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Sentinel node procedure: is a yearly ultrasound follow-up necessary?

A. Van Steen[1]

Purpose: To evaluate the place of a yearly ultrasonographical examination in the follow-up after breast cancer surgery and sentinel node biopsy.

Material and methods: From 2003 until 2009, 1.030 patients underwent breast cancer surgery and a sentinel node excision. The indications for sentinel were made according to the EUSOMA Guidelines. For the evaluation of the sentinel node a 1,2 cc solution of 10-20 MBq 99 Tc macroaggregates was injected subcutaneously above the tumor site the day before surgery. During surgery methylene blue was injected too. The lymph nodes with the highest counts as well as the blue ones were excised. When (micro)metastases were detected a complete axillary excision was done. All patients underwent a yearly clinical examination, mammography and ultrasound of the breast and axillar and infraclavicular region. All ultrasound examinations were performed on an ALOKA 5500 or alfa 10.

Results: Already one year after surgery, two relapses in the axilla were found: one patient had a large in situ carcinoma and the second patient a medially located medullary tumor. Both ultrasound and clinical examination showed the adenopathies.

Conclusion: Also based on the results of other centers a systematic investigation of the axillar region is in the future perhaps not mandatory in certain circumstances. Further long time follow-up of this group of patients is however necessary to evaluate better the additional benefit of ultrasound.

1. Dpt. of Radiology, UZ Leuven, Leuven, Belgium.

Authors	Number of patients	Mean follow-up	Clinically palpable	Axillary recurrence	%
Our study	1.030	40 months	2	2	0,2
de Kanter AY et al	149	65 months	4	4	2,7
Groetelaers RP et al	254	73 months	-	1	0,4
Veronesi U et al	3.548	48 months	-	31	0,9
Snider HC et al	289	25 months	0	0	0

New preoperative localisation procedures

A. Van Steen[1]

Due to the experience with the sentinel node procedure, some new techniques using radiopharmaceuticals have been developed.

With the Radioguided Occult Lesion Localisation (ROLL) procedure, macroaggregates of technetium-99m labelled human serum albumine are injected into the lesion, instead of the introduction of a wire hook or carbon injection.

The Sentinel Node and Occult Lesion Localisation (SNOLL) is a combination of the ROLL- and sentinel node procedure.

The technique of these procedures will be explained in detail.

The benefits of these procedures are the possibility to combine two procedures in one, which is more comfortable for the patient, and the possibility for the surgeon to choose the incision, without taking into consideration the site of injection. Thus the extracted tissue will be smaller and the lesions are more centrally located.

1. Dpt. of Radiology, UZ Leuven, Leuven, Belgium.

BIRADS-classification mammography

P.A.M. Bun[1]

The ACR breast imaging reporting and data system (Bi-rads) is a quality assurance tool designed to standardize mammographic reporting, reduce confusion in breast imaging interpretations and facilitate outcome monitoring. Newest (4th) edition: 2003

The breast imaging report should be divided into:

1. Indication for this exam
2. Breast composition
3. Findings
4. Location of lesion
5. Comparison to previous studies (if deemed necessary by the radiologist)
6. Findings ultrasound (When done)
7. Conclusion and Birads-classification

Mammographic breast composition

I. The breast is almost entirely fat (< 25% glandular)

II. Scattered fibroglandular densities (25-50%)

III. Heterogeneously dense breast tissue (51-75%)

IV. Extremely dense (> 75% glandular)

Findings

Mass and Asymmetry

A "***Mass"*** is a space-occupying (three-dimensional) structure demonstrating convex outward borders (seen in two different projections, usually evident on two orthogonal views). An ***asymmetry*** lacks convex outward borders and cannot be identified as a space-occupying lesion (if a potential mass is seen in only a single projection on mammography it should be called an "asymmetry" until it's three-dimensionality is confirmed).

