Introduction

The recurrences of Breast Carcinoma boils down to 3 levels:

1. *local*: behind the scar, around the scar and the totality of the breast,
2. *regional*: axilla, chest walls and the other breast,
3. *general*: Echographic, CT, MNR, Biologic and Scintigraphic exams.

This presentation only concerns local and regional explorations. After a brief presentation of the breast echographic technics, according to the orthogonal conventional mode and the Radial DE (Ductal Echography), we will present pattern of the scar tissue as well as the lobar surgical modifications and the possible associated pathologic findings (hematoma and lymphocela). This analysis should allow to differentiate the possible recurrences among post-surgical and post-radiotherapeutic alterations. We tempted to study more specifically doppler criteria of the involved breast because of tramps and the scar changing.

We deal with these criteria and the echographic contrast agents used in the exploration.

I. ECHO-DOPPLER CRITERIA

Localising vessels in and around the lesion is the easiest application of doppler technics in breast echography.

Unfortunately, it is very difficult to study those vessels in pulsed or continuous wave Doppler. The colored Doppler allows us to visualise the vessel lesions much better: a rigorous technic be used notably with an adapted focusing to the localisation of the tumor (which will diminish the echo attenuation and will increase the reflected beams efficiency).

Another priority: choosing the right frequency because the intensity of the reflected beam increases with the power 4 of the frequency. In otherwords if the frequency is doubled, the answer will be 16 times more powerful. Thus, the best compromise between the frequency and the depth of the examined tissue must be chosen. Hopefully, the breast is hardly ever thicker than few centimeters.

Swenson has been able to demonstrate that small millimetric lesion is able to produce angiogenetic factors which will stimulate the growth of neo-vessels within the tumor. This development is anarchic with many shunts, vessels walls abnormalities without any muscle. That is the reason why the speed of the blood flow isn’t increased, due to the high number of neo-vessels, the atipic morphology and branching. On the other hands, inside the shunt,
speed is higher. In case of malignancy, the use of colored doppler easily confirms, in most carcinomas, the increased number of vessels and ad contrario the small number in case of benign lesions. Unfortunately, benign or malign vascular doppler criterias are not precis and specific enough.

Despite this, we can remind that those semiologic criterias of malignity concern:
- the vascular distribution inside and around the tumor,
- the 90° angle of penetration concerning the direction of neo-vessels compared to the borders of the tumor,
- the increase of the number of vessels in most cancers,
- the modifications and changing of vessels directions,
- the vessels modifications in their morphology: diameter, shape, volume,
- the blood flow modifications which unfortunately shows a great number of variations (depending on the different types of tumors) provoking important index variations, (RI and PI index are important because their mesure doesn’t depend on the ultrasound beam angle), as well as increase of the systolic speed index in case of carcinoma. Because of the great variability in the flow, blood flow quantification analysis is important (but still remains very « operator-dependant ») but time-consuming and requires a sophisticated equipment.

According to Madjar, the average figure of the blood flow is:
- 20 cm/s for a carcimona,
- 11 cm/s in a benign tumor.

It is the sum evaluation of the maximum and the average speed which, according to him, is the most interesting:
- Vsum 285 cm/s for a cancer,
- Vsum 29 cm/s for a benign tumor.

After calculating the number of vessels and the sum of blood flows, Madjar also demonstrated that 90 % of the tumors can be classified in malignant or benign and that the 10 remaining per cent are false positive or negative. Hackeloer obtained a best diagnosis for 14 patients of 20 and in 13 of these cases, the echographic diagnosis was in agreement with the histologic diagnosis.

The use of the « Doppler energy » makes the breast examination easier:
* it is not modified by the breathing movement which, by the way, can be checked
* it does not depend on the angle of the ultrasound beam
* it is more sensible than the color doppler and, at the same time, it gives a good appraise of the global flow in the tumor. It, among others, allowed to confirm that a limited number of vessels, their orientation, their morphology, their regular decrease, as well as their linearly circumferential and harmoniously curvy course, all correspond to a benign lesion.

