



ȘCOALA DOCTORALĂ

REZUMATUL TEZEI DE DOCTORAT

Contribuția sonoelastografiei în diagnosticul leziunilor glandei mamare

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Cuvinte cheie: leziuni mamare focale, ecografie, sonoelastografie, clasificarea BI-RADS, scorul Tsukuba, chisturi mamare, parametrii de culoare, modificari mastozice focale

INTRODUCERE

Cancerul mamar si patologia sanului in general constituie o problema majora de sanatate publica, datorita prevalentei crescute atat la nivel national, cat si international (1 din 8 femei dezvolta cancer mamar pe parcursul vietii). Diagnosticul timpuriu si corect al cancerului mamar sau a leziunilor cu risc ale sanului reprezinta desideratele cheie in lupta cu aceste afectiuni, adeseori silentioase si pot avea un impact fundamental atat socio-economic cat si psihologic.

Progresele imagistice ale ultimei decade au imbunatatit semnificativ diagnosticul senologic. In ultimii 5 ani, alaturi de tomosinteza, rezonanta magnetica functionala, imagistica optica-moleculara, se remarca si sonoelastografia ca o tehnica non-invaziva, extrem de accesibila si cost-eficienta, integrata cu succes in evaluarea ultrasonografica a leziunilor focale mamare.

Teza cuprinde două secțiuni importante: o scurtă prezentare a stadiului actual al cunoașterii și o parte care conține cercetarea personală. Prima parte a lucrării cuprinde datele necesare pentru a aborda ipoteza de lucru a cercetării: *Care este contributia sonoelastografiei in ameliorarea si eficientizarea diagnosticului leziunilor mamare?* Principalele rezultate sunt rezumate în patru capitole. Rezultatele obtinute se inscriu in gama larga de studii din ultimii ani care atesta valoarea sonoelastografiei si totodata contin elemente de inovatie prin ipoteze de lucru abordate fie in premiera, fie dintr-o perspectiva originala. Este de mentionat faptul ca o parte din studiile prezentate au fost intre primele aparute in literatura de specialitate, fiind ulterior citate si intr-o carte de imagistica oncologica functionala de circulatie internationala.

Cercetarea de față a fost posibilă în baza a 2 granturi desfasurate in cadrul Universitatii de Medicina si Farmacie "Iuliu Hatieganu" (CNCSIS cod 1409, nr. 44/17.05.2006 and ELASTOBREAST-CEEX VIASAN nr. 149/2006), programe care au facut posibila achizitia primului aparat de ultrasonografie cu modul elastografic din Cluj Napoca si totodata au permis obtinerea unui *software* inovativ de analiza a parametrilor de culoare –software dezvoltat in colaborare cu Universitatea Tehnica din Cluj Napoca.

Studiile au fost aprobate de Comitetul de Etică al Universității. Au fost considerați pentru evaluare pacienți cu leziuni focale mamare investigati in cadrul Departamentului de Radiologie din cadrul Facultatii de Medicina din Cluj Napoca, în perioada mai 2007-decembrie 2013. Standardul de aur a fost reprezentat de rezultatele histopatologice. Pacienții au semnat consimțământ informat cu privire la examinarile efectuate și înainte de toate intervențiile diagnostice, cum ar fi biopsia mamara. S-a renunțat la consimțământul informat scris pentru analiza retrospectivă a datelor. Lotul de studiu a fost selectat folosind criteriile de includere și excludere descrise în fiecare studiu.

CONTRIBUȚIA PERSONALĂ

Studiul I. Diagnosticul senologic: Analiza concordantei dintre clasificarea BI-RADS si scorul elastografic Tsukuba

Scopul studiului. De a stabili corelatii intre clasificarea BI-RADS si scorul elastografic Tsukuba, sisteme folosite in evaluarea leziunilor mamare. Un obiectiv secundar a fost identificarea tipului de leziuni mamare care ar beneficia cel mai mult de o evaluare elastografica.

