current protocol, no attempt was made to remove extra-axillary hot nodes, such as internal mammary nodes.

The sites of the SLNs were documented in relation to the four axillary zones (A, B, C and D). All SLNs were sent for frozen-section examination; patients with positive nodes had immediate axillary lymph node dissection (ALND). Negative frozen-section specimens were sent for histopathological examination, and deferred ALND was performed in patients with positive nodes.

**Results**

During the study interval, sentinel node localization was performed in 242 patients. Both nanocolloid tracer and patent blue dye were used in 113 patients (46·7 per cent); the remaining 129 patients had either the blue dye alone (123 patients, 50·8 per cent) or the nanocolloid tracer alone (6 patients, 2·5 per cent). In 15 patients (6·2 per cent) the SLN could not be identified during the procedure; these patients underwent ALND and were excluded from the study (only five were found to have lymph node metastasis).

The remaining 227 patients had a successful SLN biopsy and were included in the study. Patient demographics and tumour staging are shown in Table 1. Table 2 shows the distribution of patients according to the location of the tumour in the breast and that of the sentinel node in the axilla. The mean number of harvested SLNs was 3·5 (range 1–6). All SLNs were found in Berg’s level I (214 of 227; 94·2 per cent) or the lower part of Berg’s level II (13 of 227; 5·8 per cent).

<table>
<thead>
<tr>
<th>Zone</th>
<th>SLN location</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>197 (86·8)</td>
</tr>
<tr>
<td>B</td>
<td>26 (11·5)</td>
</tr>
<tr>
<td>C</td>
<td>4 (1·8)</td>
</tr>
<tr>
<td>D</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

**Table 1** Patient demographics and tumour staging

<table>
<thead>
<tr>
<th>No. of patients* (n = 227)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median (range) age (years)</strong></td>
</tr>
<tr>
<td><strong>Side of tumour†</strong></td>
</tr>
<tr>
<td>Right breast</td>
</tr>
<tr>
<td>Left breast</td>
</tr>
<tr>
<td><strong>Histological staging†</strong></td>
</tr>
<tr>
<td>Tis (DCIS)</td>
</tr>
<tr>
<td>T1a</td>
</tr>
<tr>
<td>T1b</td>
</tr>
<tr>
<td>T1c</td>
</tr>
<tr>
<td>T2</td>
</tr>
<tr>
<td>N0</td>
</tr>
</tbody>
</table>

*Unless indicated otherwise. †Values in parentheses are percentages unless indicated otherwise. T, tumour category; DCIS, ductal carcinoma in situ; N, node category.

SLNs were located in zone A in 197 patients (86·8 per cent), in zone B in 26 (11·5 per cent) and in zone C in four (1·8 per cent); in no patient was the SLN located in zone D (Table 2, Fig. 3). Thus, almost all SLNs (223 of 227, 98·2 per cent) were in the medial part of the axilla adjacent to the LTV, in axillary zones A and B.

Fifty-one patients (22·5 per cent) had positive sentinel nodes, identified by frozen-section examination in 18
patients (7.9 per cent), who had immediate ALND, and by definitive histology in the remaining 33 (14.5 per cent), who underwent ALND as a separate procedure.

As all patients were injected peritumorally, an attempt was made to correlate the location of the SLN in the axilla with the site of the tumour in the breast (Table 2). Irrespective of the site of the primary in the breast, axillary zone A was the commonest location for SLNs, followed by zone B. However, tumours located in the upper pole of the breast (UIQ, UOQ and JUQ) appeared to drain more often in zone B (19 of 131, 15 per cent) in comparison with tumours in the lower pole (LIQ, LOQ and JLQ) (3 of 37, 8 per cent).

**Discussion**

In 98.2 per cent of the 227 patients in this prospective study the axillary SLN was located alongside the LTV, either below (axillary zone A, 86.8 per cent) or above (zone B, 11.5 per cent) the ICBN. This anatomical location of the SLN has not previously been demonstrated clinically. Such information could be a useful adjunct for practising surgeons and teaching purposes, not only to increase the reliability but also to reduce the morbidity of SLN procedures.

