The Evolution of Sentinel Node Biopsy in Urological Malignancy

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Abstract
Sentinel lymph node biopsy (SLNB) provides an accurate staging tool for a variety of malignancies including urological cancers. Initially introduced as a single procedure technique, SLNB has evolved into a dynamic multi-stage procedure that has an invaluable impact on the management of cancer patients.

After a thorough literature search, this article summarises the advancement of the SLNB procedure since its conception. The introduction of radioactive tracers and blue dye has resulted in a highly sensitive technique but one around which concerns persist. This paper updates existing material on the topic by examining the potential of near infra-red fluorescence optical imaging agents (NIRF) and anatomical fusion imaging as useful adjuncts to the currently practiced technique.

SLNB has an established role in penile cancer with a well documented improvement in morbidity and mortality rates. The presence of sentinel nodes in pelvic malignancy is controversial but papers have established that the technique is feasible for use in such cancers and that NIRF may have a role to play here in the future. SLNB currently has no place in the management of testicular or renal malignancy.

Introduction
In recent years sentinel lymph node biopsy (SLNB) has revolutionised the management of patients with suspected regionally advanced malignancy. Widely used in both breast cancer and melanoma as well as urological malignancy, the technique is built around Halsted’s theory which recognises that cells from the primary tumour spread sequentially along the lymph chain becoming trapped in the first node and spreading further only once that node becomes overwhelmed (1). These first nodes are known as sentinel nodes (SNs) and were initially described in parotid malignancy by Gould in 1960 (2). Removal and pathological analysis of such
nodes, allows clinicians to stage disease and identify patients in need of further regional or systemic treatment. It is preferred compared to more extensive surgery as it achieves lower morbidity rates relative to those seen in regional lymph node dissection (LND) (3).

The existence of SNs was previously confirmed and marked using lymphangiograms intraoperatively and now lymphangioscintograms preoperatively. However, dependence on these techniques alone meant that location of such nodes by the surgeon was still largely determined anatomically and did not allow for inter-patient variation (4). This changed in 1989 with the introduction of patent blue dye as a means of cutaneous lymph node mapping (5). Identification of SNs using blue dye mapping, with an injection at the site of the primary tumour, was first proposed for breast cancer in 1994 and is now widely used in SLNB for a variety of malignancies (6).

The introduction of hand held gamma radiation probes intra-operatively in SLNB was reported as an alternative to blue dye mapping by a team at the University of Vermont Medical Centre. They went on to propose that this method had a number of advantages over its counterpart, namely that it can be used to confirm that the correct node has been biopsied as well as identifying the potential existence of remaining undissected SNs (7).

In its current form SLNB is not without limitations. Several papers have raised concerns about the high false negative rates, a recent paper citing a figure as high as 15% in penile cancer (8). It is anticipated that addition of newer techniques to dynamic SNLB will improve this and literature currently available explores a number of options.

Whilst not widely implemented, a role for a portable gamma camera was proposed as a potential alternative in centres where preoperative lymphoscintigraphy was not available. Trialled in breast and gynaecology malignancy, as well as head and neck cancers, studies have shown that it may be useful in visualising and identifying nodes intra-operatively (9, 10) even identifying nodes not seen preoperatively (11). It may also have a role in confirming removal of all radioactive nodes after a surgeon has completed the resection (12). Whether a defined role for the gamma camera becomes apparent in urological SLNB remains unclear but is unlikely given that studies have demonstrated the superiority of the conventional pre operative imaging in detecting SNs (13).
More promising however, is hybrid imaging using the concept of anatomical fusion. In 2006 a study in Sweden proposed the use of hybrid single photon emission computed tomography combined with CT (SPECT–CT) as an alternative to planar imaging to improve the SLNB technique in bladder cancer. They determined a significant improvement in the localisation of SNs preoperatively, citing that preoperative lymphoscintigraphy using the hybrid technique identified 21 lymph nodes in five patients, compared to just two seen with conventional planar imaging (14). Such hybrid imaging has also been studied in penile and renal cancer with evidence that it is feasible for use in this role (15, 16) as well as in gynaecological, breast and head and neck cancers (17,18,19).

