El ganglio centinela en cáncer de mama

« Aut tace aut loquere meliora silentio »
Introduction

Background and Rationale
Breast cancer

Rationale

✓ Breast cancer is the most frequent cancer in women worldwide
✓ Accurate lymph node staging is essential for prognosis and treatment
✓ No imaging modality is accurate enough to detect lymph node metastases

Axillary lymph node dissection (ALND)

✓ Important staging procedure in breast cancer surgery
✓ Trend toward early diagnosis: many negative ALND
✓ Complications: pain, paresthesia, infection, lymphedema, mobility

Sentinel lymph node biopsy (SLNB)

✓ Applied in breast cancer about 20 y. ago and became a routine technique
✓ Accurate staging (identification rates of SLN of more than 95% in experienced multidisciplinary team: learning curve)
✓ May also detect non-axillary sentinel nodes
✓ Minimize the number of unnecessary ALND → morbidity, cosmetic results, shorter hospital stay
# SNL in breast cancer

## Techniques and results

### Technical aspects

- Injection modalities
- Volume
- Activity
- Particle size
- Time between injection and imaging / surgery

## Author | Year | Patient nb | Identified SN | False negative
--- | --- | --- | --- | ---
**Blue dye only**
Giuliano | 1994 | 174 | 66% | 11%
Guenther | 1997 | 145 | 71% | 10%
Flett | 1997 | 68 | 82% | 17%

**Probe only**
Crossin | 1998 | 50 | 84% | 13%
Krag | 1998 | 443 | 93% | 11%

**Probe and dye**
Chatterjee | 1998 | 60 | 97% | 5%
Cox | 1998 | 466 | 94% | 1%
v.d. Ent | 1998 | 70 | 100% | 4%
Doting | 1999 | 136 | 93% | 5%
Tanis | 2002 | 501 | 96% | <5%
SNL in breast cancer

The breast: multiple drainage patterns
Axillary / Internal Mammary Chain (IMC)
Indication

EANM procedure guidelines for sentinel node in breast cancer

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## Indications and contra-indications

### Common indications

<table>
<thead>
<tr>
<th>Clinical Circumstance</th>
<th>Use of SLN Biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1 or T2 tumours</td>
<td>Established</td>
</tr>
<tr>
<td>T3 or T4 tumours</td>
<td>Controversial</td>
</tr>
<tr>
<td>Multicentric or multifocal tumours</td>
<td>Controversial</td>
</tr>
<tr>
<td>Inflammatory breast cancer</td>
<td>Not recommended</td>
</tr>
<tr>
<td>DCIS with mastectomy</td>
<td>Established</td>
</tr>
<tr>
<td>DCIS without mastectomy</td>
<td>Controversial</td>
</tr>
<tr>
<td>Suspicious, palpable axillary nodes</td>
<td>Controversial</td>
</tr>
<tr>
<td>Older age</td>
<td>Established</td>
</tr>
<tr>
<td>Obesity</td>
<td>Established</td>
</tr>
<tr>
<td>Male breast cancer</td>
<td>Established</td>
</tr>
<tr>
<td>Evaluation of internal mammary LN</td>
<td>Controversial</td>
</tr>
<tr>
<td>Prior axillary surgery</td>
<td>Controversial</td>
</tr>
<tr>
<td>Prior non-oncologic breast surgery</td>
<td>Controversial</td>
</tr>
<tr>
<td>After preoperative systemic therapy</td>
<td>Controversial</td>
</tr>
<tr>
<td>Before preoperative systemic therapy</td>
<td>Established</td>
</tr>
</tbody>
</table>
Indications and contra-indications

Precautions

• Pregnancy and lactation
Pregnancy is not a contraindication for probe-guided SLN biopsy (the dose to the foetus is negligible)
The use of blue dye is not recommended during pregnancy
In nursing mothers, lactating should be suspended for 24 h after radiopharmaceutical administration

• Training
Studies should only be performed by a surgeon and a nuclear medicine specialist who have undergone specific training in this technique
At this time, no definition of the required training has been validated for the surgeon or the nuclear physician, although a minimum of 30 procedures has been proposed for the surgeon
Nuclear Medicine procedure

