

BREAST DENSITY EVALUATION: A COMPARISON BETWEEN ASSESSMENT BY A RADIOLOGIST AND THE COMPUTER-ASSISTED THRESHOLD TECHNIQUE

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ABSTRACT

Traditionally, mammographic density (MD) of the breast has been assessed by a radiologist visually. This subjective evaluation requires significant experience to distinguish the relative proportions of the fibrous connective tissue and adipose tissue in the mammary gland correctly.

The aim of this study is to compare the capabilities of the different methods (visual and computer-assisted) for assessing mammographic density.

Our sample in this study consists of 66 patients with digital mammography. The mammographic density has been evaluated using the four-grade scale of the American College of Radiology (ACR); visually, visually using an analog scale and semi-automated using UTHSCSA Image Tool 3.0, Image J and Adobe Photoshop CS6 software.

The average mammographic density calculated using the different methods is as follows: 34.8% (from 10% to 70%); 32.1% (from 10% to 60%); 23% (from 0% to 70.9%); 22.7% (from 2.5% to 78.1%) and 22.5% (from 1.5% to 72.4%).

There is a strong correlation between the results obtained visually and those calculated using a computer-assisted measurement ($p < 0.0001$). A strong correlation was found also between the results acquired using the different semi-automated programs ($p < 0.0001$).

Precise measurement of mammographic density is of great importance for the mammographic screening and evaluation of breast cancer risk. The semi-automated methods, used for this purpose are objective, accessible and reproducible tools and have some advantages over the subjective visual assessment.

KEYWORDS: mammography, breast density measurement

Introduction

Mammographic density (MD) manifested as a radiologically dense zone (consisting of epithelial and connective tissues) and represented as a percentage of the whole breast area. Although the precise mechanisms are not entirely clear, women with high-density breasts have a 4 to 6 times greater risk of breast cancer when compared to those with low-density mammary glands. [1, 2, 3] Furthermore, breast density is discussed as a prognostic factor for the outcome of invasive breast cancer. [4, 5] In 1976, John Wolte first proposed that there be an association between the "parenchymal patterns" seen in the mammogram and the risk for later development of breast cancer. He categorized

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Ansel Adams' description of zones (geared towards black and white printing)

Low values Zone 0	Complete lack of density in the negative image, other than film base density plus fog. Total black in the print. <i>We will omit zone 0 from the remainder of this tutorial; zone 1 will be considered pure black. Omitting zone 0 makes little practical difference.</i>
Zone 1	Effective threshold. First step above complete black in the print. Slight tonality, but no texture.
Zone 2	First suggestion of texture. Deep tonalities, representing the darkest part of the image in which some detail is required.
Zone 3	Average dark materials. Low values showing adequate texture.
Middle values Zone 4	Average dark foliage. Dark stone. Landscape shadow. Recommended shadow value for portraits in sunlight.
Zone 5	Clear north sky (panchromatic rendering). Dark skin. Gray stone. Average weathered wood. Middle gray (18% reflectance).
Zone 6	Average Caucasian skin value. Light stone. Shadows in snow in sunlit snowscapes.
High values Zone 7	Very light skin. Light gray objects. Average snow with acute side lighting.
Zone 8	Whites with textures and delicate values (not blank whites). Snow in full shade. Highlights on Caucasian skin.
Zone 9	Glaring white surfaces. Snow in flat sunlight. White without texture. (The only subjects higher than Zone 9 would be light sources; they would be rendered as the maximum white value of the paper surface.)

Fig. 1: Ansel Adams zone system.

breast density in four qualitative groups: N_1 , primarily fatty; $P_1 \leq 25\%$ prominent ducts; $P_2 > 25\%$ prominent ducts; and DY , dense fibro-glandular tissue. [6] Subsequently, these qualitative characteristics were added to the Breast Imaging Reporting and Data System (BI-RADS), with the aim of standardizing the mammographic assessment. To which in 2003, the American College of Radiology (ACR) added the following quantitative characteristics: low density, $D1 < 25\%$; $D2$ from 25% to 50%; $D3$ from 51% to 75%; and high density, $D4 > 75\%$. [7]

According to BI-RADS (2013, 5th ed.), there are four breast composition categories [6]:

- The breasts are almost entirely fatty
- There are scattered areas of fibro-glandular density
- The breasts are heterogeneously dense, with many obscure small masses
- The breasts are extremely dense, which lowers the sensitivity of mammography

With the widespread implementation of digital mammography, in the last couple of years, a wide variety of computer-assisted threshold techniques for MD evaluation have been employed (Cumulus, Madena, Image J, and others). However, there is still no accepted standard for their use. [1, 8, 9]

The aim of this study is to compare the capabilities of the different methods (visual and computer-assisted) for evaluating mammographic density.

