New horizons in breast Doppler ductal echography: the positive and differential diagnosis of ductal ectasia, with etiopathological correlations

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Purpose

**Terminology:** In the literature, duct ectasia syndrome was not well characterized by the non-invasive methods and has many meanings on histological and symptomatic levels, such as mastalgia, fibrocystic disease and nonpuerperal mastitis, including the special cases of granulomatous mastitis, periductal mastitis, comedo mastitis, secretory disease of the breast, plasma cell mastitis and mastitis obliterans, subareolar abscess with or without squamous metaplasia of lactiferous ducts and fistulation [1].

**Incidence:** The incidence in the population is not known, because in the past there were not available *in vivo* systematically examinations for all ages symptomatic or asymptomatic patients. However, in the pathologic reports the disease is frequently described. Browning et al. found in the histology obtained from 1256 female patients undergoing breast surgery duct ectasia in 51 (4.2%) symptomatic patients and in 103 (8.1%) patients where duct ectasia was an incidental finding [2]. The disease is usually related to the perimenopausal woman, but few cases of benignant bloody discharge in adolescent were described, with presumed mechanism of ulceration of the ductal wall or of papilloma proliferation [3; 4].

**Pathogenesis:** The common opinion considers complex pathogenesis, but there are not proved clear etiological factors. The duct ectasia is generally believed to be a result of secretory stasis (without explanation for the secretion and stasis), including stagnant colostrum, with secondary periductal inflammation and fibrosis (without explanation for the inflammatory changes). Because both duct widening and duct ectasia syndromes are frequently bilateral, systemic causes are logically to be involved. The most incriminated causes were:

- Breast tissue changes due to aging, when the composition of the "breast tissue" changes from mostly glandular to mostly fatty in an involution process, and sometimes these changes lead to blockage of a milk duct and the inflammation associated with mammary duct ectasia. This is not a reasonable explanation, because the ectasia is found in the young, dense breast as well as in the mixte or fatty breast without real aged-correlation. Moreover, duct ectasia was found associated with bloody discharge in children of both sexes, with different associations (cysts, infections, and gynecomastia) and a variety of outcomes [5].

- Smoking may be associated with widening of milk ducts, which can lead to inflammation and, possibly, mammary duct ectasia; this association is not explained, and there are not proved studies to demonstrate the absence / rarity of the disease in non-smoker women.
A newly inverted nipple is thought that may obstruct milk ducts, causing inflammation and infection, but in fact this inversion could be the effect, in the advanced stages, of the ductal ectasia with chronic galactophoritis (Fig. 1 on page 4). The newly inverted nipple in chronic galactophoritis associated to the duct ectasia is possible to be differentiated from a more serious underlying condition, such as breast cancer, by using the newer anatomical technique of breast Ductal Ultrasonography/ Echography.

**Purpose:** The aim of this study is to present a new Ultrasound technique of diagnosis of breast ductal ectasia, based on the anatomical breast architecture, named Ductal Echography of Teboul, completed with Doppler and Sonoelastography (the Full Breast Ultrasonography-FBU), which allows a better *in vivo* characterization of the lesions with etiopathological correlations.
Images for this section:

**Fig. 1:** Clinical appearance in chronic galactophoritis: the initial stage with duct ectasia and nipple surge (sometimes unapparent spontaneously), and the final stage with nipple inversion.

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Methods and Materials

We made a retrospective statistical analyze of 1340 symptomatic / screening cases investigated during September 2009- August 2012, using Ductal Echography of Teboul, the only anatomical imaging technique of breast diagnosis that provides complete visualization of normal and pathological ducts and lobules and, "unlike mammography, distinguishes them clearly from the surrounding glandular stroma" [6]. The Ductal Echography has as anatomical support the radial orientation of the mammary lobes [7], partially superposed, composed by the main duct(s) branching in secondary and tertiary ducts up to the terminal ductal-lobular units (TDLU) (Fig. 2 on page 7; Fig. 3 on page 7); moreover, the pathological findings of the "theory of the sick lobe" are well depicted by the visualization of the lobar sections on the Ductal Echography, with good illustration of the pathological size and extent of the disease, including the characterization of the multifocal and multicentric lesions [8].