Material și Metodă. S-au evaluat prospectiv un număr de 92 de pacienți cu 129 de leziuni mamare focale, detectate ecografic utilizand un aparat de tip Hitachi EUB 8500. Fiecare leziune a fost incadrata intr-o clasa BI-RADS si a primit un scor elastografic, conform criteriilor Tsukuba. Diagnosticul final s-a bazat pe biopsii obtinute percutan sau analiza pieselor de excizie chirurgicala. Leziunile tip fibroadenom sau nodul mastozic cu un caracter stationar pe durata a cel putin 3 ani, au fost considerate benigne.

Rezultate. Concordanta dintre sistemul BI-RADS si scorul elastografic in clasificarea ca benign sau malign a leziunilor mamare a fost de 81% cand au fost luate in calcul toate categoriile BI-RADS si respectiv de 78% cand analiza s-a facut excluzand categoriile tipic benign-BI-RADS 2, respectiv tipic maligne-BI-RADS 5.

Scorurile elastografice 1, 2 si BGR s-au corelat bine cu categoriile BI-RADS 2 si 3 (chisturi, hamartome, lipome, fibroadenome non-palpabile). Fibroadenomele palpabile, initial incluse in clasa BI-RADS 4a sau b au prezentat in general scoruri mici elastografice (1-2), exceptia fiind data de fibroadenomele vechi, hialinizate sau partial calcificate care au demonstrat scoruri elastografice mai mari (3 si 4). Leziunile cu caractere conventionale nespecifice clasate BI-RADS 4a sau b de tipul nodulilor mastozici au prezentat in general scoruri mici elastografice. Scorurile Tsukuba 4 si 5 s-au corelat in principal cu categoriile BI-RADS 4c si 5 reprezentate de leziuni cu risc (cicatrici radiare, papilome, adenoze sclerozante, hiperplazii epiteliale atipice) si neoplazii in situ sau invazive.

Concluzii. Clasificarea BI-RADS se coreleaza bine cu scorul elastografic Tsukuba, principala exceptie fiind reprezentata de leziunile benigne intens fibrotice sau calcificate care apar fals suspecte elastografic. Leziunile mamare de tip BI-RADS 3 si 4 beneficiaza cel mai mult de o evaluare elastografica, un scor mic incurajand monitorizarea, un scor mare impunand de multe ori confirmare anatomo-patologica

Studiul II. Aspecte sonoelastografice tipice si atipice in leziunile chistice ale sanului: impactul asupra clasificarii BI-RADS

Scopul studiului. Prezentarea aspectelor sonoelastografice ale chistelor mamare simple, complicate si complexe. Precizarea influentei elastografiei asupra clasificarii BI-RADS in leziunile chistice mamare.

Material și Metodă. S-a efectuat un studiu prospectiv in cadrul Departamentului Senologic al Clinicii Radiologice din Cluj Napoca incluzand leziunile chistice diagnosticate de acelasi medic radiolog, in perioada mai 2007-iulie 2008 Fiecare leziune a fost clasata intr-o categorie BI-RADS si a primit un scor elastografic conform criteriilor Tsukuba, dupa examinarea in prealabil pe un aparat

de tip Hitachi EUB 8500 cu modul de elastografie. Chisturile complicate si complexe au fost confirmate patologic prin prelevari percutane sau post-excisional.

Rezultate. Au fost detectate 49 de chisturi simple, 43 complicate si 14 complexe. Aspectele elastografice au fost impartite in 4 categorii: de tip classic (tristratificat BGR), aspecte caracteristice leziunilor solide (scor 1,2,3,4), alte variante de stratificare decat BGR si scor 3 inversat. Aspectul elastografic predominant in chisturile mamare a fost cel stratificat, de tip BGR. Aspectele atipice s-au intalnit predominant in cazul chisturilor complicate sau complexe. Clasificarea BI-RADS a chisturilor complicate a fost cel mai mult influentata de elastografie, care a permis intr-o majoritate a situatiilor subgradarea de la BI-RADS 3 la BI-RADS 2.

Concluzii. Cunoasterea aspectelor sonoelastografice posibile in chisturile mamare, precum si luarea in considerare a scorului elastografic, amelioreaza diagnosticul acestor leziuni si duce la eficientizarea managementului pacientilor

Studiul III. Valoarea parametrilor de culoare in analiza imaginilor elastografice ale leziunilor mamare detectate la ecografie

Scopul studiului. Principalul obiectiv a fost demonstrarea faptului ca analiza cantitativ-numerică a parametrilor de culoare afisati de imaginile elastografice poate ameliora diferentierea benign-malign. In plan secund s-a dorit identificarea acelor situatii care ar beneficia cel mai mult de o astfel de analiza.