Material and Methods

Our sample in this study consists of 66 patients with benign diseases of the mammary gland, who received surgery in the Department of Thoracic Surgery, MMA-Sofia. The average age of the patients is 53.9 years (from 37 to 76 years old).

There is no data in any of the patients' anamnesis for prior breast cancer or implants. Digital mammography of the two

breasts performed in the craniocaudal and mediolateral projections, 5-12 days after the last menstruation for premenopausal women.

All mammograms were produced using the digital mammography system Senograph 600T-FD, GE. The interpretation of the mammograms was carried out by the guidelines of ACR, by a radiologist with significant experience in breast pathology. (E.Z.)

After a visual assessment using the four degree scale of ACR ($D1$ - $D4$), a second visual evaluation was done, using the analog scale of Ansel Adams and Fred Archer, in which the gray tone from black to white has been divided into 9 easily distinguishable zones. (Fig. 1)[10]

We accepted as dense (in the mammogram) the areas that fell into the 8th and 9th zones of the scale.

The computer-assisted MD evaluation performed in the craniocaudal projection of the right breast for all of the participating in the study patients. For this assessment, we used UTHSCSA Image Tool 3.0, Image J and Adobe Photoshop CS 6 software. [11, 12] Our team has considerable experience using these software products.

Firstly, the mammogram of the right breast is saved as JPEG image. Next, a standard with a known linear size (calculated in mm) is identified on every picture. Afterward, the images are opened with the UTHSCSA Image 3.0 software. After calibrating spatial measurements, a measurement of the two-dimensional projection of the area with "dense" zones in the breast performed.

After measuring the two-dimensional projection of the whole breast, dense zones are calculated as a percentage of the entire breast. Similarly, mammographic density is calculated using Image J and Adobe Photoshop CS6 software. The area of the dense zones in the mammogram and the area of the whole breast are defined in pixels (Fig. 2a and Fig. 2b).

The measurements of mammographic density, using different software products, are presented in percentage terms. The

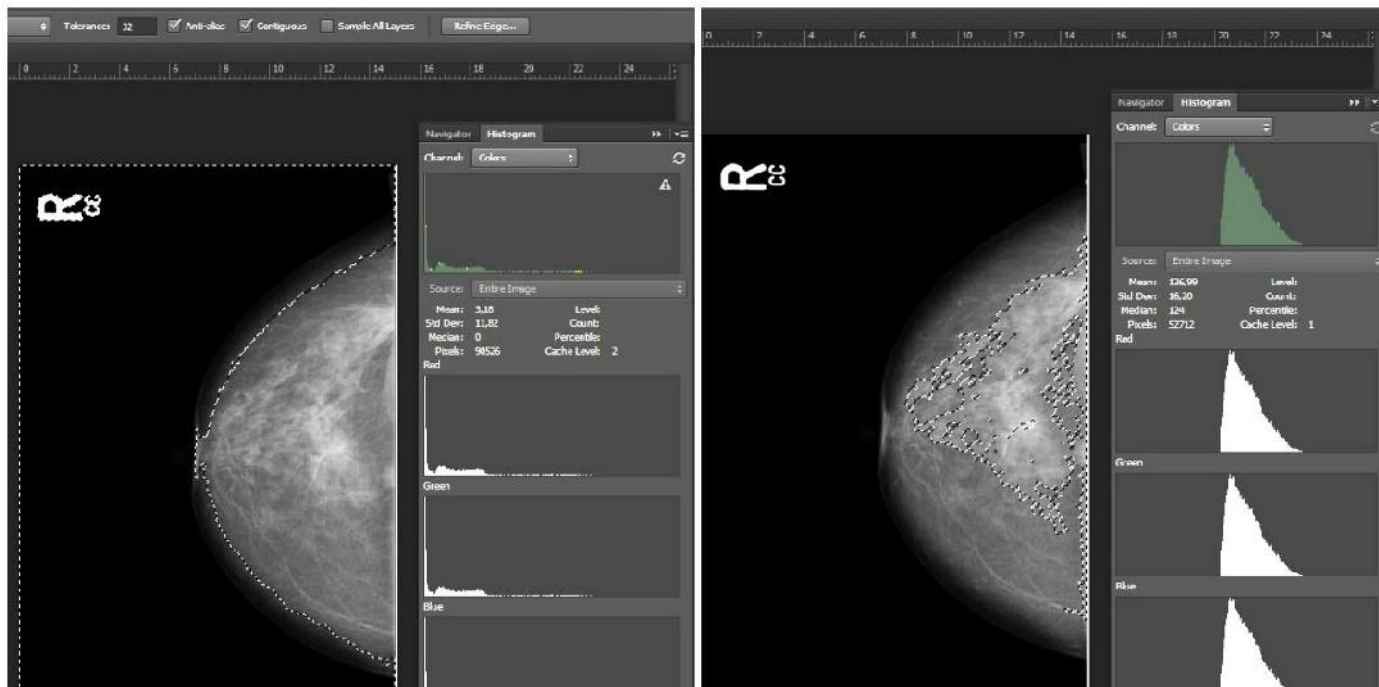


Fig. 2a: A 63-year-old patient with 52.2% mammographic density calculated using Adobe Photoshop CS6 and Image J.

