The value of Dynamic Optical Breast Imaging and Ultrasound in early breast cancer Detection

Guojuan Tan [a], Jie Wang [a], Cui Liu [a], Chunmian Li [b], Weiping Wang [b],John Zhang[c]

a.Department of Ultrasound, the Chinese PLA General Hospital, Beijing 100853, China;

b. XinAoMDT Technology Co.,Ltd,Langfang 065001,China;

c. DOBI Medical International,1200 MacArthur Blvd,Mahwah,NJ 07430 USA.

[Abstract]

Purpose   The Dynamic Optical Breast Imaging and Ultrasound were evaluated in diagnosing the early breast cancer.

Materials and Methods   62 female patients received breast biopsy were enrolled in this study. 52 patients were assessed by Dynamic Optical Breast Imaging and 35 patients were assessed by Ultrasound. Both examines were studied in 25 patients.

Results   The sensitivity, specificity, FPR(false positive rate) and FNR(false negative rate) were 84.21% 37.50% 15.79% 62.50% by using Ultrasound. Using Dynamic Optical Breast Imaging the sensitivity and specificity were 75%, the FPR and FNR were 25%. Combining the two examines the sensitivity and specificity increased 87.50% and 55.56% and omission diagnostic rate was only 12.50%.

Conclusion: The Dynamic Optical Breast Imaging is a new technology. It is non-invasive and non-radiation. It is an appropriate approach for the early diagnosing breast cancer by combining the Dynamic Optical Breast Imaging and Ultrasound. The sensitivity and specificity were 87.50% and 55.56% and the omission diagnostic rate was only 12.50%.

Key words: The Dynamic Optical Breast Imaging (DOBI); Ultrasound; breast cancer

At present, breast cancer has been becoming the first incidence rate of the women's

tumors all around the world, and the most common cancer to lead women's death. The early detection of breast cancer has great important of treatment. Dynamic Optical Breast Imaging, DOBI is such medical and optical breast imaging technique which is non-invasive and non-radioactive and can offer image-based pathological.

1.1 Research object and Sorts

There were 62 patients come to our hospital and had biopsies during the period of May,2007 to June,2008.All of them are female, the average age is 47   According to the examinations, they can be divided into 3 groups: DOBI Examination 52 cases; Ultrasound Examination of 35 cases; DOBI Examination 52 cases; Both DOBI and Ultrasound combined Examination of 25 cases, excluding patients in pregnant/lactation period and the ones that accept galactophore operation within half a year.

1.2 Instrument

Adopting DOBI Comfortscan^{TM} system utilizes light from 127 light emitting diodes (LED), mounted on an illuminator plate inclined 30° from horizontal plane. The LEDs has the wavelength of 640nm for a greater absorption and higher sensitivity of optical absorption of deoxy-hemoglobin.

1.3 Methods

1.3.1 DOBI technical inspection

By standing in front of the breast tray, which contains the LEDs for light illumination. Patients will be placed on to breast tray as much as possible, at the centre with its nipple in parallel with the tray.

In order to view more area of a breast and to have a high quantity images, patients and breasts need to have good positioning.

Though adjusts to lead of the breast tray and positing patient's body, the operator should make sure to place the breast on the breast tray as much as possible.

Based on the size of breast, three or five LED are commonly used respectively to emit the red light at the 640nm wavelength. The light emitted are recorded by a camera CCD for about 45 seconds. During the light illumination, a uniformed light pressure is applied on the breast. Through a air bladder, the pressure varies from 5mmHg(initial pressure) to 10mmHg(analyzed pressure), which last about 30s, and then to 5 mmHg again. The system collects of reaction of the breast that is the breast images. After the pressure lows to zero, the breast bracket is lifted and the image quality is checked, and then the image is stored for the further analysis. The image is analyzed by well-trained professionals with a certificate issued by the DOBI medical international Fig. 1 .

1.3.2

People checked by the ultrasound lie back or sideways and the breast are exposed completely. The probe is 10L and the frequency is 7.5 MHz. The galactophore is scanned from many directions and its both sides are observed for contrast.