Colour or Power Doppler and Sonoelastography completed the characterization of the normal and abnormal breast structures (Fig. 4 on page 8; Fig. 5 on page 9) and realized the Full Breast Ultrasonography (FBU) [9]; the method is operator-independent, because it was standardized both in the acquisition of the images and in reporting data, so the whole breast is investigated using the radial and antiradial technique following the whole radius of the mammary lobe, and the reporting follows the horary and spatial coordinates (Fig. 6 on page 10).

The **US BI-RADS characterization** was useful for the follow-up examinations and for treatment referring. This characterization was proved to be correlated with the **Ueno (Tsukuba) score** for the Sonoelastography, with some additional observations related to the normal and pathological ducts, which were not completely described by the promoters of this technique, the score being oriented especially to the characterization of the abnormal breast findings; we considered score 1 Ueno - green for the normal ducts and lobules and small duct ectasia, score 1 Ueno- green for the duct walls and red for the ductal fluid content in medium ectasia, and BGR (blue-green-red) score for the largest cylindrical or pseudo-cystic ectasia (Fig. 7 on page 11; Fig. 8 on page 12).

The examinations were performed in different imaging centers (public hospital and private laboratory) using Ultrasound machines from different manufacturers, some cases being reexamined by different operators instructed for the same radial technique, with concordant results.

The nipple discharge was referred for bacteriological tests when possible and suspect cases were selected for cytology. Mammography and breast MRI were used as
independent examinations, but it is not the intention of this study to make a statistical comparative evaluation. For the galactorrhea the Prolactin level was recommended.

The follow-up exams to at least 6 months-interval or the pathological reports after biopsies or surgical treatments were used to validate the FBU. The treatment of the pathological agents with antibiotherapy was based on the antibiogram results and a follow-up exam was performed.
**Fig. 2:** Radial scan in the left breast at 3:00 o'clock with a linear long probe provided with water - bag: the nipple in the left-upper screen-corner, the normal thin ducts and the dilated ducts are emerging together and are branching towards the periphery of the mammary lobe, located in the right screen-side; the anatomical elements, from the superficial skin-layer to the deep pectorals and ribs could be recognized by every ultrasonographers.

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Fig. 3: Radial scan with a usual short linear probe (transducer) of higher frequency (12-14MHz): the composed radius by merging the first half-screen with the nipple in the left side and the second half-screen with the periphery of the lobe approximates the breast architecture and is useful in the illustration of the breast glandular parenchyma with higher resolution, with a magnification type X3. The Doppler signal is better, proportional with the frequency of the transducer and the optimized gain.

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**Fig. 4:** Ductal Echography with radial scan and Doppler are the first steps in detection and characterization of the breast architecture: in this case, multiple ductal ectasias converging towards the nipple in a dense breast.

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Fig. 5: The same case: The final assessment is the Sonoelastography, as a complementary method of diagnosis, achieving the supplementary information about the solid/variants of fluid structures and about the risk of malignancy based on the stiffness of the tissues. All the information obtained by 2D, 4D, Doppler and Sonoelastography realize the Full Breast Ultrasonography, with the best accuracy, any other Ultrasonography being in fact incomplete, with unsatisfactory results.

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Fig. 6: The reporting of the findings in the Ductal Ultrasonography is standardized upon the geographical coordinated model: by mentioning the distance from the nipple and the clock-wise location, it is possible to check a lesion on a follow-up exam made by the same or by different operator, the mapping of the multifocal or multicentric lesions is more complete and precise, the surgeon/therapist is able to locate an impalpable tumor.

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Fig. 7: Apparently a couple of dilated ducts of the same type on the Doppler Ductal Ultrasonography

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Fig. 8: The same case: The Sonoelastography applied to the breast parenchyma illustrates the normal ducts and the benign dilated ducts with specific appearances, according to their size and contents. In duct ectasia Sonoelastography is useful in the differential diagnosis of the inspissated ducts with echogenic contents.

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Results

From all 1340 patients, 423 cases (30.6%) presented typically aspect of ductal ectasia with tubular structures radiating from the nipple, full-filled with transonic, hypoechoic or hyperechoic content, according to their etiopathogenesis (Table 1 on page 16).