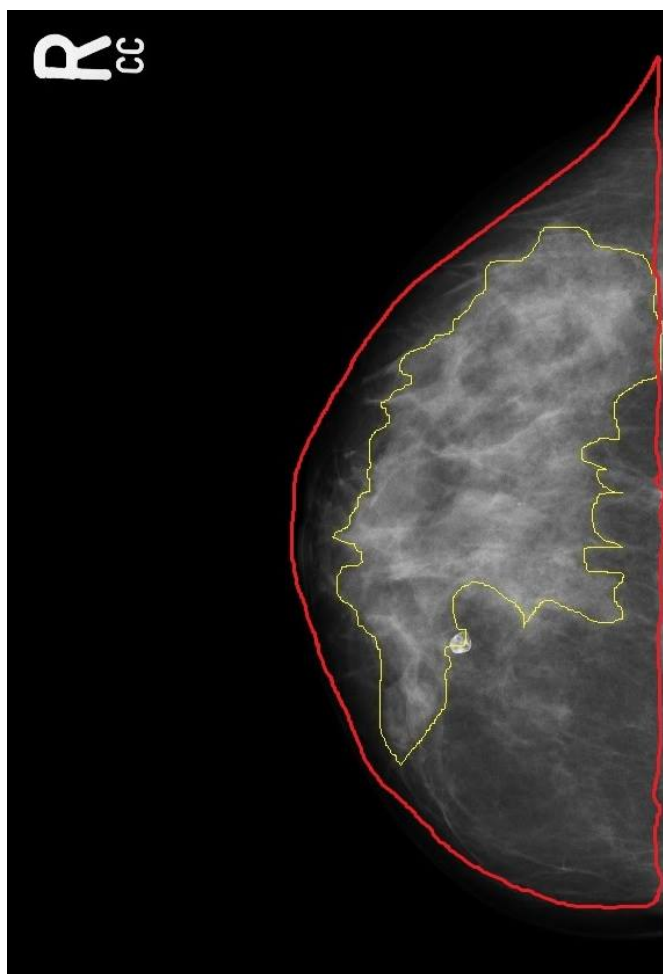


Fig. 2b: A patient measured with Image J.

results then analyzed in pairs (each method with each of the other methods), for each pair a Pearson's correlation coefficient (r) and its significance are calculated. Values of $p < 0.05$ are considered significant. The strength of the correlation defined as perfect, strong, moderate, weak or none existent according to Dancey and Reidy's (2004) guidelines. [13] For this assessment, Microsoft Excel software is used. Because of the lack of normal distribution of the studied variables, the differences between the medians of visually calculated MD and the MD, calculated using the computer-assisted methods were statistically analyzed using the Mann-Whitney (Wilcoxon) test (calculated using Statgraphics plus 2.1). Values of $p < 0,05$ were considered significant.

Results

The results obtained from MD evaluation using the various methods described are presented in Table 1.

The median MD values, calculated visually were significantly higher than those, assessed using the computer-assisted methods. The median visually evaluated value was 30% (from 10% to 70%) in comparison to the median value calculated using the semi-automated methods - 18.7% (from 0.00% to 78.1%)($W=6934.0$; $p < 0.001$). This difference is exceptionally distinguishable in the D2 density group (25% to 50%). In this group, we find half of all cases evaluated visually while only one-fourth of the patients assessed using the computer-assisted methods categorized as D2.

In 56 (84.8%) of the patients, assessed using semi-automated methods, the differences between the three methods were under 10% for each case. Only in 10 (15.2%) we found a difference of over 10% between the different types of software.

It is evident that there is a strong correlation between the visually evaluated results (by E.Z.) and those assessed visually using the analog scale of Adams and Archer (by G.B.) ($n=66$; $r=0.9664$; $P < 0.0001$).

Furthermore, a strong correlation exists between the results

Table 1 Mammographic Density Evaluation results using the various methods.