Material și Metodă. Studiul a fost unul de tip longitudinal prospectiv desfsurat in perioada Mai 2007- Septembrie 2008. Aparatul folosit: Hitachi 8500 EUB cu modul de elastografie. Leziunile suspecte au fot verificate patologic prin biopsii percutane sau chirurgicale. Parametrii de culoare urmariti au fost: valori numerice medii ale pixelilor de culoare albastru, verde si rosu; valorile numerice ale dispersiei de culoare, valorile medii ale intensitatii de culoare, precum si valorile medii ale nuantei si dispersiei de nuanta. Analiza de mai sus s-a bazat pe un program computerizat: *Image Processing Version 1.3*, dezvoltat in colaborare cu Universitatea Tehnica din Cluj Napoca.

Rezultate. 71 de paciente au intrat in analiza finala. 106 leziuni focale mamare au fost detectate ecografic in randul grupului de pacienti studiat. Cinci parametrii de culoare au fost independent asociati cu rezultatele histopatologice (valoarea numerica medie pentru culorile albastru, verde si rosu; valorile numerice ale dispersiei de culoare pentru rosu si dispersia intensitatilor de culoare). Valoarea numerica medie pentru albastru a avut din punct de vedere statistic impactul cel mai mare, o valoare mai mare de 92 indicand mai degraba malignitatea. De cealalta parte o valoare mai mare de 88 pentru culoarea verde a corespuns in principal leziunilor benigne.

Concluzii. Analiza parametrilor de culoare imbunatateste acuratetea interpretarii imaginilor elastografice problematice (mozaicate). Valori numerice crescute pentru culoarea albastru (peste 92) se asociaza cu o probabilitate mare de malignitate si impun o atitudine diagnostica mai agresiva. Pe de alta parte, valori numerice crescute (peste 88) pentru culoarea verde pot reasigura operatorul ca se afla in fata unei leziuni mai probabil benigne si indica o atitudine diagnostica de tip conservativ.

Studiul IV. Spectrul imagistic al modificarilor mastozice focale ale sanului: aspecte mamografice, ecografice conventionale, sonoelastografice si de rezonanta magnetica. Corelatii patologice si diagnostic diferential.

Scopul studiului. Sistematizarea principalelor aspecte imagistice: mamoco-elastografice si de rezonanta magnetica întâlnite în modificările mastozice focale mamare; corelarea acestora cu rezultatul histopatologic si prezentarea principalelor diagnostic diferentiale.

Material și Metodă. S-a realizat un studiu retrospectiv pe paciente investigate senologic în perioada ianuarie 2009 - decembrie 2013, la care s-au urmărit aspectele radio-imagistice, inclusiv sonoelastografice ale leziunilor clasificabile ca si modificari mastozice focale. Leziunile BI-RADS 3 ramase stationare pe durata studiului au fost considerate benigne si *a priori* ca leziuni mastozice fara risc, non-proliferative. In cazul leziunilor BI-RADS 4 s-a realizat puncție percutană sau biopsia excizionala.

Rezultate. Conform criteriilor de includere si excludere au fost selectate 120 de femei cu 135 de leziuni detectate ecografic. In 95 de cazuri s-a efectuat mamografie si la 23 de paciente investigatiile au fost completate si cu IRM mamar cu substanta de contrast. Aspectele mamografice au fost dupa cum urmeaza: *aspect oculat*-44 cazuri (46,3%), *microcalcificari*-18 cazuri (18,9%), asimetrii de densitate-16 cazuri (18,8%), *opacitati*-13 cazuri (13,7%), *opacitati plus microcalcificari*-2 cazuri (2,1%), *distorsiuni arhitecturale*-2 cazuri (2,1%). Aspectele ecografice au fost sistematizate dupa cum urmeaza: . chisturi simple, complicate sau complexe asociate sau nu cu ectazii ductale si microcalcificari-49 (36,5%), noduli mastozici -34 (25,5%), placarde mastozice -32 (23,9%), distorsiuni-19 (14,2%) Din leziunile mastozice proliferative, majoritatea au prezentat scoruri elastografice mari, peste 2 (56,5%) si hipervascularizatie (86,95%), pe cand din leziunile mastozice non-proliferative 95,5% au prezentat scoruri Tsukuba 1-2 si vascularizatie absenta (58,2%) sau redusa (31,53%). Nu a existat o corelare semnificativa statistic intre aspectele mamografice si de rezonanta magnetica (atat morfologic cat si dinamic) cu subtipurile proliferative, cu risc sau non-proliferative ale mastozelor mamare. Modificarile mastozice cu risc sau de tip proliferativ au demonstrate trasaturi radio-imagistice similare cu cele din neoplaziile in situ sau invazive ale sanului.

