Breast cancer early detection via tracking of skin back-scattered secondary speckle patterns

Aviya Bennett, Talia Sirkis, Yevgeny Beiderman, Sergey Agdarov, Yafim Beiderman and Zeev Zalevsky

Faculty of Engineering and the Nanotechnology Center, Bar-Ilan University, Ramat-Gan 52900, Israel

ABSTRACT

Breast cancer has become a major cause of death among women. The lifetime risk of a woman developing this disease has been established as one in eight. The most useful way to reduce breast cancer death is to treat the disease as early as possible. The existing methods of early diagnostics of breast cancer are mainly based on screening mammography or Magnetic Resonance Imaging (MRI) periodically conducted at medical facilities. In this paper the authors proposing a new approach for simple breast cancer detection. It is based on skin stimulation by sound waves, illuminating it by laser beam and tracking the reflected secondary speckle patterns. As first approach, plastic balls of different sizes were placed under the skin of chicken breast and detected by the proposed method.

Key words: Speckle; Tissue characterization; Medical optics instrumentation;

1. INTRODUCTION

Breast cancer has become a major cause of death among women [1]. The lifetime risk of a woman developing this disease has been established as one in eight [2]. The most useful way to reduce breast cancer death is to treat the disease as early as possible. Most primary breast cancers are detected by the patients themselves when the average size is about 2.5 cm. The survival chance of breast cancer drops from a rate of about 95% when the lump is about 0.5 cm size, to a rate of 75% when the cancer is treated at a size of about 2.5 cm. Hence, finding an accurate, simple and effective diagnostic method is very important [3]. Breast palpation found to be a simple and brief clinical screening test for breast cancer [4]. In addition, there is general agreement that screening mammography reduces the rate of death from breast cancer among women [5]. However, studies show that screening can be over diagnosed causing women undergo surgery, radiation therapy, hormonal therapy, chemotherapy, or usually a combination of these [6]. Moreover, the sensitivity of mammography ranges from approximately 70% to 90% [7-9] and has a high false diagnosis ratio for cancer [10]. Therefore, further improvement in mammographic sensitivity is needed [11]. Another tool for breast cancer diagnosis is the MRI, which provides high soft tissue contrast, but it has to be made more practical for application in breast imaging [10, 12].

Another optical tool is diaphanoscopic which is based on the difference in absorption coefficients of various tissues. It enables the detection of non-homogeneities in the breast. The areas of dense tumor look darker, while the pockets of cyst look clearer as compared to the surrounding tissues. However, breast cancer detection rate using this method is about 30% [13]. Ultrasound Tagging of Light (UTL) was proved to be useful in the detection of breast cancer. Photon localization in turbid tissue is achieved by cross modulating a laser beam with focused, pulsed ultrasound. Light which passes through the ultrasound focal spot is `tagged' with the frequency of the ultrasound pulse. However, much work remains to be done to prove the feasibility of UTL technique as a breast cancer imaging system [14].

Near-infrared spectroscopy has gained importance for non-invasive or minimally invasive cancer diagnostic applications in cancer. It is based on differences of endogenous chromophores between cancer and normal tissues. The method provides diagnosis and therapy monitoring of several cancers [15, 16]. Optical coherence elastography was also examined in view to diagnose breast cancer. Tumor was identified by obtaining higher Young's modulus [17-19]. Speckle is a common phenomenon in coherent imaging systems and is an artifact degrading target visibility. It occurs when a coherent source and a detector are used to interrogate a medium, which is rough on the scale of the wavelength. Previous works used speckle pattern in order to characterize tissues. For example, Ruey-Feng Chang et al. evaluated breast masses in pathologically-proven tumors based on analysis of ultra-sound (US) speckles for classifying breast tumors [20]. Jun Li et al. found that the contrast of the speckle pattern formed by the transmitted light decreased when ultrasound acted on the tissues. By measuring the variation of the speckle contrast with the location of ultrasonic column,

