The diagnosis of gynecomastia by Doppler ductal ultrasonography: Etiopathogenic, endocrine and imaging correlations

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Learning objectives

To illustrate the utility of Doppler Ductal Ultrasonography (DDUS) in the positive and differential diagnosis of the gynecomastia and in distinguishing, for the first time in the literature, of various endocrine aetiologies.
Background

**Gynecomastia** represents the development of the mammary bud in true mammary glandular structures in men. Usually, the diagnosis of gynecomastia is made by the physician by just simple observation and palpation and the presenting history.

There are few imaging illustrations of male breast pathology, despite the "classical" aspect on Ultrasonography and mammography that are rather presenting the differential diagnosis of the malignant from the benign conditions, than describing gynecomastia itself (Figure 1).

The breast anatomy in gynecomastia is considered to be the same as in the female breast, but there are some specific morphological types according to the stage of evolution and to the type of dishormonal pathology (Figure 2); the classical methods of diagnosis did not make a clear discrimination between them.

**The development of gynecomastia** is better understood when we know the development of the breast in female (Figure 3).

In the literature there is not a clear demarcation between the "physiological" and the "pathological" gynecomastia; in practice, gynecomastia is considered as a "physiological" or a "benignant" condition and no treatment is recommended if the esthetical reason is not important. In fact, gynecomastia could be considered "physiological" in neonate and puberty, and "disease" at any age if it is related to other dysfunctional or tumoral endocrine/ non endocrine condition (Figure 4).

Understanding the imaging aspects of gynecomastia requires to understand the breast anatomy in male, which is hormonal-dependent and logically has a dynamic architecture. As in female breast, the glandular structures are represented by a number of lobes radially oriented from the nipple, with a specific glandular architecture, with partial spatial superposition, but being anatomically and functionally distinct (Figure 5).

**The classical imaging diagnosis of the male breast** is based on the mammography, but there are some limitations and inconvenients; the "classical" Ultrasonography (US) has the main purpose to differentiate the cystic from the solid lesions, but it is unable to describe the gynecomastia itself, because the scanning and the interpretation are not anatomical, since only the glandular parenchyma is identified. Male breast MRI is an interesting tool, but it is not available for all and could not visualise the specific parenchyma, thus MRI has limited applications for the diagnostic of suspected masses (Figure 6).

In the last 15 years US was developed especially based on the engineering and computational achievements, but had less developments based on the pure medical
reasons. For the breast application of US, the "classical" method uses the axial, sagittal, random oblique, radial and antiradial scans, 3D and panoramic SieScape-type acquisitions, without any correlation with the breast anatomy; moreover, the analysis of the US images is based on the mammographic lexicon, completed with a number of specific terms. As results, US became a complementary method in the diagnosis of breast tumors, with limited applications in the male's breast. In the same time, the systematical radial ultrasonography, issued more than 15 years ago, named Ductal Echography (DE) by its promoters [5, 8, 9, 12], began more appreciated and gained many supporters, due to its advantages.

**DDUS** is a new concept based on the radial breast scanning (DE) upon the Teboul-Amy standardized technique, completed with the characterisation of the vasculature using the Doppler techniques. Actually DDUS represents the unique imaging method that visualises the anatomical structure of the breast, with some indoubtable advantages:

**ADVANTAGES OF DOPPLER DUCTAL ECHOGRAPHY (DDUS):**

1- an intelligent and intelligible US examination of the breast, available for all, of both sexes and of any age, because it is based on the anatomical radial structure and orientation of the mammary lobes [8, 9];

2- an intelligible interpretation and standardized reporting of the findings based on the analysis of the galactophorous tree (ducts and lobules) and its connections with the eventually pathological masses of the breast: reporting L (left) and R (right) followed by the clockwise annotation with the measuring of the distance from the nipple allows the reproducible scans, by any operator with different machine, and the interventional precise approach (biopsy or surgical treatment);

3- the most available, cheap (Doppler characterisation is cheaper than the use of the contrast agents in MRI or classical US examinations) and without side-effects method of imaging diagnosis of the breast; DDUS demonstrates not only the millimetrical abnormalities of the parenchyma, but also the premalignant changes: ductal hyperplasia, ectasia, papillomas, adenosis [5, 9, 12];

4- in men, DE is the method of choice before any interventional procedure, because the anatomical analysis offers the positive and differential diagnosis of gynecomastia and could characterise the subtypes of gynecomastia, with recommendation for targeted hormonal tests and imaging exams, reducing the time and the costs of overall diagnosis.
DEFINITION

**Gynecomastia** represents the development of the mammary bud in true mammary glandular structures in men. The clinical appearance as a retroareolar painful lump (at least in the florid stage) has usually asymmetrical development, but rarely is found unilateral.