Concluzii. Aspectele radio-imagistice intalnite in modificarile mastozice focale sunt extrem de variabile, de la tipic benigne la inalt suspecte. Leziunile fara risc proliferativ se prezinta mai degraba cu aspect non-rigid elastografic si hipovascularizate, pe cand cele de tip proliferativ sunt de cele mai multe ori rigide si hipervascularizate. Diagnosticul diferential al leziunilor proliferative cu neoplaziile mamare in situ sau invazive este imposibil de realizat pe criteria strict imagistice si necesita control anatomopatologic.

ORIGINALITATEA ȘI CONTRIBUȚIILE INOVATIVE ALE TEZEI

Cancerul mamar reprezinta o problema majora de sanatate publica si obtinerea unui diagnostic timpuriu este elementul cheie in lupta cu aceasta afectiune.

Radiologii specializati in diagnosticul senologic se bazeaza pe evaluarea vizuala a unei leziuni mamare, clasificand-o ca benigna, cu risc sau maligna in functie de trasaturile demonstrate la investigatiile efectuate. Asadar, o evaluare facila, accesibila, de tip calitativ a leziunilor mamare, precum sonoelastografia, este in bine primita in mediile de specialitate.

Dupa ce metoda sonoelastografica a fost pentru prima data promovata in randul senologilor de catre faimosul studiu al lui Ueno si Itoh publicat in prestigiosul jurnal *Radiology* in 2006, a aparut nevoia logica de a dezvolta si conduce noi studii care sa ii certifice si amplifice potentialul si respectiv aplicatiile clinice. In acest respect, capitolul al treilea din partea de *Contributii Personale* a tezei este dedicat uneia dintre primele publicatii aparute *post Ueno*, care certifica valoarea metodei, aratand totodata concordanta buna a scorului elastografic Tsukuba cu sistemul BI-RADS de clasificare a leziunilor mamare.

Ca si o continuare mai nuantata sau focusata a acestui studiu, capitolele 4 si 6 din partea personala a tezei, sunt dedicate aparent banalelor chisturi si modificarilor mastozice ale sanului . In aceste capitole se dovedeste valoarea elastografiei in alegerea celei mai potrivite atitudini in cazul leziunilor chistice si respectiv leziunilor de tip mastozic, situatii in care metoda indica corect si eficient fie o monitorizare conservativa, fie o biopsie mamara.

Alt aspect, abordat pentru prima data in literatura de specialitate dedicata diagnosticului senologic, este cel al evaluarii cantitativ-numeric a imaginilor elastografice problematice-extrem de mozaicate, pentru care discriminarea oculara simpla intre benign (scor 2) versus suspect (scor 4) se dovedeste de multe ori dubitativa. Astfel a fost pus in valoare un *software* capabil sa cuantifice pixelii de culoare demonstrati de fiecare imagine, program cu potential clinic imediat, mai ales in cazul unor operatori cu mai putina experienta (sub 6 luni) in elastografia si imagistica mamara pentru care discriminarea vizuala calitativa poate fi dificila .

Conform celor sintetizate mai sus teza de doctorat se inscrie in randul lucrarilor care dovedesc valoarea diagnostica a sonoelastografiei mamare si deschide perspectiva unor studii viitoare, centrate pe abordarea multi-imagistica a sanilor problematici de tip mastozic sau aflati la risc genetic.