Nanoscale Imaging, Sensing, and Actuation for Biomedical Applications XV, edited by Alexander N. Cartwright, Dan V. Nicolau, Dror Fixler, Proc. of SPIE Vol. 10506, 1050603 · © 2018 SPIE
CCC code: 1605-7422/18/$18 · doi: 10.1117/12.2286791

they could detect optical inhomogeneities inside the tissue [21]. Tuchin stated that speckle based methods are applicable for various tissue structure imaging and can be suitable in many areas of medicine [22]. Ulyanov and Tuchin showed the use of low-coherence speckles in the field of bioflow measurements [23], Ulyanov et al. analyzed the fundamentals and applications of speckles induced by laser beam [24]. Zalevsky et al. presented a novel technique for remote noncontact blood pulse pressure measurement. It is based on tracking the temporal changes in both the position and the amplitude of reflected secondary speckle patterns produced in human skin when illuminated by a laser beam [25]. Using the same method, Sirkis et al. measured continuously pulse wave velocity and pulse pressure [26]. It was proposed by Zalevsky et al. to have the camera focused on the far field and the object itself being defocused. Such configuration transforms tilt vibrations of the object to a lateral shift of the speckle patterns. In this way, the movement of the object creates a situation in which the speckle patterns are only moving or vibrating in the transversal plane [27].

2. THE METHOD

Breast tumors associated with micro calcifications, mainly composed of hydroxyapatite, which is a very hard material compared with breast tissues. Therefore, a modality that is sensitive to the elastic properties of tissues would likely be suitable for detection of micro calcifications. This group of imaging techniques is called elasticity imaging [28]. The general approach in elasticity imaging is to measure the response of tissue to an excitation force [29]. The excitation force used in current work is an acoustic pulse of specific frequency. The magnitude of the pressure gradient caused by an acoustic beam travelling through an absorbing medium is proportional to the acoustic intensity in the beam and to the absorption [30].

During the acoustic wave propagation in the tissue, it is reflected as a function of the tissue properties and the reflected signal interfere with the agitation signal affecting the surface, resulting on skin oscillation. Once the acoustic excitation is stopped, the oscillation is damping. We assume that the presence of cancer tissue simulated by a plastic ball having different acoustic properties from the healthy tissue, will affect the damping. The sound wave reflected from the plastic ball will increase the oscillation decline and oscillation will damp faster. It could predict presence of plastic ball or micro calcifications related to breast cancer. The under forced damped harmonic oscillation of the skin surface is:

$$\ddot{x} + b\dot{x} + kx = 0 \tag{1}$$

In case $b^2 \geq 4k$ the oscillation is damped or over damped. Such situation was observed under initial testing of the skin sample. See Fig. 1:

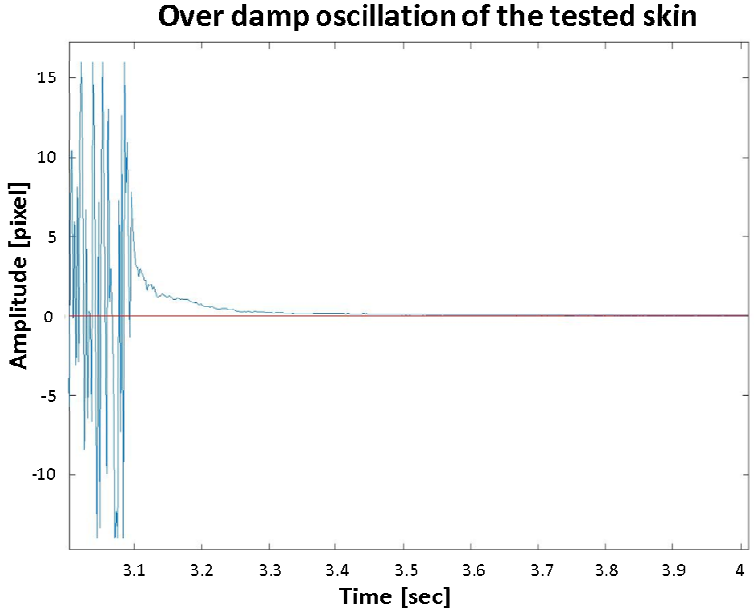

Fig. 1. Over damp free oscillation of the tested skin.

For over damped oscillation the solution of Eq. 1 could be described as follow:

$$x(t) = C_1 e^{r_1 t} + C_2 e^{r_2 t} \tag{2}$$

Where

$$r_1 = \frac{-b + \sqrt{b^2 - 4k}}{2} \qquad r_2 = \frac{-b - \sqrt{b^2 - 4k}}{2}$$

Constants C_1 and C_2 could be determined from initial condition $x(0)=A_{max}$ (maximum amplitude) and $\dot{x}(0)=0$. Where b and k can be determined from the over damped curve approximation.

