Breast Doppler Ductal Ultrasonography: Definition, History, and Advantages

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1.1 Definition and History: Galactography and Ductal Echography

The only method of diagnosis of the breast ductal pathology used in the past and still recommended is galactography/ductography of the breast, considered as an underused procedure that often helps define the cause of unilateral, single-pore, spontaneous nipple discharge [1]. It is recommended to search papilloma or carcinomas that can be responsible for nipple discharge and to help guide accurate surgical intervention. Galactography is useful because it refers to ducts, but it has some inconvenient facts:

- It increases the effects of the X-ray exposure, as follow-up a mammography.
- It is an interventional procedure, with risk of complications and with possible artifacts such as air bubbles or extravasations of the contrast iodinate agents.
- It cannot measure the thickness of the duct's wall nor the ductal tree distal from a stenosis.
- Most importantly, this procedure cannot visualize the surrounding tissues, the lobules, nor the lymph nodes or the pathological nearby vasculature.
- The optimal quantity of iodinated contrast agent and the best degree of breast compression could not be calculated: too much or too less?
- The lobar ductal branching is distorted by the compression of the tissues; indeed, the lobar projection appears too large in all views, with the false perception of the lobar volume and a wrong conservative therapy planning.
- The ductal enlargement is overestimated, because the initial content is increased by the iodinated contrast agent added by instillation; moreover, there are ductal ectasias misdiagnosed in cases without salient nipple surge; thus, not all ectasias are evaluated.

With regards to performance, galactography/ductography is as limited for the breast diagnosis as the urography for the urinary system, or barium meal for the upper digestive tube.

The breast pathology was redefined by T. Tot and L. Tabar, which developed *the theory of the* "sick lobe" [2–4]: the breast carcinoma is a lobar disease, with simultaneously or asynchronously appearance (either in situ or infiltrative type) of multiple tumor foci originated in a single lobe of the breast. This theory affirms that the malignant process is initiated when the *sick lobe* is differentiated, in early embryonic life, as an explanation for the almost simultaneous transformation of the whole lobe. *The sick lobe theory* is proved by the frequent *multifocality* of the lesions in the same lobe, while the *multicentricity* with two or more lobes simultaneously involved is rarely found. The branching ducts inside the lobe were reproduced by Ichihara and Ohitake [5] and demonstrated by numerous pathologists. The explanation of the origin of the *sick lobe* in the embryonic life is nevertheless unbelievable, because there is not any small embryonic or fetal model of the breast with little lobes, similar to the embryonic cartilaginous model of the bones, for example, or an embryonic branching tracheal-bronchial tree; indeed, the newborn has a not divided mammary bud, and the branching process during thelarche is progressive: initially the homogeneous bud becomes heterogeneous, and then the main ducts appear at the periphery and are surrounded by the simultaneously growing glandular stroma; in the next stage, the secondary segmental ducts develop and finally appear in the lobules, with the terminal ductules and the acini. If the moment of the origin of the *sick lobe* seems to be thelarche, it is possible to be determined by the amount of hormonal and neural receptors or by a mutation of the responsible genes during the cellular multiplication. The *sick lobe* could be determined even later, related to pregnancy, dishormonal pathology, substitution hormonal therapy, or other unknown factors. We find this explanation concordant with the statistically risk factors for breast malignancies such as precocious thelarche, late pregnancy, birth control pills, or postmenopausal substitution therapy.

The greatest value of the "sick lobe theory" consists in removing the concept of "breast cancer as a lump;" thus, the radical excision of the whole "sick lobe" should theoretically

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represent the best conservative curative intervention. This is sustained by the fact the mammary lobes may overlap, but there are not directly communications between their ductal-lobular trees, so the cancer is spreading initially via the lobar tree inside the same lobe before to extend to the surrounding lobes or other tissues. For achieving this target, we need a technique of imaging able to visualize the anatomy of the breast lobe, and the only technique that is noninvasive, in real time, operator independent, and accessible for all is the ductal echography (DE) imagined by M. Teboul and his collaborators and further developed by promoters such as D. Amy.

