

The Performance of Elastographic Diagnostic of Breast Tumor in Dr. Soetomo Teaching Hospital Surabaya

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Abstract

Background: Elastography in breast cancer cases has not become a routine examination that is conducted in the radiodiagnostic unit in Dr. Soetomo Teaching Hospital Surabaya. These last few years, elastography has been an addition examination modality which is promising to assess breast lesions that are detected by ultrasound. **Objective:** The aim of the present study is to observe the performance of elastography in breast tumor cases. **Method:** This cross-sectional study was conducted in Dr. Soetomo Teaching Hospital Surabaya. The elastography is applied in 65 females (the average age is 49,1 years old) and it was found 66 lesions with a definitive diagnosis (34 benign tumors, 32 malignant tumors) which was proved through a fine-needle aspiration biopsy. The grayscale result is classified into benign and malignant categorizations with examining five descriptors including shape, margin, orientation, echo pattern, and posterior features. **Results:** The elastography score showed that the sensitivity is 87,5 %, the specificity is 94,1 %, and the accuracy is 90,9 %. The strain ratio showed 93,8 %, 94,1 %, 90,9 % in sequence. On the other hand, the grayscale result showed 96,9 %, 91,2 %, and 95,5 %. The combination of elastography and grayscale showed a better performance with the 97,1% of sensitivity, 94,1 % of specificity, and 93,8 % of accuracy. There was a significant correlation between the lesion size and the quality of elastography result ($P = .034$) while there was no correlation with the lesion depth ($P = .624$). **Conclusion:** The combination of elastography and grayscale have a better diagnostic performance in distinguishing benign breast tumor with malignant breast tumor.

Keywords: Breast Tumor; Elastography Score, Strain

Background

Elastography is a non-invasive imaging technique that can be applied to describe the strain of a tissue as a response to a given mechanical power. The basic of elastography is still developed, so the implementation in the clinical practice has become a debate in the scientific community and its functions remain unknown¹. This technique is initially addressed to differentiate between the benign lesions and malignant lesions. However, it is implemented to assess 'probably benign lesion'².

Several studies reported that the elastography did not give any additional information to the ultrasonografi (USG) diagnosis of breast cancer, in which the accuracy of the diagnostic is similar to the USG of grayscale³. However, other studies revealed that this method can only be applied to the lesions which are no more than 2 cm⁴. On the other hand, several other studies asserted that elastography could give additional information regarding the elasticity (strain) that cannot be achieved through the routine imaging modalities. It can also increase the specificity in the (USG) of grayscale so that it can decrease the biopsy number in benign lesion cases through the dubious grayscale USG and it can be postponed for one year^{5,6,7,8}.

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The elastography application in the imaging elastographic properties of tissues was proposed in one study. A conducted study categorized in a static method and based on the facts that a hard tissue has a small strain¹. On the other hand, one of the conducted study referred to the dynamic method and based on the fact that a hard tissue has a high velocity of propagation⁹. There was a scoring system called Tsukuba Elasticity Score (TES) based on the diagnosis of more than 100 breast tumor cases in 2006. This scoring system categorizes the color scheme of the breast tumor elasticity into five classes, from benign (score 1-3), to malignant (score 4-5), and BGR score for cystic lesions⁵.

Thus, this method is not applied to replace the conventional USG to diagnose a breast tumor but as a complementary by giving information about the strain of a tissue which is not obtained in other imaging modalities. So far, there has been no data related to the use of elastography in breast tumor cases in radiodiagnostic unit Dr. Soetomo Teaching Hospital. Therefore, the present study aims to understand the elastography functions in diagnosing a breast tumor in radiodiagnostic unit of Dr. Soetomo Teaching Hospital. In addition, it also aims to recognize the elastography variations in breast tumors and explore the factors that can affect the elastography result.

Method

The independent variable was used for the

elastography result and the related variable was used for the FNAB result. The present study conducted an examination hosted by the radiology residents that has been through an ultrasound stage for 5 months and supervised by the technical appliance and used Hitachi machine type Hi-Vision Avius with probe EUP-L74M 5-13 MHz.

All notes were submitted next to do a tabulation of data and statistic analysis. The present study also used a statistic analysis by calculating the sensitivity, specificity, and accuracy of the Chi-Square method. The trust limit that was used is 95% (95% CI) with the value of p is considered significant if it is <0,05. The statistic calculation was conducted with the assistance of SPSS software. Ethically, the researcher has received ethical clearance permission from Medical Research Ethics Commission Dr. Soetomo Teaching Hospital Surabaya.