2.1 Biological setup

The current work is based on the assumption that micro calcification related to breast tumor could be modeled by means of a plasticized ball inserted in the tissue. Different sizes of plasticized balls were inserted at different depths under the chicken breast skin as shown in Fig. 2.

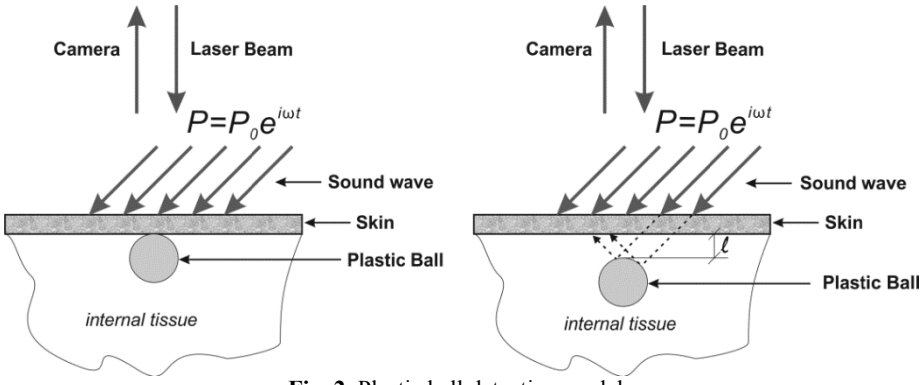

Fig. 2. Plastic ball detection model.

At the first stage we tried to find influence of small plastic balls with different diameters being placed under the skin on the free skin oscillations. It was assumed that it is possible to detect different sized bodies by exciting and illuminating the same area with laser beam.

Plastic balls of 2, 4, 6 and 8mm were prepared for the experiment. As breast simulated tissue we used 2cm thick chicken breast part covered by skin.

At the first stage, the balls were placed directly under the skin inside the tissue so that the top of the balls touched the internal part of the skin. A HJ 532nm wavelength green laser was used to illuminate the tissue. After the acoustic excitation stopped, tissue free oscillation response was evaluated.

At the second stage the different diameter plastic balls were placed inside the tissue at different depths. The setup remained the same but the balls were placed 2.5 & 5mm deeper into the tissue. For both experiments, the possibility to detect the objects of different physical properties placed under the skin was examined.

Please note that in our experiments the sound absorption have not been evaluated. Only the scattering of the light from the oscillated surface was analyzed. Our assumption is that the skin vibration is affected by the presence of the under-dermal plastic ball which affects the skin's oscillation after the agitation stopped.

2.2 Optical setup and system configuration

The optically-based monitoring infrared device was positioned 28.5cm from the examined chicken tissue containing plastic ball. The system contains a fast camera and a laser. A HJ 532nm green laser was used to illuminate the tissue. Its reflections were analyzed using a "PixeLINK" high sampling rate digital camera. The camera's focal length was 55 mm with an F-number of 2.8. The illuminating beam was 3mm in diameter. The focusing was performed on a focal plane that fulfills the far field conditions of diffraction applied in respect to the back-reflecting surface that in our case was the skin. Specifically, the focusing plane was a few meters away from the skin surface. The skin was agitated by sound waves with excitation frequency of 300Hz (see section 3.1). Each frame presented a secondary speckle pattern being correlated to the next frame. The position of the correlation peak was derived and its time depended position was plotted

using Matlab software. The signal amplitude designates the shift in the location of the correlation peak in pixel units of the camera. A sketch of the constructed setup and the experimental setup configuration is given in Fig. 3.

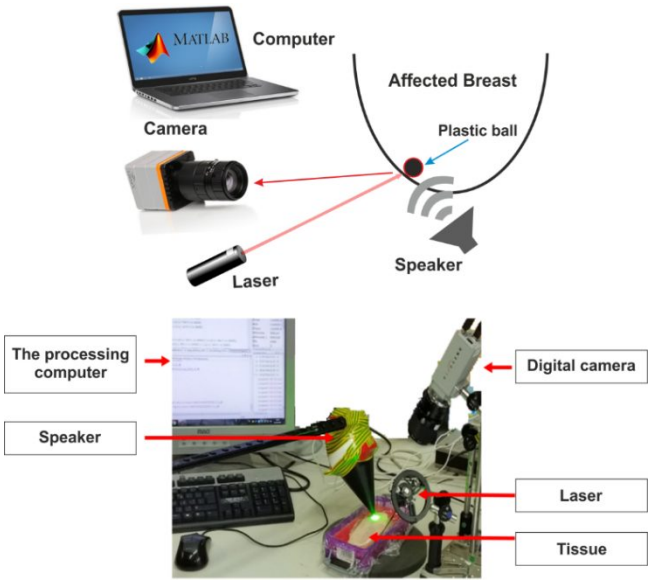

Fig. 3. Implemented optical configuration for breast cancer simulated remote measurement (a) Sketch of the optical system. (b) The breast cancer simulated experimental setup configuration.

