Original Article

Can Shear Wave Elastography Increase Specificity in Diagnosis of Benign and Malignant Breast Masses?

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Objective: To determine whether shear wave elastography [SWE] can increase specificity in diagnosis of benign and malignant breast masses in BI-RADS category 3 and 4.

Materials and Methods: Data were collected retrospectively between January 2013 and December 2015 at King Chulalongkorn Memorial Hospital. Breast sonography with supplementary SWE of BI-RADS category 3 and 4, according to the ACR BI-RADS 2013, which had histopathology-proved diagnosis or at least two years of stability, were randomly reviewed by the researchers. Elasticity values were all generated by Supersonic Imagine ultrasound system. Minimal elasticity [Emin], mean elasticity [Emean], and maximal elasticity [Emax] values were separately evaluated among benign and malignant groups.

Results: One hundred sixteen lesions in 107 female patients were eligible for the present study. Eighty lesions (68.9%) were benign and 36 lesions (31.0%) were malignant. All Emin, Emean, and Emax showed statistically significant difference between benign and malignant lesions (*p*-value 0.022, 0.001, and <0.001, respectively). The area under the receiver operating curve [AUC] for elasticity value was slightly higher for maximum (0.733) than mean (0.710) values. The cut-off value of Emax was 110 kPa, showing sensitivity 63.9%, specificity 78.8%, PPV 57.5%, NPV 82.9%, and accuracy 74.1%. All BI-RADS category 3 lesions were benign, as well as all BI-RADS category 4c lesions, were malignant. The cut-off value of Emax below 48 kPa in BI-RADS category 4a lesions proved to be all benign except medullary carcinoma. Maximal Emax value was 300 kPa, which was proven to be diabetes mellitus mastopathy and some malignant lesions.

Conclusion: Emin, Emean, and Emax values were significantly different between benign and malignant masses and the specificity was increased as compared with conventional ultrasound alone, especially in BI-RADS category 4a. The present study showed Emax value at 110 kPa had good specificity and high NPV. Elasticity values primarily reflect the degree of fibrosis of breast lesions, which help the diagnosis.

Keywords: Shear wave elastography, Diagnostic accuracy, Benign, Malignant, Breast masses, BI-RADS 3 and 4

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Breast cancer is the most common cancer among females in the Asia-Pacific region and the fourth most common cause of cancer-related deaths. Survival from breast cancer depends mainly on early detection that leads to optimal treatment[1]. Since Asian breasts tend to have denser tissue than western breasts, the possibility of missed lesion from mammography in the Asian population is increased[2]. Ultrasound is one of the current gold standards, according to the American College of Radiology, Breast Imaging Reporting and Data System [ACR BI-RADS] Atlas 2013[3] (Table 1). BI-RADS Category 3 is reserved for specific imaging findings containing the probably benign finding(s), known to have more than 0% but 2% or less likelihood of malignancy. The initial short-term follow-up interval is usually six months to assess stability for category 3. BI-RADS Category 4 is used for findings that do not have the classic appearance of malignancy but are adequately suspicious to justify a recommendation for interventional procedures. The likelihood of malignancy for category 4 is more than 2% and less than 95%, which cover quite a wide range[3]. The present study is concerned about the different management between BI-RADS category 3 and 4. The limitation of the conventional ultrasonography is low specificity, while good sensitivity and negative predictive value [NPV] are achieved[4]. Shear wave elastography [SWE] is a new diagnostic tool for detecting tissue elasticity (stiffness) by applying vibration energy irradiation via real-time ultrasonography. This method brings both

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Table 1. American college of radiology BI-RADS Atlas 2013

Assessment	Management	Likelihood of cancer
Category 0: Incomplete, need additional imaging evaluation	Recall for additional imaging	N/A
Category 1: Negative	Routine screening	Essentially 0% likelihood of malignancy
Category 2: Benign	Routine screening	Essentially 0% likelihood of malignancy
Category 3: Probably benign	Short-interval (6-month) follow-up or continued surveillance	>0% but ≤2% likelihood of malignancy
Category 4: Suspicious	Tissue diagnosis	>2% but <95% likelihood of malignancy
Category 4a: Low suspicion for malignancy Category 4b: Moderate suspicion for malignancy Category 4c: High suspicion for malignancy		>2% to ≤10% likelihood of malignancy >10% to ≤50% likelihood of malignancy >50% to <95% likelihood of malignancy
Category 5: Highly suggestive of malignancy	Tissue diagnosis	≥95% likelihood of malignancy
Category 6: Known biopsy-proven malignancy	Surgical excision when clinically appropriate	N/A

N/A = not applicable

qualitative and quantitative diagnostic assessment in kiloPascal [kPa] unit[5]. Benign lesions tend to be soft, while malignancy tends to be stiffer[6].

