

Review Article

DUCTAL ORIENTED DOPPLER SONOELASTOGRAPHY – THE ALTERNATIVE OF CHOICE TO DRAW THE BENIGN VERSUS MALIGNANT FRONTIER IN BREAST DISEASES

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Abstract

The trial is aiming to assess *Ductal Oriented Breast SonoElastography* (DODSE) compared to mammography and to the pathological reference, hoping to reduce furtherly the number of breast biopsies. For some unclear breast lesions defined as BI-RADS 3 or 4, DODSE could stand for referee, as well as MRI or biopsy. Between 2008-2011 we evaluated 1758 patients by sonography; 232 patients were found to have unclear nature lesions and submitted to digital fullfield mammography, elastography and pathological examination. Considering the pathological report, 207 of the 232 (89.22%) were conclusively redefined as benign or malignant, but only 179 (77.15%) by digital mammography. Considering the whole trial, with 1526 patients categorically classified by ultrasonography and the additional 207 patients conclusively classified by sonoelastography, in 98.57% of patients the DODSE evaluation proved to be correct. This included 8 of our 11 cases of DCIS in our trial.

Key-words: *Ductal Oriented Breast SonoElastography (DODSE), mammography, breast biopsies, unclear breast lesions*

Rezumat

Studiul își propune să evalueze *SonoElastografia Doppler Ductal-Orientată* (SEDDO) comparativ cu mamografia sub arbitrajul anatomiei patologice, în speranța de a reduce în viitor numărul biopsiilor mamare inutile. Pentru unele dintre leziunile mamare incerte,

definite ca BI-RADS 3 sau 4, SEDDO poate fi discriminatorie, la fel ca RMN sau biopsia. Între 2008 și 2011 am evaluat 1758 paciente prin ecografie; 232 paciente au prezentat leziuni de natură neclară și au fost examinate prin mamografie digitală, elastografie și biopsie. În urma rapoartelor anatomo-patologice a rezultat că 207 (89,22%) din cele 232 paciente au fost corect clasificate ca leziuni benigne sau maligne de către SEDDO, în timp ce numai 179 (77,15%) dintre ele au fost categorisite corect de către mamografia digitală. Având în vedere întregul lot, cu 1526 de paciente clasificate fără echivoc de către ecografie și cele încă 207 paciente cu leziuni clarificate în urma sonoelastografiei, SEDDO s-a dovedit exactă la 98,57% dintre paciente, inclusiv în 8 din cele 11 cazuri de carcinom ductal in situ din lot.

Cuvinte cheie: *SonoElastografia Doppler Ductal-Orientată (SEDDO), mamografia, biopsiilor mamare, leziunile mamare incerte*

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Introduction

The border between fibro-cystic disease and (micro-)invasive carcinoma is crossing-over the dysplasias with epithelial proliferation (either typical or atypical) as well as carcinomas in situ of all grades (low, mild or high).

The lesions defining the benign-malignant frontier are endo-cystic proliferation, severe or atypical dysplasia, plasma cell mastitis, borderline tumors (such as Phyllodes tumor) or even in situ carcinomas (DCIS, LCIS). Geographically, the border may be designed by the intraductal dissemination, the presence of multiple neoplastic foci or lymphatic diffusion nodules (1, 2).

But who is drawing the benign versus malignant (B/M) frontier? These won't be the patients, ranging from indolence to cancerofobia, nor the practitioners, often confused by misjudgments and physical exam's limitations. But they may be the explorers (radiologists or ultrasonographers) assessing the lesions by the BI-RADS. The no man's land will be a bit confusingly stated by the scores of 3 (meaning that the lesion is very probably benign, but asking, however, a close follow up) or 4 (meaning that lesion's nature is not clear and requiring breast biopsy). The only ones to be sure about B/M discrimination are the pathologists, but they need a breast biopsy for this purpose.

Concerning which images shall we trust and how much it is to be said that digital mammography has 30% false negative and 10% false positive results and can suggest a borderline lesion showing areas of microcalcifications, poorly defined dense lesions or architectural distortions. Better data are offered by the *ductal oriented Doppler sonoelastography* (DODSE), defined by 10% false positive and 5% false negative results, revealing evidence of epithelial proliferation, slightly irregular shape, blurred limits, posterior shadowing, ductal

relationship, increased vascular density, different speeds of blood stream, Cooper ligament and/or skin thickening.(3). Addition of sonoelastographic data may reveal the lack of compressibility. Magnetic Resonance Imaging may have 3% false negative and 40% false positive results mainly based on revealing slightly irregular lesions with rapid uptake, short plateau and rapid wash out signal. The best seems to be PET scan, with only 1% of false negative and 5% false positive results (4).