Doppler illustrated increased periductal vasculature in breast-feeding ectasias (used as reference cases) (Fig. 9 on page 16) and pathological hyperprolactinemia (Fig. 10 on page 17) (in total 52 cases-12.2%), some cases of galactorrhea presenting pituitary micro-adenoma proved on MRI examination of the hypophysis. The Galactorrhea was found in woman with/without menstrual disturbances and evenly in man with gynecomastia, initially misdiagnosed by other methods of examination and treated by conservative surgery. As a curiosity, galactorrhea with hyperprolactinemia had rarely proved a pathogenic agent and almost only in the acute/subacute mastitis. In addition, Doppler was useful in the characterization of the malignancy risk of the proliferative lesions associated to duct ectasia (Fig. 11 on page 18).

371 (69.4%) cases without salient periductal increased vasculature and normal levels of the Prolactin presented various nipple discharges, even in the same breast; in 340 cases the biological tests were positive and the follow-up exams found good response to the antibiotherapy. The most frequent as expected were Staphylococcus aureus and Staphylococcus white haemolyticus, but we found also Streptococcus haemolyticus, Escherichia coli, Klebsiella or Proteus; rare cases presented Candida albicans, and most of the Staphylococci considered saprophyte (S. saprophyticus, S. epidermidis) presented resistance to many antibiotics and were treated in the symptomatic cases, being considerate potential pathogen (opportunistic) (Table 2 on page 19). The so-called “sterile” cases presented sometimes greenish, brownish or gray surge, without any proliferative findings, but we could not identify bacterial or fungi agents, maybe because of the previous uncontrolled antibiotherapy, or because of some viral agents that we had not possibility to isolate.

In the most cases of ductal ectasia the lesions were multiple, usually bilateral symmetrical/asymmetrical and in the same breast the wider ducts were present in the lower lobes from the lower quadrants, possible according to the gravitational accumulation of the fluids. Ductal ectasia was rarely isolated, but FBU detected associated lesions such as fibro-cystic dysplasia (frequent, some chronic infected cysts punctioned presenting the same pathological agent), intraductal papillomas, ductal segmental hyperplasia (Table 3 on page 20), and ductal/lobular carcinoma (rare).
The axillary lymph nodes presented either a normal aspect in the ductal ectasia (Fig. 12 on page 21), or more specific features in the chronic galactophoritis: a normal peripheral hypoechoic avascular cortex, a hilum with less salient vasculature but with a less hyperechoic central part, this aspect being the corresponding image to the pathological description of a benignant histiocytosis (Fig. 13 on page 22). The acute lymphadenitis preserved the hyperechoic hilum aspect, but with increasing centrifuge vasculature (Fig. 14 on page 23). All these variants presented benignant-type Sonoelastography, while the malignant lymph nodes were suspected when presented thicker cortex, peripheral new-formation vasculature and malignant-type score upon Ueno (Fig. 15 on page 24).
Table 1: The distribution of the cases

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Fig. 9: FBU aspects of the lactation breast, with long-probe and short high frequency probe: the diffuse increased vasculature is significant, associated with ductal ectasia and lobular apparently hyperplasias, scored 1 Ueno, and less perimammary fatty tissue

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Fig. 10: FBU in pathological hyperprolactinemia, with similar findings as in the previous case

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Fig. 11: Doppler Ductal Ultrasonography in a case with impalpable invasive ductal carcinoma with multiple metastases (brain, lung, liver and bones), without mammographic significant findings and with doubtful MRI enhancement curve: the new formation vasculature with incident plunging angle was significant for malignancy and the targeted biopsy after Ultrasound localization confirmed the diagnosis. The patient presented no more lung metastases after 1 year-survival under chemotherapy.

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**Table 2:** The distribution of the pathogen agents at the bacteriological tests of the nipple surge in Ductal Ectasia

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Table 3: The pathological associations of the Ductal Ectasia

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**Fig. 12:** Full Ultrasonography of a normal axillary lymph node; the concept of Ultrasonography completed with Doppler and Sonoelastography should be the gold standard in Ultrasound examination when application is technological developed, as it was in small parts as thyroid, salivary glands or superficial lymph nodes, in prostate, uterus.