The purpose of the present study was determined whether SWE could differentiate benign and malignant breast lesions in BI-RADS category 3 and 4.

Materials and Methods

The present cases were randomly collected between January 2013 and December 2016 at King Chulalongkorn Memorial Hospital [KCMH]. The clinical information and imaging findings were reviewed from the medical record and the Picture Archiving and Communication Systems [PACs]. Two hundred forty-three breast masses with BI-RADS category 3 or 4 by conventional ultrasound and supplementary quantitative elastography between January 2013 and December 2016 were included. One hundred nine lesions had qualitative assessment with no region of interest [ROI] placement were excluded. One patient with multiple masses in the same quadrant of each breast was excluded due to the unability to correlate lesion on ultrasound with the pathologic results. Seventeen lesions with inconclusive definite diagnosis due to inadequate tissue histopathology were also excluded. Masses without pathological report but stable size for at least two years follow up were defined as benign lesions.

Both conventional ultrasound and elasticity values were generated by the Aixplorer® (SuperSonic Imagine, Aix en Provence, France). Five experienced radiologists performed both qualitative and quantitative assessment by placing the ROI box at the location of maximum stiffness. The minimal, mean and maximal elasticity values were obtained in every lesion in kPa unit. Elastography application was used to calculate tissue elasticity based on the propagation speed of shear waves[3].

Image findings were interpreted according to the ACR BI-RADS 2013 (fifth edition).

Case record form was composed of patient's age, clinical presentation, the maximal length of each lesion, BI-RADS categories, pathological report, stability for at least two years follow-up, minimal elasticity [Emin], mean elasticity [Emean], and maximal elasticity [Emax] values.

Statistical analysis

Differentiate elasticity between benign and malignant breast masses was the primary outcome in the present study. Sample size was calculated by using two independent means. The SWE parameters for calculating sample size were Emean and standard deviation [SD] of benign and malignant breast masses, which was published on a prior study[7]. Elasticity values were presented as number (%), mean ± SD. Statistical analysis was performed using the SPSS Statistical 17.0 software. The average Emin, Emean, and Emax values were compared between benign and malignant masses by using unpaired t-test, which two-tailed *p*-values of less than 0.05 was indicated as statistical significance. Receiver operating characteristic [ROC] curves for Emean and Emax values were analyzed to evaluate diagnostic performance. The authors selected cut-off value aimed high specificity without losing sensitivity of the conventional ultrasonography. Then, the sensitivity, specificity, positive predictive value [PPV], NPV, and accuracy of the selected cut-off value were achieved.

Furthermore, the average Emax values of all breast masses were analyzed by subcategorized pathology among benign and malignant lesions.

Results

One hundred sixteen lesions in 107 patients were eligible for the present study. All patients were female. The mean patient's age was 52 years (range from 25 to 90 years). Of these 116 masses, 20 masses (17.2%) were incidentally found due to screening ultrasound, and 96 masses (82.8%) were presented with a symptom. Grouping definite diagnosis into benign and malignant lesions according to BI-RADS categories are shown in Table 2.

The Emin (p-value 0.022), Emean (p-value 0.001), and Emax (p-value <0.001) values reveal higher values with statistical significance for malignant lesions than all benign lesions. The highest diagnostic performance was Emax value. The longest dimension was subcategorized and compared with average Emax values for each diagnosis group (Figure 1). The Emax values for each pathological definite diagnosis are shown in Table 3.

Regardless of the Emax values, all BI-RADS category 3 lesions were all benign. In addition, all BI-RADS category 4c lesions were all malignant.