Eventually, according to different authors the mammography / echography / « Color Doppler Energy » + contraste association significantly raises the diagnosis precision, and most of all, reduces the number of useless biopsies generated by the different exams used separately.
II. RECALL OF ALTERATIONS OF THE DUCT AS WELL AS IN THE LOBULAR AXIS, IN CASE OF AN EARLY BREAST CARCINOMA

Both carcinoma propagation modes at an early stage are longitudinal in the duct, perpendicular throughout the Cooper ligament.

Consequences: recurrence in both sides of the duct scar after a local lumpectomie or along the ligament and the subcutaneous connective axis of the scar.

III. SCAR MODIFICATIONS IN ECHOGRAPHY IMAGES

Echography semiology:
- in case of adenosis,
- in case of adenosclerosis, adenofibrosis,
- in case of cystosteatonécrosis,
- in case of recurrence.

There is an astonishing ressemblance between these 4 lesions with the echography: it is impossible to surely differenciate an adenosis or a cystosteatonécrosis from recurrence: there is an heterogene, with irregular borders, hypoechogone zone with indirect ligament signs, most of the time a posterior shadow of attenuation, a lesion which is larger than at an early stage (in case of development along the Cooper ligament), surrounded by a hyperechogenic crown and with cutaneous and sub-cutaneous scar changings:
- in case of hematoma
- in case of lymphocela
- in case of lymph node recurrences
- in case of parietal lesions

IV. PROGRESSING IN BREAST ECHO-DOPPLER BY USING CONTRAST

Contrast agents like LEVOVIST are perfectly adapted to the study of breast carcinomas: their use provokes a huge raise of the signal/noise ratio (amplification by 20 db of the arterial and veinous signals, thus a better vascular mapping of a lesion with better differenciation of benign and malignant criteria).

The minobubbles are small enough to get through the pulmonar vascular barrier and stable enough to remain several minutes in the flood flow.

The microbubbles that are appearing after the galactose microparticules dilution have got an excellent capacity to upraise the echo signal reflected in the vessels. Thanks to the adding of palmitic acide, the bubbles are stabilized for a few minutes before dissolving in the flood flow.

We used a 300 mg microparticules/ml concentration, in 8 ml of water injected through a 16 or 19 G butterfly, as fast as possible, before injecting 10 ml of Isotonic Sodium Chloride.
Modifications of the blood flow appear 20 to 30 seconds after the injection. The raise can continue to last a few minutes (up to 9/10 minutes) This retention phase is very important (related to the number of arterio-veinuous shunts, and to the modified flow inside many carcinomas). In case of carcinoma, the response appears soon after a maximum pick of early raise, with the presence of a great number of vessels which have irregular and tortuous diameters. The upraise can lost few minutes after the injections. The wash out, longer and more emphasized seems to favour the malignity (except in case of inflammation). In case of pur scar tissue, of fibrosis, the blood flows are not upraise. In case of benign tumors, the response is delayed, the pick less intense, less extended, the regular circulation vessels are fewer, more regular and harmonious.

V. CONCLUSION

Echography itself is unable to differenciate with certainty a breast carcinoma recurence from an adenosis, an adenofibrosis or a cysosteatonecrosis lesion. The use of Doppler (color + energy) with the addition of contrast agent seems to be an interesting alternative to confirm a recurence. The contrast amplified the small tumorous vessels blood flow signal which cannot be seen without contrast. This underlines the sensibility when detecting small carcinomas, recurrences and metastatic lymph node lesion.

A multicentric european study is in progress (levovist). Its target is to classify the benign/malign and scar/recurence differenciation criteria.

The coming up development of the harmonic imaging for which the microbubbles resound at different frequences of the ultrasound beam, will allow a better localisation of breast lesions. It also seems that after the first results of the different studies, one can speak of carcinoma forecast since angiogenesis is a factor testifying from the biological agressivity of a tumor. This is to be confirmed by larger study with contrast agent.