Mass morphology

Shape: round, oval, lobular, irregular

Margin: circumscribed, microlobulated, "obscured", indistinct (ill-defined), spiculated

Density: high-, equal- (isodense), low density (not fat-containing), fat-containing, radiolucent

Calcifications

Morphology (most important)

Typically benign

- Skin
- Vascular
- Coarse/popcorn-like (fibroadenoma)
- Large rod-like (secretory calc./plasmacel mastitis)
- round (0,5-1 mm)/punctuate (< 0,5 mm)
- Lucent- centered calcifications (< 1 mm 1 cm >)
- Eggshell or Rim calcifications
- Milk or Calcium (sedimented calcifications in macro-or microcysts)
- Suture calcifications
- Dystrophic (coarse > 5 mm often lucent center)

Intermediate concern, suspicious calcifications

- Amorphous or indistinct calcifications: (small, hazy: no better morphologic classification determined). Diffuse/Scattered: can usually be dismissed as benign (baseline magnification view). Regional, segmental, clustered or linear distribution warrant biopsy.
- Coarse heterogeneous calcifications: > 0,5 mm irregular, conspicuous tend to coalesce. Bilaterally clustered usually benign (fibroadenoma), single cluster low suspicion, linear en segmental distribution suspicious.

Higher probability of malignancy

- Fine pleomorphic calcifications: irregular, usually < 0,5 mm, varying in size and shape.
- Fine linear or fine linear branching calcifications: may be discontinuous and < 0,5 mm in width, irregular linear of curvilinear (suggests filling irregular duct lumen breast ca).

Distribution modifiers

- Benign: diffuse/scattered, regional (> 2 cm)
- Intermediate: grouped or clustered (> 4 in < 1 cm)
- Suspicious: linear, segmental

Conclusion and Birads-classification

- Birads assessment categories provide guidance and management recommen - dations. They are divided into incomplete (category 0) and final (complete assessment) categories (categories 1-6)
- Both mammography and ultrasound done: one report with separate paragraphs detailing each and one integrated final assessment
- Overall final assessment category based on the most worrisome findings (examination with highest suspicion)

Assessment categories

- **Category 0**: need additional imaging evaluation and/or prior mammograms for comparison ("screening" situation)
- **Category 1**: nothing to comment on
- **Category 2**: benign finding (s) ("normal"assessment, choice to describe benign finding (calcified fibroadenoma, fat or mixed density lesions, implants, surgical scars))
- **Category 3**: Probably benign finding – initial short interval follow-up suggested (< 2% risk of malignancy): (noncalcified circumscribed mass nonpalpable, on baseline mammogram (unless benign with us), focal asymmetry, cluster punctate calcifications. Follow-up: 6 months, then bilateral 6 months, bilateral 12 months: unchanged: Birads 2 (or after 3 yrs). Mammography and US features fibroadenoma (palpable or not))
- **Category 4**: Suspicious abnormality - biopsy should be considered (subdivision A,B, C): from 2 to 95% = wide range of risk of malignancy
  Optional subdivision
  A: low suspicion of malignancy (not expected malignant report or benign biopsy is appropriate)
  B: intermediate suspicion: close radiologic/ pathologic correlation
  C: moderate concern, not classic (ill defined irregular solid mass, new cluster pleiomorphic calcifications) benign result should encourage pathologist to inititiate further evaluation
- **Category 5**: Highly suggestive of malignancy- appropriate action should be taken (probability malignancy ≥ 95%) = classic breast cancer: spiculated irregular high density mass (with pleiomorfic calcifications), segmental/ linear arrangement of fine linear calcifications. Pathology benign: multidisciplinary meeting: sample error??
- **Category 6**: Known biopsy-proven malignancy- appropriate action should be taken.

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1. Dpt. Radiology, LRCB Nijmegen, The Netherlands.