PHD SCHOOL

SUMMARY OF THE PhD THESIS

Strain sonoelastography contribution in the diagnosis of breast lesions

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Key words: breast lesions, ultrasound, sonoelastography, BI-RADS, Tsukuba elasticity score, breast cysts, color parameters, focal mastopathic changes

INTRODUCTION

Breast cancer represents a worldwide major public health problem, with an alarmingly rapid increase of its national and international prevalence (1 in 8 women will eventually be affected of this disease during their life course). Early diagnosis is a cornerstone when it comes to fighting with better odds against this silent developing affliction.

Advancements in Breast Imaging have provided the opportunity to revolutionize how we image and evaluate patients with mammary lesions. In addition, to conventional diagnostic techniques such as mammography, gray scale ultrasound and MRI, sonoelastography may play a central role in the early detection of breast carcinoma or potentially risk lesions due to its unique ability of identifying stiffer tissues as opposed to normal soft surroundings. And within the breast as well as within the thyroid, salivary glands, testicles, prostate or other superficially soft tissues, what is stiffer is usually harmful or potentially malignant.

The first stage of the doctoral research was to summarize within a state of the art paper the main sonoelastography techniques and its major clinical applications in breast diagnosis. Further on the aim was to contribute to already published data with novel studies meant to confirm the value of elastography in breast diagnosis. Thus we decided to compare the well known and largely utilised BI-RADS diagnostic system with the Ueno-Itoh (Tsukuba) elasticity score when assessing breast focal lesions. To the best of our knowledge it was one of the first published comparison of this type being also cited in a book chapter (Richard G Barr's *Functional Imaging in Oncology*). Relevant clinical data derived from this study: firstly we were able to indicate which types of breast lesions would benefit most from an elastographic assessment and another step forward was achieved when the research focused on elastography patterns of breast cystic lesions. Another goal was to test an innovative software using advanced color parameters analysis in order to optimized elastographic image interpretation

Lastly the usefulness of sonoelastography was once more proven when assessing breast focal mastopathic changes - a group of entities sparsely addressed in literature data in spite the fact that a lot of breast cancers may ultimately derive or begin within this large and heterogeneous pathologic family. In this respect, our study was meant to realize a more systematized approach of this particular spectrum of breast lesions and tried to integrate the role of elastography in their evaluation.

We were able to perform our research and enrol patients with breast focal lesions that undergone sonoelastographic examinations by virtue of two grant programs (*CNCSIS cod 1409, nr. 44/17.05.2006 and ELASTOBREAST- CEEEX VIASAN nr. 149/2006*) conducted and finalized under the supervision of Radiology Professor. Sorin Marian Dudea, grants which provided the US machine with strain elastography option and a dedicated software used to analyse color parameters of elastographic images

PERSONAL CONTRIBUTION

Study I. Breast diagnosis: Concordance analysis between the BI-RADS classification and Tsukuba sonoelastography score

Purpose. To establish the correlations between the ultrasound (US) BI-RADS classification and Tsukuba elastography score when assessing breast lesions. To determine which type of breast lesion (BI-RADS category) would benefit most from an elastographic assessment.

Material and Methods. The investigated sample of imaging comprised a number of 129 images belonging to 92 subjects examined with a Hitachi 8500 US device. Each lesion was assessed according to the BI-RADS and Tsukuba elastography score. Histopathology was obtained by means of percutaneous biopsy or post-surgery. Fibroadenoma-like lesions unchanged over a period of 3 years were considered benign.

Results. The concordance between the BI-RADS system and Tsukuba elasticity score when it came to correctly classify as benign or malignant breast lesions was of 81% when all BI-RADS categories were considered and respectively of 78% when typically benign –BI-RADS 2 and typically malignant –BI-RADS 5 lesions were excluded from the study.

The 1, 2 and BGR Tsukuba scores mostly correlated with BI-RADS 2 and 3 lesions such as cysts, hamartomas, lipomas, hematomas, non-palpable fibroadenomas. Palpable fibroadenomas initially included in BI-RADS 4a/b category, usually received benign elasticity scores (1 or 2), the exception being represented by a minority of cases of old, fibrotic or calcified lesions (elastic score 3 or 4). Non-specific BI-RADS 4a/b lesions, such as mastopathic nodules demonstrated rather soft, elastic properties on elastogram (score 1 or 2). The 4 and 5 Ueno-Itoh scores were predominantly correlated with BI-RADS 4c and 5 categories represented by high risk lesions (radial scar, papillomas, atypical epithelial ductal hyperplasia) and in situ or invasive carcinomas.