In 1995, the first *Atlas of Ultrasound and Ductal Echography of the Breast,* by Michel Teboul and Michael Halliwell, was published [6, 7]. The new technique was presented as a *newer, more effective diagnostic tool in breast disease*. Despite the argued challenges in the technique of examination and diagnosis of breast pathology related to the normal anatomical lobes of the breast, with the description of the ductal US features, of the lobules, and their relationship with the surroundings tissues, this method of diagnosis rested almost unknown until the publication in 2003, in Spain, of the *Practical Ductal Echography (D.E.): Guide to Intelligent and Intelligible Ultrasonic Imaging of the Breast,* by Michel Teboul and F. Javier Amorós Oliveros [8]. This was a best seller, the ductal approach became more familiar, and many specialists from Europe, Japan, and the USA became adepts of this method.

M. Teboul sustained his method in Congresses and Conferences such as *The 13th International Congress on the Ultrasonic Examination of the Breast, April 6–8, 2003* [9]. He revealed the progress of the technique, especially after 2000, when the release of high-quality fully digitized equipment has still further increased DE performance. *New digital equipment has highlighted the superior aspects of DE over conventional investigation and reinforced the sense of reliability in the relationship between the DE display and the macroscopic pathological situation.* With better resolution, the visual evaluation of lesions was improved to such a point that the use of needle aspiration was often bypassed, and surgical biopsies were directly performed with a high rate of reliability. This method is opposed to breast MRI, for instance, which increased biopsies and needs a complementary method such as mammography or US to complete diagnosis. DE added confidence to surgeons in the US technique, so that the *American College of Breast Surgeons* has recommended adopting, teaching, diffusing, and utilizing ultrasound and DE for the management of breast diseases [9]. It seems the *American College of Radiologists* was more conservator, because it is easier to learn a new technique than to change an old, well-known technique with another newer, even better one. This is an observation of one of the most active promoters of DE, Dominique Amy, who worked formerly in DE at the Francophone Center of Formation in the USA, of Aix-en-Provence, coordinated by the University of Nimes, France.

However, we can read many publications about breast US that are referring of the radial and antiradial scans in classical breast US, but used as complementary targeted scans, after the "classical" longitudinal and transversal scans; this approach has as goal to *find the lesion*, while DE intends to analyze *the breast anatomy*, because only searching the whole "forest," we are able to localize, recognize and characterize all its "trees" as normal elements, and thus we become able to detect all the abnormal changes. By using DE, it proves a feasible diagnostic procedure of the subcentimeter breast carcinoma, as presented by Amy at the *13th International Congress on the Ultrasonic Examination of the Breast: Thanks to its systematic anatomical analysis it's a perfectly reproducible technique and moreover it became interpretable by everyone*.

In the studies of Amy, 2003 [10, 11], with 1400 files analyzed, focused on the lesions of 4–5 mm to 10 mm, DE was evaluated in comparison with mammography. There were classified three categories of cases:

- Positive mammography: the US was used to confirm a carcinoma and to search additional lesions.
- Doubtful mammography: US allowed the identification of suspect zones and a wide lesion assessment.
- Negative mammography: US made it possible to detect lesion clinically and radiological dumb.

Contrary to certain publications, this author never met a mammographically visible lesion which was not detected by US. Moreover, the analysis of the multicentric cancers confirmed and raised the literature data that affirms more than 43 % of multiple lesions, this percentage increasing with the new equipment to be above 55 %. The very significant number of multifocal cancer (more than 1 out 2), of infracentimetric dimensions, certainly will involve surgical and chemotherapeutic treatment adaptations.

The DE is not a different technique of examination, but an US with another method of acquisition and interpreting the images, based on the anatomy and sustained by the most recent theories of breast pathology. There are some models of the primary site and the spreading ways of ductal and lobular cancers [12], which offered a three-dimensional network showing the ductal-lobular system, where the papilloma develops in the main ducts, while the cancers arise in the periphery, in *the terminal ductal-lobular specific units (TDLUs).* This model explains the branching ductal-lobular system, where several duct systems overlap one another in the same radius of the breast, and may mimic a multilobar simultaneous pathology.