BIRADS-classification ultrasound

P. De Visschere[1]

In 2003, the American College of Radiology (ACR) mammographic Breast Imaging and Reporting Data System (BI-RADS) classification was adapted for ultrasound and MRI. BI-RADS aims at providing a uniform lexicon for breast imaging, standardizing the reporting system and selecting lesion descriptors that emphasize the distinctions between benign and malignant. The recommended sonographic terminology shows significant overlap with the mammographic terminology, but descriptors such as echogenicity, posterior acoustic features and orientation with reference to the skin line are specific for ultrasound.

There are seven categories in the BI-RADS classification: incomplete assessment (BI-RADS 0), negative examination (BI-RADS I), benign findings (BI-RADS II), probably benign findings (< 2% malignancy risk; BI-RADS III), probably malignant findings (BI-RADS IV), findings highly suggestive of malignancy (BI-RADS V), and biopsy-proven malignancy (BI-RADS VI). Category BI-RADS IV is further divided into small (IVa), moderate (IVb) and substantial (IVc) malignancy risk. The reported interobserver variability is good in BI-RADS I, II and V, but only fair in BI-RADS III and IV. In these latter categories, the radiologist has to decide whether a lesion is suspicious for malignancy and should be biopsied, or attributes such a low risk for malignancy that the option of short-interval follow-up can be offered as an alternative to biopsy. One of the reasonable and achievable goals for diagnostic ultrasound should be to help identify this subgroup of low-malignancy risk lesions (BI-RADS III) and consequently prevent unnecessary biopsies.

Breast cancer varies greatly, not only from one nodule to another, but even within an individual nodule. The entire surface of the lesion must be carefully evaluated to detect suspicious findings. The ACR's ultrasound BI-RADS lexicon identifies irregular shape, microlobulations, spiculated or angular margins, non-parallel orientation, posterior acoustic shadowing and thick echogenic halo as suspicious findings. Benign findings are elliptical shape, gently lobulated margins, hyperechoic echotexture, parallel orientation and complete thin echogenic capsule. Whenever there is a mixture of suspicious and benign findings within an individual nodule, the benign findings must be ignored and the lesion should be classified BI-RADS IV which warrants biopsy.

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1. Dpt. of Radiology, UZ Gent, Ghent, Belgium.

Introduction of nationwide digital breast cancer screening in The Netherlands

P. A. M. Bun[1]

The breast cancer incidence in the Netherlands is one of the highest in the world (1/7 women get breast cancer). There are more than 13.000 new cases per year and according to the most recent data 3300 deaths.

The RIVM (National Institute for Public Health and the environment) provides a free nationwide breast cancer screening for all women between 50 and 70 years. Almost one million women are examined per year. The examinations are performed in 14 fixed units and 52 mobile screening units. The examinations are organized, assessed and archived by 5 regional screening organisations, coordinated by one central organisation. The national expert and training centre and the national evaluation team cover training, quality control, audits and evaluation.

Starting with a referral rate of 1% which even dropped below this, an optimization study was carried out, indicating that the referral rate should be increased. In 2006 this was 1,6% accompanied by an increase in the detection rate in the following rounds to 5 per 1000. From 1989 to 2006 mortality in the 55-75 year old age group was reduced by 24%.

With the experience of 4 digital pilots the government is currently implementing a program of modernisation in which the analogue mammography units are being replaced by new digital systems, linked via a nationwide image management system with a central archive and 25 reporting units at various locations in the country, staffed by specially trained screening radiologists, who perform the double reading. The workstations in the reporting units have two high-resolution screens and a regular screen for textual information (paperless system). These are connected directly to a central archive via a nationwide optical network.

A programme of requirements was written, with digital archiving as a central issue. More detailed issues to be men-

tioned are: scanning priors, availability, presentation (same size),speed, availability information radiographer, possibility double reading, arbitrage and reporting, feed- back- training- communication (also with hospitals). The RIVM invited tenders from a number of manufacturers. After selection and testing one manufacturer was chosen as project manager, who leads a consortium of specialised suppliers.