3. RESULTS

3.1 Excitation frequency and signal amplitude evaluation

In order to find the excitation frequency with most significant response, several frequencies within (100-300Hz) were examined. The frame rate (FPS) of the digital camera was three times higher than the frequency measured, in order to fully fulfill the Nyquist ratio requirements. Furthermore, in order to find the most powerful response, we applied the excitation signal under the mentioned frequencies with two different sound wave amplitudes (92dB and 100dB). After the preliminary tests, based on the damping duration, the agitation frequency of 300Hz@100dB and camera working at 900 FPS were selected for further experiments. See Fig. 4.

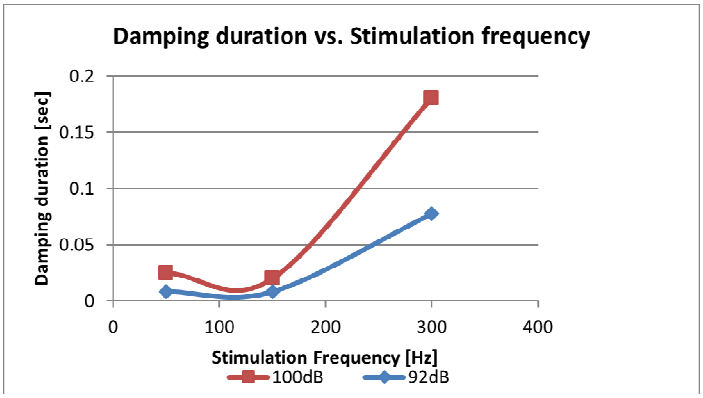

Fig. 4. Damping duration of skin free oscillation vs. stimulation frequency.

3.2 Plastic balls detection under the skin of the chicken breast

In order to check the possibility of detection of plastic balls under the skin simulating breast cancer calcification, a chicken breast was used as the examined tissue. Cuts under the skin surface were performed for planting four different sized balls (of 2, 4, 6 and 8mm in diameter). The top of balls was positioned exactly under the skin surface. As a

reference, the tissue was also tested independently without any ball inserted into it. The tissue was brought to vibration by sound waves with acoustic excitation frequency of 300Hz@100dB from an external speaker. After agitating the tissue surface for few second, the signal was turned off and the damped oscillation of the skin was recorded and analyzed for the period when speaker was turned off till the amplitude of the skin free damped oscillation reached the average noise level. An example of skin damped oscillation presented by asymmetric pattern is shown on Fig. 5.

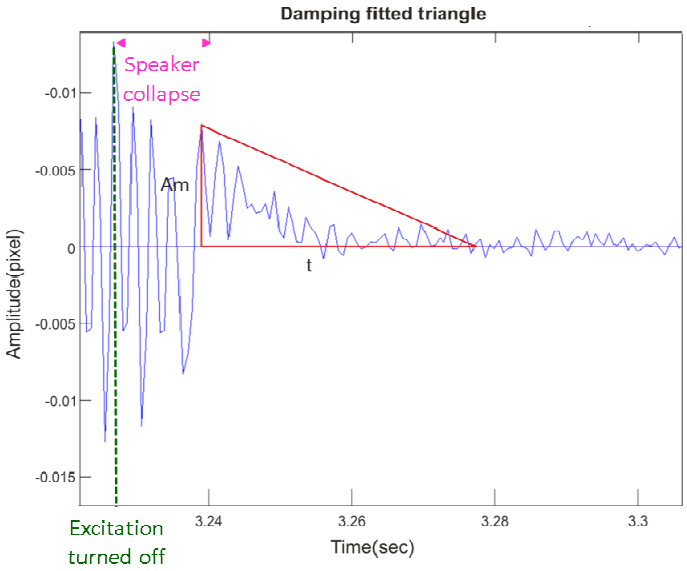

Fig. 5. Example of free damped oscillation of the skin.