**Interest of the study:**
- There are few imaging data in the literature, despite the high clinical incidence and the complex endocrine endogenous or exogenous etiology;
- Some cases mask breast cancers usually diagnosed in advanced stages, because there is no screening test of the male breast cancer even in cases with estrogenic therapy;
- The clinical overdiagnosis is frequently followed by unnecessary biopsy or surgical treatment.

**Fig. 0:** Definition and interest of the study

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**Fig. 0:** Anatomical/Pathological classification

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**Table 1. Gynecomastia - Anatomical/ pathological types classification**

<table>
<thead>
<tr>
<th>Gynecomastia</th>
<th>Female breast</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute florid/ Developing (&lt; 6 months)</td>
<td>Thelarch</td>
</tr>
<tr>
<td>Chronic</td>
<td>Young/Adult type</td>
</tr>
<tr>
<td>Secretor/ Galactorrhea</td>
<td>Lactation/Galactorrhea</td>
</tr>
<tr>
<td>Ductal hyperplasia</td>
<td>Ductal hyperplasia, Adenosis</td>
</tr>
<tr>
<td>Benign/ Malignant mass</td>
<td>Benign/ Malignant mass</td>
</tr>
</tbody>
</table>
**FEMALE BREAST DEVELOPMENT**

**Embryological stage**

The breast develops from the breast bud which is formed in the first six weeks of life *in utero*.

Further normal breast development does not occur until puberty.

**Adolescent breast development**

The female breast contains 12-16 mammary lobes radially oriented from the nipple; each lobe is a morphological and functional unit and determine a pathological unit (the “sick lobe theory”) [1, 2]

Each lobe develops:

- A branch of the mammary bud continues to branch out and growth of breast ducts;
- Simultaneous development of hormonally-responsive specialized periductal stroma;
- Development of lobules, the milk secretor units - a prolonged process that is accelerated by pregnancy; the terminal ductal-lobular (specific) unit (TDLUs) is thought to be the beginning site of breast malignancies.

**Fig. 0:** Female breast development

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DEVELOPMENT OF GYNECOMASTIA

The development of gynecomastia follows the same process as the developing breast in female, but the lobules are rarely present. Gynecomastia is simultaneous proliferation of ducts and stroma without encapsulation, so it must blend into the surrounding fat tissue.

Gynecomastia is considered to have 3 peaks of incidence:
- neonate: transplacental estrogens, with spontaneous resolution in a few weeks;
- puberty: 13-16 years, up to 60% boys, with spontaneous resolution in 2 years;
- elderly men (65% of breast masses).

In our experience, except the “physiological” gynecomastia of neonate and puberty, gynecomastia as disease (causing discomfort, pain, mental shock, embarrassment, associated with infertility, male hypogonadism, endocrine tumours) could be present in patients of any age.

Fig. 0: Development of gynecomastia

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BREAST ANATOMY IN GYNECOMASTIA

As in female breast, the glandular structures are represented by a number of lobes radially oriented from the nipple.

Male breast lobes:

1. **Breast parenchyma** is the key functional/ specialized glandular tissue represented by the mammary bud, which is branching in:
   a) The ductal system: nipple ➔ the major duct or sinus ➔ intermediate lactiferous ducts ➔ minor ducts ➔ distal lactiferous ducts or acini.
   b) The lobules/ the lobular units, responsible for the production of milk – rarely seen in gynecomastia.

2. **Stroma**: the supportive framework of an organ/ gland, composed of connective tissue; the stroma contains the blood vasculature, the lymphatic vessels and the nerves.

The TDLUs is located in ductal echography (DE) at the intersection of the main ductal axis and the Cooper’s ligament; TDLUs is thought to represent the beginning site of the most breast cancers in females and males patients.