In July 2008 the nationwide digitization started in one region. All regions are expected to be fully integrated in July 2010. The transition to the new system is complex requiring cooperation of all parties including the radiologists. Because of one nationwide system harmonisation of radiological working procedures is necessary. To achieve this and get insight into other effects of digitization like temporary recall peaks, all radiologists followed a training programme at the National Training and Expert centre.

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1. Dpt. of Radiology, LRCB Nijmegen, The Netherlands.

Imaging of the axilla

L. Steyaert[1]

Different imaging modalities can show the lymph nodes (LN) in the axilla and the other tributary locations.

NUCLEAR MEDICINE can show LN by tracing the uptake of Technetium colloid in the nodes. The technique is well know from the sentinel node procedure, currently widely used in case of tumorectomy for smaller breast tumours. It is not used as a preoperative staging modality.

PET CT is a good technique to search metastatic locations of tumors, and is therefore capable of showing abnormal LN. The spatial resolution is not that high so only nodes of 1 cm or bigger are well detected. This technique is not currently used as a (pre-operative) staging modality. It is not cost-effective and less available than other imaging modalities.

CT scan of the thorax can show enlarged LN in the axilla and periclavicular areas. The technique is not sensitive for minor involvement since criteria of abnormality are mainly based on size. It is well know that there is a large variety of size of the LN from patient to patient. Probably the easiest detectable nodes are the mammaria interna nodes; they are only well seen when they are abnormal.

MAMMOGRAPHY can show enlarged LN only in a limited number of cases. Frequently the nodes are deeper in the axilla and cannot be visualised routinely on the standard axillary projection. The sensitivity is insufficient to rule out LN involvement. When they are visible, normal LN are seen as an ovoid structure, with a thin, dense periphery and a radiolucent fatty hilum. There is a considerable variation in normal size, ranging from less than 5 mm to over 4 cm. Pathologic LN are usually seen as homogeneous dense structure, with disappearance of the fatty hilum.

MRI is more and more used in breast imaging, and certainly in preopartive staging, where the value of the technique is well established. Axillary LN are more difficult to visualise than the breast, since they are situated more posteriorly, further away from the antennas in the coil, and in an area where there are more flow artefacts. The use of higher field strengths, larger antennas with better coverage of the axillary part, and improved sequences and noise reduction algorythms have largely improved the detectability. Size, shape and contrast enhancement are the main pathologic criteria; however contrast uptake curves are not so reliable, since most LN show a 'malignant' type curve. Despite that, the LN adjacent to the breast should be carefully studied when performing an MRI exam. Second look US can be performed in case of abnormalities.

ULTRASOUND is probably by far the best imaging modality for studying the LN, and it should always be included in a breast exam. LN are located sufficiently superficial to be studied with the same high frequency transducers used in breast imaging. Many technological evolutions have raised ultrasound imaging quality considerably.

The use of frequencies of > 10 MHz (up to 18), high element probes and matrix probes improve the resolution. Harmonic imaging and compound imaging are probably the most important advances in recent years. Increased spatial and contrast resolution, with reduction of image noise contribute to the high image quality available nowadays on high end equipment. Good focalisation according to the examined depth is important. Sometimes lower frequencies are required in obese patients. Trapezoidal imaging can provide a wider view of deeper areas.

NORMAL LN are seen on US as 'kidney-like' structures, with a central reflective fatty hilum and a thin hypoechoic cortex, usually less than 2 mm thick, with even thickness over the complete LN. The afferent lymphatic vessels reach the LN in the periphery, and the efferent vessels are situated in the hilum, next to the vascular pedicle, that can be seen easily with color Doppler. So involvement of the LN starts in the periphery, and therefore the most important sign of metastatic involvement is a cortical thickening (> 2.5 mm), frequently asymmetric. More important involvement makes the fatty hilum disappear partially or completely, and produce a more rounded hypoechoic LN, where a normal LN is rather oval shaped. Irregular contours of the LN may suggest capsular rupture and invasion of the surrounding tissue. Pathological hypoechoic areas may show an increased vascularity on color Doppler.