Perhaps the most significant recent step in the evolution of sentinel node biopsy was the introduction of near infrared fluorescence optical imaging agents (NIRF). NIRF provides a non radioactive, more penetrative, real time alternative to the tracers currently in use. It was studied in mice in 2003 (20) and in 2005, Melancon and colleagues demonstrated this to be a more effective method of identifying SNs in breast cancer, identifying all six superficial cervical nodes compared to T1 weighted MR which identified just four (21). In 2011 NIRF, in the form of indocyanine, was introduced to urological malignancy and used to identify lymphatic pathways in 14 patients with prostate cancer (22). Studies since then have shown that it can be used in a similar role for bladder cancer (23) but it was only earlier this year, after successfully identifying sentinel drainage in nine out of ten patients with bladder cancer and 38 of 50 patients with prostate cancer, that NIRF has been demonstrated as a feasible technique for aiding SLNB in robotically assisted procedures (24, 25).

The concept of a hybrid tracer, combining the success of radioactive tracers and NIRF imaging was first suggested for prostate cancer in 2011 (26). In 2012, Brouwer and colleagues proposed indocyanine green-(99m)Tc-nanocolloid, a multimodal tracer as an replacement for blue dye in penile cancer. They not only demonstrated increased sensitivity, citing that it allowed visualisation of 96.8% of SNs compared to blue dye which stained just 55.7%, but that it could have a dual role as a suitable replacement for (99m)Tc-nanocolloid with which it has the same lymphatic drainage pattern (27, 28). The concept of the hybrid tracer has yet to be widely implemented but there is support for its use in penile, prostate and breast cancer (29, 30).

Whilst there is evidence to support the use of all the above discussed techniques independently, the majority of recent studies have demonstrated the benefits of synergistic use of the
techniques. It is in combination, mainly that of pre-operative lymphoscintigraphy, radioactive tracer and patent blue dye with gamma probe detection, that it is used in dynamic sentinel lymph node biopsy for urological malignancies today.

Use in penile cancer

The use of SLNB in penile cancer was first recommended by Cabanas in 1977 (31). By studying 100 patients he was able to support the existence of a sentinel node in disseminated penile malignancy. He performed lymphangiogram guided sentinel lymph node biopsies on 46 patients concluding that a positive SLNB was a good indicator that a patient should proceed to full inguino-iliaic LND.

Despite support from Cabanas, SLNB fell out of favour with urologists due to poor reproducibility. It was only after positive experiences from both breast cancer and melanoma, as well as the introduction of patent blue dye injection and radiolabelling, that acceptance of the use and reliability of SLNB in the management of locally advanced penile malignancy was achieved (32,33,34).

Concerns regarding false negative rates remained until 2007 when Leijte and colleagues demonstrated that the combination of SLNB with ultrasound with or without fine needle aspiration cytology further increased sensitivity (35), a finding that was supported by Crawshaw and colleagues in 2009 (36). A recent paper studying 500 inguinal basins carried out at a tertiary centre, cited a 94% sensitivity per patient when SLNB with ultrasound was used, compared to 91% with blue dye and gamma probe guided SLNB alone (37).

Since the introduction of SLNB, there has been a significant improvement in both morbidity and mortality of patients with penile cancer. A study by Djajadiningrat and colleagues published in the journal of urology in 2014 looked at the 5 year cancer specific survival of patients with squamous cell carcinoma of the penis. They compared the 5 year cancer survival rate before the introduction of SLNB and after and found a statistically significant difference, 91% compared to 82%, with a p value of 0.021 (38). This was not the first paper with such findings. A Dutch study in 2005, cited 3 year cancer specific survival of patients with positive lymph nodes at 84% for those who underwent SLNB and immediate lymphadenectomy and at 35% for those who had lymph nodes excised only after they became clinically palpable during a period of surveillance. They
concluded that SLNB led to earlier identification of positive nodes and that the subsequent early resection directly resulted in a survival benefit (39). The introduction of SLNB has also seen a reduction in morbidity. A study which assessed a group of 48 patients who underwent radical lymphadenectomy, found that 21 suffered with early complications and 18 with late complications, compared to just three early complications seen in the 22 patients who underwent SLNB (40).

SLNB in penile cancer has a high sensitivity and there is well documented, albeit largely retrospective, evidence that it reduces morbidity and mortality. In most patients it allows for more accurate staging but despite this, not all studies have found in its favour. Hungerhuber et al (41), reported on the limited value of sentinel lymph node biopsy in patients with clinically suspicious lymph nodes and it is the existence of such papers that explains why inguinal node dissection with frozen section or pre operative fine needle aspiration remains the preferred procedure in such patients.