Injection technique, detection technique

SPECT-CT: 3D Volume rendering
Procedure

- Quality control
  - of the gamma camera and image display
  - of the gamma probe for sentinel node detection in the operating theatre

- Patient preparation
  - no special preparation for the test is needed

- Radiopharmaceuticals

<table>
<thead>
<tr>
<th>99mTc-based agents</th>
<th>Particle size max (nm)</th>
<th>Particle size mean (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulphur colloid (USA)</td>
<td>350-5000</td>
<td>100-220 (filtered)</td>
</tr>
<tr>
<td>Nanocolloidal albumin (Nanocoll ®) (Europe)</td>
<td>100</td>
<td>5-80</td>
</tr>
<tr>
<td>Antimony trisulphide (Canada and Australia)</td>
<td>80</td>
<td>3-30</td>
</tr>
<tr>
<td>Tin colloid</td>
<td>800</td>
<td>30-250</td>
</tr>
<tr>
<td>Labeled dextran</td>
<td>800</td>
<td>10-400</td>
</tr>
<tr>
<td>Hydroxyl-ethyl starch</td>
<td>1000</td>
<td>100-1000</td>
</tr>
<tr>
<td>Stannous phytate</td>
<td>1200</td>
<td>200-400</td>
</tr>
<tr>
<td>Sulphide nanocolloid (Lymphoscint ®)</td>
<td>80</td>
<td>10-50</td>
</tr>
<tr>
<td>Rhenium sulphide nanocolloid (Nanocis®)</td>
<td>500</td>
<td>50 - 200</td>
</tr>
</tbody>
</table>
Injection techniques

Size of colloids

sulfur colloid (5-80 nm) or albumin nanocolloid (5-30 nm)

Volume - Concentration

Total injected volume: 0.2-0.5 mL (physiologic)
- if less: slow drainage
- if more: saturation
Injection techniques

Activity - Timing

- If injection the same day of surgery: 5-30 MBq
- If injection the day after the surgery: 150 MBq max

Early: intravascular activity; multiple vessels leading to a single sentinel node
### Injection site

<table>
<thead>
<tr>
<th></th>
<th>Subdermal</th>
<th>Peritumoral</th>
<th>Intratumoral</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Injection</strong></td>
<td>Multiple</td>
<td>Multiple (4)</td>
<td>single</td>
</tr>
<tr>
<td><strong>Drainage (speed)</strong></td>
<td>fast</td>
<td>slow</td>
<td>fast or slow</td>
</tr>
<tr>
<td><strong>Injection site on scan</strong></td>
<td>large</td>
<td>very large</td>
<td>circumscript</td>
</tr>
<tr>
<td><strong>Internal Mammary nodes</strong></td>
<td>rare</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td><strong>Intramammary nodes</strong></td>
<td>never</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td><strong>Reflects tumor’s drainage</strong></td>
<td>+/-</td>
<td>+</td>
<td>++</td>
</tr>
</tbody>
</table>
ROLL technique

Radioguided Occult Lesion Localisation

In non-palpable breast lesion replace hooked wired localization
Intratumoral administration guided by ultrasound/stereotaxis
Followed by immediate surgical resection, guided by probe
Can be associated to SLN
Peritumoral injection site

**Injection technique**

- **Palpable breast carcinoma**
  - 3-4 injection around the tumor

- **Non-palpable breast carcinoma**
  - Administration guided by ultrasound/stereotaxis

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Peritumoral injection site

Characteristics

- Visualization of IMC
- ROLL and SLN detection

Internal Mammary Chain (5-20%)
Axilla (98%)

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Superficial injection sites

Injection technique

Subareolar/Periareolar (Sappey’s subareolar plexus)

1 – 4 injection at the skin level (subdermal/intradermal)

Over the lesion
Subdermal injection sites

Characteristics

Subareolar/Periareolar

- Impalpable and multicentric tumours

Easy technique, rapid uptake

Over the lesion

- Better accuracy (elderly)