The following parameters were calculated in order to find relation with the plastic ball diameter:

1. Time of the free damped oscillation up to the noise level (τ)
2. Area under the oscillation graph for the same τ period (S)
3. Free damp oscillation area divided by the damping fitted triangle area (μ) according to:

$$\mu = \frac{2S}{A_m \tau}. \tag{3}$$

Where τ is the time of the free damped oscillation up to the noise level, S is the area under the oscillation graph for the same τ period and A_m is the amplitude in maximum overshoot.

4. Average signal amplitude (A) within the mentioned period according to:

$$A = \frac{S}{\tau} \tag{4}$$

5. Amplitude in maximum overshoot (A_m) divided by (τ) according to:

$$tg(\varphi) = \frac{A_m}{\tau}. \tag{5}$$

6. Parameters of exponential fit

Average values, standard deviation and coefficient of variations were calculated for the above-mentioned parameters in order to insure that the tests repeated ten times are statistically significant (95% confidence interval with 10% selected margin of error).

It was found that parameters 4-6 are not correlated with the plastic ball diameter. For the rest of the parameters average values show strong correlation with the plastic ball size as shown on the Figs. 6-8.

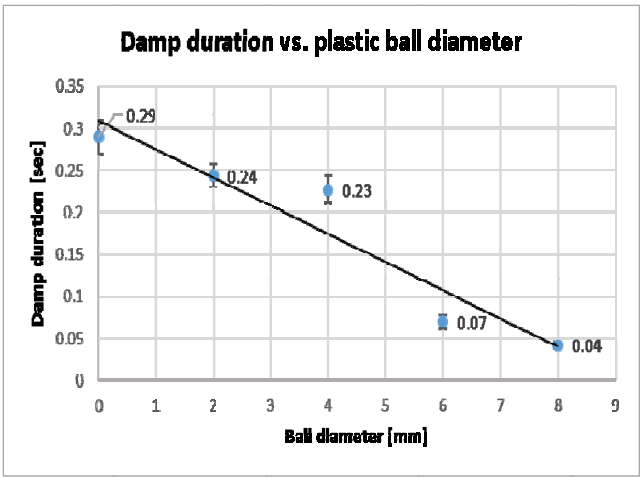

Fig. 6. Correlation and linear regression between the skin free damped oscillation duration and plastic ball diameter.

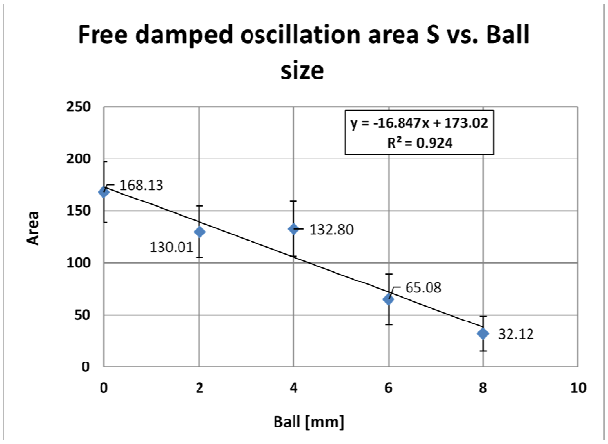

Fig. 7. Correlation and linear regression between the area S and plastic ball diameter.

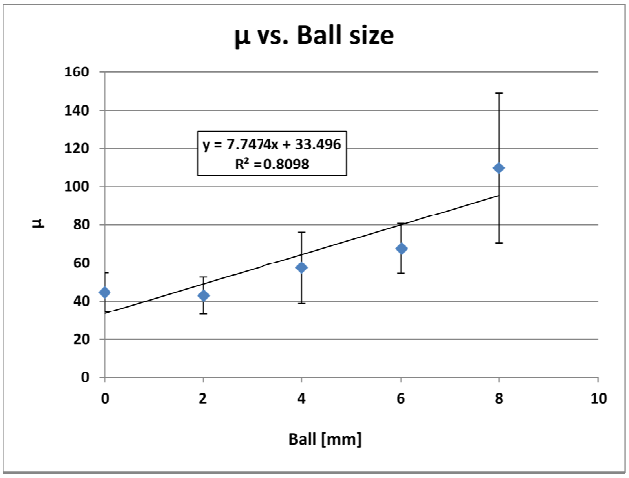

Fig. 8. Correlation and linear regression between parameter μ and plastic ball diameter.