Table 1: Summary table: SLNB in penile cancer

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Cohort size</th>
<th>Methodology</th>
<th>Conclusion</th>
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<tbody>
<tr>
<td>Introduction and Development of technique</td>
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<tr>
<td>Cabanas et al, 1977</td>
<td>46</td>
<td>Prospective</td>
<td>Feasibility of SLNB in penile cancer (lymphangiograms alone)</td>
</tr>
<tr>
<td>Horenblas et al, 2000</td>
<td>55</td>
<td>Prospective</td>
<td>Feasibility of dynamic SLNB in penile cancer (lymphoscintigraphy, patent blue dye and gamma probe)</td>
</tr>
<tr>
<td>Utsunohi et al, 2009</td>
<td>64</td>
<td>Prospective</td>
<td>Superiority of SLNB combining dynamic SLNB and US guided fine needle aspiration over dynamic SLNB alone which would miss between 5 and 10% metastases</td>
</tr>
<tr>
<td>Igartia et al, 2009</td>
<td>16</td>
<td>Prospective</td>
<td>Superiority of SPECT CT over conventional lymphoscintigraphy</td>
</tr>
<tr>
<td>Broecker et al, 2014</td>
<td>21</td>
<td>Prospective</td>
<td>Successful use of preoperatively acquired SPECT/CT for intraoperative navigation</td>
</tr>
<tr>
<td>Alomar et al, 2015</td>
<td>32</td>
<td>Prospective</td>
<td>Superiority of hybrid tracer over patent blue dye</td>
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<tr>
<td>Validating the technique</td>
<td></td>
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<tr>
<td>Tanis et al, 2002</td>
<td>33</td>
<td>Prospective</td>
<td>80% sensitivity of dynamic SLNB</td>
</tr>
<tr>
<td>Leijte et al, 2007</td>
<td>35</td>
<td>Retrospective</td>
<td>Reduction in false negative and complication rate with introduction of pre operative FNAC and intraoperative palpation</td>
</tr>
<tr>
<td>Tang et al, 2013</td>
<td>37</td>
<td>Retrospective</td>
<td>DSNB combined with US demonstrates high sensitivity staging of penile cancer with low false negative rates (94% vs 92%)</td>
</tr>
<tr>
<td>Examining outcomes</td>
<td></td>
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<tr>
<td>Perdona et al, 2005</td>
<td>48</td>
<td>Retrospective</td>
<td>Dynamic SLNB has similar results to radical inguinal lymphadenectomy but with lower morbidity</td>
</tr>
<tr>
<td>Jager et al, 2014</td>
<td>1000</td>
<td>Retrospective</td>
<td>Contemporary management of regional lymph nodes has led to an improvement in 5 year survival (92% vs 89%)</td>
</tr>
<tr>
<td>Conclusion</td>
<td></td>
<td></td>
<td>With high sensitivity and specificity data and strong morbidity and mortality outcomes, this author recommends the use of SLNB is recommended for use in penile cancer</td>
</tr>
</tbody>
</table>
Use in pelvic malignancies

Knowledge of the extent of lymphatic invasion in prostate and bladder cancer allows clinicians to stage disease and determine duration and strength of adjuvant therapy. In fact, excision of positive nodes in the absence of distant metastases can even be curative (43). However, views on the use of sentinel nodes in pelvic cancer differ.

Being almost unchanged in size and with microscopic metastases and untraceable using radiological techniques, positive lymph nodes in the pelvis are often difficult to identify. The use of SLNB can address this but controversy surrounding the pattern of lymphatic drainage and the extent of subsequent lymphadenectomy required persists. **It is agreed however that with the prostate and bladder being midline structures, lymph may drain to either side indiscriminately and thus that lymph nodes from both sides should be sampled with findings being reported not only per person but per side, as is already the case in cervical cancer (44)**.

Lymph from the prostate drains via one of three routes, either draining to internal iliac lymph nodes, to external iliac lymph nodes and thus forming a paravesical plexus or travelling posterially to sacral lymph nodes (45). Elucidation of the drainage of prostate cancer cells would allow better management of patients with medium or high risk cancers but studies thus far have failed to clearly define this except to note that tumour location within the gland can have an impact (46).