Results

The Subject Characteristic of the Study

In this study, 66 samples are obtained aged between 32-80 years old with the mean 49,1 ± 8, 94 years old in which the most age group are 40-49 years old. The age average in the group with the benign cytology is 45,94 ± 7,32. However, the age average in the group with the malignant cytology is 52,41 ± 9,29.

The Sample Distribution Based On The Result Of Elastography And Cytology

Table 1. The imaging of elastography result and cytology result

Parameter	In general		Benign		Malignant	
	f	%	f	%	f	%
Elastography score						
0 (BGR)	17	25,8	17	25,8	-	-
1	5	7,6	5	7,6	-	-
2	8	12,1	7	10,6		
3	8	12,1	5	7,6		
4	18	27,3	-	-	18	27,3
5	10	15,2	-	-	10	15,2
Total	66	100,0	34	51,5	32	48,5
Strain Ratio						
< 4,5	34	51,5	32	48,5	2	3,0
≥ 4,5	32	48,5	2	3,0	30	45,5
Total	66	100,0	34	51,5	32	48,5

From the first elastography examination, it is found that SE means in the group with benign cytology is 2. On the other hand, the SE mean in the malignant cytology group are 4. Secondly, from the SR assessment is found the SR mean in the benign cytology group is $3,03 \pm 1,28$. The elastography score is range from 0 until 5. In score 0, it is obtained 17 persons (25,8%) with benign tumors. In score 1, it is found 5 persons (7,6%) with benign tumors.

Score 3 found 8 patients (12,1%) with benign tumors. Score 4 obtained 18 patients (27,3%) with malignant tumors. In score 5, there are 10 patients (15,2%) with malignant tumors. The strain ration $<4,5$ are 34 patients (51,5%) with benign tumors and 2 persons (3%) are the malignant tumor patients. On the other hand, the strain ration $\geq 4,5$ are 32 persons with 2 patients with benign tumors (3%) and 30 patients with malignant tumors (45,5%).

The Sample Distribution Based on The Result of Cytology

Table 2. The Sample Distribution Based on The Result of Cytology

Category	Frequency	Percentage(%)	SE	Mean SR
Benign				
Benign cystic lesion	17	25,8	BGR,2	2,41
FAM	10	15,1	1-4	3,78
BEH	4	6,1	2-3	3,67
FCC	2	3,0		
Phylloides	1	1,5	1	3,31
Total	34	51,5		
Malignant				
Invasive ductal ca	22	33,3	2,4-5	7,85
Mucinous ca	3	4,5	4-5	6,74
Invasive lobular ca	2	3,0	3,5	6,85
Invasive ca of NST	2	3,0	3-4	6,58
Susp. malignant	2	3,0	4	6,87
Malignant round cell ca	1	1,5	3	3,46
Total	32	48,5		

From 66 samples, 26 samples have been confirmed with the histopathology result. The benign tumor category includes 34 persons (51,5 %) which the benign cystic lesion are 17 patients (25,8 %) and FAM are 10 patients (15,1 %). There are 32 subjects (48,5 %), which are included in the malignant category, and invasive ductal Ca are included 22 patients (33,3 %) (Table 3).

The Diagnostic Performance of The SE and SR combination

Table 3. The diagnostic performance of the combination of SE and SR

SE + SR	FNAB			Malignant	Total
	Benign				
Benign	32			2	34
Malignant	2			30	32
Total	34			32	66
Sensitivity	= 93,8 %		PPV	= 93,8 %	NPV = 94,1 %
Specificity	= 94,1 %		FP	= 6,3 %	FN = 5,9 %
Accuracy	= 93,9 %				

The results of the examination of SE and SR benign tumor elastography score and benign tumor FNAB are 32 patients while the malignant tumor examinations are 2 patients. The results of elastography score in malignant tumor and FNAB in benign tumors are 2 patients while the results of the examination in the malignant tumor are 30 patients. The sensitivity result of the diagnostic performance of SE is 93,8%, the specificity is 94,1%, the accuracy is 93,9%, PPV is 93,8%, FP is 6,3%, NPV is 94,1%, and FN is 5,9%.(Table 3).

