Laparoscopic sentinel-node biopsy in cervical cancer

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Blue dye

- **Advantages**: easy, low cost, no use of radio-active products, good sensibility (?)..
- **Disadvantages**: per-operative detection requiring a relatively large surgical dissection, reduced rate of detection (?)
Isotopic method

- **Advantages**: performing a pre-operative scintigraphy in order to localize sentinel nodes in other territories than pelvic, per-operative detection easy to perform with help of endoscopic probes, reproducibility, efficacy (?)..

- **Disadvantages**: handling of isotopic products, cost.
Sentinel node

- Isotopic method (Technetium 99)
  » Colloidal particles
- Possibility of location of abnormal lymphatic drainage (scintigraphy)
- Problems: size of the particles and injected volume
Technique

- Cervical injection (4 quadrants)
- Time between injection and detection of the sentinel node: function of the technique
  - blue dye: 10 to 20 minutes
  - isotopic method: variations of time depending on size of the particles (2 to 18 hours)
FOIE + RATE

X crete iliaque

<---- POINTS D'INJECTION

X symphyse pubienne

VUE ANTERIEURE
Lymphatic drainage of the uterus

- 3 drainage directions
- Main channel = along the uterine pedicles
- Accessory channel along the infundibulo-pelvic pedicles
- Accessory channel going from the posterior part of the uterus
Lymphatic drainage of the uterus

- Main drainage (uterine pedicles) goes to the external iliac nodes
- Channel along the infundibulo-pelvic pedicles goes to the para-aortic supra-mesenteric nodes
- Posterior channel goes to the presacral nodes
- Skip metastases are rare (< 5%)
Material:

- October 1998 to October 2003,
- 123 patients with cervical cancer stage IA2-IB1.
- A systematic full pelvic laparoscopic lymphadenectomy was performed in all cases.
Results:

- 1 sentinel node (or a group of 2 or 3 adjacent sentinel nodes) were found in 97.5% of cases.
- When looking at the rate of detection by pelvic side, it is 87%.
- In 6 patients, sentinel nodes were found in different places.
Results:

- **Localization** of the sentinel node:
- 86% in external iliac position (described by Leveuf and Godard)
- 14%: Lucas-Championnière, obturator, common iliac, presacral
Results:

- Metastases were found in the sentinel nodes in 24% of patients.
- When the sentinel nodes were negative, the other pelvic nodes were always negative also, the negative predictive value = 100%.
Specific histological analysis of the sentinel node

- Serial sections (each 200µm)
- Immunohistochemical study with antibody against cytokeratins:
  - Discovering micrometastases
  - Increasing the rate of node positive patients by 15%
Early cervical cancer, risk of relapse after radical hysterectomy
Ph VAN TRAPPEN Lancet 2001

<table>
<thead>
<tr>
<th>Type of Metastasis</th>
<th>Patients</th>
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<tbody>
<tr>
<td>Nodal metastases</td>
<td>1/4 patients</td>
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<tr>
<td>Micrométastases*</td>
<td>3/16 patients</td>
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<tr>
<td>No nodal metastases</td>
<td>0/12 patients</td>
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</table>

* Detection with RT-PCR looking for CK19 mRNA
Material

- Prospective series of 43 patients
- January 2001 to May 2004
- Mean age = 41 years
- Squamous carcinoma = 31 (72%), adenocarcinoma = 12.
- Tumoral diameter > 2 cm = 20 (46%).
Method

- All the nodes (sentinel and non sentinel) were extensively analyzed.
- Serial sectioning each 200 µm with HES staining.
- If the node was negative with this technique, an immunohistochemical analysis with a anti-cytokeratins antibody was performed on all sections.
Results

- Detection rate of the sentinel node = 100%.

- 3 patients positives with frozen sections (8%)
Results

- 1 patient with macrometastasis in a SN with the classical histological technique
- 6 cases of micrometastases.
- Of these, 3 were real micrometastases (< 2mm and > 200µm)
- And 3 were tumor cells embolism (< 200µm)
CK: AE1-AE3
IHC : CK+

Tumor cells embolism
IHC : CK+
IHC : CK+
Results

- Of the 6 cases with micrometastases, these were located in 3 cases in the SN, but in NSN in 3 patients.
- 15% of micrometastases.
- Negative predictive value of the SN = 91.6%.
- But 3/10 (30%) false negative rate.
Correlation between SN and NSN

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<th>NSN -</th>
<th>NSN +</th>
<th>Total</th>
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<tbody>
<tr>
<td>SN -</td>
<td>33</td>
<td>3</td>
<td>36</td>
</tr>
<tr>
<td>SN +</td>
<td>6</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>39</td>
<td>4</td>
<td>43</td>
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</table>
## Results

<table>
<thead>
<tr>
<th>Name</th>
<th>Type of node</th>
<th>Nb of node</th>
<th>Serial sections with HES</th>
<th>IHC</th>
<th>Type of meta</th>
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<tbody>
<tr>
<td>Br</td>
<td>SN</td>
<td>4</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>NSN</td>
<td>18</td>
<td>-</td>
<td>+</td>
<td>Cell embolism</td>
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<tr>
<td>Ma</td>
<td>SN</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>NSN</td>
<td>12</td>
<td>+</td>
<td>+</td>
<td>&lt; 2mm</td>
</tr>
<tr>
<td>Ka</td>
<td>SN</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>NSN</td>
<td>39</td>
<td>+</td>
<td>+</td>
<td>&lt; 2mm</td>
</tr>
</tbody>
</table>
Explanations for the false negative cases

- No isotopic detection in 27 cases, including the 3 false negative cases.
- Multiple channels of drainage.
- Lost of nodal material during the frozen sections procedure.
- Metastases inside the parametrium.
Results:

- Mean follow-up of 22 months (4-38).
- Recurrence occurred already in 1 patient (2.8%).
- It was a squamous Ib1 cervical carcinoma with LVSI, all pelvic nodes were negative with classical histological exam, but a micrometastasis onto a SLN was detected only with IHC. The recurrence was either in the pelvic area and distal (liver metastasis).
Conclusions

- SN biopsy seems a reliable technique when looking with classical histological technique.

- But multilevel sectioning with cytokeratin immunohistochemistry may identify more patients with nodal micrometastases.

- However it identifies cases where micrometastases were present in nonsentinel nodes when the sentinel node was negative.
Conclusions

- This high false-negative rate of the sentinel node biopsy rises questions about the validity of the sentinel node concept in cervical carcinoma.

- A multicentric study is ongoing in France in order to elucidate the place of SN biopsy in early cervical cancer.