ROC curve analyses of the Emax and Emean were performed, yielding the area under the receiver operating curve [AUC] 0.733 and 0.710, respectively (Figure 2). The optimal cut-off value of Emax was 110 kPa, showing sensitivity 63.9% (95% confidence

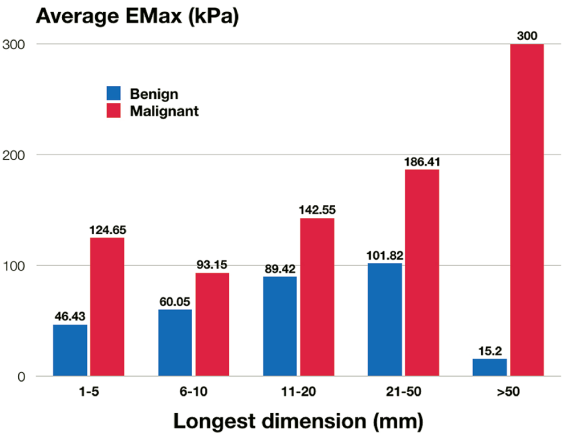

Figure 1. The longest dimension comparing with average Emax values for each benign and malignant groups.

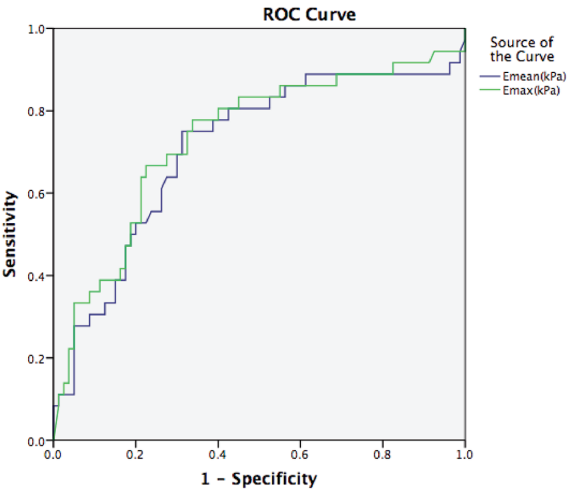

Figure 2. ROC curve analysis of the Emax and Emean, showing a slightly higher diagnostic performance of the Emax as compared with the Emean.

Table 2. Definite diagnosis grouping into benign and malignant lesions according to BI-RADS categories

Diagnosis	BI-RADS, n (%)			
	3	4a	4b	4c
Benign	30 (25.9)	30 (25.9)	20 (17.2)	0 (0.0)
Malignant	0 (0.0)	7 (6.0)	11 (9.5)	18 (15.5)

BI-RADS = Breast Imaging Reporting and Data System

Table 3. Distribution of Emax values for each pathological definite diagnosis

Definite diagnosis	n (%)	Emax (mean ± SD)	Range
Benign	80 (68.97)	74.99±64.48	5.8 to 300
Stability at least 2 years	26 (22.41)	54.05±43.44	5.8 to 168.2
FIbroadenoma	27 (23.28)	75.50±58.20	10.1 to 251.6
Adenosis	5 (4.31)	115.70±64.06	46.8 to 171.7
Phyllodes Tumor	4 (3.45)	75.63±65.44	15.2 to 141
Intraductal papilloma	3 (2.59)	83.47±24.35	60.8 to 109.2
Diabetes mastopathy	2 (1.72)	293.55±9.12	287.1 to 300
Cyst	3 (2.59)	38.63±8.38	31.6 to 47.9
Benign findings	10 (8.62)	78.80±98.08	19 to 225.4
Malignant	36 (31.03)	141.80±86.83	4 to 300
Ductal carcinoma in situ	4 (3.45)	133.63±100.01	17.9 to 246.8
Invasive ductal carcinoma	21 (18.10)	127.13±81.32	4 to 300
Invasive lobular carcinoma	5 (4.31)	155.48±85.34	86.8 to 298.5
Mucinous carcinoma	2 (1.72)	167.45±42.64	137.3 to 197.6
Invasive mammary carcinoma	3 (2.59)	260.83±36.13	228.8 to 300
Medullary carcinoma	1 (0.86)	5.70±0.00	5.7 to 5.7