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Injection method does not significantly affect the identification of SLN

- superficial injection is easy to perform
- deep injections may require ultrasound or sterotaxic guidance but allow detection of extra-axillary nodes
Imaging is strongly recommended before any operative procedure (variability in breast lymphatic drainage into the axilla and extra-axillary)

- **Patient position:**
  Supine or prone (with hanging breast position or upright)
  Anterior, 45° anterior oblique and lateral imaging can be obtained

- **Imaging:**
  Performed within 15-30 min after the injection and 2-4 hours after
  Images acquired for 3-5 min, pixel size of about 2mm (256x256 or 128x128 matrix)
  57Co or 99mTc flood source for delineation of patient’s body contour
  SPECT/CT optional images: better contrast and spatial resolution

- **Localisation:**
  The site of any suspected SLN can be localized on overlying skin, preferably on the 45° anterior oblique oblique image
DRENAJE LINFÁTICO

← Ganglios axilares (Niveles I, II y III de Berg) (N1-N3)
← G. del parénquima mamario
← G. de la cadena mamaria interna (N1-N3)
G. de la zona supraclavicular (N3)

← G. de la cara lateral del cuello (M1)
← G. de la axila contralateral (M1)
Detection techniques

Localization

IM: incidence = 20%

30%
46%
17%
4%

Detection techniques

Localization

Supraclavicular 0.3%
Infraclavicular 1.2%
Interpectoral 2.0%
Intramamary lateral 5.3%
Intramamary medial 2.0%

Others: incidence = 11%

Detection techniques

Landmark

- Anterior projection
- Axillary projection
- Lateral projection
Detection techniques

Imaging

The ideal case!
Detection techniques

Timing

Role of early/delayed images
Detection techniques

Imaging

Two SLN
Detection techniques

Imaging

One SLN
Detection techniques

Imaging

One or two SLN?
Detection techniques

Imaging

Intra-mammary SLN
Detection techniques

Imaging

Exclusively non-axillary SLN

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Detection techniques

Imaging

All in one!
The majority of patients with preoperative lymphoscintigraphic SLN non visualization will have at least one SLN detected intraoperatively. In approximately 1%-2% of patients, SLN will not be detected intraoperatively, and the status of axillary nodes cannot be determined. Old age, obesity, tumor location other than in the upper outer quadrant, and non-visualization of SLN on preoperative lymphoscintigraphy may be associated with failed SLN localization. There is no definitive consensus on what to do if the SLN cannot be visualized. However, current standard patient care recommends axillary lymph node dissection.
Captación débil o ausente en el ganglio centinela

1. Radiotrazador
   a. Dosis escasa
   b. Baja calidad
   c. Cifra de partículas insuficiente

2. Imágenes
   Intervalos demasiado cortos o largos entre la administración del radiotrazador y la linfogammagrafía

3. Paciente
   a. Edad avanzada
   b. Mamas grandes / grasas
   c. Cuadrante superoexterno
   d. Invasión tumoral
   e. Cirugía / biopsia de mama previa

Overweighted patients with breast cancer

Improved sentinel node identification by SPECT/CT

Lerman et al. JNM, 2007
SPECT-CT
Advantages

SLN better localization

Two parietal lymph nodes clearly shown only on SPECT-CT
Advantages

Specific location of the SLN

Level I and Level II axillary lymph nodes clearly shown on SPECT-CT
Advantages

Specific location of the SLN

Deep intra-mammary lymph nodes
Advantages

Additional Lymph Nodes

An intra-mammary lymph node is seen only in SPECT-CT
Advantages

Intra-mamary lymph node detection
Advantages

Intra-mammary and axillary lymph node detection
Enlarged axillar lymph node with uptake of the tracer only at the pole clearly shown on SPECT-CT
SPECT-CT

Advantages

Anatomic Information: Surgical Planning
Procedures during surgery

SN exeresis and analysis

While removing too few nodes may result in missing potential metastasis in regional lymph nodes, indiscriminate removal of axillary nodes may cause morbidity similar to that of axillary lymphadenectomy.
Surgical techniques