**Fig. 0:** Breast anatomy in gynecomastia

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Fig. 0: Imaging diagnosis of gynecomastia

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TECHNIQUE OF DDUS: TRANSDUCERS (PROBES)

DDUS is performed using both a long-linear water-bag probe for the completely exploring of the mammary area (Figure 1) and the mapping of the abnormal structures (Figure 2) and a short, higher frequency probe for detailed tissues characterization, including the Doppler analysis and the Real-time Sono-Elastography (RTSE) (Figure 3).

TECHNIQUE OF DDUS: RADIAL SCANNING

The radial scanning of the breast has standardized orientation of the images: the nipple in the upper-left corner of the screen and the peripheral region of the scan of the lobe to the right screen-side; the body mark on the screen respects the clockwise annotation and each main duct with its branches is followed entirely by small angulations of the probe around the orthogonal scanning plan (Figure 4). The antiradial axis is used in the determination of the volume of a lesion and in the analysis of the anatomical rapports (Figure 5). The Doppler analysis and the RTSE could be done in any axis, but it is logically to be performed in the radial axis because of better correlation with the ductal tree. DE completed with Doppler and RTSE represent the "true" breast examination with US, a new concept [12], briefly named the Full Breast Ultrasonography (FBU). The lymph nodes are examined allways using Doppler US and RTSE, with better results in the evaluation of the sentinel node than in the "classical" US; not only the axillary and sub-/suprACLAVicular stations are investigated, but Doppler US is useful for the internal mammary lymph nodes characterisation. Reporting the imaging findings is the same as in US BI-RADS, with a better characterisation of the lesions when it is proved their connection to the ductal-tree.

IMAGING FINDINGS IN GYNECOMASTIA USING DE/DDUS/FBU

We present an analysis of 47 cases with "true" gynecomastia, aged 8 months - 67 years old, found in a series of 65 males.

The breast anatomy is the same in gynecomastia as in young female normal breast or in the pathological female breast. In male, however, we can identify some correlations of the pathological forms of gynecomastia with the endocrine pathology based on the analysis of the breast parenchyma.

DDUS is a non-invasive method allowing the identification of three histological elements of diagnosis of gynecomastia:
1- **Parenchyma** is represented by the retroareolar bud, branching in lactiferous ducts, rarely ended with small lobules. The ductal system has a monostratificated ductal epithelium surrounded by a myo-epithelium, lying on an uninterrupted basement membrane. The mammary bud is usually hypoechoic, as a mass with irregular borders, with progressive branching in ducts. The ducts are hypo/izoechoic and usually contain a hyperechoic central line, *the central line sign*, representing the virtually ductal lumina, a pathognomonic sign for the mammary ducts, or a double line in ductal ectasias with fluid content.

The lobules, also called the lobular units, are responsible for the production of milk - rarely seen in gynecomastia.

2- **Stroma**, generally the supportive framework of an organ (or gland or other structure), is composed of connective tissue. The stroma contains the breast vasculature, lymphatic vessels and nerves. Stroma surrounding the parenchyma is absent in pseudogynecomastia (Figures 6, 7). In gynecomastia as well in thelarche the both elements parenchyma and stroma are related and are simultaneous developing.

3- The formation of **new vessels** is the third element, consistent with the painful developing gynecomastia (Figure 8) and the malignancy. The old/chronic gynecomastia may present less visible vessels, as in normal female breast. The chronic gynecomastia could be visualised at any age, and it is less painful (Figures 9, 10, 11, 12).

The familial gynecomastia could be assigned to some genetic or nutritional factors (food contaminants) (Figures 13, 14).

In our group of patients, 5 cases presented ductal ectasias, correlated with hyperprolactinemia, one of which with milk secretions presented a microprolactinoma (Figures 15, 16, 17). 7 cases presented ductal-lobular thickening up to 3 mm diameter, presumed as hyperplasia, were correlated with hyperestrogenemia (Figures 18, 19): in one case was identified on US and MRI an adrenal adenoma (Figures 20, 21, 22, 23), in 3 cases diffuse adrenal hyperplasia (Figure 24) and 3 cases were interpreted as dietary hormonal changes. No feminizing testicular tumors were found in this small group of patients.