We must remember, in 1842, Doppler presented his paper to the Royal Bohemian Society with his most famous idea

entitled**:** "On the Coloured Light of the Double Stars and Certain Other Stars of the Heavens." This paper presented for the first time the Doppler principle which relates the frequency of a source to its velocity relative to an observer. Nowadays, it is not conceivable to perform US without Doppler, and for the breast, this technique is very useful in the differential diagnosis of the benign and malignant changes. Doppler will be part of the full ductal Doppler US or simply the full breast ultrasonography (FBU), represented by breast US in radial scanning and interpreting (DE), completed with Doppler and sonoelastography. The last was developed from the beginning of the 1990s in Japan and almost simultaneously in the USA. There is almost a consensus about the value of the qualitative Doppler, eventually associated with 3D acquisitions, in the differential diagnosis of the malignant breast lesions; despite the differences of opinions at the beginnings, sonoelastography both qualitatively and quantitatively demonstrated its contribution in increasing the overall accuracy of US.

1.2 The Advantages of the Breast Doppler Ductal Echography

Breast Doppler DE represents a useful diagnostic tool, both for the diagnosis of the infracentimetric breast cancer and fibroadenoma and for the group of four benign lesions that are generally omitted/underdiagnosed by the mammography and the classical US, *ductal ectasias*, *papillomatosis*, *adenosis*, and especially *ductal hyperplasia*, which are considered forerunner for fibroadenomas, cysts, and breast cancer [8]. The noninvasive diagnosis of these benign but not mammographically visible lesions allows the treatment of the symptomatic patients, usually referred for painful breast mostly related to the endocrine disorders [13]. The most important progress is the opportunity to develop differential diagnosis criteria between infracentimetric benign and malignant lesions, with these small lesions generally having less specific features upon the Stavros criteria, and thus to reduce unnecessary biopsies and to prevent the advanced breast cancer.

We present the most important risk factors for breast cancer upon the analysis of OMS published in 2005 [14]; these factors increase 4–5-folds the risk of breast cancer by determining the premalignant changes of breast parenchyma:

- Oral birth control pills
- Hormonal substitution treatment
- Food with animal fat (steroids depot), contaminants (xeno-estrogens and some pesticides, these factors being controversial)
- Beast irradiation (especially the therapeutically irradiation associated with the epithelial proliferative lesions, the most important being atypical hyperplasia)

Doppler DE is able to diagnose small parenchymal lesions with better characterization of the premalignant ones and of the less 10 mm diameter cancers; contrary, following the mammographic screening any 2 years in patients after 50-year old, in the advanced countries, the breast cancer incidence is constant and the mortality was reduced with only 30 % [15].

The most important argument for using Doppler DE is the fact that 90 % of the human cancers are carcinomas, epithelial or glandular tumors, which in the breast are related to the ductal-lobular system; from these, 80 % are ductal carcinomas, 15 % are lobular, and the rest of 5 % are tubular, medullar, or other types. "In situ" carcinomas without microcalcifications are difficult to detect by mammography, but they are visible on Doppler DE, supposing that the findings are not yet proved to be malignant. There are either the ductal-type (ductal carcinoma "in situ"—DCIS), whom 30 % develop to invasive ductal carcinomas, or the lobular-type (lobular carcinoma "in situ"—LCIS), usually multifocal/multicentric, uni-/bilateral, with estrogens receptors in young woman, considered on high risk of raising invasive cancer, in despite of discordant opinions of different authors [14]. In the future, it is presumed Doppler DE could represent an alternative to IRM in the diagnosis of the multicentric breast cancer.

Doppler DE visualizes less 5 mm diameter lesions, either dysplastic, without visible vasculature, or tumoral, with salient suspect new vasculature, offering an anatomical precise localization and characterization (shape, volume, structure, ductal connection).

Doppler DE is superior to 3D/4D US in the diagnosis of the following:

- Nipple discharge
- Symptomatic ductal ectasia
- Diffuse or segmental ductal hyperplasia
- Breast-feeding pathology
- "True" gynecomastia, generally difficult to diagnose on mammography or MRI
- Breast pathology in children and teenagers
- Multifocal cancer, the disease spreading by the ductal way in a centripetal or centrifugal direction toward the intraluminal lowest pressure

3D/4D US is useful in the diagnosis of solid tumors, adenosis, sclerosing adenosis, and fibro-micro-cystic dysplasia, with less than3 mm cysts, which may not be mammographically recognized, especially in the nodular form. Doppler DE better visualizes the complex cysts, with differentiation between the intracystic papilloma, septae, pseudo-septae, debris, and peripheral inflammation.