The obtain results (figures 6-8) show that the proposed method allows detection of bodies with diameter of 2mm and higher which are located under the skin. Tumors of this size are considered to be in the early stages of breast cancer disease. Therefore, it is assumed that the proposed methodology could allow detecting breast cancer tumors located

under the skin in their early stages, which can greatly contribute to the disease recovery chances. Therefore, further investigation of the proposed methodology on in-vivo real breast cancer cases is recommended and to be conducted in the near future to verify the presented approach.

One important comment is related to the question of how one can detect the presence of the tumor if a reference measurement without the tumor is not available. For this it is important to note that one can always make comparisons to the second breast and to use the luck of symmetry between the two measurements as part of the calibration and detection process.

3.3 Plastic balls detection deep under the skin of the chicken breast

The difference between the current experiment and the previous is related to the balls position inside the tissue. The plastic balls were placed (2.5mm and 5mm) under the skin to check the possibility of ball detection in deeper locations. The tests were repeated 10 times with green laser and average values were calculated. Significant correlations between the ball size and selected parameters under the tested agitation frequency and intensity have not been observed at this stage.

4. CONCLUSIONS

Experiments for detection plastic balls of 2 to 8mm in diameter placed under the skin of chicken breast sample by agitating the area above the ball and analyzing the secondary speckles reflected from the surface during damped free oscillation of the skin were conducted for the first time.

The results show strong correlation between most of the selected parameters and the ball size. Therefore, the balls could be detected in case placed under the skin so, that the top of the ball, placed within the tissue, touches the internal part of the skin. Based on the obtained results the proposed method should be clinically investigated for breast cancer detection feasibility.

In case the balls were placed deeper inside of the tissue, correlation between the ball size and output was not observed at this stage. Further investigations are required with higher agitation intensity and frequency. Thus, in the present study we were only capable of demonstrating detection depths in which the balls were touching the internal surface of the skin.

REFERENCES

[1] C. DeSantis, J. Ma, L. Bryan, A. Jemal "Breast cancer statistics, 2013," CA a cancer Journal for Clinicians, 64, 52-62 (2013).

[2] E. J. Feuer, L. Wun, C.C. Boring ,W. D. Flanders, M. J. Timmel, T. Tong, "The Lifetime Risk of Developing Breast Cancer," J Natl Cancer Inst 85(11), 892-897 (1993).

[3] S. B. Colak, M. B. van der Mark, G. W. Hooft, J. H. Hoogenraad, E. S. van der Linden, and F. A. Kuijpers, "Clinical Optical Tomography and NIR Spectroscopy for Breast Cancer Detection," IEEE Journal of selected topics in quantum electronics 5(4), 1143-1158 (1999).

[4] L. Mahoney and A. Csima, “Efficiency of palpation in clinical detection of breast cancer,” CMA Journal 15(127):729-730 (1982).

[5] L. L. Humphrey, M. Helfand, B.K.S. Chan, S. H. Woolf, "Breast Cancer Screening: A Summary of the Evidence for the U.S. Preventive Services Task Force,” Annals of Internal Medicine 137, 347-360 (2002).

[6] A. Bleyer and H. G. Welch, "Effect of Three Decades of Screening Mammography on Breast-Cancer Incidence," The new England Journal of Medicine 367, 1998-2005 (2012).

[7] T.M. Kolb, J. Lichy and J.H. Newhouse, " Comparison of the performance of screening mammography, physical examination, and breast US and evaluation of the factors that influence them: an analysis of 27,825 patient evaluations," Radiology 225(1), 165-175 (2002)

[8] K. Kerlikowske, P. A. Carney, B. Geller, M. T. Mandelson, S. H. Taplin, K. Malvin, V. Ernster, N.Urban, G. Cutter, R. Rosenberg, R. Ballard-Barbash," Performance of screening mammography among women with and without a first-degree relative with breast cancer," Annals of Internal Medicine 133, 855-863 (2000).

[9] R. E. Bird, T. W. Wallace, and B. C. Yankaskas, "Analysis of cancers missed at screening mammography," Radiology 184(3), 613-617 (1992).

[10] E. F. Conant and A. D. Maidment, “Breast cancer imaging,” Science and medicine 3(1), 22–31 (1996).