The results in RMN contrast agent injection enhancement are quite superposabled to those obtain in contrast Doppler Breast examination. Now, Doppler results with contrast allow to follow, in an efficient way, the chimiotherapic treatment. The study, after a breast carcinoma treatment, of scar itself musn’t exclude the seek for associated lesions, at distance, unrecognized meanwhile former tests, plurifocal carcinomas, contro-lateral carcinoma, chest-small lesions (recurences, hematomata, lymphocela) which cannot be explored throughout mammography and will only be seen by echography or MNR.
MULTIMODARITY DIAGNOSIS FOR BREAST CONSERVING THERAPY

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On performing breast conserving therapy (BCT), the most important factor preventing ipsilateral breast tumor recurrence (IBTR) is to perform the local resection to be stump negative for cancer. In contrast to the BCT in period of 1980’s, when only gross removal of the primary was necessary and after that, radiotherapy (RT) was expected to eradicate the subclinical amount of residual cancer, in later half of 1990’s, more elaborate and precise resection is began to be expected and also to be practiced for the purpose of so called complete resection.

In the Cancer Institute Hospital, Tokyo we began BCT in 1986 and our fundamental attitude was that thorough and complete resection is preferable in doing local resection. For this purpose, multi-modality diagnosis is necessary and permissible larger resection is better, and ultimately serial pathological examination of resected specimens is a basic procedure for safer BCT and if stump is proved by the pathological examination, RT is not added but avoided.

For the multimodality diagnosis of the cancer spreading
1. High quality MMG is fundamental, especially for cases that show microcalcification or multi-nodular lesions.
2. US is important for detecting breast duct dilatation or irregularity by cancer spreading, not showing microcalcifications on MMG.
3. Subtraction MRI is very useful for detecting cancer spreading through vascularity in cases of no microcalcifications on MMG and no duct dilatation on US.
4. Fine needle aspiration cytology is mandatory for all palpable tumors (in some cases, US guided) moreover, stereotactic core needle biopsy (containing Mammoitome) is essential for nonpalpable microcalcifications on MMG.
We performed 1074 cases of BCT by 1997. Of them 679 cases (63.2%) were analyzed as stump negative and no RT added. Under 4.3 year mean observation period, 23 cases (3.3%), annually 0.79% showed IBTR. And these figures are lower than those of usual BCTs with RT. Of 23 cases, 9 cases were proved to be recurrence and 14 as a manifestation of a new primary cancer.

Considering the results mentioned above, BCT could be done even without RT if multimodality diagnosis, appropriate surgery and serial pathological examination were excellent.

The use of broad band transducers determined a great increase in spatial, contrast and vascular resolution of ultrasound probes dedicated to breast studies. Providing better definition of normal as well as pathologic features, high resolution sonography improves the specificity of the diagnosis for the majority of malignant nodules and allows a better definition of both local and regional staging. The most impressive results have been achieved in the evaluation of multifocal and multicentric carcinomas, in determining the size of the tumor, its degree of invasion of the surrounding tissues and of the ducts. Color and power Doppler offer further characterization that may be particularly useful in evaluating tumor vascularity during therapies that are planned before surgery. These new staging possibilities must push the radiologists to adequate their instruments and their methods to provide up-to-date and more accurate informations to the surgeon.

Carcinoma is the main breast disease, at the point that the diagnosis of all other benign abnormalities becomes significant because it rules out cancer. Mammography is the main diagnostic tool to detect cancers that are not palpable; pathology is the gold standard to differentiate masses.

The role of sonography is to add more diagnostic parameters to those already found with clinical examination and mammography.

Staging of carcinoma includes the evaluation of multiple parameters: tumor size, vascularity and fixation, local infiltration and ductal invasion for local staging; skin, underlying fascia and muscle invasion and lymphatics infiltration for regional staging (table 1).

Most of these can be adequately assessed with high frequency sonography (9, 10, 11).