Among these imaging methods DODSE may be proffered because it has no contraindications, it is harmless (no trauma, no radiation, no claustrophobia), it is affordable and accessible and repeatable whenever is needed. It reveals the different breast tissues as well as the breast (ductal) anatomy and also the lesion's structure, vascularisation and compressibility, fair enough to characterize correctly the lesion's nature. In order to reach this goal, sonography had to fulfill a long journey, starting with the first breast scanning of Wild and Reid (1953), renouncing in mid seventies at the tub immersion for hydro-gel lubrication, introducing in the eighties the multicrystal transducers and continuing to improve in the nineties, achieving the use of harmonic frequency, digital signal, Doppler assessment, contrast dye and immersion bag [5, 6]. These enabled breast sonography to differentiate benign from malignant lesions, especially in young or pregnant patients, in case of breast implants and whenever mamography is questionable. Then the American College of Radiologists advocated sonography as the second breast imaging method (after digital mamography), but still didn't recommend it for screening purposes. In the past decade, sonography achieved 3D representation, computer assisted diagnosis and elastography (DODSE), becoming more prone to standardization and almost operator independent. Concerning elastography, an application allowing the imaging assessment of tissue structure's elasticity, it took some 15 years from designing the principle by Ophir and Parker (1991) to render the technology available for Hitachi by Tsuyoshi Shiina, Ako Itoh and Ei Ueno (from Tsukuba University, Japan) till Ako Itoh proposed the qualitative elastographic (Tsukuba) (6) score. According to it the lesion's compressibility may be classified as:

- 1 = uniform, similar to surrounding tissues (defining normal structure)
- 2 = not uniform, with "puzzle" pattern (defining mild dysplasias);
- 3 = low compressibility (with some peripherically compressibility defining breast fibroadenoma or „three colors badge" image in case of a large cyst)
- 4 = uniformly uncompressible lesion in a compressible atmosphere
- 5 = absolutely uncompressible lesion laying in a less compressible atmosphere

These are to be combined to the morphological sonographical features suggesting malignancy (spicular extensions, taller than wide, angular margins, posterior shadowing, hypodensity, small calcifications and ductal extension). The principle of elastography consists in defining soft tissues as viscoelastic structures (behaving as liquid and solid in the same time), characterized by:

- *Elasticity module* (Young) = E (elastic deforming tension)
- *Shear module* = G (shearing/deforming tension)
- *Bulking module* = K (volumetric tension/volumetric bulking)
- *Poisson ratio* (transverse to axial tension)

The optimal evaluation consists in assessing the shearing +/- bulking modules (3D elastography) with varieties inducing compression from outside the tissues (vibrating compression or decompression) or inside the tissue (by the supersonic compression). The differentiation comes from the observation that malignant lesions may be at least 9 times less compressible than subcutaneous soft structures! [7, 8, 9].

Material and method

We used elastography for the evaluation of hypodense masses, areas with microcalcifications, zones with structural or vascular distortions, especially if the axillar lymph nodes were enlarged. Considering the technical aspects we restricted its indications in case of unhomogenous structures, when no masses or distortions were present, for large lesions (dimensions of more than 2.5 cms), in presence of scars or fat necrosis or in coloidlike lesions. We tried to achieve the best sonographical conditions by a Hitachi EUB 6500 US scanner, using always the ductal approach and Doppler assessment performed using a high resolution panoramic multicrystal transducer (9.6 cms) with immersion bag. Performing the elastography, we tried to center the assessment on the region of interest, to encompass sufficient breast volume around the lesion, to avoid having ribs within the evaluation frame, to inflict low pressure (not to deform the structures) and to combine the qualitative feature evaluation with the numeric quantification.

Our trial consisted in evaluating all the patients presenting themselves for an initial breast diagnosis between January 2008 to December 2010. Out of the 3926 breast sonograms performed in that period, 1758 were initial presentations and were included in the trial. Usually conventional morphology and Doppler offered enough data for the benign versus malignant discrimination. This was the case of 1526 of patients (86.8%), but 232 patients belonging to this trial (13.2% of 1758) were unconclusively classified (BIRADS 3 or 4) by conventional sonography. They were furtherly submitted to elastography. Being informed that no imaging

method can provide certain results and they have a suspicious lesion, the large majority of those patients (202) consented a microscopic evaluation consisting in 81 core-biopsies and 121 FNA cytologies. If irrelevant, the pathological examination was repeated (in 19 patients). All the 1758 patients were followed up to 18 to 48 months.