1.3.3

If the patient accepts the both DOBI technology and ultrasound examinations, generally the DOBI technology scan is prior to the ultrasound galactophore check. If the ultrasound galactophore check is done first, the DOBI scan should be done after 20 minutes of ultrasound. Because the non-uniform pressure of probe to galactophore in the process of the ultrasound has an effect on the DOBI scan.

1.3.4 Biopsy

Patients lie back or sideways and the breast exposed completely. Conventional disinfection and clothes with holes and partial anaesthesia are done. With the guide of the ultrasound, the suspicious parts checked by DOBI or ultrasound are probed. The tissue

got by the probe is sent to pathology for check.

1.4 Statistical process

Sensitivity(SE),specificity(SP),the rate of misdiagnosis( ) and the rate of missed diagnosis(β) of DOBI technology and ultrasound and their combination's diagnosis to breast carcinoma are calculated and compared.

2   Result

Sensitivity (SE), specificity (SP), the rate of misdiagnosis ( ), the rate of missed diagnosis (β)of DOBI technology and ultrasound and their combination 's diagnosis to breast carcinoma are calculated.

2.1 Diagnosis of breast cancer by DOBI technology（Fi g. 2)

Patients only accepted DOBI inspection, and had biopsy for the suspicious sites. The sensitivity (SE) = a / a + c = 14/19 = 73.68%; specificity (SP) = d / b + d = 25/33 = 75.76%; the rate of misdiagnosis (a) = b / b + d = 8 / 33 = 24.24 percent; the rate of missed diagnosis (β) = c / a + c = 5 / 19 = 26.32%. (Table-1)

2.2 Diagnosis of breast cancer by Ultrasound

Patients only accepted ultrasound examination, and did biopsy for the suspicious sites provided by ultrasound. The sensitivity (SE) = a / a + c = 16/19 = 84.21%; specificity (SP) = d / b + d = 6 / 16 = 37.50%; the rate of misdiagnosis (a) = b / b + d = 10 / 16 = 62.50 percent; the rate of missed diagnosis (β) = c / a + c = 3 / 19 = 15.79%. (Table-2)

2.3 Diagnosis of breast cancer by both DOBI and ultrasound technologies .

Patients accepted two technical inspections, generally DOBI first, and then ultrasound, did biopsy for the suspicious sites provided by them. sensitivity (SE) = a / a + c = 14/16 = 87.50%; specificity (SP) = d / b + d = 5 / 9 = 55.56%; the rate of misdiagnosis (a) = b / b

+ d = 4 / 9 = 44.44%; the rate of missed diagnosis (β) = c / a + c = 2 / 16 = 12.50%. (Table-3)

The results shows that: for diagnosis of breast cancer, the sensitivity of ultrasound is slightly higher than DOBI technology, but the specificity is lower, only 37.50 percent, the missed diagnosis rate is lower but the rate of misdiagnosis is higher, up to 62.50 percent. DOBI diagnosis of breast cancer, the sensitivity and specificity are at or close to 75%, the rates of misdiagnosis and missed diagnosis are about 25%. The combination of then will enable the diagnosis of breast cancer sensitivity up to 87.50%, the specificity increased to 55.56 percent, the rate of misdiagnosis was just 12.50 percent.

3 DISCUSS

Breast cancer is the most common cancer that led to the deaths of women. The latest statistics of Chinese Health Ministry illustrate that in China the incidence of breast cancer is high among women whose age is from 30 to 54-year-old, it is earlier 10-15 years than Western countries. The data from Chinese anti-cancer Association (CACA) shows that in 2005 the incidence of breast cancer in China's major cities has increased 31.7 percentage than nine years ago, the mortality rate increased 37%, and each year the incidence of breast cancer is risen at a rate of 2%. US Medical Institute pointed out that the intervenning the development of early breast cancer can reduce breast cancer mortality. Clinically on the basis of keeping breast intact as much as possible, more than 90% of patients with early breast cancer can survival for about decade.

Breast biopsy is the only way to examine the existence of breast cancer. While it is also a kind of more expensive and harmful checks which will make patients painful and anxious. Ultrasound is a kind of imaging technology for detecting small tumors and determining they are benign or malignant, the specificity is lower, which is in line with the results of this study. DOBI technology [3] is a new non-invasive, non-radiation medical imaging system, which provides much new image-based pathological information.