In 2013, Joniau and colleagues used a combination of radioactive tracer, planar scintigraphy and SPECT imaging in order to map lymphatic drainage in 74 patients with prostate cancer. They identified sentinel nodes mainly in 5 regions: obturator fossa (25%), internal iliac (25%), external iliac (19%), common iliac (14%), presacral (13%) but noted sentinel nodes also in the pararectal, paravesical and para-aortic regions, in mesenteric fat and at the aortic bifurcation. Their findings reiterated concerns that sentinel nodes are often widely spread suggesting potential for positive lymph nodes in a large number of areas that current lymphadenectomy margins do not account for (47).

Pelvic lymphadenectomy can be broadly categorised into three divisions. 1) Standard lymphadenectomy, which involves resection of all lymphatic and fibrofatty tissue that comprise the external iliac nodes and obturator nodes. 2) Limited lymphadenectomy, which is the removal of the external iliac nodes only, whilst 3) extended lymphadenectomy excises the hypogastric nodes as well as the external iliac and obturator nodes, although some surgeons may also remove...
the subaortic and presacral nodes (48). The margins of an extended lymphadenectomy remain controversial with two separate studies suggesting that resection at current margins allows for the possibility to undissected lymph nodes and consequently proposing new wider alternatives (47, 49). A recent prospective study demonstrated that standard or limited dissection alone would have missed 51.9% and 74.1% of metastatic lymph nodes in a cohort of 200 prostate cancer patients (50). With this and previous studies in mind, prior to SLNB, extended pelvic lymphadenectomy was accepted as the only reliable way for a surgeon to stage the patient’s disease despite being associated with higher morbidity when compared to standard lymphadenectomy (51,52).

The decision to proceed to lymphadenectomy in pelvic cancer is made based on validated mathematical algorithms such as Partin tables and Briganti nomograms for prostate cancer (53, 54) and nomograms set out by Green et al. and karakiewicz et al. in bladder cancer (55,56). Such algorithms calculate the likeliness of tumour extending beyond the primary organ and those deemed to have low risk cancer do not proceed to lymphadenectomy. Previously, with no way to accurately differentiate between those with lymph positive disease and those without, all patients calculated to have medium or high risk cancer underwent extended lymphadenectomy despite the associated high morbidity, now such patients undergo SLNB instead. In 2012, Winter and colleagues questioned the validity of existing algorithms when used with SLNB. They found that previous algorithms (validated on extended pelvic node dissections) were underestimating the incidence of LN involvement (57) and therefore introduced the first LN involvement probability table for use with SLNB.

Along with penile and breast cancer, the use of a multimodal tracers such as indocyanine green, has been proposed in pelvic cancers. In 2012 Jeschke et al. successfully demonstrated that, using a combination of fluorescence navigation and radiolabelling, technetium labelled indocyanine green provides an equally effective, real time alternative to blue dye, a finding supported by Manny et al in 2014 (58, 24, 25). This is likely to be the future of SLNB in pelvic malignancies.

Prostate cancer

The use of SLNB in prostate cancer was first proposed by the Augsburg group in 1999. They initially examined eleven patients using dynamic lymphoscintigraphy with preoperative
radionucleotide being administered transrectally and detected using an intra-operative gamma probe (59). Having successfully demonstrated the success of that technique they performed a larger study with 117 patients, 25 of whom had lymph node metastases and in 24 of the 25 demonstrated 96% sensitivity (60).

Since then many studies have reiterated the high sensitivity and specificity of SLNB in prostate cancer (61,62,63). The largest of these examined 2020 patients who underwent SLNB over a ten year period. They cited an intra-operative detection rate of 98% when using a preoperative gamma camera and an intra-operative gamma probe. As in penile cancer, false negatives were identified as a potential concern (a 6.2% false negative rate was cited). One potential cause for false negatives were macrometastases blocking lymph node channels and the recommendation was made that all patients being considered for SLNB should first undergo a CT to exclude these (64).

As in penile cancer, SPECT CT was explored as alternative to planar scintigraphy but here with poor results (65). Immunoscintigraphy using monoclonal antibodies was also explored (66), although lymphoscintigraphy combining SPECT CT and MRI was found to be more effective with combined use increasing the sensitivity from 40% with CT alone to 88.9% (67).

In 2006 Corvin and colleagues proposed the idea of laparoscopic sentinel node dissection postulating that this would result in lower morbidity, less postoperative pain and shorter hospital stays. Using a gamma camera for preoperative lymph mapping and a laparoscopic gamma probe intra-operatively they proved that laparoscopic sentinel node biopsy can be an acceptable alternative to extended pelvic LND (68), a hypothesis that has since been supported by experience in gynaecological cancers (69).