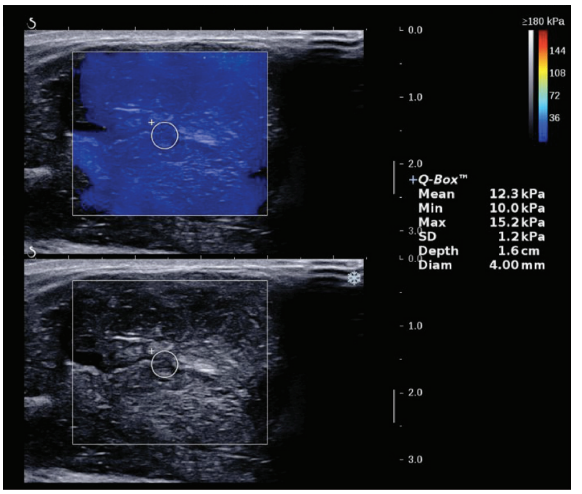

Figure 3. A case presented with a palpable right breast lump, ultrasonography revealed a large circumscribed heterogeneous echoic mass with soft elasticity (Emax 15.2 kPa) at the right upper part, classified as BI-RADS 4b. The histology was benign phyllodes tumor.

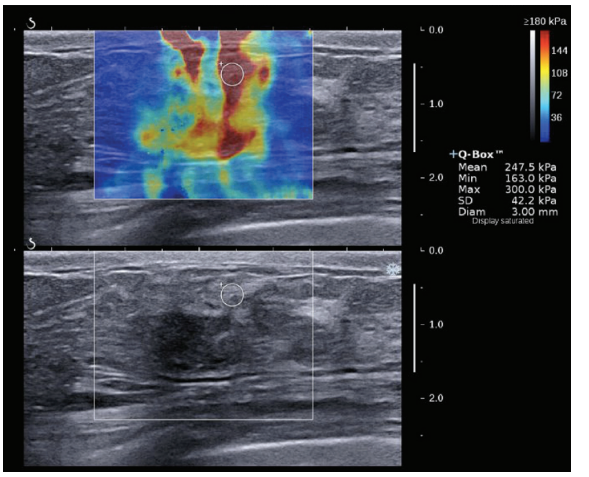

Figure 4. A case with diabetes mellitus was sent to follow-up bilateral breast masses. Ultrasound revealed the mass with posterior shadowing and hard elasticity value (Emax 300 kPa) in right breast, classified as BI-RADS 3. The histology was diabetic mastopathy.

interval [CI] 46.2 to 78.7), specificity 78.8% (95% CI 67.9 to 86.8), PPV 57.5% (95% CI 41.0 to 72.6), NPV 82.9% (95% CI 72.2 to 90.2), accuracy 74.1% (95% CI 65.5 to 81.2), false negative 36.1% (95% CI 27.4 to 44.8), and false positive 21.3% (95% CI 13.9 to 28.7).

For BI-RADS category 4a masses, the threshold values of 110 kPa showed PPV 25% (95% CI 4.5 to 64.4), NPV 82.8% (95% CI 63.5 to 93.4), sensitivity 28.6% (95% CI 5.1 to 69.7), and specificity 80% (95% CI 60.9 to 91.6). For BI-RADS category 4b lesions, the threshold values of 110 kPa revealed PPV 44.4% (95% CI 22.4 to 68.7), NPV 76.9% (95% CI 46.0 to 93.8), sensitivity 72.7% (95% CI 39.3 to 92.7), and specificity 50% (95% CI 27.9 to 72.1).

Discussion

The best diagnostic performance of SWE to differentiate benign and malignant breast masses in BI-RADS 3 and 4 was the Emax value. The present study revealed average Emax values were significantly higher in malignant masses (141.8±86.63 kPa) than in benign masses (74.99±64.48 kPa) (p-value <0.001), consistent with the previous study[8]. Subcategorized masses by longest dimension also showed higher average Emax values of the malignant masses as compared to the benign masses. The present study also demonstrated that benign lesions tend to be soft, for examples, fibroadenoma, intraductal papilloma, and benign phyllodes tumor (Figure 3), similar to a previous report[6].

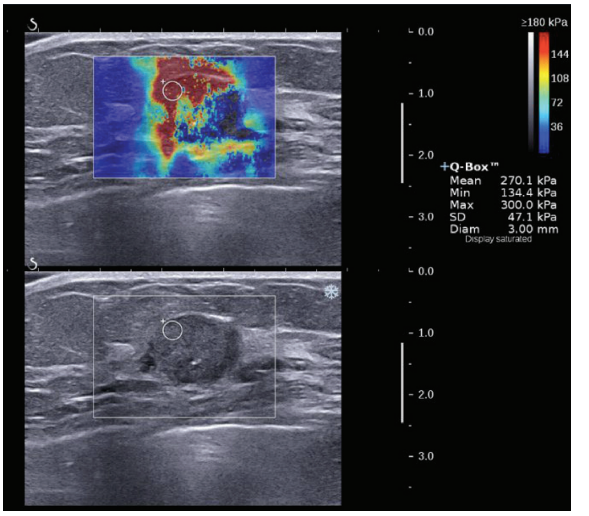

Figure 5. A case with palpable lump on her left breast, ultrasonography showing a partially circumscribed hypoechoic mass with hard elasticity (Emax 300 kPa). This mass was classified as BI-RADS 4b. The histology was invasive ductal carcinoma.