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Table 1. Parameters involved in local and regional staging of breast tumors
Most clinical investigations are concentrated on multifocality and ductal invasion; these two parameters are crucial in planning a more extensive use of conservative surgery. Cancer may be multifocal, multicentric and bilateral. Multifocality indicates that several unabridged tumors lie in one quadrant; multicentricity indicates that tumors are located in two or more quadrants. Subserial whole-organ sectioning demonstrated a 74 percent incidence of multicentricity (4); 50 percent were multicentric in situ carcinomas. Higher incidence has been showed for moderate to large size tumors and histological types like lobular and tubular carcinoma. Residual cancers after operations designed to preserve the breast without other therapy may therefore result in high local recurrence rates, ranging from 18 to 37 percent (12). Consequently the attempt of mapping the tumoral growth must be considered a preliminary step in the staging procedure. The discrete accuracy of sonography in preoperative detection of multicentric carcinomas has already proven in a series of 34 histologically confirmed cases in which ultrasound was correct in 87 percent (17). Recognition is made easier with sensitive Color Doppler or contrast enhancers (figure 1). Helical CT provides similar sensitivity (18) but there are some false positive cases due to small cysts; contrast enhanced MR provides better sensitivity (5) but the availability of adequate scanners is still limited.

Fig. 1. Small nodules of multifocal carcinoma of the outer upper right quadrant (7 and 3 mm).

Several studies indicate a strong correlation between the size of the cancer and prognosis with a definite decrement in survival associated with an increasing tumor diameter; nodal involvement is also related to tumor size. A correct determination of tumor size is therefore important for patient management, particularly in case of breast conservation therapy. The poor correlation between mammographic and clinical estimates with the size measured on the pathologic specimen is well known. Sonography has shown the best correlation with pathologic cancer size when compared to mammographic and clinical measurements. High resolution annular arrays show better accuracy in tumor size determination than do lower frequency linear transducers. First, high resolution sonography can accurately differentiate the mass from desmoplasia that is highly echogenic; a mixture of strands of collagen fibers, proliferating tumor cells and fatty inclusions is responsible for the high echogenicity (16). Desmoplasia cannot be differentiated with palpation, and is just as dense as cancer growths on the mammogram.
Second, high resolution sonography provides a better assessment of tumor margins. Morphology is the main pattern to clarify the type of tumor growth: expansive or infiltrating. There are two main morphologic patterns for malignant masses: stellate and circumscribed (1, 2). An infiltrating growth shows irregular and spiculated margins, that appear even more irregular, when associated to reactive desmoplasia; high resolution sonography magnifies this characteristic. Spiculation seems to be the most distinctive pattern of breast cancer, having a 99.4 percent of specificity and, respectively, a 91.8 percent and a 88.8 percent of positive or negative predictive value (13). In a retrospective evaluation of 65 cancers we have found that the 7.5 MHz transducer missed 18 percent of spiculations seen with the 13 MHz transducer.

Well circumscribed masses have rounded or oval shape, slightly blurred or well-defined margins that simply push into the surrounding tissues, causing compression, and dislocation, but no distortion. High resolution probes allow good resolution through all the field of view and permit very clear real time assessment of the relationships between the different tissues. A slight change of shape and a gliding motion inside breast tissues can be shown by probe compression on a circumscribed, non infiltrating mass. The same is not seen with hard, infiltrating masses. The interface may be an irregular, thick, hyperechoic rim, surrounding the mass, and representing desmoplasia; an increased echogenicity of surrounding fat as a reaction to infiltration, and an architectural distortion, that pulls on the fibrous stroma of the gland. On the contrary, circumscribed carcinomas do not cause changes in the surrounding tissues, besides compression. The borders are quite well-defined, sometimes only blurred or lobulated.