Ductal and lobular hyperplasia, associated or not with ductal ectasia, despite the presence of the estrogen receptors

is not related to the menstrual cycle; otherwise, diffuse/localized increasing breast vasculature associated with ductal-lobular hyperplasia is suspected for atypical hyperplasia, and the short-interval Doppler DE follow-up associated with the dynamic research of the tumoral serum markers such as CA 15-3 may be useful, because the biopsy cannot be used as screening of the premalignant lesions.

Diffuse increasing vasculature associated with ductal ectasia with/without significant hyperplasia is usually related to the physiological or pathological hyperprolactinemia, while ectasia without hyperemia is found in chronic infections either with saprophyte bacteria, which become resistant to antibiotics (opportunistic infections), such as *Staphylococcus epidermidis* and *Staphylococcus albus*; or with pathogen bacteria such as *Staphylococcus aureus*, *Streptococcus haemolyticus*, and *Escherichia coli*; or even with fungus such as *Candida albicans*.

In the painful breast with ductal ectasia on Doppler DE and without spontaneous nipple discharge, it is useful to actively squeeze out the nipple for the cytological and bacteriological tests; in galactorrhea, the hyperprolactinemia may direct to a pituitary prolactinoma.

The malignant microcalcifications are less than 0.1 mm and are better visualized on mammography; high-resolution Doppler DE could detect small intraductal or intratumoral calcifications, which appear as hyperechoic spots. For the actual probes, it is possible to detect microcalcifications over 0.4 mm, and when present, the benign lesion is defined. There were not proved US microcalcification features highly corresponding to the radiological findings; most cases of so-called microcalcifications on US represent in fact artifacts of the fibro-micro-cystic dysplasia, explained by the posterior tiny enhancement effect with marginal small shadowing of the millimetric cysts and proved on sonoelastography, which demonstrates a summation-BGR scoring upon Ueno.

The presence on Doppler DE of a multiple subcentimeter nodules attached to the same duct, with salient vasculature, with a centripetal or centrifugal descending scale of rank development, is highly suspicious for ductal carcinoma with intraductal dissemination, even without the classical signs of probable malignant breast lesion (acoustic shadowing, marginal spicules, taller-than-wide, etc.). The connection of a lesion with the ductal tree is essential in the diagnosis, and this aspect was introduced by ED, while the classical US and the 3D US, including the automated breast volume scanner (ABVS) with the plane "C," cannot visualize simultaneously all the foci related to the same ductal tree.

The proven connection of the most lesions with the ductal-lobular tree allows a better definition of the isoechoic lesions, such as fibroadenoma or atypical cancers, with differentiation from the lipomatous tissues especially in fatty breasts, while these lesions are usually misdiagnosed in the classical US; once the isoechoic lesion is found on DE, we can improve the contrast by using the tissue harmonic intensifier (THI), and when available, the sonoelastography demonstrates this particular strain.

Doppler DE is the sectional imagery with the best resolution, with continuous scans less than 1 mm thick and measurements less than 0.5 mm, as compared with MRI that usually, without dedicated machines, has a resolution of several millimeters and does not allow the scanning in the axis of the main ducts.

Doppler DE is useful in the monitoring, guided biopsies, and conservatory surgical treatment [16], being proved that large surgical mastectomies did not significantly improve the lifetime of the patients.

For illustration, we will present some images related to the technique, the results of ductal echography compared with the MRI aspect in the same case, and the influence of the imaging diagnostic approach to the surgical therapy (Figs. 1.1, 1.2, 1.3, 1.4, and 1.5).