Results

The trial showed up a good capacity of ductal oriented Doppler sonography which was able only by itself to classify correctly 1526 of the 1758 patients (86.8%), which is consistently better than mammography, obtaining some 70-78% correct assessments. Out of the 232 (13.2%) patients with lesions of unclear nature classified BI-RADS 3 or 4, elastography helped to clearly discriminate benign versus malignant nature in 207 cases. In 6 patients the diagnostic was invalid (4 DCIS, 1 colloid cancer, 1 scar) and in 19 patients BI-RADS rest unconclusive even after performing sonoelastography (retroareolar lesions, deep lesions in large breasts, marginal lesions, lesions in areas of fat necrosis or fibrosis).

Finally, the 1526 patients conclusively BI-RADS classified by sonography (86.8%) altogether with the 207 supplementary patients conclusively reclassified on elastography (total 98.57%). In 6 cases (0.34%) the classification proved to be wrong and in other 1.43% of cases, it remained inconclusive, but these results are quite acceptable. About the benign-malignant frontier, it is to be highlined that in 16 cases of suspicious ductal thickening with elastographic classification of BI-RADS 5, multiple guided core-biopsies identified 14 DCIS.

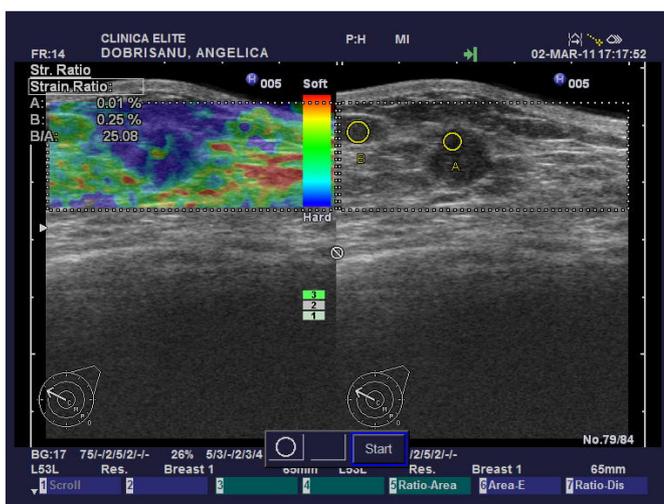


Figure 1: Invasive ductal carcinoma (9x8mm)

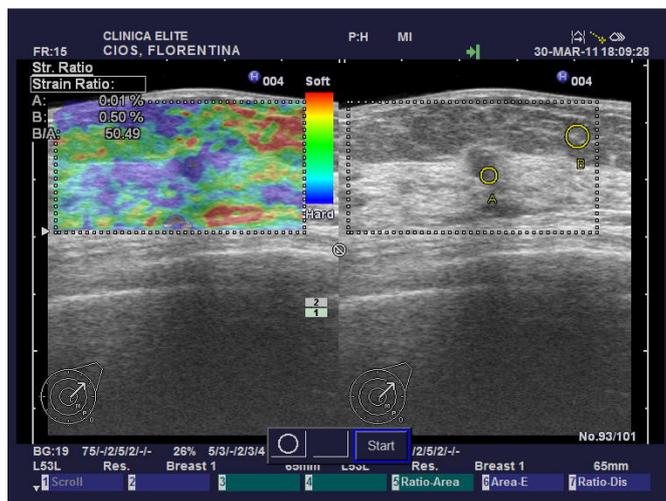


Figure 2: Invasive lobular carcinoma (0.7mm)

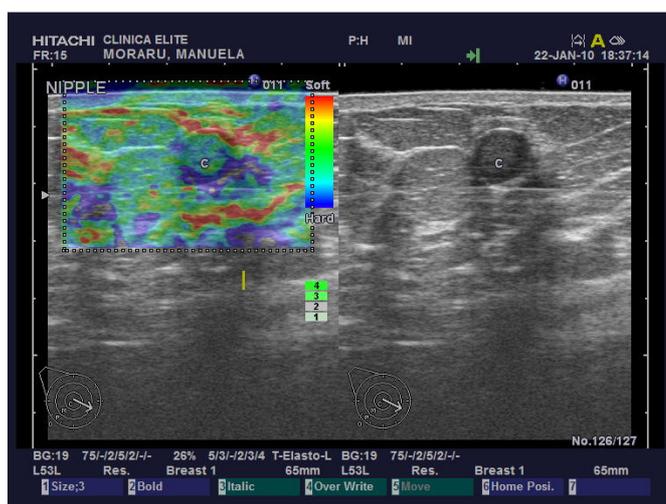


Figure 3: Complex cyst and DCIS

In this trial, combining Doppler with ductal-oriented sono-elastography driven to a more than fair sensitivity of about 89.2%, an excellent specificity of 96.6% and an accuracy of 90.9%.

