Radionuclide detection of sentinel lymph node

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BACKGROUND

- The prognosis of malignant disease is determined by the metastatic potential of the primary tumor.
- The status of the regional LNs is the most important prognostic factor for pts with malignancies. Moreover, the detailed histological assessment is a strong determinant in the choice of the therapy.
- CLND was the standard procedure
- Minimal invasive surgery (SN biopsy) combined with lymphatic mapping:
  - lower risk of operative morbidity
  - more accurate detection of microscopic disease
  - significant prognostic information
  - identification of those pts who should undergo lymphadenectomy
Which one is the sentinel node?

1992 Morton et al: the initial lymph node upon which the primary tumor drains directly.
Techniques in SLN detection

Preoperative (dept of Nuclear Medicine)
- Conventional lymphoscintigraphy (planar)
  - SPECT- CT
  - PET/CT
  - γ probe

Intraoperative
- Hand held gamma probe
  - Portable γ camera

- Accurate preoperative identification of regional LNs basins at risk and the real SLN
- Accurate intraoperative localization and biopsy of the SLN
- Accurate pathologic evaluation of the removed SLN

2 steps: preoperative and intraoperative

Non radioisotopique

Blue
INJECTION TECHNIQUES

99mTc-labelled colloids (0.3 mCi/0.2ml)

99mTc tilmanocept: a receptor based tracer

ICG-99mTc nannocolloid: a hybrid tracer (indocyanine green)

intradermal injection around the tumor or around the biopsy scar.

Peritumoral (deep) injection (experience, non palpable??, multifocal??, shine through??)

Intratumoral injection

Periareolar (superficial) subdermal injection (simple, quick, extraaxillary LNs??)

Periareolar intraparenchymal injection (modified technique)
Conventional lymphoscintigraphy (CLS)

• To demonstrate which lymphatic drainage basin(s) are potential sites of metastatic disease

• b. To determine the number and location of SLNs within those drainage basins

• c. To demonstrate alternative lymphatic drainage basins

• d. To mark the location of any SLNs for subsequent surgical dissection

• e. To try to distinguish SLNs from second-tier lymph nodes
Conventional lymphoscintigraphy (CLS)

- Planar delayed static images after radiotracer administration. The first hot spot = SLN

- Dynamic imaging: road map melanomas (head and neck, trunk centrally located melanomas) visualization of lymphatic ducts time of appearance radioactivity

CLS can distinguish the real SN from a second tier node (falsely interpreted in static images)
dLSC: malignant melanoma
dLSC: breast cancer: optional
Hybrid imaging

- Limitations:
  False negative: skin contamination, shine through effect, leakage from the wire tract, sternoclavicular joint uptake, mediastinal uptake in blood vessels, age, body mass, metastatic nodes, technical errors

- Anatomic information?
  exact location
  depth
  anatomical relationship with the surrounding tissue
• Immediately after conventional lymphoscintigraphy
• Questions:
  type of used CT (low dose vs diagnostic CT), AC, SC
  role in daily clinical practice
  Appropriate use and optimal timing
  predict the metastatic SLN?

• Low dose is not suitable for SLNs staging having small rate of sensitivity, specificity, PPV, NPV, accuracy: 36%, 84%, 50%, 74%, 60% respectively.

• AC: is the best solution (detection rate: 98,2%)
• AC+SC: 78,6%
• Without AC,SC: 89,3%
SPECT/CT and BREAST CANCER

Questions: role in daily clinical practice

- Its systemic use is not recommended in all cases (combination of CLS+hand held gamma probe+intraoperative identification) achieves very high detection rates and few FN results (1-2%).

- Indications:
  a) improves the anatomical localization, the identification of the extraaxillary in pts with breast cancer, overweighted pts (50% no visualization), unusual lymphatic drainage
  
  a) reduces the FP results
  
  a) change the surgical approach


SPECT/CT and melanomas

- Head and neck melanomas
- Posterior trunk melanomas
- In detecting SLNs close to the injection site and the level of the SLNs
- Is helpful in differentiating skin contamination from nodal uptake
- SPECT/CT has significant advantages over CLS static images but it can't replace dynamic CLS


- Additional cost
- additional Time
- Additional radiation exposure (mSv vs µSv) (Eur J Rad, 2012, e717-720)
Can 18-FDG PET/CT replace SNB? Not yet!!!!!!