Conclusions. Generally the BI-RADS classification correlates well with the Tsukuba elasticity score, the main exception being represented by fibrotic, calcified lesions which falsely appear more suspicious post-elastography. BI-RADS 3 and 4 lesions would benefit most from an elastographic assessment, a low Tsukuba score allowing a less invasive approach, while a high score imposes histopathological evaluation.

Study II. Typical and unusual sonoelastographic patterns of breast cystic lesions: impact on BI-RADS classification

Purpose: To describe the sonoelastographic appearance of breast cysts (simple, complicated cysts with sedimentation and complex-cysts with internal solid parts). To assess the influence of sonoelastography on the BI-RADS classification of complicated cysts.

Materials and Methods: A prospective study was conducted and all cysts diagnosed by the same radiologist between May 2007 and July 2008 in our breast unit were included. Each lesion was assessed according to BI-RADS and the Tsukuba elasticity score using a Hitachi 8500 US device. Cytology or histopathology was obtained for complicated and complex cysts.

Results: 49 simple, 43 complicated and 14 complex cysts were detected. The elasticity patterns were divided into 4 categories: typical BGR (blue-green-red) pattern, appearance similar to that described for solid lesions, variants of BGR, an inverse score of 3. The BGR pattern was predominant in breast cysts. Atypical elasticity patterns were mostly associated with complicated and complex cysts. BI-RADS classification of complicated cysts before and after elastography showed a statistically significant difference in terms of final category assessment (most of the complicated cysts were downgraded to BI-RADS 2 after elastography).

Conclusion: Being aware of the wide spectrum of elastographic patterns of breast cysts and considering elastography when assessing the BI-RADS category of complicated cysts may lead radiologists to better patient management.

Study III The added value of color parameters in analysing elastographic images of ultrasound detected breast focal lesions

Purpose: The purpose of the study was to determine if color quantitative analysis obtained on elastographic images of breast lesions can amend benign-malignant differentiation. and to identify some of the circumstances which would benefit most from such an analysis.

Material and Methods. The study design was a longitudinal prospective one, all data being acquired between May 2007 and September 2008. The US device used: Hitachi 8500 EUB machine with elastography option For suspicious breast lesions histopathology was obtained by means of percutaneous biopsy or post-surgery. Followed color parameters (numeric values): average color (red, green, blue), color dispersion, average intensity, average hue, hue dispersion. Calculus modality: Image Processing Version 1.3, a program developed in collaboration with Technical University of Cluj Napoca.

Results. 71 women were selected for the study. A hundred and six circumscribed breast lesions were detected by means of ultrasound in the studied group. Five color parameters were independently associated with the histological diagnosis (AvgBlue, AvgGreen and AvgRed; DispRed and DispIntensity) with AvgBlue parameter making the most important contribution ($p < 0.0001$); greater the values of AvgBlue (more than 92), higher the chances of malignancy and greater the values of AvgGreen (more than 88), higher the chances for a benign lesion.

Conclusion: High numeric values for Avg Blue (more than 92) would increase the probability of malignancy and thus recommend a more aggressive diagnostic management (biopsy) while high numeric values for AvgGreen (more than 88) would reassure the examiner to proceed conservatively with short interval or routine follow-ups.

Study IV. Imaging spectrum of breast focal mastopathic changes: mammography, conventional ultrasound, elastography and MRI appearances; pathology correlations and differential diagnosis

Purpose: The paper goals were to describe in a more exhaustive and systematized manner the imaging appearances of breast mastopathic changes, to discuss the relationship between imaging aspects and histopathological subtypes and to approach the main differential diagnosis of these entities.

Methods and Material: Our analysis was based on a retrospective study conducted on women examined during a period of four years (January 2009- December 2013). There were analyzed only breast lesions classifiable as mastopathic for which we followed imaging features on mammography, ultrasound, sonoelastography and MRI. BI-RADS 3 lesions were considered benign and *a priori* risk free if they were stationary during the 4 years time frame. BI-RADS 4 lesions were pathologically confirmed by means of percutaneous or surgical biopsies.