Discussions

The screening method for breast cancer remains the mammography, even breast specialists are increasingly dissatisfied by the radiological assessment. Breast sonography, the most unfairly underestimated method of breast imaging, becomes now a real challenge for the most valued means of breast assessment, the

MRI. In fact, it is the only method able to reveal breast lobe anatomy and to correlate the lesion with the network of ducts and Cooper ligaments, most important in understanding breast structures and dysplastic pathology. The addition of elastography is enhancing method's efficacy like providing an infrared lens to a snyper. Michel Teboul described mammography like „a wrong tool, displaying a wrong tissue in a wrong way” because it is painful, uses radiation and is blind to breast epithelium, seeing only indirect signs (as microcalcifications). This is in contrast with harmless, office practice suitable and available tool, is able to draw the anatomy of the breast from ducts to lobules and vascular frame of Cooper ligaments, to see sharply the initial point of breast pathology (very often where the ligament is crossing the duct) [10, 11].

We considered this and were amazed by the very rich amount of informations given by DODSE. Combined with elastography, the ductal sonography could identify microinvasive cancers of 4 mms in largest diameter and could strongly suggest the presence of a DCIS (proved in 8 of 11 cases in our trial). Considering the elasticity of fat (18-22 kPa), normal gland (28-66 kPa), fibrous tissue (96-144 kPa) and breast cancer (22-560 kPa), the cut-off 95% being between 100 and 140 kPa (5 to 7 times less compressible than the fat). This feature can discriminate very accurately benign from malignant, fact noticed by the majority of authors, even there are also unsatisfied users. Some explanations may be a wrong use of the method (ignoring anatomy), limited expertise („encyclopedical” sonographer), bad indication (large tumor in small breast) or debatable choice of equipment. (Tabel no 1).

Tabel no 1. statistical dates of the literature

	Ss /US	Ss /elasto	Sp /US	Sp /elasto	Ac /US	Ac /elasto
Tanter, 2005		84		92		
Itoh, 2006	83.3	89.3	86.7	93.1		
Schaefer, 2006	57.8	76.0	96.1	96.9	69.2	82.9
Thomas, 2007		77.6		91.5		
Tan, 2008		78.9*		98.5*		89.5*
Voiculescu, 2011		89.2*		96.6*		90.9*

The prospectives of DODSE lay on its excellent conventional diagnostic skills, but also in its use as extended diagnosis facilities (real time FNAC or core biopsy guidance as well as guidance for a cyst evacuation or for properly injecting contrast dye for santinel node or even imaging assistance for ductoscopy). But one must not forget its therapeutic facilities such as radioablation probe guidance, assesement for evacuation or lesional radioablative changes, assesement for drainage tube's position or postchemotherapeutic assesement of lesion's size or volume, lesion's changes in morphology, density, vascularity or compressibility [11,12,13].

The post-therapeutic facilities of DODSE are the assessment of the intra-mammary scar and of the gland's structural alignment, the possibility to reveal easily hematomas, seromas, abscesses or postoperative necrosis as well as phlebitis and (lymph)oedema, duct ectasiae due to stenosis or ligation and to show the presence of enlarged lymph nodes or axilar fluid collections. After esthetic surgery, DODSE should analyze implant's situation in terms of position, folding, peri-implant collections, implant's ruptures and capsular contraction. After reductional mammoplasties, it can reveal bridging scars, oily cysts or other forms of fat necrosis [14, 15].

Speaking about prevention at the benign – malignant frontier we emphasize patient's role (in terms of active life style, healthy diet, regular self breast control), the much more important role of periodic breast imaging control (breast cancer screening!), the use of breast biopsies whenever the patient has an inconclusive BI-RADS of (3)-4. In terms of action, we may speak about preventional therapy (for all moderate to severe discrynias and displasias, tamoxifen or raloxifen being the favorite drugs of prevention), but also about "surgical prevention" (solid lesions' removal, with proper study of the margins)

Conclusions

- Benign versus malignant discrimination isn't always neat and perpetual;
- Standard report according BI-RADS is mandatory to establish the optimal attitude;
- Associating breast imagistic methods results in enhancing diagnostic efficacy;
- Breast imaging may draw the frontier with some liabilitaty, but for unclearly defined lesions - biopsy is mandatory!
- The sono-elastography may significantly reduce the ratio for lesions of uncertain nature, so it may reduce the need for breast biopsies.

- May be, somehow, we may talk about medical or surgical prevention at the benign versus malignant frontier, being more prone to remove solid lesions appeared after the age of 40.

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