[11] R. F. Brem, J. Baum, M. Lechner, S. Kaplan, S. Souders, L. Gill Naul and J. Hoffmeister, "Improvement in Sensitivity of Screening Mammography with Computer-Aided Detection: A Multiinstitutional Trial," American Journal of Roentgenology 181(3), 687-693 (2003).
[12] E. A Sickles, "Computed tomography scanning, transillumination, and magnetic resonance imaging of the breast," Recent results in Cancer Research 105, 31-36 (1987).
[13] B. Drexler, J. L. Davis, G. Schofield , "Diaphanography in the diagnosis of breast cancer," Radiology 157(1), 41-44 (1985).
[14] F.A. Marks, H. W. Tomlinson, G.W. Brooksby, "A comprehensive approach to breast cancer detection using light: photon localization by ultrasound modulation and tissue characterization by spectral discrimination," Proc. SPIE 1888, 500-510 (1993).
[15] V.R. Kondepati, H. M. Heise and J. Backhaus, "Recent applications of near-infrared spectroscopy in cancer diagnosis and therapy ", Analytical and Bioanalytical Chemistry 390(125), 125-139 (2008).
[16] N. Shah, A. Cerussi, C. Eker, J. Espinoza, J. Butler, J. Fishkin, R. Hornung and B. Tromberg, "Noninvasive functional optical spectroscopy of human breast tissue," PNAS, 98(8), 4420-4425 (2001).
[17] B. F. Kennedy, P. Wijesinghe and D. D. Sampson “The emergence of optical elastography in biomedicine,” Nature Photonics 11(4), 215–221 (2017).
[18] K. M. Kennedy, L. Chin, R. A. McLaughlin, B. Latham, C. M. Saunders, D. D. Sampson and B. F. Kennedy, “Quantitative micro-elastography: imaging of tissue elasticity using compression optical coherence elastography,” Nature 5, 15538 (2015).
[19] J. Ophir, I. Céspedes, H. Ponnekanti, Y. Yazdi and,X. Li “Elastography: A quantitative method for imaging the elasticity of biological tissues,” Elsevier 13(2), 111-134 (1991).
[20] R.F. Chang, W.J. Wu, W. K. Moon, D.R. Chen, "Improvement in breast tumor discrimination by support vector machines and speckle-emphasis texture analysis," Ultrasound in Medicine & Biology 29(5), 679–686 (2003).
[21] J. Li, G. Ku and L. V. Wang, "Ultrasound-modulated optical tomography of biological tissue by use of contrast of laser speckle," Applied Optics 41(28), 6030-6035(2002).
[22] V. V. Tuchin, “Coherent optical techniques for the analysis of tissue structure and dynamics,” Journal of biomedical optics 4(1), 106–124 (1999).
[23] S. S. Ulyanov and V. V. Tuchin, “Use of low-coherence speckled speckles for bioflow measurements,” Applied Optics 39(34), 6385-6389 (2000).
[24] S. S. Ulyanov, D. A. Zimnyakov and V. V. Tuchin, “Fundamentals and applications of dynamic speckles induced by focused laser beam scattering,” Optical Engineering 33(10), 3189-3201 (1994).
[25] Y. Beiderman, I. Horovitz, N. Burshtein, M. Teicher, J. Garcia, V. Mico and Z. Zalevsky, "Remote estimation of blood pulse pressure via temporal tracking of reflected secondary speckles pattern," Journal of biomedical optics, 15(6), 061707-061707 (2010).
[26] T. Sirkis, Ya. Beiderman, S. Agdarov, Ye. Beiderman and Z. Zalevsky," Monitoring vital bio signs using secondary speckles pattern," Optics Express 24(24), 27899-27909 (2016).
[27] Z. Zalevsky, Y. Beiderman, I. Margalit, S. Gingold, M. Teicher, V. Mico and J. Garcia, "Simultaneous remote extraction of multiple speech sources and heart beats from secondary speckles pattern," Optics Express 17(24), 21566-21580 (2009).
[28] M. Fatemi, L. E. Wold, A. Alizad and J. F. Greenleaf, "Vibro-Acoustic Tissue Mammography," IEEE Transactions on Medical Imaging 21(1), 1-8 (2002).
[29] H. C. Starrittt, F. A. Duckt and V. F. Humphrey, "Forces acting in the direction of propagation in pulsed I ultrasound fields," Phys. Med. Bid 36(11), 1465-1474 (1991).
[30] K. Nightingale, R. Bentley and G. Trahey, "Observations of Tissue Response to Acoustic Radiation Force: Opportunities for Imaging," Ultrasonic Imaging 24,129-138 (2002).