Performing **DDUS and RTSE** in the same examination realises the FBU with the complete analysis of gynecomastia: the additional RTSE offers the possibility of better differentiation of the breast parenchyma from the stroma and the fatty tissue (Figure 25); the parenchyma is the softest structure in breast, colored in red and green, while the stroma is more stiff, coloured in light blue, in concordance with the radiological absorption law, therefore this could explain why the breast parenchyma is not visible on mammography.

The gynecomastia could be associated with the pathology of the thyroid: the diffuse goitre, nodular solid or colloidal-cystic goitre (Figure 26) with hyper- or hypo-thyroid
function seems to be correlated with the breast pathology, in gynecomastia as well in woman, in our experience and in the literature [15, 16].

**The relation of gynecomastia with the male breast cancer** is not very clear, because of the limited possibilities of the "classical" radiological and imaging techniques of diagnosis (Figure 27). There are some general assumptions in the literature:

- Male breast cancer occurs in one breast and it is seen in older males.

- In the majority of cases of gynecomastia, there is no cancer associated; however, any male over the age of 50 with a sudden increase in a single breast is suspect.

- Breast cancer in males presents just like in females: a mass is identified in a single breast, there is generally no pain or nipple discharge but the mass may be hard to touch.

- The only way to tell if it is cancer is by a biopsy.

However, DDUS is able to precise the connection of the lesion with the ductal tree, its spreading ways along the surrounded ducts and along the Cooper's ligaments; the (male) breast cancer develops for long time only inside the same lobe as says the "theory of the sick lobe" [1, 2]. These signs of malignancy are logical and correspond to the pathological findings. Moreover, Doppler application demonstrates the malignant features of the new vasculature: the incidental angle appropriate to 90º [17], the tortuous course of unequal dilated vessels with centripetal orientation and high velocities as comparing with the rest of the breast. When adding the RTSE to the DDUS, the accuracy of the diagnosis of the breast cancer in gynecomastia as well in female breast is over 95% in the presented papers and in our experience (Figure 28), but unfortunately there are few publications so far, because of the recent use of RTSE and of few sonographers trained on DE [5, 9].

**DISCUSSIONS**

**Endocrine-imaging-pathological correlations in gynecomastia**

- A report of a positive correlation between E2 and FSH (r = 0.67, p < 0.0001) in a group of 106 infertile men [14] confirms the correlation of the hyperestrogenism (gynecomastia) with the infertility (hypogonadism). Importance of this study: *gynecomastia as a symptom could be easily demonstrated by DDUS and easier to interpret than the more expansive set of hormonal blood tests.*

- A report presented a 10-year-old boy with congenital adrenal hyperplasia and associated hyperplastic testicular adrenal rests, which had high serum concentrations of 17-OH progesterone (17-OHP), estradiol (E2), testosterone (T), and basal and TRH-stimulated TSH and PRL, but normal thyroid hormones (T3, T4, FT3, FT4) and thyroxine-binding globulin (TBG). This case suggests that E2 does stimulate the secretion of basal and TRH-elicited both TSH and PRL [19]. Importance: *this report confirms the pathogenic*
relation between E2 (gynecomastia) and TSH and PRL, and also the possibility of presence of a goitre with normal T3, T4.

- Hyperprolactinemia in man has multiple etiologies [13], and DDUS could be a good follow-up examination, less expansive and time-consuming than the serologic hormonal tests.

- Hyperestrogenemia may be related to the coronary thrombosis in man [20], similar to the menopausal substitution treatment. Importance: when floride gynecomastia or ductal hyperplasia are demonstrated on DDUS, the serum concentration of E2 must be evaluated as a risk factor for coronary thrombosis.

- A report presents a 71-year-old man with clinical signs of Kennedy disease including dysarthria, dysphagia, palatal and oral mandibular fasciculations, lower-extremity weakness, gynecomastia, and testicular atrophy, proved the correlation with an increased estrogen level of 180 to 220 pg/mL [21]. Importance: this paper demonstrates gynecomastia in elderly man as a symptom of hyperestrogenemia, thus it must be considerate as a pathological condition, while in the literature the gynecomastia in elderly is "physiological".