Different areas are to be examined to have a complete staging of LN involvement.

The mammaria interna chain is seen along the arteria mammaria interna, in the parasternal intercostal spaces. This is done with a sagittal parasternal and axial intercostal orientation of the probe. Normal LN are very small and extremely difficult to see in these areas; if LN can be seen, then they are most of the time pathological.

Axillary and infraclavicular LN are divided in 3 groups or levels; the M. Pectoralis minor is an important landmark. Level 1 is situated lateral from the M. Pectoralis minor, level 2 is behind this muscle and level 3 medial to it. The Rotter's space or interpectoral space is situated between M. Pectoralis maior and minor, and can also contain pathologic LN. In severe stages, supraclavicular LN can also be involved.

The lateral and most superficial LN in the axilla are best viualised with the arm elevated 90°, with the US probe in the armpit. The infraclavicular LN (level 2 and 3, Rotter) are best visualised using a sagittal orientation of the probe, with the arm along the body. The landmarks, M. Pectoralis minor and maior are easily seen with this approach.

When pathological features (cortical thickening, asymmetry, increased volume, ...) are present, US guided FNA or core biopsy can be performed. This makes a better selection for sentinel node procedure possible.

1. Dpt of Radiology, AZ Sint-Jan, Brugge, Belgium.

Sonography and punctions of the axillary lymph nodes

C. Dillenbourg[1]

We try to find a preoperative procedure that would allow selection of those patients who should directly undergo axillary dissection.

The sonographic examination: we have to find the best criteria to determine the pathologic axillary lymph nodes. The size criteria is not relevant enough. The morphological criterions are more interesting. We can consider that a lymph node is pathologic when: it is round, or with an eccentric cortical hypertrophy, or with a diffuse cortical thickening, or with a hypoechoic hilum. With the use of sonography alone, applying morphological criterions to establish malignancy, approximately half of the axillae with metastasis would be detected (sensitivity about 48%) with a high specificity (96%).

The punctures: fine needle aspiration and core biopsy. It is difficult to synthetize and to compare the different studies, because they use different methods (morphological criterions, types of punctures, size of the primary tumor ...). The

cytological and histological diagnosis of metastasis reaches 100% specificity. With both methods, we obtain a good sensitivity (75% for FNA and 82% for CB) with slightly more advantages for the core biopsy. But the difference is not relevant and the core biopsy is more expansive and more dangerous.

So we can propose, as a general method: if you have a patient who could benefit from a sentinel node biopsy: during your sonographic examination, try to find pathological lymph nodes. For these nodes, you can do a FNA, rather than a core biopsy. If you obtain positive cytology, the patient must have an axillary dissection. If the axillar sonography or if the cytological analysis is normal, the surgeon can proceed with a sentinel node biopsy. If there is an indication of SNB regardless of the primary tumor size, it is possible to avoid SNB in +/- 30% of cases.

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1. Dpt. of Radiology, St Josef Klinik, St Vith, Belgium.

Pathologic evaluation of the axillary lymph nodes by breast carcinoma
M. Drijkoningen[1]

- pN in the TNM-classification (7th edition)
- Macrometastase: one or more localisations of > 2 mm (pN_{1-2-3})
- Micrometastase: one or more localisations of > 0,2 mm or > 200 tumorcells (pN_{1mi})
- Isolated tumorcells = submicrometastase ($pN_0(i+)$)
- Capsula = part of the lymph node: tumorcells in the lymphvenes of the capsula = metastase
- Postoperative investigation: histologic slice = 4 µ: less than 0,1% of the lymph node is investigated.
- Sentinel node investigation: 1-3 lymph nodes: better investigation is possible. The purpose is to find all macrometastases/micrometastases: slices of 200 µ, with specific IHC colouring.

Peroperative investigation of the sentinel node: cutting into thin slices – macroscopic investigation – depcytology or frozen slice (only for macrometastases). The sensitivity gives 1 on 5 false negative for macrometastases and 4 on 5 false negative for micrometastases.