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Patient No.</th>
<th>Ref.</th>
<th>PET/CT Sensitivity (%)</th>
<th>PET/CT Specificity (%)</th>
<th>PET/CT PPV (%)</th>
<th>PET/CT NPV (%)</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wahl et al[10]</td>
<td>2004</td>
<td>360</td>
<td>ALND</td>
<td>61</td>
<td>80</td>
<td>62</td>
<td>79</td>
<td>FDG PET was limited in detection of micrometastasis</td>
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<tr>
<td>Veronesi et al[9]</td>
<td>2007</td>
<td>236</td>
<td>SLNB</td>
<td>37</td>
<td>96</td>
<td>88</td>
<td>66</td>
<td>High specificity of FDG PET/CT indicated that patients with positive PET should have ALND directly</td>
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<tr>
<td>Ueda et al[8]</td>
<td>2008</td>
<td>183</td>
<td>SLNB and/or ALND</td>
<td>58</td>
<td>95</td>
<td>85</td>
<td>83</td>
<td>Diagnostic accuracy of PET/CT was nearly equal to ultrasound</td>
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<tr>
<td>Kim et al[7]</td>
<td>2009</td>
<td>137</td>
<td>ALND or SLNB</td>
<td>77</td>
<td>100</td>
<td>100</td>
<td>94</td>
<td>FDG PET/CT could help to select patients for either ALND or SLNB</td>
</tr>
<tr>
<td>Heusner et al[6]</td>
<td>2009</td>
<td>61</td>
<td>SLNB</td>
<td>58</td>
<td>92</td>
<td>82</td>
<td>77</td>
<td>FDG PET/CT could not replace invasive approaches for axillary staging</td>
</tr>
<tr>
<td>Choi et al[5]</td>
<td>2012</td>
<td>154</td>
<td>Biopsy or additional imaging and follow-ups</td>
<td>37</td>
<td>96</td>
<td>83</td>
<td>74</td>
<td>FDG PET/CT could not be recommended as a primary diagnostic procedure</td>
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<tr>
<td>Groheux et al[4]</td>
<td>2011</td>
<td>70</td>
<td>SLNB or US-FNA</td>
<td>63</td>
<td>91</td>
<td>63</td>
<td>91</td>
<td>FDG PET/CT might impact cancer management in small portions of patients</td>
</tr>
<tr>
<td>Koolen et al[3]</td>
<td>2012</td>
<td>290</td>
<td>SLNB or US-FNA</td>
<td>82</td>
<td>92</td>
<td>98</td>
<td>53</td>
<td>FDG PET/CT could be recommended as a standard staging procedure</td>
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<tr>
<td>Pritchard et al[2]</td>
<td>2012</td>
<td>325</td>
<td>SLNB or ALND</td>
<td>24</td>
<td>100</td>
<td>96</td>
<td>75</td>
<td>FDG PET/CT was not sufficiently sensitive to detect positive axillary nodes</td>
</tr>
</tbody>
</table>

EIO EXPERIENCE
21/9/2016

- PRESELECT PTs FOR CLND
- is superior to CI for IMNs
- select patients for postoperative radiotherapy

**Sensibility**
- PET: 46.3%
- SLN: 95.8%
- ALND: 100%
- SN biopsy: 86.5%
- PPV: 91.7%
- NPV: 100%
PSF: point spread function:
• improve the diagnostic performance
• improve the spatial resolution
• Detect smaller metastasis (<7mm)
• minimize the PVE

<table>
<thead>
<tr>
<th></th>
<th>All patients</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>OSEM</td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>76 (58 – 89)</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>75 (47 – 92)</td>
</tr>
<tr>
<td>Positive predictive value (%)</td>
<td>87 (68 – 96)</td>
</tr>
<tr>
<td>Negative predictive value (%)</td>
<td>60 (36 – 80)</td>
</tr>
<tr>
<td>Accuracy (%)</td>
<td>76 (62 – 86)</td>
</tr>
<tr>
<td>Positive LR</td>
<td>3.06 (1.28 – 7.29)</td>
</tr>
<tr>
<td>Negative LR</td>
<td>0.31 (0.16 – 0.59)</td>
</tr>
</tbody>
</table>
• Are very contributary as they can identify and localize LNs and reduce the length and the morbidity of surgery.
• Spatial resolution

Which one is the real sentinel node using γ probes?

• The absolute nr of counts in the nodes
• In vivo or ex vivo counts of LNs/ bkgr or neighbouring LNs
• Threshold is >10% of the counting rate in the hottest node
• 4/1996 - 5/2016: 299 pts with malignant melanoma (Breslow >1 mm, high mitotic rate)

• Detection rate: 99% (296/299)

• Positive SLN: 18% (54/296)

• Accuracy: 97% (286/296)

FN: 16% (10/64)

3% (10/296)
Hand held gamma probe

- Detection rate: 99%
- FN rate: <3%

Intraoperative (dept of surgery)

Is there any benefit from sentinel lymph node biopsy using the combined radioisotope/dye technique in breast cancer patients with clinically negative axilla? Sophia Koukouraki et al. Nuclear Medicine Communications 2009, 30:48–53

It is mandatory for NM community to reach a consensus on the radioactive counting rate threshold in order to guide the surgeon in the identification of the real SLNs.

<table>
<thead>
<tr>
<th>In situ</th>
<th>Ex vivo</th>
<th>Incision area</th>
<th>evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>+</td>
<td>-</td>
<td>Total excision</td>
</tr>
<tr>
<td>+</td>
<td>-</td>
<td>+</td>
<td>Not true SLN</td>
</tr>
<tr>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Additional lymphnodes</td>
</tr>
<tr>
<td>+</td>
<td>-</td>
<td>-</td>
<td>Technical failure</td>
</tr>
</tbody>
</table>
For SLNB concept the preoperative identification of SLNs is essential. But this complicates the organization of surgery and takes additional time.

The road to real time intraoperative imaging

Portable mini gamma camera vs SPECT/CT: sensitivity 83%

Detection rate: >95%

Its role is very important to confirm the adequate safety margins of the removed lesion.
• Radioisotopique techniques in the concept of SLNB are highly successful and accurate and is a part of the routine surgical management of oncological patients.

• dLSC + IOD has a high success rate.

• SPECT/CT may be used in specific situations. AC is useful. More studies must be done in proving the clinical impact.

• PET/CT cannot replace SNB.

• Radiation risks to staff and patients are minimal (far below harmful levels).

• Best protocol, optimal nr of removed nodes.