- There are a lot of drugs associated with adrenal adenoma: Adalat, Avastin, Clofarabine, Evista, Fosamax, Hydrochlorothiazina, Nifedipine, Sildenafil, Tegretal, Valsartan, Zocor, Zoledronic etc. It seems logically to present the risk to the patients and to recommend a screening US examination of the mammary area and of the adrenals.

- Male breast cancer coexists with gynecomastia, but there are confusions in the management of these diseases, while the classical methods of diagnosis could not demonstrate the benign mammary ducts. The general assumption is gynecomastia is benign or physiological; however, 50% of cases with gynecomastia are selected for mammography [22]. In elderly males gynecomastia makes up 65% of all breast lesions; 25% is carcinoma and 10% are other lesions. In fact, estrogen receptors are more commonly present in males with breast cancer than in women, occurring in 75-94% of males with cancer [23]. The breast tissue in males responds to the hormonal stimulation, with growth of ducts and connective tissue resulting in gynecomastia. The overwhelming histologic subtype of breast carcinoma in men is ductal or unclassified (93.7%), followed by papillary (2.6%). Infiltrating lobular carcinoma is rare in males, likely because of the rarity of terminal lobules in the male breast. Importance: DDUS can demonstrate both the gynecomastia and cancer, with visualisation of non-palpable infracentimetric tumors.

- In our experience, floride gynecomastia with salient new vasculature or the type with ductal hyperplasias are correlated with hyperestrogenemia at the time of the examination, while chronic gynecomastia may be associated with normal values of the steroid tests.
Images for this section:

Technique of examination in DE with application in gynecomastia:

1. Long linear probe with water bag device
   - better than the panoramic view (SieScape techniques) because of high precision and thus better reproducibility of the scans;
   - the water-bag allows the reproducing of the breast shape without deforming and improves the examination of the skin and of the subcutaneous fat.

2. Short higher frequency linear probe
   - better resolution for the characterisation of the structures of interest;
   - the probe of choice for Doppler applications and RTSE.

Fig. 0: Transducers used in DE/DDUS

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Fig. 0: Water-bag probe scans

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**Fig. 0:** High frequency probe applications

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Fig. 0: The radial axis

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The transversal, sagittal or randomly oblique scans used still by the large majority of the sonographers are non-anatomical, difficult to analyze and are looking just for a lesion in an unknown surrounding “breast tissue”. This technique is susceptible to omissions/“blind” regions of the breast and the examination is not reproducible.

The radial and antiradial scans used in DE (examples colored in yellow), are logical, repeatable and easy to locate respecting the clockwise annotation; first, we are searching the normal anatomy of the whole breast and then the eventually lesion/abnormality related to the normal anatomical architecture.

**Fig. 0**: "Classical" US versus Ductal Echography (DE)

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Case 1: 48-year-old male patient presented the small/normal mammary bud indistinguishable from the nipple; there is no glandular stroma and the vasculature is reduced to the periareolar anatomical ring. There is an amount of fatty tissue behind and all-around the nipple representing the pseudo-gynecomastia.

**Fig. 0:** Pseudo gynecomastia I

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Case 2: 49-year-old male patient with pseudo-gynecomastia, presenting a mass located subdermal, anterior to the *fascia superficialis* (▲), with a thin hyperechoic capsule (●), discrete hyperechogenicity, posterior acoustic enhancement, no detectable vasculature and score 2 Ueno with low FLR 3.32. This is a typical aspect for lipoma.

**Fig. 0:** Pseudo gynecomastia II

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**Fig. 0:** Recent/acute florid gynecomastia

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**Case 6:** 1-year-old male presenting bilateral symmetrical gynecomastia, with probable exogenous etiology (nutritional); motion Doppler artefacts are the inconveniences of the examination at this age, but the anatomy is well demonstrated.

**Fig. 0:** Infantile gynecomastia

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**Fig. 0:** Pubertal gynecomastia

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**Case 9:** DDUS in a 24-year-old male patient demonstrates on R9:00 – 3:00 the enlarged mammary bud as a hypoechoic retroareolar area, with irregular borders represented by short ductal branches, surrounded by little amount of stroma. This is the aspect of “small” gynecomastia.

**DDUS on L3:00** demonstrates the advanced gynecomastia with a developed mammary lobe: ducts with the central line sign and stroma prolonged by the Cooper’s ligaments (>). The composed double screen image, with contiguous radial scans, was performed with a high resolution probe to demonstrate the whole long axis of the mammary lobe.