Due to its better contrast, high resolution sonography also provides the best assessment of the L/AP nodular ratio and allows a preliminary differentiation between carcinomas and benign nodules. Evaluating the sonographic characteristics of 750 breast nodules, Stavros et al. (13) reported a 41.6 percent of sensitivity for breast cancer and a 98 percent of specificity for taller than wide shapes. The odds ratio of this sign turned out to be second only to the spiculated margin, having a very high positive predictive value.

Infiltrating ductal carcinoma may have an extensive intraductal component which causes local recurrence in case of very conservative surgery (12). Mammography may have a good predictive value to determine the possibility of an extensive intraductal component; cancers showing calcifications on the mammogram are associated with an extensive intraductal component in 65 percent of cases (14).

High resolution sonography may suggest ductal spread of carcinoma (1, 6, 11, 17). An asymmetric, dilated duct or stretched and stiff hypoechoic, tubular structures at the periphery of cancer are the most distinctive characters (figure 2).
The diagnostic accuracy of this sign (figure 3) suggests the use of routine radial scanning at the periphery of a suspicious lesion.

The demonstration of tubular structures at the periphery of a mass must be considered along with the nodule's size and multicentricity an invaluable information for the surgeon planning conservative surgery.

Fig. 2. A 9 mm carcinoma becomes a 32 mm tumor considering the satellite nodules (→) and the invaded, stiff and dilated ducts (⃣).

Fig. 3. The predictive value in the evaluation of ductal invasion is very high. Results reported from a controlled group of 51 T1N0 carcinomas.

The demonstration of tubular structures at the periphery of a mass must be considered along with the nodule's size and multicentricity an invaluable information for the surgeon planning conservative surgery.
Regional staging involves evaluation of the skin and the subcutaneous tissues; these structures can be well evaluated only with high frequency, highly focused transducers. The sonographic pattern of normal skin is a more or less homogeneous band that is more echogenic than the underlying fat tissue. Normal skin thickness varies between 0.5 mm and 2 mm, and is usually maximum in the lower quadrants, towards the inframammary fold. The subcutaneous region contains fat and lymphatics. Subcutaneous fat is crossed by thin, echogenic lines, of the superficial fascia and the Cooper's ligaments. These ligaments go from the skin to the deep pectoral fascia and are well visualized both in subcutaneous fat as well as in fatty breasts, with a regular orientation and in contrast with hypoechoic fat. Superficial masses, besides causing changes in subcutaneous fat, usually infiltrate the skin, that thickens or changes its echogenicity (figure 4). Less superficial cancers may also cause skin changes by pulling on Cooper's ligaments, and by changing their orientation. As it concerns the possibility of evaluating the invasion of the deeper muscular planes high resolution sonography is still limited if compared to magnetic resonance; nonetheless diagnosis is correct in 95 percent of the cases. Underestimation may usually occur in very large glandular breasts.

Breast lymphatics form a microscopic network in the superficial areas of the breast, mainly between the skin and subcutaneous tissues and also along ducts. Normal lymphatics cannot be visualized, but in case of dilatation - due to inflammation or carcinomatous infiltration - they can be demonstrated as hypo-anechoic, thin lines, parallel and perpendicular to the skin, forming a network (1).

Axillary and supraclavicular nodes are the most frequent localization of breast cancer, starting from the outer breast quadrants. Sonography can easily detect enlarged lymph nodes, show size and shape, and evaluate if the echogenic hilus is maintained. The most specific sign for the diagnosis of secondary deposit is the absence of the hilus (3). When compared to mammography and clinical examination, sonography has a higher sensitivity in the detection of axillary lymph nodes; the better contrast provided by high resolution sonography permits a better visualization of nodes dispersed in the fatty tissues.