Method:	Visual	Visual with Analog Scale	Image tool	Image J	Photoshop CS6
D1	20	28	42	44	46
D2	38	90	16	14	12
D3	8	8	4	4	8
D4	-	-	2	2	-
Average (%)	34.8%	32.1%	23%	22.7%	22.5%
Varying between	(10-70%)	(10-60%)	(0-70.9%)	(2.5-78.1%)	(1.5-72.4%)
Total	2300	2120	1520.6	1796.6	

assessed visually and those using the semi-automated method with Image tool (by I. Iv) (n=66; r=0.9166; p<0.0001), with Image J (by I. In) (n=66, r=0.8465; p<0.0001) and with Photoshop CS6 (by G. B)(n=66, r=0.9125; p<0.0001).

We conclude that there is a strong correlation between the MD values (in percentages) assessed using the analog scale and those evaluated semi-automatically using Image Tool software (n=66, r=0.9213; p<0.0001).

The results assessed visually correlate strongly with those calculated using Image J (n=66, r=0.8464; p<0.0001) and with those evaluated using Photoshop CS6 (n=66, r=0.9226; p<0.0001). Furthermore, we found a strong correlation between the results evaluated semi-automatically with Image Tool and those using Image J (n=66, r=0.8583; p<0.0001) and those using Photoshop CS6 (n=66, r=0.9253; p<0.0001).

There is no significant difference in the time needed to calculate the MD of one patient, from one to three minutes using the analog scale and from 2.5 to 5.5 minutes using the computer-assisted methods (Table 2).

Discussion

Mammographic density evaluation has been the primary subject of a variety of studies in the last 20 years. Traditionally, MD of the breast has been visually assessed by a radiologist using a standard mammogram. This subjective evaluation requires significant experience for one to be able to assess the relative proportions of fibrous connective tissue and adipose connective tissue in the breast correctly. There is evidence for significant differences in MD evaluations by different radiologists. [14] With the widespread implementation of digital mammography and its accessibility, it was just a matter of time before software products for computer-assisted and fully automated MD evaluation were developed and utilized. These improved methods could potentially be beneficial for a more precise quantitative assessment of breast cancer risk and its timely assessment. It is exceptionally important because breast density can alter by important factors like hormones, diet, and the patient's age. [3, 15]

According to the legislation in 21 American states, currently doctors are required to inform patients if their breasts are mammographically dense, and must recommend additional examinations and follow-ups in such cases. An evaluation of the 5-year

risk of the subsequent development of breast cancer (Gail model) combined with assessment of MD could help in the identification of women with high risk and the subsequent implementation of additional screening methods in such cases. [16, 18]

Although there are some differences in the assessment of dense zones in the breast (higher values evaluated subjectively in comparison to those calculated using the semi-automated methods) in our study we did not find a statistically significant difference in the final groups (D1-D4). According to other authors who analyzed a significantly greater series of cases, there is a tendency in the visual evaluation for overestimating the area of the dense zones. [18, 19, 20] Regarding the time needed to perform MD evaluations using various computer-assisted methods our results are in line with existing literature. [18]

A recently published study (Alonzo-Proulx et al., 2015) compares MD evaluation with semi-automated methods to using fully-automated methods (Volpara, Quantra). The study finds no significant difference in the end results. [21]

Although an in-depth discussion of the image processing software for fully automated analysis is outside the reach of this article, exploring its possibilities is important and should be researched further with a greater number of cases.

We believe that tomosynthesis of the breast, CT and MRI could also be utilized in MD evaluation, but for now these methods are not routinely used for screening and diagnostics in our practice. According to some studies, there is a considerable correlation between results from computer-assisted methods for evaluating digital mammograms and MRI results. [9, 14, 20]

Conclusion

We can state that accurate MD evaluation has great importance for improving the mammographic screening and assessment of individual breast cancer risk. The semi-automated methods used for this purpose are objective, non-invasive instruments that have a better reproducibility than the subjective visual assessment, which requires significant experience in breast pathology.

Taking into account that most of the computer-assisted threshold techniques are widely available and easy to use, they are one of the possibilities for evaluating the different types of breast tissue in the modern digital age.

Table 2 Time needed (in minutes) to evaluate the MD with the different methods. The time required to turn the digital mammo-gram from DICOM format into JPEG (2 to 3 minutes) is not included.

Visually	Visual with Analog Scale	Image Tool	Image J	Photoshop CS6
1.5 (average)	2.2	3	3.5	4.5
1 to 2	1.5 to 3	2.5 to 4	2.5 to 4.5	3 to 5.5

Although, a “gold standard” for assessing MD still does not exist. We recommend Image J for everyday use in the clinical practice. The Image J software is freely available, runs on Java and is thus not based on any specific platform. Furthermore, it does not require substantial expertise to run the macros for processing mammograms. Its open-source design makes Image J more easily adaptable than many other packages.

Authors’ Statements

Competing Interests

The authors declare no conflict of interest.

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