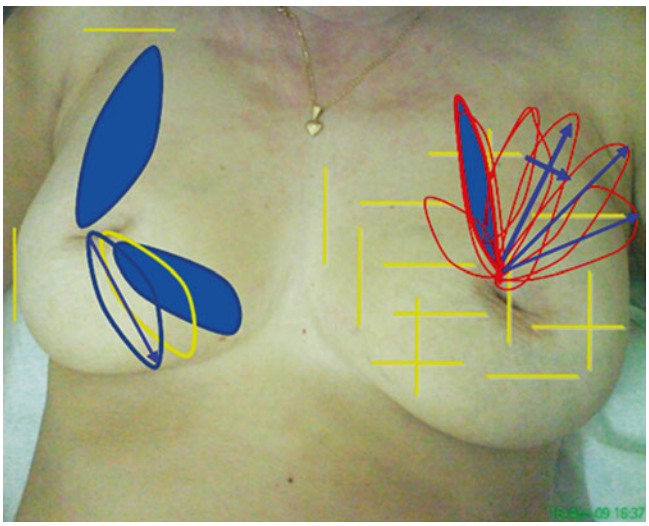

Fig. 1.1 Radial and antiradial scan planes used in DE (examples colored in *blue*) are logical, repeatable, and easy to locate; we visualize on the first intention the normal anatomy, and consequently, we are able to identify eventually a lesion; the transversal and sagittal planes which are still used by the large majority of ultrasonographers (examples colored in *yellow*) are nonanatomical, are difficult to analyze, and are looking just for a lesion in an unknown surrounding "breast tissue"