The Medical and scientific basis of DOBI technology is the angiogenesis imaging system,

which is to identify early breast cancer associated with the growth of capillaries instantaneous changes .Tumor growth over "1 millimeter least", tumor cell will grow their own blood supply system, that is "angiogenesis" [5], adequate blood supply makes the explosive growth of tumor cells and the spread of a wide range. This unique "features of the new angiogenesis," includs high-density and high blood content [6], high resistance to blood flow [7], the new blood vessels under pressure outside is more likely to collapse, high oxygen consumption and the spread of light attenuation [8]. Deoxy-hemoglobin in the 600-900nm band observes absorption of spectrum, and shows the attenuation characteristics of spread of light .

light-emitting diode (LED) used by DOBI can launch 640nm wavelength red light, which is sensitive to the wavelength   hemoglobin ,with a high absorption rate [9]. DOBI ues silicon soft air chamber to exert mild pressure to the breast on the uniform, when added external pressure around the breasts, blood will be redistributed, vascular and capillary was crushed, the dynamic changes stimulated by these pressure are different between the normal and abnormal breast tissue. the new blood vessels   associated with cancer can absorb more light than normal tissue, so it will show a low bright region in the images. Benign or normal tissues have normal distribution of blood vessels, and the rate of metabolism is lower, light absorption will not have any major changes.

In the images, bright areas indicate normal or benign , and dark blue means it may be malignant. Through comparing, it shows that DOBI has the ability to confirm the existence of breast cancer and distinguish it with benign lesions and normal tissues. Due to changes of blood vessels occurred in the early stages of the cancer development, image such changes may detect breast cancer in the early development of cancer.

This study shows that, diagnosing breast cancer by DOBI technology, the sensitivity and specificity are at or close to 75%, the rate of misdiagnosis and missed diagnosis rate is about 25%; sensitivity, although slightly lower than ultrasound, but the specificity is far greater than ultrasound. The combination of DOBI and ultrasound technologies will enable the diagnosis of breast cancer sensitivity to incerese 87.50%, specificity reach 55.56 percent, the missed diagnosis rate to decrease to 12.50 percent.

DOBI technology is a new medical imagingtechnology, with the characteristics of non-intravenous injection , non-invasive, no radiation and no pain ,but in clinical practice we found that at present DOBI of ComfortScan^{TM} dynamic optical breast imaging system still has its limitations: for Small breasts, dense breast imaging has poor results, due to the different of positions breast; tumor closed to the chest wall or near the armpit (as a result of away from the imaging area) is easily missed; larger breasts can not be completed during one inspection; squeezing the breast before inspection make difference   on imaging and so on.

Although DOBI is a new medical imaging technology, the combination with ultrasound diagnosis of early breast cancer is a suitable imaging form. While it needs a large number of case studies to distinguish malignant and benign tumors, including in different stages of cancer development, with different physical signs in patients, quantify the metabolic rate of malignant and benign tumors by statistics and so on.

REFERENCE

1. China Medical Devices Net, www. zgylqxw. cn/Html/ 2007-03-10/ 320313. shtml.

2. Nass SJ, Henderson C, Lashof JC, et al.. Mammography and Beyond: Developing Technologies for the Early Detection of Breast Cancer. Washington, DC: National Academy Press. 2001. Prepublication copy:13.

3. Alexandra Athanasiou, Daniel Vanel, Corinne Balleyguier, et al. Dynamic Optical Breast Imaging: A New Technique to Visualise Breast Vessels: Comparison with Breath MRI and Preliminary Results. European Journal of Radiolog. 2005, 54: 72-79.

4. McDonald DM, Choyke PL. *Imaging of Angiogenesis: From Microscope to Clinic.* Nature Medicine. 2003, 9(6): 713-725.

5. Li WW, Tumor angiogenesis: molecular pathology, therapeutic targeting and imaging. *Academic Radiology*   2000,7:800-811.

6. Weidner N, Semple JP, Welch WR, Folkman J. Tumor angiogenesis and metastasis – correlation in invasive breast carcinoma. New England Journal of Medicine. 1991, 324:1-8.