SLN biopsy has become the standard minimally invasive alternative to ALND in staging patients with clinically node-negative disease. Although all patients in this study had no node involvement clinically, 22.5 per cent had metastatic nodes on histological examination, similar to previously reported rates in the much larger Axillary Lymphatic Mapping Against Nodal Axillary Clearance (ALMANAC)\(^\text{14}\), American College of Surgeons Oncology Group (ACOSOG) Z0010\(^\text{15}\) and National Surgical Adjuvant Breast and Bowel Project B-32\(^\text{29}\) trials. Sentinel node biopsy was originally developed to avoid the morbidity of ALND. However, the morbidity rate associated with SLN biopsy, although significantly lower than that of ALND, is not negligible. In the ACOSOG Z0010 trial, which included 4,975 patients, the recorded 6-month morbidity rates of SLN biopsy were as follows: proximal lymphoedema 6.9 per cent, paraesthesia 8.6 per cent and decreased upper extremity range of motion 3.8 per cent\(^\text{15}\). Similar complication rates were reported in the 515 patients assigned to the SLN biopsy arm of the ALMANAC trial\(^\text{14}\). In a prospective Swiss multicentre study of 659 patients that compared the morbidity of SLN biopsy with that of SLN biopsy followed by ALND, 39 per cent of patients in the former group developed at least one complication (lymphoedema, numbness, impaired shoulder mobility and pain)\(^\text{8}\). These studies demonstrated that, although SLN biopsy harvests fewer nodes, the procedure can still result in significant intermediate- or long-term morbidity. It is therefore imperative to investigate the aetiology of these complications as well as to identify potential ways of reducing them. It is possible that the morbidity of SLN biopsy is associated with the extent of dissection. Thus, knowledge of the exact location of the sentinel node should help to focus the dissection and...
reduce the morbidity of SLN biopsy procedures without compromising sensitivity.

Berg30 used the pectoralis minor muscle to divide the axillary lymph nodes into three levels. The majority of early and screen-detected breast cancers drain primarily to levels I and II axillary lymph nodes22. The exact location of the SLN in the axilla is, however, difficult to define, as Berg’s levels have never been subdivided anatomically. Therefore, further anatomical classification is needed to facilitate the precise location of the SLN. In the present study, the lower part of the axilla (Berg’s levels I and II) was divided into four zones based on the crossing of two constant anatomical structures, the LTV and the second ICBN. The LTV is a constant landmark in Berg’s level I of the axilla (Figs I and 2). It drains the breast laterally, then courses vertically upwards in the axilla to intersect with the second ICBN before joining the axillary vein anterior to the thoracodorsal vein16–21. The second ICBN is the lateral cutaneous branch of the second intercostal nerve. It supplies the skin of the second intercostal space at the medial wall of axilla and the skin of the floor of the axilla, as well as the medial side of the upper part of the arm. The nerve enters the axilla by piercing the serratus anterior muscle in the mid-axillary line. It traverses the axilla obliquely, lying within the axillary fat pad where it gives cutaneous branches to the floor of the axilla. It then communicates with the medial cutaneous nerve of the arm (arising from the brachial plexus) and pierces the deep fascia supplying the skin on the medial side of the upper arm17–31.

The present study has demonstrated that SLNs are neither equally distributed nor randomly scattered in the four defined zones of levels I and II of the axilla. Almost all SLNs (98·2 per cent) were located in the medial part of the axilla (zones A and B) adjacent to the LTV (Fig. 4). This has not been demonstrated previously in a clinical study, and highlights that the breast lymphatics follow the venous drainage. In only one small autopsy study, Pavlista and colleagues34 used a similar technique for localization and dissection of the SLN. The axilla was divided into four zones using the intersection of the thoracoepigastric vein (located lateral to the LTV) and the third ICBN as anatomical landmarks (Fig. 2). Despite small numbers, the results were similar to those in the present investigation: 87 per cent of SLNs were located in the lower and upper ventral quadrants of the axilla, which correspond to zones A and B in the present study.

There is much debate about whether or not the whole breast drains into the same SLN25–28,35. The second aim of the present study was therefore to identify the association, if any, between the site of the tumour in the breast and the location of the SLN in the axilla. Some authors injected two tracers at two different sites (peritumoral and periareolar) and found a concordance rate of 94–98 per cent with regard to the location of the SLN36,37. The concept that the whole breast drains into the same SLN has positive practical implications: a periareolar injection could be used whether or not the tumour is palpable, and regardless of its location in the breast, as recommended in the UK New Start sentinel node biopsy training programme. However, this is still debated, as other investigators have demonstrated that, although most of the breast does drain into the same SLN, different areas can drain into separate nodes25,28. Therefore, until definitive evidence is obtained, the present authors still inject all patients peritumorally, even for non-palpable tumours, which are injected under ultrasonographic guidance24.