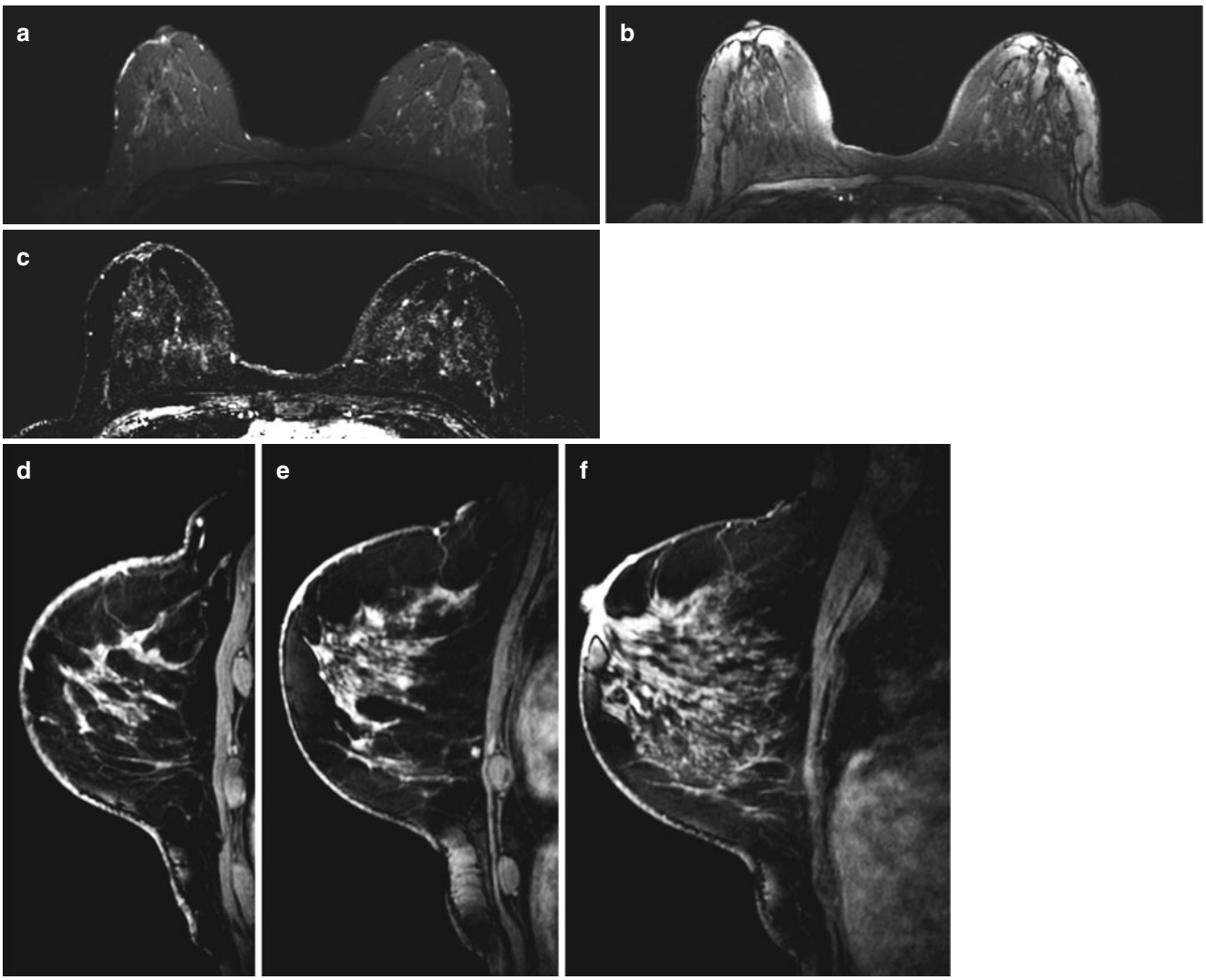

Fig. 1.2 Breast MRI in a 40-year-old patient: upper acquisitions in the axial plane on T2-fat sat, T1 with contrast and T1 with contrast agent and subtraction weighted sequences (**a**–**c**); lower sequences in the sagittal plane T1 with contrast and fat suppression (**d**–**f**). MRI exam is suggesting bilateral multiple small lesions, with unspecific character, but no section is able to present the anatomy inside a mammary lobe, despite the resolution enough for visualization of the normal Cooper ligaments. The enhancement curves were more specific for benignity, but they must be performed for each lesion before the final diagnosis, with higher costs due to the contrast agent and being time consuming than a ductal echography with Doppler and sonoelastography (FBU)

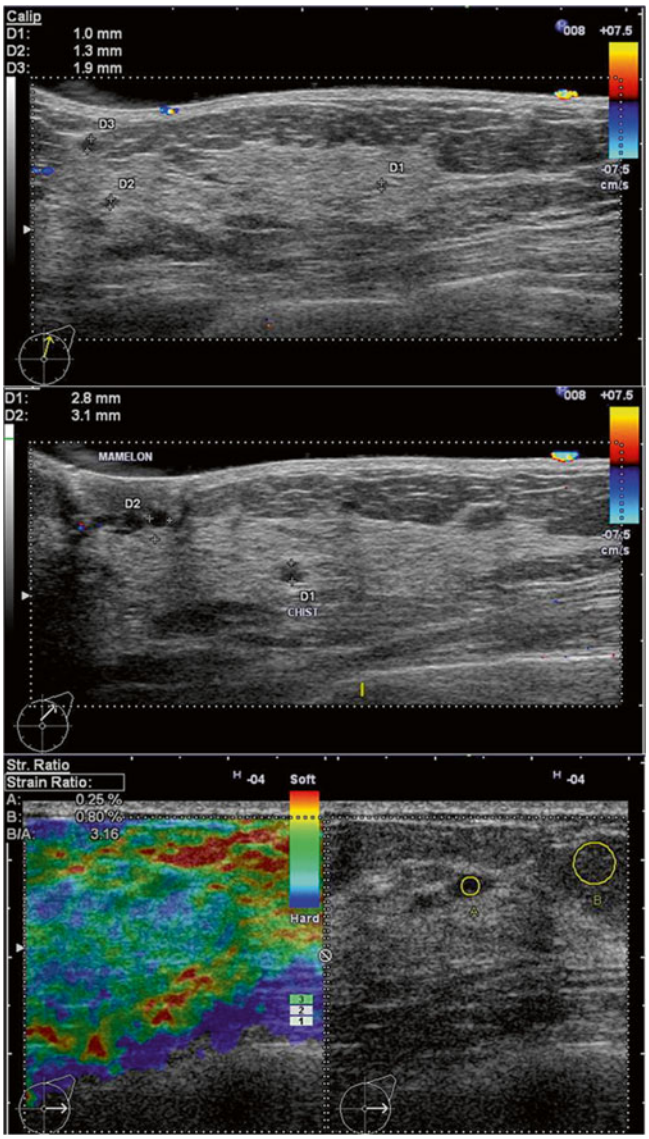

Fig. 1.3 The same case: Doppler DE and sonoelastography present the lobar anatomy with tiny ducts connected to the abnormal findings of 1–3 mm corresponding to microcystic fibrous dysplasia, scored 2 Ueno with "benign" FLR of less 4.70