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Fig. 13: Full Ultrasonography of an axillary lymph node with less vasculature but with hypoechoic central region of the hilum, is suggesting chronic lymphadenitis.

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**Fig. 14:** Acute benign axillary lymphadenitis, with increased vasculature of centrifugal-type

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**Fig. 15:** Suspect axillary lymph node, with focal thickening of the cortical, presenting new formation vasculature of peripheral type, associated with significant Sonoelastographic changes of the stiffness in the same area. When the whole lymph node was involved with both vasculature and strain of malignant-type, the biopsy was considered no more necessary.

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Conclusion

The noninvasive methods of breast diagnosis used to determine *in vivo* the duct diameter are available only recently (last decades), such as 3D/4D US [10] or MRI (Fig. 16 on page 28; Fig. 17 on page 28), but the benign lesions are yet insufficient described and there are not clear correlations in the literature between these findings and the results of the older mammographic Ductography (Galactography) or the results from biopsies. In fact, the usual worldwide US approach is limited only to the periareolary area, where the ducts are better depicted by the usually short 4-5cm linear transducers, and the periphery of the mammary lobar ducts remain unexplored. Galactography still represents for many specialists the best preoperative method of diagnosis in nipple discharge (Fig. 18 on page 29), but not all duct ectasias can be proved by this symptom, some nipple pores being obstructed [11]. The diagnostic Mammography, even using the full technique of examination, is less performing in the delimitation of the ductal tree, because both of the superposed tridimensional structures on a 2D image and of a lower opacity of the breast parenchyma than of the connective, stromal tissue. Breast Tomosynthesis even with its possibility to visualize series of breast sections, is unuseful because the section plans are not anatomical oriented, so the enlarged ducts appear as variable segmental discontinuous opacities.

In our experience, there were identified on FBU at least 4 pathogenic mechanisms that could determine 4 groups of duct ectasia, with clinical, bacteriological and pathological correlations:

1. *Dishormonal factors*, which determine the **Galactorrhea**, with milk or appropriate milky secretions without normal period of lactation breast; when the seric Prolactin level was raised, the breast vasculature was more intense on Doppler Ductal Echography, similar to the normal lactation breast; the response to the anti-Prolactin treatment (Dostinex/ Cabergoline) was concordant with less Doppler findings; in men Galactorrhea represents a rare form of Gynecomastia, and FBU is the best method of imaging diagnosis (Fig. 19 on page 30);

2. *Chronic infections*, which determine **Chronic galactophoritis**, with proved bacterial/fungus agents (Staphylococci, Streptococcus, E. coli, Proteus, Candida) in the nipple discharge or in the associated chronic inflamed cysts evacuated by punction-aspiration, but without salient breast increased vasculature on Doppler; these cases were associated with chronic inflammatory-type changes in the axillary lymph nodes on FBU, with good response to the treatment with antibiotics according to the antibiogram; the evolution without treatment was found in the long-evolution cases presenting periductal fibrosis and nipple inversion (Fig. 20 on page 31);

3. *Dysplastic mechanism*, many cases of duct ectasia being associated with some fibro-cystic changes in the same lobe, according to "the thick
lobe theory”, with the observation of an asymmetrical distribution between lobes and between the two breasts: when duct ectasia was more extended (in size and number), the cysts were less large and inversely (Fig. 21 on page 32; Fig. 22 on page 33); the chronic infection may appear as a consequence of secretor unidentified conditions;

4. - **Tumoral pathogenic factors**: it could be found either an intraductal **benign** proliferative lesions, usually in the central periareolar part, which could produce secretions or may cause bleeding, such as **papillomas** (Fig. 23 on page 34; Fig. 24 on page 35), or ductal-connected **malignant** lesions, usually peripheral and in a TDLUs location, with secondary duct widening (Fig. 25 on page 36; Fig. 26 on page 37; Fig. 27 on page 38; Fig. 28 on page 39). Some cases with non-bloody nipple discharge may present diffuse non-palpable intraductal carcinoma [12].

The symptomatology was frequently absent, but when present the dominant sign was pain, stings, sometime pasty nipple discharge of various colors: white, serous, citrine, gray, green, brown or bloody; the nipple retraction or inversion happened lately, sometime associated with squamous deposits or increasing pigmentation of the nipple and areola.