The present study did not show that different quadrants of the breast drained into different axillary zones; zone A remained the main draining area for all tumours irrespective of their location in the breast. It might be concluded from these results that there is only one sentinel node draining the entire breast. Alternatively, the study may have been limited in that the number of tumours in each quadrant of the breast was not large enough to demonstrate a significant difference in the location of the SLN.

Only 1·8 per cent of SLNs in the present study were located laterally in zone C, the lateral axillary area outside zone A. None was found in zone D, the lateral axillary area outside zone B. These findings complement emerging information on the association between the lymphatic drainage of the arm and that of the breast38. In the past 3 years there has been growing interest in the axillary location of the SLN draining the arm38–42. The aim of these studies was to preserve the lymphatic drainage of the arm in patients undergoing ALND and consequently to minimize the risk of lymphoedema. Axillary reverse mapping (ARM) studies have demonstrated that ARM-specific nodes almost never harbour metastatic involvement from breast cancer. Nos and co-workers38 have demonstrated previously that the dominant node draining the arm is usually situated in the lateral pillar of the axilla underneath the axillary vein and above the second ICBN, an area that corresponds to zone D in the present study.

On the basis of observations in the present study and those of the ARM studies38–42 it is hypothesized that there are two distinct lymphatic pathways in the axilla: a medial chain draining the breast, centred around the LTV and extending upwards and medially behind the pectoralis minor muscle to level II nodes (zones A and B), and a lateral chain (zones C and D) draining the arm (Fig. 5).
Thus, during SLN biopsy, attention should be focused on zone A and, to a lesser degree, on zone B. If the SLN is not found in either of these two areas, the authors recommend that zone A should be palpated carefully for suspicious nodes that are neither hot nor blue. Conversely, it could be argued that any dissection lateral to zones A and B in the search for the breast SLN is unnecessary and might explain the small, but not negligible, risk of arm lymphoedema following breast SLN biopsy procedures.

Similarly, the common practice during axillary SLN biopsy of removing enlarged palpable non-sentinel nodes could be questioned. The majority of these nodes are found in zone D and a systematic excision might explain the persistence of lymphoedema in large SLN studies, even when a small number of nodes has been removed. On the basis of the present study it is recommended that, unless highly suspicious, lateral dissection and harvesting of lateral palpable non-sentinel nodes be avoided.

Breast SLNs are not located randomly in the axilla. In order to determine the precise location of the SLN in the axilla, and to harmonize future research, a new anatomical classification of the lower axilla based on the crossing of two constant anatomical structures, the LTV and the second ICBN, is proposed. This classification will be of value to breast surgeons performing SLN biopsy procedures.

Acknowledgements
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References
New anatomical classification of the axilla with implications for sentinel node biopsy (Br J Surg 2010; 97: 1659–1665)

This paper represents the first advance in our anatomical appreciation of the pattern of axillary lymphatic drainage in operable breast cancer since the work of John Berg in the 1950s. Whereas Berg described an anatomical classification...
of axillary lymph drainage applicable to the surgical practice of axillary lymph node clearance, Clough and colleagues have described a classification fit for the new era of sentinel lymph node (SLN) biopsy. Although this is a relatively small study, the data show convincingly that in the vast majority of patients with operable breast cancer the SLN will be found medially in level 1 adjacent to the lateral thoracic (central) vein below its intersection by the second intercostobrachial nerve (ICBN), and in the remainder it will be located medially above the level of the second ICBN.

I am confident this paper will inspire further studies. If, in addition to predicting the site of the SLN, it becomes possible to predict the location of involved lymph nodes when the sentinel node is involved, a more focused and less radical axillary dissection to remove the disease might be performed. This would be especially valuable in patients with low-volume or micrometastatic disease in the SLN, many of whom have no further disease in the axilla and are therefore exposed to the morbidity of axillary clearance with no additional benefit.

In combination with preoperative axillary staging and intraoperative analysis of the sentinel node, this new anatomical classification of the axillary lymphatic system has the potential to minimize axillary, arm and shoulder morbidity for the majority of patients with breast cancer. A few selected patients with advanced axillary disease may still require a full ‘Berg’-type clearance, but extra care when dissecting laterally, particularly close to the origin of thoracodorsal bundle (to latissimus dorsi), may spare even this group some arm morbidity.

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**Reference**