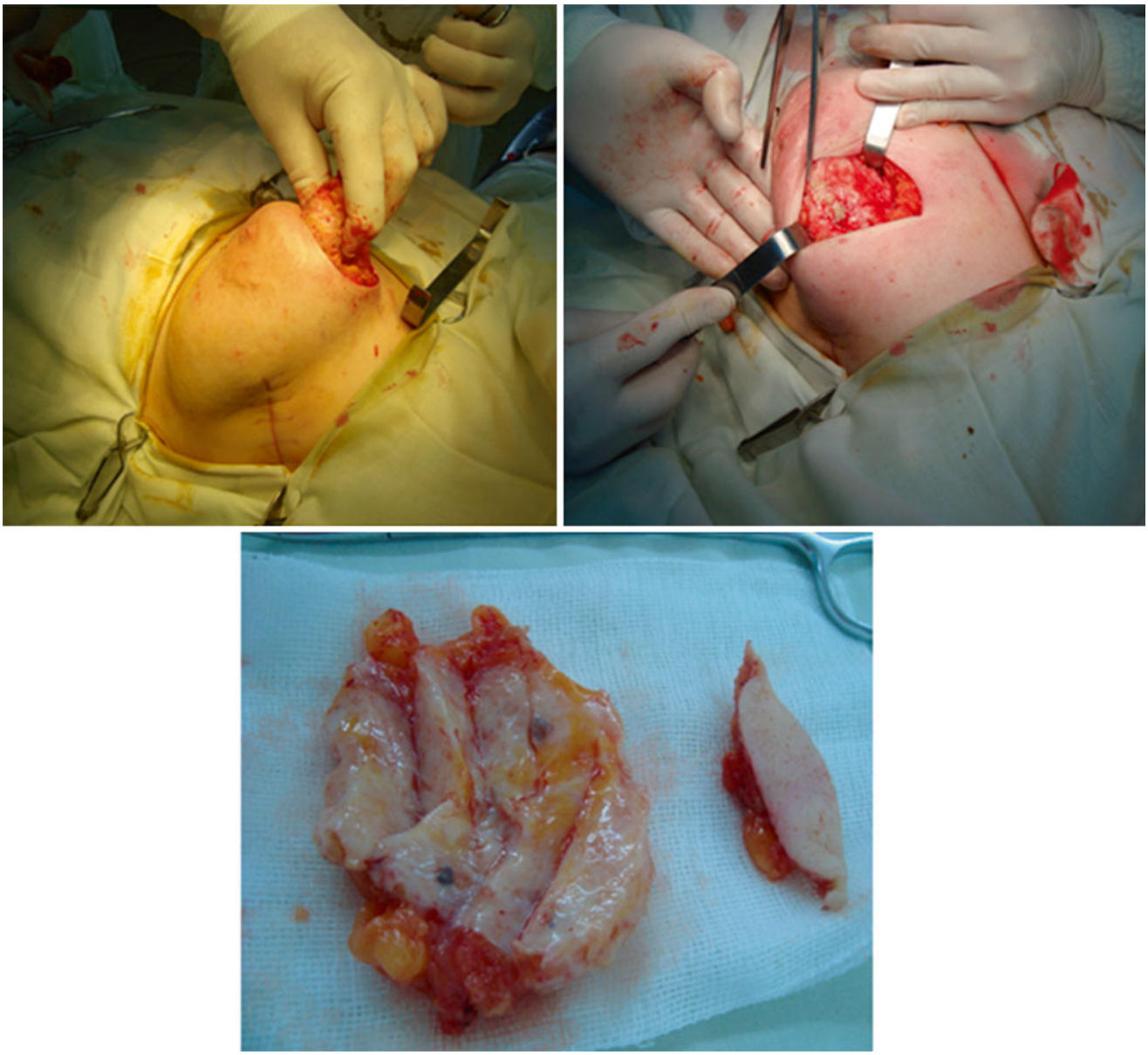

Fig. 1.4 A wrong imaging approach, referred only to the lesion, leads to a wrong therapeutic approach, such as lumpectomy, or segmentectomy. Misinterpreting the anatomy and ignoring the "sick lobe" are proved by the incomplete, repeated lumpectomy with random axes and by illogical random section of the specimen

