Aims and objectives

Thoraco-abdomino-pelvic Computer Tomography (CT) is routinely used to stage high risk breast cancer patients (pN+), most of the time after breast surgery (1-2). It may also be helpful in preoperative assessment to approach the disease burden in the axilla: less or more than four axillary suspected nodes (3-6). This information should allow for a more limited selective axillary dissection (SAD) in patients limited axillary disease (N1, less than 4 nodes involved) sparing them the morbidity of more extensive surgery (7,8).

The current standard for patients who are known to be node-positive after FNA or core biopsy continues to be completion axillary dissection (AD) where a minimum of ten lymph nodes are removed. Pathological results demonstrate that most pN + patients have only pN1 disease with between 1 and 3 lymph nodes involved (9). If more reliable preoperative axillary imaging were available that could predict the number and location of involved nodes, a more limited AD could be performed for the majority of these patients who have only N1 disease. This more limited procedure would be a selective axillary dissection (SAD), removing more lymphatic tissue than a Sentinel node biopsy (SNB) but less than an AD. SAD combined with axillary reverse mapping (ARM) should result in a more focused and accurate dissection of diseased nodes resulting in less surgical morbidity (figure1). We wanted to determine if CT imaging, routinely used in staging node-positive patients, could also reliably predict regional lymph node involvement (10-12).
Fig. 1: Selective axillary dissection with Axillary Reverse mapping: the objective is to preserve the main lymphatic chain for arm drainage during axillary dissection. This technique can be proposed for patients with limited axillary disease (less than 3 metastatic nodes).

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Methods and materials

Inclusion criteria were breast cancer patients at risk for pN1 nodal involvement after clinical and ultrasound examination. From 2009 to 2013, 194 consecutive patients underwent pre-operative CT scanning using a specific protocol for lymph node imaging called Thoraco-Abdomino-Pelvic-Nodes (TAP-N): abdomino-pelvic study at portal time and then thoracic study at later venous time (images obtained 120 sec after administering contrast medium). We studied the TAP-N predictive value for determining which patients had N2 or N3 disease, not eligible for SAD.

We decided to study the thoracic nodes regions in late venous phase, an average of 120 seconds after injection of contrast. The studies were performed on a Siemens Somatom multi-detector CT with a slice thickness of 0.5mm, respecting the recommended maximum X-Ray dose of 1000 mGray / exam. Non ionic contrast medium (120ml; 340mgI/ml) was perfused at a rate of 3ml/sec. Three studies were performed: a liver unenhancement study, then an abdominopelvic enhanced study during portal phase and finally a thoracic study in late venous phase (on average 120 sec after contrast injection). (figure 2) Contrast injection was performed contralateral to the side of the tumor to avoid the "blush" seen in the axillary vein which can mask visualization of deeper structures.

Images were interpreted prospectively by a breast radiologist with 15 years of experience. Lymph nodes were evaluated and compared to the contralateral healthy side.

Axillary lymph nodes were considered abnormal if they were greater than 6 mm in little axis with one additional of the following criteria: overall deformation of the shape with loss of the fatty hilum, irregular contour, focal cortical thickening, heterogeneous enhancement or enhancement of more than 20 Hounsfield units compared to the contralateral healthy nodes (figure 3).

Any detectable internal mammary lymph nodes were considered suspect in the absence of recent breast surgery or an existing implant (figure 4). The use of Minimum Intensity Projection frontal reconstructions helped to reliably and easily locate and visualize the axillary lymph nodes along the lateral thoracic artery (figure 5) and to better identify nodes in the IMC.

When unknowned metastatic axillary nodes was suspected at CT-N, ultrasound studies was performed, with fine needle aspiration (FNA) as standards recommendations (13) (figure 6). This procedure allowed the surgeon to choose between SNB when negative and AD when positive.

Between 2008 and 2013, 194 patients at risk for pN1 disease was explored by CT-N before treatment. The patients were divided into two groups depending on their initial
treatment: surgical group or neoadjuvant chemotherapy group. In the surgical group, the CT-N scan was performed one or two weeks before breast and axillary surgery (SNB or AD).

We aimed to answer the following questions:

- Is it possible to determine which patient has significant N2 or N3 disease (more than 3 positive lymph nodes)?
- Can we reliably assess the lymph nodes of the internal mammary chain (IMC)?
- How efficient is our scanning technique for determining overall metastatic burden?