**Fig. 0:** Chronical adult gynecomstia

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**Fig. 0:** Chronic adult asymmetrical gynecomastia

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Fig. 0: Familial gynecomastia - the son

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Case 12: 52-year-old patient, the father, with chronic gynecomastia (4 years) presents the mammary lobes with long ducts, irregular ductal thickening/hyperplasias; the hyperechoic stroma is larger and there are thick premammary and retromammary fatty layers (type of mixte breast in woman).

Fig. 0: Familial gynecomastia - the father

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**GALACTORRHEA IN MAN**

Case 13: 54-year-old male patient after right gynecomastia, misdiagnosed and partially removed (segmentectomy), with local evolution and finally contralateral development. Clinically the patient presented exophthalmia and Doppler US demonstrated diffuse goitre with moderate increasing of the vascular activity compared to a witness patient, as we technically recommend.

**Fig. 0:** Galactorrhea in man I

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The same case: DDUS demonstrated large central ductal-ampullar ectasia (▲), peripheral thickened lobules connected to the ending ducts (▲) and new vasculature with arterial/venous flow, similar to the lactating breast. Previous surgical treatment had proven milky ducts.

Fig. 0: Galactorrhea in man II

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**Fig. 0: Galactorrhea in man III**

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HYPERESTROGENEMIA IN MAN

Case 14: DDUS scan at L 4:00 visualises a typical mammary lobe in a 20-year-old male patient, similar to a lobe in a dense female breast; the segmental thickening of the ducts up to 2 mm with the presence of the characteristic central line sign and without periductal new vasculature is suggestive for ductal benign hyperplasia, correlated with a high hyperestrogenemia.

Chronic gynecomastia with thin ducts and without salient development of vasculature, clinically not painful, may present normal values of the sexual hormones.

Fig. 0: Hyperestrogenemia in man I

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**Fig. 0**: Hyperestrogenemia in man II

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Case 15: Recent gynecomastia in a 33-year-old male patient with Cushing's syndrome: obesity, round-shaped face, red skin vergetures, folliculitis and arterial hypertension; the couple's infertility could be correlated with these endocrine disorders [14].

DDUS demonstrates at L10:30 the branching mammary bud and lobes with predominantly parenchymal component (^) and thin stroma (\), mimicking the fatty tissue; a localized hypoechoic thickening of the superficial layers of the skin is due to folliculitis (▲).

**Fig. 0:** Hyperestrogenia and adrenal adenoma I

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Fig. 0: Gynecomastia and adrenal adenoma II

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**Hyperestrogenemia in man**

The same case: Axial T1WI and T2WI MRI demonstrate a right adrenal mass with heterogeneous hypersignal and with mark on the right kidney. WFT1 WI changes in a heterogeneous hyposignal, demonstrating the lipid component of the tumor.

**Fig. 0:** Gynecomastia and adrenal adenoma III

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**Hyperestrogenemia in man**

The same case: coronal T1WI demonstrates the pathological mass located in the area of the cortical of the right adrenal gland, indistinct from the perirenal fat, located between the medullar adrenal area and the right kidney.

The adrenal medulla is the only one seen on MRI and CT, while US visualizes all the adrenal gland without differentiation between its components, thus the volume of the lesion is overestimated in US!

Axial “out-of-phase” images demonstrate the change in hyposignal of the tumour, the “chemical shift”/“signal dropout” sign, characteristic for the adrenal adenoma.

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**Fig. 0:** Gynecomastia and adrenal adenoma IV

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Gynecomastia in Cushing's Syndrome (2)

Case 16: A 54-year-old male patient with Cushing’s syndrome and typical gynecomastia, with the retroareolar branching bud and the specific glandular stroma; the ducts are typical, with the central hyperechoic line sign on DE, but the RTSE better demonstrates the breast parenchyma with high elasticity, in red color, with the score 1 Ueno/Tsukuba and low FLR 0.66.

FBU is useful in the characterization of the malignant lesions as well of the benign lesions and of the anatomical structures.