Results . According to the inclusion and exclusion criteria a number of 120 women were finally selected for the study. US and USE were performed in all patients and 135 circumscribed breast lesions were detected and assessed. Mammography was performed in 95 patients and MRI in 23 cases.

Mammography aspects were as follows: *occult*-44 cases (46,3%), *microcalcifications*-18 cases (18,9%), asymmetrical densities-16 cases (18,8%), *opacities*-13 cases (13,7%), *opacity plus microcalcifications*-2 cases (2,1%), *architectural distortions*-2 cases (2,1%). Ultrasound appearances were systematized as follows: . cysts (simple, complicated sau complex) associated or not with duct ectasia and microcalcifications-49 (36,5%), mastopathic nodules -34 (25,5%), mastopathic placards -32 (23,9%), distortion-19 (14,2%) Within the pathologically proven, proliferative mastopathic group of lesions, the majority(56,5%) displayed high scores (above 2) on elastography and increased vascularity on Doppler examination (86,95%), whereas most (95,5%) of the pathological entities included within the non-proliferative group, displayed low scores on elastography (1-2) and showed absent (58,2%) or reduced vascularity (31,53%). There was no statistically significant correlation between mammography and MRI aspects (both morphological and dynamic) ant the pathology proliferative or non-proliferative subtypes of mastosis . However the proliferative mastopathic entities showed radio-imaging features similar to those found in invasive or in situ breast neoplasia.

Conclusions:The imaging spectrum of breast mastosis comprises a large, heterogeneous group of appearances from typically benign aspects to non-specific or highly suspicious features

Soft, hypovascular mastopathic changes are usually associated with non-proliferative lesions, whereas stiff, hypervascular lesions better correlate with proliferative changes. For most cases with imaging risk features, such as hypervascularity on Doppler examination, stiffness on elastography or regional enhancement with wash-out on MRI, differential diagnosis with in situ or invasive neoplasia is impossible on imaging criteria alone.

In the light of our preliminary data we may speculate that using the elastography assessment in conjunction with Doppler examination it is possible to better assess the malignancy potential of

focal mastopathic changes of the breast. Thus, the soft, hypovascular ones may be rather followed than excised or biopsied with less anxiety for the patient and less burden for the medical system, whereas the stiff, hypervascular lesions should be pathologically confirmed.

ORIGINALITY AND INNOVATIVE CONTRIBUTION

Breast cancer represents a worldwide major public health problem, thus, preventing its development and reaching a timely diagnosis are cornerstone goals when it comes to fighting with better odds against this widely spread affliction.

Radiologists are depending on their visual assessment to establish the diagnosis of focal breast lesions. According to various imaging features they may decide to dismiss the detected anomaly as typically benign or they may opt to follow it or further on to perform a biopsy. Therefore, the development of a qualitative assessment method such as elastography, meant to improve detection of potentially malignant or risk lesions is largely welcomed.

After the the US elastography was promoted starting with the famous Ueno and Itoh paper from Radiology journal, 2006, the need of other studies to confirm elastography potential had risen. In this respect the third chapter from our Personal Contribution section was based on one of the first publications which stated that strain sonoelastography may be a reliable method of evaluation for breast focal lesions, comparable or in agreement with the already widely used ACR's BI-RADS. As a continuations two other innovative studies were conducted and published, studies which proved the elastography role in choosing the most appropriate and economically advantageous attitude when it came to breast cystic lesions and focal mastosis. In these circumstances elastography reinforced the radiologist opinion towards follow-up or towards a biopsy. Another aspect, to the best of our knowledge firstly approached in our research was finding a solution to amend interpretation of problematic elastographic images displaying an intricate mosaic aspect, difficult to classify as Tsukuba score 2 or 4 Thus it was proved that a software able to numerically analyze color parameters of elastographic images may significantly aid in differentiating the benign score 2 from the suspicious score 4, particularly if the image acquisition or interpretation is performed by a less experienced operator.

From the point of view of the importance of evaluation of breast focal lesions, this thesis falls into the current trend validation of non-invasive imaging diagnosis techniques.

According to our results, strain sonoelastography has proven its diagnostic value. The multi-modality imaging approach of breast potentially risk lesions such as focal mastopathic changes will be our main concern for the near future.