Maximal Emax value was 300 kPa, which proved to be diabetes mellitus mastopathy (Figure 4) and some malignant lesions including, invasive ductal carcinoma (Figure 5) and invasive mammary carcinoma, in agreement with a previous study[9]. Elasticity primarily reflects the degree of fibrosis of breast lesions. The stiffness of malignant lesions was believed to be influenced by desmoplastic reaction owing to neoplastic infiltration of the interstitial

tissue[10]. In addition, a previous study proved that diabetic mastopathy shows increase consistency and density secondary to fibrous proliferation[11]. Their pathologies revealed areas of fibrosis with predominant B cell-lymphocytic infiltration.

The combination of conventional ultrasound and SWE can improve management of breast lesions by increasing specificity. The authors' data presented the cut-off value of 110 kPa for differentiating malignant from benign lesions, which is close to the previous report of 106 kPa[8].

BI-RADS category 4a showed benefit from elastography with high specificity of 80% and high NPV of 82.8%, reducing unnecessary biopsies for masses with Emax less than 110 kPa. A PPV of 25% appeared to be higher than the likelihood of malignancy, which is between 3% to 10% of BI-RADs category 4a masses with Emax at least 110 kPa. In addition, the cut-off value of Emax below 48 kPa in BI-RADS category 4a lesions proved to be all benign lesions except one, which was medullary carcinoma (Figure 6). This is in line with a previous study stating that tumors with low malignant consistency included medullary carcinoma, mucinous carcinoma, and papillary carcinoma[10].

BI-RADS category 4b masses had the likelihood of malignancy between 11% to 50%, consistent with the present study showing PPV 44.4% at the threshold values of 110 kPa.

Some limitations have occurred in the present study. First, BI-RADS category assessments were retrospectively established by five radiologists, causing inter-observer variability. Second, not all malignant and benign breast lesions were included in the present study. There was no malignant cases of lobular carcinoma in situ [LCIS], invasive papillary carcinoma, and tubular carcinoma as well as other uncommon inflammatory and reactive breast disorders, which could mimic malignancy, such as granulomatous mastitis and Mammary tuberculosis[12].

A future study with large-scale validation including a greater variety of breast diseases may increase the level of confidence for combined SWE with the conventional ultrasonography in the evaluation of various breast masses.

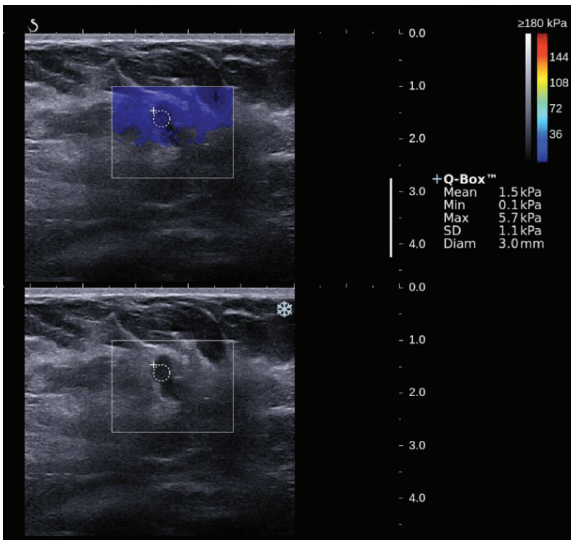

Figure 6. A case with lobulated hypoechoic mass with soft elasticity value (Emax 5.7 kPa) in her left breast, classified as BI-RADS 4a. The histology revealed medullary carcinoma.