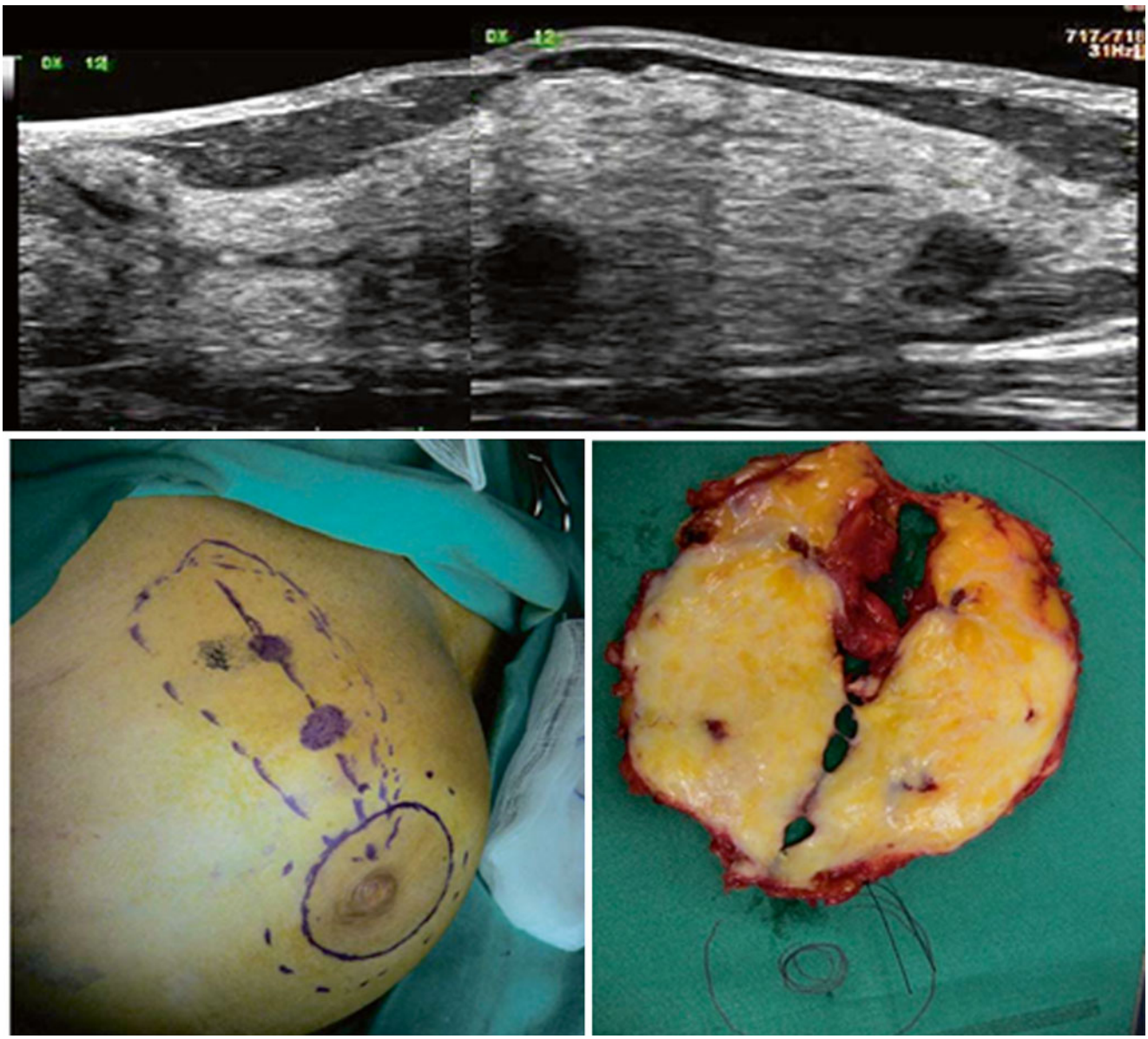

Fig. 1.5 The "intelligent and intelligible" DE of Teboul offers the best therapeutic approach, lobectomy being the ideal treatment for multicentric carcinoma. Conservatory surgery involves not only the lesions but also the whole sick lobe, confirmed by the radial section of the specimen (Courtesy of M. Teboul)

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