Fig. 0: Gynecomastia in Cushing's Syndrome

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Case 17: 63-year-old male patient having asymmetrical gynecomastia with advanced differentiation on the right side; the left mammary bud presents a pseudotumoral hypoechoic aspect, with irregular margins represented by the developing ducts demonstrated on RTSE (score 1 Ueno and very low FLR 0.56-0.60).

Fig. 0: Full breast Ultrasonography of gynecomastia

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**Fig. 0:** Gynecomastia and goitre

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BREAST CANCER AND GYNECOMASTIA

General assumptions in the literature:

✓ When it does occur, male breast cancer occurs in one breast and it is seen in older males.
✓ In the majority of cases of gynecomastia, there is no cancer associated; however, any male over the age of 50 with a sudden increase in a single breast is suspect.
✓ Breast cancer in males presents just like in females: a mass is identified in a single breast, there is generally no pain or nipple discharge but the mass may be hard to touch.
✓ The only way to tell if it is cancer is by a biopsy.

Fig. 0: Male breast cancer and gynecomastia

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DDUS AND MALIGNANT GYNECOMASTIA

Case 19: DDUS in a 52-year-old male demonstrates at L 4:00 a hypoechoic eccentric mass, with irregular spicular borders represented by thickened connected ducts, the long axis parallel with the lobular radius and presenting malignant-type new vascularity: multiple poles, with acute angular penetration [17], centripetal orientation and tortuous course. The extension of the tumoral margins following the ducts and the vessels along the Cooper's ligaments («) is highly predicting for malignancy. RTSE would be concluding as an additional tool, avoiding unnecessary biopsies [18].

MALE BREAST CANCER OF INVASIVE DUCTAL CARCINOMA TYPE CAN BE DIAGNOSED ON DDUS/ FBU WITHOUT BIOPSY!

Fig. 0: DDUS and male breast cancer

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Conclusion

We must evaluate the utility of DE and DDUS, in addition to the "classical" methods of diagnosis of the gynecomastia, by multicentric comparative studies (Figure 1).

DDUS and better consecutive FBU is a new, performing and non invasive tool in the diagnosis of the male breast cancer (Figure 2).

The differential diagnosis of the gynecomastia is easier using DDUS, because the classification of the lesions that do/ do not occur in man could be done referring to the connection of a lesion to the ductal tree (Figure 3).

DDUS is suitable instead of the "classical" US because it is a standardized technique of breast imaging:

- applicable for all (both sexes, any age);
- it is not sonographer dependent, but it is only anatomical-dependent;
- it could be easily repeated identically;
- it is readable by everyone.

DDUS is the unique anatomical imaging method of breast diagnosis:

- useful in the positive and the differential diagnosis of gynecomastia;
- proves the connection of the possible pathological masses to the mammary ductal-tree.

The radial US demonstrates the precise location and morphology of the mammary ducts:

- demonstrates the pathological ducts: ductal ectasia, ductal hyperplasia;
- useful in the etiological endocrine diagnosis with targeted hormonal tests (prolactinemia in ductal ectasia, oestrogens in floride gynecomastia and ductal hyperplasia);
- recommended as follow-up examination (i.e. in the treatment with bromocriptine, or antiandrogens in prostate cancer etc [13]).
The vascular analysis by Doppler techniques is useful in the positive diagnosis of recent/florid gynecomastia and in the diagnosis of the pathological masses:

- it must be avoided the overestimation of Doppler as a unique US finding;

- the value of Doppler or contrast enhanced US (CEUS) is similar to contrast MRI of the breast, but Doppler is less expansive; however, the use of CEUS proved better results in the "classical" US and DE.

- Doppler characterisation is useful in addition to the Stavros [25] and US BI-RADS criteria [26], and the most pitfalls in the breast US are due to neglecting Doppler features (malignant lesions with benign Stavros criteria, pseudo-malignant lesions on classical US, indeterminate lesions).

DDUS supplemented with RTSE represents the FBU, the only accomplished US examination of the breast and of the soft tissues, but there are some problems:

- not yet standardized RTSE: different machines with different soft and scales of interpretation;

- not yet enough trained sonographers in DE and RTSE.