**Table 1**: patients characteristics in surgical group

<table>
<thead>
<tr>
<th>Metastatic Nodes</th>
<th>pN0</th>
<th>pNi ou pN1</th>
<th>pN2 et plus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor size</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1cm</td>
<td>35 (54.7%)</td>
<td>17 (26.5%)</td>
<td>12 (18.8%)</td>
</tr>
<tr>
<td>1-2cm</td>
<td>28 (43.8%)</td>
<td>18</td>
<td>8</td>
</tr>
<tr>
<td>2-3cm</td>
<td>21 (32.8%)</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>&gt;3cm</td>
<td>13 (20.3%)</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Grade</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>12 (18.8%)</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>32 (50%)</td>
<td>17</td>
<td>11</td>
</tr>
<tr>
<td>3</td>
<td>20 (31.2%)</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>HER2+</td>
<td>8 (12.5%)</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Histological feature</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lobular carcinoma</td>
<td>15 (23.4%)</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>Canalar carcinoma</td>
<td>47 (73.4%)</td>
<td>23</td>
<td>13</td>
</tr>
<tr>
<td>Over</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>
**Table 2:** Final histology in surgical group

<table>
<thead>
<tr>
<th>Metastatic Nodes</th>
<th>pN0 (35)</th>
<th>PN+ (29)</th>
<th>pNi</th>
<th>pN1</th>
<th>pN2 and more</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>(2)</td>
<td>(15)</td>
<td>(12)</td>
</tr>
<tr>
<td>TAP-N: N0</td>
<td>17</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>TAP-N: N1</td>
<td>18</td>
<td>1</td>
<td>11</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>(1 to 3 suspected nodes)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TAP-N: N2 or more</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>(4 suspected nodes or more)</td>
<td></td>
<td></td>
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</table>
Fig. 1: Selective axillary dissection with Axillary Reverse mapping: the objective is to preserve the main lymphatic chain for arm drainage during axillary dissection. This technique can be proposed for patients with limited axillary disease (less than 3 metastatic nodes)

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Fig. 2: TAP-N use a specific protocol with a thoracic study at late venous phase, on average 120 sec after contrast injection.
**Fig. 3:** Abnormal nodes: size > 6mm with morphologic changes or specific enhancement. After CT study, abnormal nodes are evaluated by Ultrasound with fine needle aspiration.

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**Fig. 4:** Internal mammary lymph node. MIP reconstruction

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**Fig. 5:** Axillary lymph nodes: comparison with healthy side.

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**Fig. 6:** Abnormal lymph node near to the lateral thoracic artery. Correlation with ultrasound study before fine needle aspiration.

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Results

Among the 194 patients, 130 underwent neoadjuvant chemotherapy and 64 went directly to surgery and axillary dissection.

1- Evaluation of nodal extension: N0/N1 versus N2/N3 (n=64)

The correlation between imaging and final histology was only possible for the surgery group (n=64).

Histological features and patient characteristics are presented in Table 1.

The correlation between final histology and the TAP-N scan results for the surgical group are shown in Table 2.

Correlation between TAP-N and final histology was studied on the 64 surgical patients: 45.3% were pN+ (29/64), 26.5% were pN1 (17/64) and 18.8% were pN2 or pN3 (12/64). These pN2-pN3 metastatic extensions were not suspected by clinical or ultrasound studies but clearly seen by CT-N.

All patient who had pN2 or greater disease were identified as N+ on CT.

TAP-N could differentiate between N0-N1 versus N2-N3 disease with a sensitivity of 83.3%, specificity of 96.1%, NPV of 96.1%, PPV of 83.3% and an accuracy of 93.7%.

In 2 cases, the scan underestimated axillary disease predicting N1 disease when there were actually 4 or 5 positive lymph nodes on permanent section. One of the false negative results involved a nodal metastasis of less than 5 mm not seen on CT. The other was a patient with a poorly vascularized tumor (lobular) with little enhancement on imaging and a metastasis of less than 5 mm on final pathology.

In 2 patients with false positive results, CT CAP-N predicted N2 or N3 disease but finally pathology revealed only 2 or 3 positive lymph nodes. The lymph nodes that were false positives seen on CT were small (<8 mm) with normal morphology but misinterpreted as they enhanced strongly after contrast injection.

2- Imaging of the IMC (n=194)
8.2% of patients (16/194) had at least one suspicious IMC lymph node. In five of these patients, there was no evidence of axillary disease and the tumor locations were medial and/or deep. In the remaining 11 patients, the axilla had extensive disease (>3 positive lymph nodes) with extension into Berg's Zones 2 and 3 for eight patients.

We have no histological correlation for these imaging findings as the lymph nodes observed were mostly small (< 6 mm) not amenable to ultrasound-guided FNA.

3- Assessment of metastatic burden and second primary lesions (n=194)

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6.2% of patients (12/194) had evidence of metastatic disease or second primary lesions. 8 patients were found to have asymptomatic metastatic disease and four patients had four synchronous primary lesions: 2 kidney tumors, 1 pancreatic tumor and 1 lung tumor. Finally, two patients had evidence of contralateral breast lesions which were confirmed on mammogram and ultrasound.
Conclusion

The TAP-N provides the surgeon with relevant preoperative information regarding regional nodal involvement and can help with surgical planning. Our protocol does not allow differentiation between N0 and pN1 patients, but between patients with limited pN1 disease and those with more extensive pN2-N3 disease. The radiologist sends the surgeon high quality anatomical images where we clearly see the thoraco-lateral and axillary vessels.

The TAP-N is extremely effective at detecting N2 axillary disease and greater. Such pre-operative CT using a specific lymph node protocol can reliably predict which patients do not have extensive axillary disease, eligible for a less morbid Selective Axillary Dissection.
References