The Diagnostic Performance of the Combination of Elastography And Grayscale

Table 4. The diagnostic performance of the combination of elastography and grayscale

Elasto & Gray Scale	FNAB		Total
	Benign	Malignant	
Benign	33	3	36
Malignant	1	29	30
Total	34	32	66
Sensitivity	= 90,6 %	PPV = 90,6 %	NPV = 91,2 %
Specificity	= 91,2 %	FP = 9,4 %	FN = 8,8 %
Accuracy	= 90,9 %		

The results of the gray scale in benign tumor and FNAB in the benign tumor are 33 persons and the score of elastography in benign tumor and FNAB in the malignant tumor are 3 persons. The results of the gray scale in malignant tumor and FNAB in the benign tumor are 1 persons and the score of elastography in malignant tumor and FNAB in the malignant tumor are 29 persons. The sensitivity result of the diagnostic performance of SE is 90,6%, the specificity is 97,1%, the accuracy is 93,9%, PPV is 96,7%, FP is 3,3%, NPV is 91,7%, and FN is 8,3%.

Discussion

This study revealed that there are 2 lesions with FNAB-FCC result. Theoretically, FCC must result in the benign elastography. However, this study is obtained 1 case with malignant elastography (SE = 4; SR = 4,61). After analyzing it, it is indeed found that the lesion location, in this case, is deep (depth +/-1,1 cm) compared to the other FCC that has been diagnosed accurately. As Thomas et al stated, the depth of lesion location which is more than 1 cm cannot be evaluated adequately with elastography. However, from the data analysis of the study, it is obtained that there is no false positive/negative in the lesion with 1,5 cm deep.

This study revealed that 3 lesions with FNAB-BEH result and all of them have tendency to benign elastography. However, two of them have the grayscale result that tends to be malignant. In accordance with the study conducted by Barr et al., the BEH case had a grayscale result and malignant elastography.

This study found 22 cases with FNAB-IDC and two cases with FNAB-ILC result. There are 3 cases such as (2 IDC, 1 ILC) with the benign elastography result (SE = 2-3; SR = 3,20), but the grayscale result tends to be malignant. The false negative is also reported in the two conducted^{5,10}. IDC and ILC are categorized as "hard carcinoma" compared to other malignant tumors¹¹. IDC/ILC low grade and intermediate usually related to the intensified esmoplastic process. So it will appear as a hard lesion. On the other hand, IDC high grade is related to the high rate of mitosis and necrosis area so that it appears to be a mild lesion. Thus, it causes the false negative result.

This study found 3 cases with FNAB mucinous ca and 2 cases with NST result. Mucinous ca and NST are categorized as "soft carcinoma"¹¹. It is usually related to the cystic component or a collection of mucin so that it appears to be soft. Based on the result of this study. It is found mean SE and SR for lower mucinous compared to IDC/ILC. This study revealed that one case with malignant round cell ca result (referred to NHL). The result of elastography and grayscale tend to be benign (SE = 3, SR = 3,46. Similar to the previous studies conducted by Thomas et al. dan Barr et al., there are 2 cases of false negative which are lymphoma.

On the other hand, the result of this study tends to be benign. It referred to the facts that the discovery of conventional radiography does not usually assist in distinguishing the primary lesion with metastatic. We

found that the cutoff value is SR 5.1. As a comparison, a conducted study found that the SR value in breast cancer diagnosis was 3.08¹². In addition, a study found that the SR value is 4,5 as it is used to be the standard in this study¹³. However, previous conducted study found that the SR value is 2,8¹⁴.

In this study, SE possesses the sensitivity of 87,5 %, 94,1 % of specificity, the accuracy is 90,9 %, the false positive is 6,7 %, the false negative is 11,1 %. While, SR possesses 93,8 % sensitivity, 94,1 % of specificity, 93,9 % of accuracy, 6,3 % of false positives, and 5,9 % of a false negative. While grayscale has 90,6 % sensitivity, 91,2 % specificity and 90,9 % accuracy. If it is all combined with the grayscale sensitivity, specificity, and accuracy, it obtains 90,6 %, 97,1 %, 93,9 %. From the results above, it can be concluded that the elastography can increase the specificity of grayscale. It is in accordance with the results of some studies⁵. Some previous studies found that asserted that elastography could increase the specificity in breast tumor diagnosis¹².

There is a significant correlation between the tumor size and the result of elastography ($P = .034$). The result of this study is in accordance with the two related previous studies (Itoh, et al. 2014), (Rizzato 2001). However, there is no significant correlation between the depth of tumor and the result of Elastography ($P = .624$). It Is Not In Accordance With The Two Conducted Studies^{15,14}

However, there is no significant correlation between the depth of tumor and the result of elastography. The breast tumor with 3 scores are not considered as the benign one but it is considered as indeterminate and suggested to do biopsy.. All tumors with 3 scores underwent a biopsy to minimize the findings of a false negative, because it would increase the sensitivity in 2007. However, this study still suggests that biopsy must be undergone by considering the result of gray scale USG first.