Depcytology is preferred: less tissue damage, no loss of tissue and both sides of the slice can be investigated. A lot of experience is however necessary.

Preoperative staging: all lymph nodes that are suspect on ultrasonography need a FNAC: in 25% of cases the sentinel procedure can be omitted.

This is a gain of time for the patient and the surgeons.

1. Dpt. of Radiology, Virga Jesse Hospital, Hasselt, Belgium.

Radiological diagnosis of precursor and pre-invasive breast lesions
C. Van Ongeval[1]

The precursor lesions of invasive breast cancer according to the WHO classification consist of the lobular neoplasia (LCIS, ALH), ductal intraepithelial neoplasia (DIN) and intraductal papillary neoplasms. The DIN group includes flat epithelial atypia (FEA), atypical ductal hyperplasia (ADH) and ductal carcinoma in situ grade 1-2-3 (DCIS). In the group of the intraductal papillary neoplasms, benign intraductal papilloma, noninvasive papillary carcinoma and encysted papillary carcinoma can be found. A complex sclerosing lesion/radial scar is classified as a benign epithelial neoplasm, but as there is an increase in ADH and DCIS in these lesions, they are discussed as well. Precursor lesions are frequently diagnosed by screening programs, performed to detect early stages of breast cancer.

Microcalcifications are the most frequent presentation of lobular neoplasia and the DIN lesions. Whereas ADH was previously incidentally diagnosed in biopsies for palpable masses, the incidence of ADH increases as more biopsies are performed for the BIRADS-3 and 4 microcalcifications and as larger needles are used.

Approximately 80% of the comedo type DCIS shows a typical branching pattern, but 20-25% and the non-comedo DCIS fail to exhibit these characteristics.

Sonography is less important in the evaluation of microcalcifications, but is excellent to guide percutaneaous biopsies for the evaluation of radial scar, papillary lesions and palpable lesions. Vacuum assisted biopsy has a higher accuracy compared to large core biopsy for the evaluation of precursor lesions and it is therefore the preferred technique for their preoperative evaluation.

Although mammography can detect up to 83% of DCIS, it underestimates the extent of the disease. Magnetic resonance imaging (MRI) is better in predicting the extent of the disease and of multifocality.

The role of MRI in the evaluation or follow-up of precursor lesions is not clear yet: most of the precursor lesions will show enhancement and differentiation between the grades of proliferation is not yet possible.

1. Dpt. of Radiology, University Hospitals Leuven, Belgium.

Rare presentation of breast cancer
A. Rappaport[1]

The case of a 67-year-old woman with a large lump in the left axillary region and the left breast is presented.

Pathologic investigation of these masses in 2 hospitals was inconclusive.

Further work-up in our radiologic department showed beside the presence of the two tumoral masses, abnormalities with the radiologic characteristics of granulomatous mastitis. Final pathologic analysis showed the presence of an invasive ductal carcinoma in the two masses in combination with a granulomatous stromal reaction.

1. Dpt. of Radiology, University Hospitals Leuven, Belgium.

Breast hemangioma
H. Claes[1]

On routine screening mammograms, a small lobulated nodular mass was found in the left breast of a 66-year-old woman. Additional tomosynthesis confirmed the presence of the lesion, which could not be depicted on ultrasound. Because of severe obesity, MR imaging was not possible. Six months later, the lesion was unchanged on follow-up mammograms. Repeat ultrasound examination revealed a small inconspicuous hyperreflective area which correlated, after placement of a localization wire through the area under ultrasound guidance, with the small mass visible on plain film. Core needle biopsy proved this lesion to be a hemangioma.

Breast hemangiomas are very rare, except for the clinically not detectable perilobular subtype. They cannot be completely distinguished from malignant tumors (breast tumors and more importantly angiosarcoma) by imaging and should be excised completely to confirm the diagnosis.

1. Dpt. of Radiology, KULeuven, University Hospitals Leuven, Leuven, Belgium.