Conclusion

Elasticity values between benign and malignant BI-RADS category 3 and 4 masses were significantly different. Emax showed the highest diagnostic performance. Elasticity primarily reflects the degree of fibrosis in lesions, which help the diagnosis. Our cut-off value of Emax was 110 kPa, showing increased specificity as compared with ultrasound alone. Emax of at least 110 kPa masses tend to be malignant while lower Emax masses tend to be benign. However, malignancy without desmoplastic reaction and benign masses with fibrosis could cause false negative in 36.1% and false positive in 21.3%, respectively. We found that all BI-RADS category 3 masses were all benign as well as all BI-RADS category 4c masses were all malignant regardless of elasticity values and sizes. BI-RADS category 4a showed benefit from elastography with high specificity and high NPV, leading to a reduction of unnecessary biopsies for Emax less than 110 kPa masses.

What is already known on this topic?

Shear wave ultrasound elastography brings both qualitative and quantitative diagnostic assessment of breast masses. Benign lesions tend to be soft, while malignancy tends to be stiffer.

What this study adds?

The purpose of this study was to determine whether SWE can differentiate benign and malignant BI-RADS category 3 and 4 breast masses because physicians concern about different management between these two categories. The authors reported diagnostic performance of the proper cut-off value. The authors also found that BI-RADS category 4a

showed benefit from supplement elastography with high specificity and high NPV, leading to a reduction in unnecessary biopsies for masses with Emax less than 110 kPa.

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Potential conflicts of interest

The authors declare no conflict of interest.

References

1. Youlden DR, Cramb SM, Yip CH, Baade PD. Incidence and mortality of female breast cancer in the Asia-Pacific region. Cancer Biol Med 2014; 11:101-15.
2. Kolb TM, Lichy J, Newhouse JH. Comparison of the performance of screening mammography, physical examination, and breast US and evaluation of factors that influence them: an analysis of 27,825 patient evaluations. Radiology 2002;225:165-75.
3. Mendelson EB, Böhm-Vélez M, Berg WA, Whitman GJ, Feldman MI, Madjar H, et al. ACR BI-RADS Ultrasound. In: ACR BI-RADS Atlas: Breast imaging reporting and data system. 5th ed. Reston, VA: American College of Radiology; 2013.
4. Balu-Maestro C, Tardivon A, Chapellier C, Athanasiou A, Tourasse C, Juhan V. European Congress of Radiology. Clinical benifits evaluation of shear wave elastography in ultrasound examination of breast lesions [Internet]. 2011 [cited 2015 Sep 18]. Available from: http://www.50505.ru/stati/spetsialnye/Breast%20ECR2011.pdf.
5. Nakashima K, Shiina T, Sakurai M, Enokido K, Endo T, Tsunoda H, et al. JSUM ultrasound elastography practice guidelines: breast. J Med Ultrason (2001) 2013;40:359-91.
6. Evans A, Whelehan P, Thomson K, McLean D, Brauer K, Purdie C, et al. Quantitative shear wave ultrasound elastography: initial experience in solid breast masses. Breast Cancer Res 2010;12:R104.
7. Lee EJ, Jung HK, Ko KH, Lee JT, Yoon JH. Diagnostic performances of shear wave elastography: which parameter to use in differential diagnosis of solid breast masses? Eur Radiol 2013;23:1803-11.
8. Klotz T, Boussion V, Kwiatkowski F, Dieu-de Fraissinette V, Bailly-Glatre A, Lemery S, et al. Shear wave elastography contribution in ultrasound diagnosis management of breast lesions. Diagn Interv Imaging 2014;95:813-24.
9. Matsubayashi RN, Imanishi M, Nakagawa S, Takahashi R, Akashi M, Momosaki S, et al. Breast ultrasound elastography and magnetic resonance imaging of fibrotic changes of breast disease: correlations between elastography findings and pathologic and short Tau inversion recovery imaging results, including the enhancement ratio and apparent diffusion coefficient. J Comput Assist Tomogr 2015;39:94-101.
10. Goddi A, Bonardi M, Alessi S. Breast elastography: A literature review. J Ultrasound 2012;15:192-8.
11. Navarro-Aguilar V, Montoliu G, Viguer Benavent RM, Sánchez Fuster MÁ, Camacho Alcazar JL. Diabetic mastopathy: spectrum of radiological findings. Proceedings of the European Congress of Radiology 2014 Mar 6-10; Vienna, Austria; 2014.
12. Sabaté JM, Clotet M, Gómez A, De Las Heras P, Torrubia S, Salinas T. Radiologic evaluation of uncommon inflammatory and reactive breast disorders. Radiographics 2005;25:411-24.