Table 2: Summary table: SLNB in prostate cancer

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<thead>
<tr>
<th>Author, year</th>
<th>Cohort size</th>
<th>Methodology</th>
<th>Conclusion</th>
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<tbody>
<tr>
<td>Augsburg group, 1999</td>
<td>11</td>
<td>Prospective</td>
<td>Feasibility of SLNB in prostate cancer</td>
</tr>
<tr>
<td>Corvin et al, 2006</td>
<td>28</td>
<td>Prospective</td>
<td>Introduction of Laparoscopic SLNB in prostate cancer</td>
</tr>
<tr>
<td>Wynant et al, 2006</td>
<td>40</td>
<td>Prospective</td>
<td>Immunoscintigraphy can be used to identify positive LNs in prostate cancer</td>
</tr>
<tr>
<td>EAU guidelines, 2011</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Van der Poel, 2011</td>
<td>34</td>
<td>Prospective</td>
<td>Patients with a more than or equal to 7% risk of having lymph node metastases from prostate cancer (calculated using nomograms) should undergo lymph node dissection</td>
</tr>
<tr>
<td>Briganti et al, 2012</td>
<td>1441</td>
<td>Retrospective</td>
<td>CT is a poor tool for identification of prostate cancer lymph node metastases with high specificity and low sensitivity</td>
</tr>
<tr>
<td>Hardie et al, 2013</td>
<td>19/12</td>
<td>Retrospective</td>
<td>Combining SPECT CT and MRI increases sensitivity and specificity of identification of lymph node metastases in prostate cancer (sensitivity of CT: 40%, combined 88.9; specificity of CT: 96.7%, combined 98.5%)</td>
</tr>
</tbody>
</table>
Validating the technique
Holl et al, 2009
2020 Retrospective SLNB has 98% intraoperative detection rate with a false negative rate of 6%

Conclusion
There is good evidence to support the use of SLNB in prostate cancer but concerns around false negatives persist. This procedure does have potential but in the absence of further outcome data we cannot recommend its use.

Bladder cancer

The concept of sentinel node biopsy was introduced to bladder cancer in 2001. Using a combination of scintigraphy, radioactive tracer and blue dye, Sherif and colleagues identified SNs in thirteen patients awaiting radical cystectomy. After extended pelvic lymphadenectomy has occurred, histopathology confirmed that all of the four positive SNs were detected using the pre operative techniques despite three of them lying outside the standard lymphadenectomy area (71). This study cited a false negative rate of 0% however a larger study looking at 75 patients with invasive bladder cancer quoted 19%, a figured that highlights one of the persistent concerns around SLNB. Despite this, the study successfully demonstrated that the use of pre and intra-operative lymphoscintigraphy, patent blue dye and ex vivo examination with a gamma probe along-side extended serial sectioning improved bladder cancer nodal staging in 25% of patients (72). It is in this form that dynamic SLNB is currently performed in patients with bladder malignancy. However, the introduction of robot assisted sentinel node excision and NIRF is likely to change that in the coming years.

Table 3: Summary table: SLNB in bladder cancer

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<tr>
<th>Author, year</th>
<th>cohort size</th>
<th>Methodology</th>
<th>Conclusion</th>
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<tbody>
<tr>
<td>Introduction and Development of technique</td>
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<tr>
<td>Sherif et al, 2001</td>
<td>13</td>
<td>Prospective</td>
<td>Introduction of SLNB (pre operative scintigraphy, radioactive tracer and patent blue dye) in bladder cancer</td>
</tr>
<tr>
<td>Sherif et al, 2006</td>
<td>6</td>
<td>Prospective</td>
<td>Use of SPECT CT imaging allows for better pre operative identification of lymph nodes in patients with bladder cancer than planar imaging</td>
</tr>
<tr>
<td>Inoue et al, 2012</td>
<td>12</td>
<td>Prospective</td>
<td>Introduction of NIRF in bladder cancer</td>
</tr>
<tr>
<td>Manny et al, 2014</td>
<td>10</td>
<td>Prospective</td>
<td>NIR is feasible for use in robotically assisted procedures</td>
</tr>
<tr>
<td>Validating the technique</td>
<td></td>
<td></td>
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<tr>
<td>Liedberg et al, 2006</td>
<td>75</td>
<td>Prospective</td>
<td>Use of dynamic SLNB (pre and intra-operative scintigraphy, patent blue dye and ex vivo gamma probe examination) along with extended serial sectioning increases bladder cancer nodal staging by 25% but with a false negative rate of 19%</td>
</tr>
</tbody>
</table>