Conclusion

Ethical Clearance: This study protocol was approved by ethical clearance Dr. Soetomo Surabaya, Indonesia teaching hospital research.

Conflict of Interest: This study protocol was approved by ethical clearance Dr. Soetomo Surabaya, Indonesia teaching hospital research.

Source of Funding: This study is done with

individual funding.

References

1. Barr, Mr H., N. Krasner, P. B. Boulos, P. Chatlani, and S. G. Bown. "Photodynamic Therapy for Colorectal Cancer: A Quantitative Pilot Study." *BJS (British Journal of Surgery)* (BJS Society) 77, no. 1 (1990).
2. Bojanic, Kristina, et al. "Implementation of Elastography Score and Strain Ratio in Combination with B-Mode Ultrasound Avoids Unnecessary Biopsies of Breast Lesions." *Ultrasound in Medicine & Biology* (Science Direct) 43, no. 4 (2017): 804-816.
3. Bussière, Clémence, Jonathan Sicsic, and Nathalie Pelletier-Fleury. "The Effects of Obesity and Mobility Disability in Access to Breast and Cervical Cancer Screening in France: Results from the National Health and Disability Survey." *Plos One* (Plos One) 9, no. 8 (2014).
4. Carlsen, Jonathan F., Caroline Ewertsen, Lars Lönn, and Michael B. Nielsen. "Strain Elastography Ultrasound: An Overview with Emphasis on Breast Cancer Diagnosis." *Diagnostics* (MDPI) 3, no. 1 (2013): 117-125.
5. Gheonea, Dan Ionuț, Costin Teodor Streba, Tudorel Ciurea, and Adrian Săftoiu. "Quantitative Low Mechanical Index Contrast-enhanced Endoscopic Ultrasound for The Differential Diagnosis of Chronic Pseudotumoral Pancreatitis and Pancreatic Cancer." *BMC Gastroenterology* (Springer Nature), 2013.
6. Giuseppetti, G. M., A. Martegani, B. Di Cioccio, and S. Baldassarre. "Elastosonography in the Diagnosis of the Nodular Breast Lesions: Preliminary Report." *Radiology Medical* 1, no. 2 (2005): 69-76.
7. Goddi, A., M. Bonardi, and S. Alessi. "Breast Elastography: A Literature Review." *Journal of Ultrasound* (Elsevier) 15, no. 3 (2012): 192-198.
8. Gong, C, et al. "Beclin 1 and Autophagy are Required for the Tumorigenicity of Breast Cancer Stem-like/Progenitor Cells." (*Ocogene*) 32 (2013): 2261-2272.
9. Itoh, Hiroaki, et al. "Dietary Cadmium Intake and Breast Cancer Risk in Japanese Women: A Case-control Study." *International Journal of Hygiene and Environmental Health* (Science Direct) 217, no. 1 (2014): 70-77.
10. Ophir, J., et al. "Elastographic Imaging." *Ultrasound in Medicine and Biology* (Elsevier) 26, no. 1 (2000): 23-29.
11. Parker, Joel S., et al. "Supervised Risk Predictor of Breast Cancer Based on Intrinsic Subtypes." *Journal of Clinical Oncology* (American Society of Clinical Oncology) 27, no. 8 (2009): 1160-1167.
12. Rizzatto, Giorgio. "Towards A More Sophisticated Use of Breast Ultrasound." *European Radiology* (Springer) 11, no. 12 (2001): 2425-2435.
13. Sadigh, Gelareh, Ruth C. Carlos, Colleen H. Neal, and Ben A. Dwamena. "Ultrasonographic Differentiation of Malignant from Benign Breast Lesions: A Meta-analytic Comparison of Elasticity and BIRADS Scoring." *Breast Cancer Research Treatment* (Springer) 133, no. 1 (2012): 23-35.
14. Thomas, Eva S., et al. "Ixabepilone Plus Capecitabine for Metastatic Breast Cancer Progressing After Anthracycline and Taxane Treatment." *Journal of Clinical Oncology* (American Society of Clinical Oncology) 25, no. 33 (2007).
15. Zhi, Xiangcheng, et al. "BRCA1 and BRCA2 sequence variants in Chinese Breast Cancer Families." *Human Mutation* (Wiley Online Library) 20, no. 6 (2002).