7. Dyachenko A. Dynamic imaging of breast lesions; one dimensional optical model. *Asian Journal of Physics* 2001, (10)4:1-18.

8. Netti PA, Roberage S, Boucher Y, Baxter LT, Jain RK. Effect of transvascular fluid exchange on pressure—flow relationship in tumors: a proposed mechanism for tumor blood flow heterogeneity. *Microvascular Research.* 1996, 52:27.

9. Gatzemeier W, Scelsi M, Galetti K, et al. Dynamic Optical Breast Imaing: A non-invasive, adjunctive method to detect breast cancer. San Antonio Breast Cancer Symposium. 2004, (12):6011.

Corresponding author at: Department of Ultrasound, the Chinese PLA General Hospital, Beijing 100853, China. Major: Ultrasound.

E-mail address:
Guojuan Tan's adress:cmli0303@sina.com
Jie Wang's address   wangjie@301hospital.com.cn
Cui Liu's address: LJW301@yahoo.com
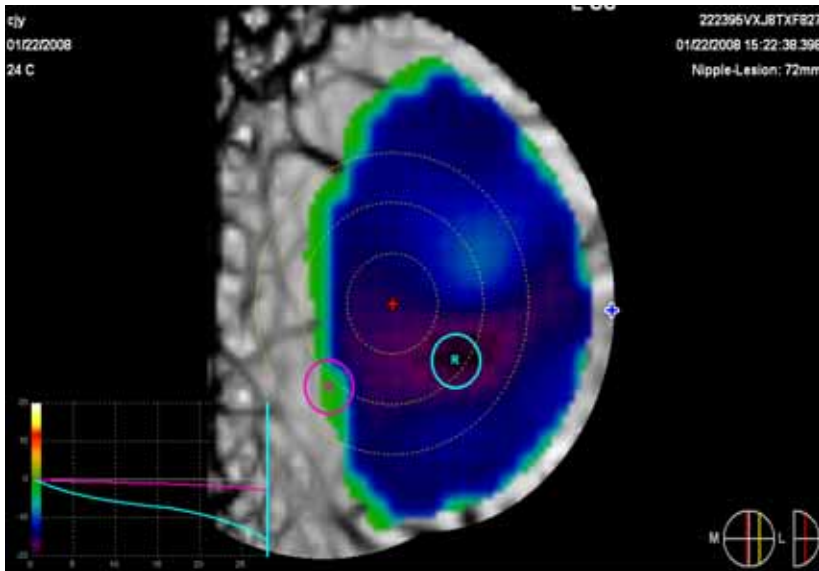Chunmian Li's address: liermao8188@126.com
John Zhang's address: dobigjzhang@yahoo.com.cn
Dr Wang's address:w_p_wang@hotmail.com

Fig.1. The ComfortScan optical mammography system. The patient stands upright and her breast is placed in the breast holder. The entire procedure takes less than 10 min.

Fig. 2. Optical image of 43-year-old patient. The navy-blue pixels in the optical image represent pixels with a temporal absorption curve suspect of malignancy.

Table-1 Evaluate 4 situations of diagnosis of breast cancer by DOBI technology

DOBI	Pathology		SUM
	Cancer	Non-cancer	
+	14 real + a	8(false +b	22(a+b)
_	5 false _c	25 real _d	30(c+d)
SUM	19 (a+c)	33 (b+d)	52(a+b+c+d)

Table-2 Evaluate 4 situations of diagnosis of breast cancer by Ultrasound

Ultrasound	Pathology		SUM
	Cancer	Non-Cancer	
+	16 Real +a	10 False +b	26 (a+b)
_	3(False_c	6(Real+d	9(c+d)
SUM	19 (a+c)	16 (b+d)	35(a+b+c+d)

Table-3 Evaluate 4 situations of diagnosis of breast cancer by both DOBI and Ultrasound

DOBI and Ultrasound	Pathology		SUM
	Cancer	Non-Cancer	
+	14 Real +a	4 False +b	18(a+b)
_	2 False _c	5 Real +d	7(c+d)
SUM	16 (a+c)	9 (b+d)	25(a+b+c+d)