In rare cases the inflammation became acute or subacute with tenderness in the nipple or surrounding breast tissue, redness of the nipple and sometimes large surrounding area, usually in the lower quadrants. Rarely, it may suddenly develop a painful breast lump or thickening near the clogged duct.

We can conclude there are many cases with ignored chronically galactophoritis, confirmed by the bacteriological tests and the satellite lymph nodes with benignant histiocytosis. Irregular thickening, frondlike tissue, or masses within the duct should avoid biopsy because intraductal carcinoma or papillomatosis considered a high risk of malignancy could be detected in the first 5mm diameter by FBU; short-time follow-up after antibiotherapy by non-invasive diagnosis, such as Sonoelastography or breast MRI is mandatory.
Fig. 16: Application of 3D Ultrasonography in ductal ectasia, confirming the diagnosis in multiplanar reconstructions; the reproducibility of the images and the characterization of the lesions are less performing than by Ductal Echography.

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Fig. 17: Breast MRI contrast T1-weighted sequence in the Sagittal plan at the nipple level, from 12:00 to 6:00 o'clock with thick reconstruction, may illustrate the ducts and the radial distribution of the branching parenchyma; this "anatomical" acquisition could not be realized in the outer or inner quadrants, because of the oblique section of the mammary lobes; the same thing for the axial scans, the only "anatomical" reconstruction is possible just for the scan at the nipple level, passing from 9:00 to 3:00 o'clock, the upper or lower quadrants being excluded.

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Fig. 18: Mammographic Galactography with inconvenient: the pathological, complete obstructed ducts are not salient; a suspect lesion has not a precise location because of the projection of a 3D structure on a 2D image and of the mammographic compression; there is not information about the risk of malignity because we can not visualize the surrounding ductal walls; technically the irradiation is supplementary increased, and we cannot approximate the quantity of the iodinated contrast agent: too much (falsely dilated ducts) or not enough (less ducts opacified).

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Fig. 19: Gynecomastia was characterized by the three specific features of a mammary developed (developing) gland: the parenchyma represented usually by the branching ducts, rarely ended by lobules, all surrounded by glandular hyperechoic stroma containing salient new-formation vasculature; in this case, gynecomastia presented duct ectasia with increased mammary vasculature characteristic for galactorrhea (surgical proved).

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Fig. 20: Chronic galactophoritis in postmenopausal woman, with lobar atrophy characterized by less hyperechoic glandular stroma, thin ductal walls, ductal ectasia without salient periductal vasculature, with/without nipple inversion.

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Fig. 21: Chronic galactoforitis associated with fibro-cystic dysplasia, with bacteriological agent identified in the nipple surge: thin ductal ectasia ended by small lobular cysts, without significant stromal vasculature.

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Fig. 22: Nipple surge in thin ductal ectasia but associated with huge number of various size of mammary cysts in the Reclus’ disease; the selected antibiotherapy has proved to be useful.

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**Fig. 23:** FBU: Ductal ectasia and intraductal papilloma.

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Fig. 24: FBU: differential aspects of ductal ectasia in intraductal papilloma and simple ectasia, with score 2 Ueno with low FLR and respectively score 1 Ueno with the green walls and the red fluid-filled lumen.

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**Fig. 25:** FBU in suspect intraductal lesion: the score 4 Ueno (constant determination), but without salient vasculature, can be assessed BI-RADS 4a category, and it is frequently associated with the intraductal carcinoma.

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Fig. 26: A radial scan with a long-probe provided with water-bag in a case with bloody nipple discharge, detected a deep suspect lesion in L13:30.

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Fig. 27: The same case: the Doppler scan with a short high-frequency transducer illustrated a ductal ectasia connected to the lesion, and the incident angle of the plunging artery increased the suspicion of malignant-type lesion.

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Fig. 28: The same case: the Sonoelastography completed the characterization on FBU of the associated lesion to the ectasia, presenting a score 5 Ueno with a high FLR. In our experience, the malignant-type new vasculature associated with a malignant Sonoelastographic score of 4 or 5 Ueno are the most important descriptors and should be included in the US BI-RADS assessment.

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