Fig. 4. Skin infiltration increasing the echogenicity of the subcutaneous fat (→). The superficial fascia is interrupted.
of the axilla or of the peripheral breast. In the series of Strauss et al. (15) the sonographic
detection of axillary node metastases had a sensitivity of 90% and a specificity of 91.7% in
relation to all tumor stages and a sensitivity of 100% and specificity of 89.6% in relation to
T1 tumors. Verbanck et al. (19) found a sensitivity of 92%, with a specificity of 95%, a
positive and negative predictive value of 96% and 91%, respectively. Youg et al. (20) did
not find significative advantages in adding color Doppler; flow signals can be showed in
both normal and metastatic axillary lymph nodes. Miner et al. (8) demonstrated that US
guided injection improves localization of the sentinel lymph node, perhaps as a result of
more accurate placement of the radionuclide marker.

In summary high resolution sonography is useful in the characterization of solid masses of
the breast. It improves the diagnostic specificity reducing the need for biopsy; furthermore
it allows better local and regional staging of tumors. The potential for cost reduction and
better treatment planning promotes high resolution ultrasound as a standard procedure to
evaluate patients with breast cancer. Radiological departments must upgrade their breast
technology with this new facility to enhance the quality of their diagnostic performances.

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ULTRASOUND OF THE TREATED BREAST

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There has been little written about the applications of ultrasound in imaging the breast after conserving surgery and radiation therapy for carcinoma. (1,2) Ultrasound (US) can be used to follow the early changes that resolve slowly, such as the fluid collections, which only very rarely become infected, edema and skin thickening in a breast that may be difficult to compress sufficiently for optimal mammography in the first six to twelve months after treatment. The fluid collections might be mistaken for recurrent tumors mammographically, except that they are circumscribed and oval. US can display the internal contents, depict the sharp borders, and the posterior acoustic enhancement.

Mammographic views of the surgical site may be limited by the projection of the density of the thickened skin of the incision over the tumor bed obscuring the site of tumor removal. A view tangential to the incision site can show separation of the skin incision, the tract leading from the skin to the surgical bed, and the unobscured tumor removal site. A second technique is to mark the site of tumor removal with surgical clips for radiation treatment planning and for follow-up mammography. US, however, is a reliable technique to image the tumor bed, which is focused upon each time these patients return for follow-up imaging. On orthogonal views, the extent of scarring can be assessed, particularly as sequential studies show the progression of healing as the enhancing fluid collections are resolved and replaced by jagged, fibrotic tissue with posterior acoustic shadowing. Scrutiny of the lumpectomy site is crucial because recurrent tumor is found at or within 2 cm of the lumpectomy site for approximately the first seven years after therapy, with mean time to recurrence being three years. (3)

When recurrent tumor presents as a new mass, its recognition apart from the scar is facilitated by familiarity with the appearance of scarring, becoming over time progressively contracted and more linear. Stability of a scar is reached between one and three years. US imaging of the area of tumor removal can heighten confidence in interpretation.

In 1988, we published results of a study of 100 patients and found five recurrences. (1) These five recurrences of carcinoma were all at or near the lumpectomy sites. Four presented as masses, two of which were suspected clinically as new palpable lesions at the lumpectomy areas. Two were identified by imaging along (mammography and US). In one case where recurrence was suspected clinically, mammographic parenchymal density obscured the lumpectomy site, and US, compared to previous sonograms, confirmed the new mass. With US, recurrent tumor was imaged in four out of
five cases; in the fifth case, recurrent tumor was unsuspected clinically, but new microcalcifications were identified on the patient’s mammogram. Continuing to image the tumor bed of every lumpectomy and radiation therapy patient who presents for follow-up study in our center, we have been able to corroborate our mammographic findings sonographically, recognizing recurrence as a new or enlarging mass and confidently excluding recurrence in the majority without resorting to ambiguous written interpretations, to MRI, or to unnecessary rebiopsy of the lumpectomy site either percutaneously or surgically. Our protocol for follow-up imaging after breast conserving therapy and irradiation calls for a preradiation mammogram. Baseline mammography and sonography are performed at six months, with imaging of the treated breast at six-month intervals until stability (no change of a resolving or evolving finding on two successive studies) is recognized, at which time, resumption of annual breast imaging is suggested. For the contralateral breast, annual mammographic screening is recommended with sonographic evaluation as indicated.

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