Injection of Patent Blue Dye

Operative Detection
(hot and blue SN)
Blue dye localisation

- patent blue V, isosulfan blue, methylene blue
- 0.5-1 mL of blue dye
- injected around primary tumour, 10-20 min prior surgery

Within 5-15 min the SLN is coloured. Washout after about 45 min

In most cases, the same SLNs are detected by the two methods
Detection probes

Able to detect the SLN from the skin surface and within the exposed surgical cavity:
- must be well collimated to discriminate activity
- can be used to select the optimum location for incision
- must be used to check the wound site for remaining activity
- must be used to re-check removed SLN before sending for histology

Deep SLN are difficult to detect (tissue attenuation): to avoid false negative results, the open axilla should be palpated and suspicious lymph nodes harvested, even if these are neither hot nor blue
INDICACION CLINICA

T1 <2cm
Ausencia clínica de metástasis linfáticas

T2 2-5 cm

BIOPSIA DEL GANGLIO CENTINELA

VISUALIZACION 95%

LOCALIZACION QUIRURGICA 98%

Resultados

Falsos negativos = 3 % (0-10%)  VPN = 98%
SNL in breast cancer

HCL protocol

✓ Local anesthesia: None
✓ Tracer activity: 40 MBq in 1/4 injection (0.2 mL), for surgery the day after
✓ Particle type: Nanocis® or Nanocoll®
✓ Injection site: Intradermal/Periareolar
✓ Time between injection and imaging: early static images at 30’, eventually late static images at 2h (if Nanocis®, normally not necessary if Nanocoll®)
✓ Acquisition: 5’, 256² matrix, parallel hole high resolution collimator,
✓ Projections: anterior (supine) and lateral (prone, hanging breast)
✓ ⁵⁷Co flood source: eventually (medical option)
✓ SPECT-CT: Yes if BMI > 25, otherwise eventually (medical option)
  ✓ SPECT parameters: 128² matrix, 32 images of 15”, zoom 1.23
  ✓ CT parameters: 3mm slices, pitch 1.5
✓ Landmarks: Yes
Issues requiring further clarification

**T3-T4 tumours**
False negative rate and axillary recurrence reported similar to T1-T2

**Multifocal and multicentric tumours**
Prevalence of axillary metastases is higher
High false negative rates
However, the reported axillary recurrence rates are acceptable

**DCIS and breast conservation**
DCIS does not metastasize to regional lymph nodes. However, invasion is missed in up to 40% of patients. Therefore, sentinel node biopsy is recommended only in patients undergoing mastectomy

**Suspicious palpable nodes.**
Palpable axillary nodes may be tumour negative in 40% of cases. Thus, SLN biopsy could be performed also in patients with palpable nodes, if negative in the preoperative diagnosis (FNAB)

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Issues requiring further clarification

Evaluation of internal mammary and other extra-axillary nodes

Detection rate is affected by the depth of injection
The significance of internal mammary SLN biopsy is under debate
More evidence is necessary to support the idea that mapping of IMN will improve the outcome of treatment and survival

Prior excisional biopsy or breast surgery
The lymph drainage is probably changed. However, previous breast surgery probably do not affect the accuracy of SLN procedure

Neoadjuvant chemotherapy
Before nCT, SLN biopsy is useful but can postpone the treatment
After nCT, SLN biopsy may lead to an underestimation of the initial stage, with unknown clinical significance
New trends in SLN
Instrumentation

Small field of view portable imaging devices

Gamma-Node ® (Clerad)

Sentinella S102®
(Oncovision)

Last generation portable gamma camera fitted with a pin-hole collimator, with improved ergometrical details and adequate support system for intra-operative use

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Radiopharmaceuticals

Bimodal tracers

Simultaneous radioguided and fluorescent detection

Preoperative injection → Preoperative imaging

Gamma tracing/imaging + NIR fluorescence imaging → Post-excision gamma imaging

Intraoperative injection → Visual detection

Brouwer OR, Ann Surg Oncol (2012)

F.Giammarile
Thanks for your attention

Congress 2013