Conclusion
There is good evidence to support the use of SLNB in bladder cancer but concerns around false negatives persist. This procedure does have potential but in the absence of outcome data we cannot recommend its use.
Use in Other Urological Malignancies

Testicular cancer

The use of SNs in testicular malignancy is a relatively new concept. Taking a lead from penile and prostate cancer, Tanis and colleagues introduced SLNB to testicular cancer in 2002 (74). They demonstrated that pre operative dynamic lymphoscintigraphy using technetium-99m nanocolloid could be used to identify SNs in testicular cancer. In 2005, using a cohort of 22 patients, urologists in Japan built on this further by demonstrating that SLNB using a combination of lymphoscintigraphy using technetium 99m labelled phyrate and intra-operative hand held gamma probe yielded detection rate of 95% in stage one testicular cancer (75).

In light of limited evidence in support of its use, and the use of adjuvant chemo and radiotherapy in achieving very low recurrence rates using standard lymphadenectomy, SLNB does not currently have a role in lymph node mapping in testicular malignancy with EAU guidelines suggesting that CT scans be used for staging instead (76).

Table 4: Summary table: SLNB in testicular cancer

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<th>Author, year</th>
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<th>Methodology</th>
<th>Conclusion</th>
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<tbody>
<tr>
<td>Introduction and Development of technique</td>
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<tr>
<td>Tanis et al, 2002</td>
<td>5</td>
<td>Prospective</td>
<td>Introduction of SLNB in testicular cancer using pre operative lymphoscintigraphy</td>
</tr>
<tr>
<td>Satoh et al, 2005</td>
<td>22</td>
<td>Prospective</td>
<td>Introduction of dynamic SLNB introduced to testicular cancer using pre operative lymphoscintigraphy and hand held gamma probe</td>
</tr>
<tr>
<td>Conclusion</td>
<td></td>
<td></td>
<td>There is currently no evidence to support the use of SLNB in testicular cancer over other less invasive techniques.</td>
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</tbody>
</table>

Renal cancer

As a malignancy that has a well recognised haematogenous spread and an unpredictable lymphatic drainage, LND in renal cancer has a limited role (77,78,79). Metastatic spread has been shown to have a high correlation with size of tumour (80), so with advancing technology allowing for earlier diagnosis of smaller tumours, SLNB may have both a prognostic and therapeutic role to play by identifying and removing nodal disease in patients without distant metastases.

The use of SLNB in renal cancer was first studied in porcine models by Bernie et al (81). Using preoperative radionuclide tracer in combination with US, CT and SPECT scanning and intra-operative hand held gamma probes Bex and colleagues successfully demonstrated that Bernie’s technique could be used to identify SNs in six of eight human patients (16). This was supported by
a study of thirteen patients in Sweden which concluded that radioguided surgery in combination with imaging modalities and patent blue dye could identify SNs in renal cancer but that further work was needed to decide the combination of the most efficacious modes of detection (82). At time of writing, LND and extended LND continues to be the accepted management of those with clinically node positive disease without distant metastases or to reduce tumour bulk in those with distant metastases.

**Table 5: Summary table: SLNB in renal cancer**

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<tr>
<th>Author, year</th>
<th>cohort size</th>
<th>Methodology</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bex et al, 2010</td>
<td>8</td>
<td>Prospective</td>
<td>SLNB has potential for use in renal cancer in humans</td>
</tr>
<tr>
<td>Sherif et al, 2012</td>
<td>13</td>
<td>Prospective</td>
<td>Radioguided surgery and patent blue dye can be used to identify positive nodes in patients with metastatic renal cancer</td>
</tr>
</tbody>
</table>

**Conclusion:**

Since its introduction SLNB has shown itself to be invaluable in the management of urological cancer. Introduced to improve staging at a lower morbidity cost and initially solely dependent on lymphangiograms, SNLB in its current form has evolved to become a dynamic technique with excellent sensitivity and specificity figures. With a role in penile cancer well defined, its feasibility in pelvic cancers well established and with the introduction of NIRF and hybrid tracers, SLNB will continue to improve the management, morbidity and mortality of patients with urological cancers in the future.
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