FBU is recommended before the biopsy and the surgical treatment, especially in gynecomastia or paediatric patients, avoiding the inconvenient side-effects such as pain, haematomas [27] or scars.
**Table 2. The Diagnosis of Gynecomastia**

<table>
<thead>
<tr>
<th>Clinical presentation</th>
<th>Age newborn - 70’s, soft, mobile on the pectoral fascia, tender in florid stage or painless, subareolar/central but asymmetrical, unilateral/ bilateral, usually associated endocrine pathology</th>
</tr>
</thead>
</table>
| Mammography           | Limited applications related to the age and breast size, does not visualise the ducts, requires biopsy:  
  • Nodular glandular (acute florid phase): fan shaped  
  • Dendritic (chronic fibrotic phase): subareolar density with extensions into fat  
  • Diffuse glandular: similar to the dense breast in woman |
| Breast MRI:            | Less availability, does not visualise the ducts, less specific for the benign lesions, requires biopsy |
| Classical US           | The hypoechoic retroareolar “breast tissue” (incomplete characterisation), requires biopsy |
| Doppler Ductal US with RTSE = FBU | Mammary bud with more or less developed branching ducts, surrounded by stroma and with new vasculature better visualised in the florid stage; simple / pathological ducts; RTSE demonstrates soft parenchyma; not usual biopsy required |

**Fig. 0:** The methods of diagnosis of the gynecomastia

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CONCLUSIONS

Table 3. The Diagnosis of Breast Cancer in Man

<table>
<thead>
<tr>
<th>Clinical presentation</th>
<th>Age 60’s, soft or hard, mobile or fixed, usually painless, subareolar usually eccentric, usually unilateral, recent evolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mammography</td>
<td>Limited applications due of breast size, does not visualise the ducts, rarely evidence of micro-califications, requires biopsy [22]:</td>
</tr>
<tr>
<td></td>
<td>• Large mass: lobulated border</td>
</tr>
<tr>
<td></td>
<td>• Small mass: spiculations</td>
</tr>
<tr>
<td>Breast MRI:</td>
<td>Less availability, does not visualise the ducts, paramagnetic contrast agents, requires biopsy</td>
</tr>
<tr>
<td>Classical US</td>
<td>The hypoechoic retroareolar eccentric mass similar to the “breast tissue” (incomplete characterisation), more or less regular contour, requires biopsy</td>
</tr>
<tr>
<td>Doppler Ductal US with RTSE = FBU</td>
<td>Pathological mass connected to ducts, new vasculature with tortuous shape, increased incidental angle of penetration [17] and centripetal orientation; RTSE with score 4 or 5 Ueno/Tsukuba and high FLR &gt; 4.30 – 4.70; biopsy ±</td>
</tr>
</tbody>
</table>

Fig. 0: The diagnosis of breast cancer in man

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**Table 4. Lesions that Do Occur in Man [24]:**

<table>
<thead>
<tr>
<th>Gynecomastia with secondary lesions (related to breast parenchyma):</th>
<th>Non – gynecomastia</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Ductal hyperplasia</td>
<td>- Pseudogynecomastia</td>
</tr>
<tr>
<td>- Ductal ectasia (galactorrhea)</td>
<td>- Myofibroblastoma</td>
</tr>
<tr>
<td>- Papilloma</td>
<td>- Granular cell tumor (neural origin)</td>
</tr>
<tr>
<td>- Adenoma</td>
<td>- Epidermal inclusion cyst</td>
</tr>
<tr>
<td>- Fibrocystic change</td>
<td>- Cystic lymphangioma</td>
</tr>
<tr>
<td>- Diabetic mastopathy</td>
<td>- Varix</td>
</tr>
<tr>
<td>- Paget’s disease (more common than in woman)</td>
<td>- Leiomyoma</td>
</tr>
<tr>
<td>- Breast cancer</td>
<td>- Lipoma</td>
</tr>
<tr>
<td></td>
<td>- Pleomorphic hyalinizing angioectatic tumor of soft tissues</td>
</tr>
</tbody>
</table>

**Table 5. Lesions that Do not Occur in Man or Are Extremely Rare**

(there are rare cases with presence of the lobules, as precursor lesions):
- Fibroepithelial lesions: Fibroadenoma
  - Phyllodes tumor
  - Carcinosarcoma
- Lobular carcinomas

**Fig. 0:** DDUS and the differential diagnosis of gynecomastia

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