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Evaluation of laser computer mammography (CTLM) usefulness in differentiation benign and malignant breast lesions

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Summary

Background:

To evaluate the usefulness of the CTLM method in differentiation between benign and malignant neoplasms in female breast tissue (benign and malignant breast lesions).

Material/Methods:

Retrospective analysis of 482 lesions in female breast tissue, verified histopathologically on the basis of material obtained by core biopsy. In this study, the CTLM diagnosis was established prior to biopsy, so the radiologist describing the CTLM examination was unaware of the histopathology finding; he/she was however familiar in most cases with the outcome of mammography, was involved in performing/evaluating the mammography and/or performed an ultrasound examination. CTLM examinations not applicable for evaluation because of artifacts were excluded from the analysis. A CTLM examination result was counted as positive, i.e. the presence of angiogenesis was detected, when an area of enhanced laser light absorption was visible and that area was not a normal vascular structure.

Results:

In 2005, angiogenesis was observed in 25 out of 65 malignant lesions (38.46%) and in 40 cases (61.54%) areas of enhanced laser light absorption were not detected. Among 142 benign lesions, in 57 cases (40.14%) enhanced laser light absorption (ELLA) was observed, whereas in 85 cases (59.86%) it was absent. Coefficients calculated for data acquired in 2005 were as follows: sensitivity = 38%, specificity = 60%, positive predictive value (PPV) = 30%, negative predictive value (NPV) = 68%, diagnostic accuracy = 53%.

In 2006, angiogenesis was detected in 46 out of 97 cases (47.42%), whereas in the remaining 51 (52.58%) cases ELLA was not observed. Among 178 benign lesions, in 46 cases (25.84%) ELLA was observed, whereas in 132 cases (74.16%) it was not. Coefficients calculated for data acquired in 2006 were: sensitivity = 47%, specificity = 74%, positive predictive value (PPV) = 50%, negative predictive value (NPV) = 72%, diagnostic accuracy = 65%.

The presented data reveal that an increase of absorption of laser light was observed by us more often in cases of malignant lesions than of benign ones (47.42% vs. 25.84%, $p < 0.001$, data from 2006).

Conclusions:

The obtained results demonstrate that indeed a positive CTLM reading is observed more often in malignant rather than benign lesions, and that the examination is a valuable method adjunct to classic X-ray mammography.

Key words:

CTLM • breast cancer • optical imaging • laser technique

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Background

CTLM (Computed Tomographic Laser Mammography) is one of the new techniques available in breast imaging [1].

Despite the use of x-ray mammography, ultrasound and magnetic resonance imaging in breast diagnostics, the number of benign lesion biopsies is still high. X-ray mammography is the basic method of breast cancer diagnosis. It has many important advantages, but unfortunately it also has disadvantages. The primary disadvantages are the use of ionizing radiation and relatively low sensitivity in case of high density breast tissue. Ultrasound imaging is a very good method of differentiation between solid and cystic lesions, however, it is far less effective in differentiating between benign and malignant lesions. At present, high hopes for changing this situation are attached to ultrasound elastography [2, 3, 4].

Magnetic resonance mammography is the most sensitive method. However, it is costly, still not widely available and burdened with a high rate of false positive results [5]. The diffusion imaging (DWI) and MR spectroscopy remain in the clinical trial phase rather than in daily practice.

The quest for new, secure methods for highly sensitive, highly specific imaging diagnosis of breast cancer – the most common malignant cancer in women – is therefore highly commendable [6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16].

The first approaches to utilize laser light for „scanning“ breasts dates back to the years 1970-1980, however, the initial results were not promising [17, 18, 19]. It was only after the association of laser imaging with computerized tomography that far superior results were obtained. This was how CTLM i.e. computed tomography laser mammography came to be.

The CTLM method is based on two phenomena:

- The neoplasm secretes angiogenic substances, thus stimulating the growth of functionally and structurally pathological blood vessels. This phenomenon is called angiogenesis and is described in many malignant tumors and some benign tumors [20, 21, 22, 23]. A malignant neoplasm is accompanied by angiogenesis – new blood vessels are essential for the tumor's growth.
- Various tissues have different coefficients of laser light absorption – the wavelength of the laser beam in CTLM (808 nm) is absorbed much more by hemoglobin (both oxidized and deoxidized) than by surrounding tissue. There is practically no absorption of this wavelength by water and fatty tissue.

In fact, CTLM produces a „hemoglobin angiogram“ of the breast. Tissue with high hemoglobin content has a high absorption coefficient, whereas tissue with little Hb content has a low or very low coefficient. This is why healthy tissue demonstrates low absorption of laser light of 808 nm wavelength. Benign lesions should also be characterized by low absorption of laser light, however, a part of these lesions is accompanied by angiogenesis [7, 24]. Malignant lesions, in particular those with a diameter above 1 cm, are

characterized by a high coefficient of laser light absorption [25, 26]. It may be expected that imaging with CTLM should characterize the lesion so well that this could lead to a reduction in the number of benign case biopsies.

The aim of the study is the evaluation of the usefulness of CTLM in differentiating malignant and benign breast lesions.

Materials and methods

Examinations of 482 women were analyzed. These patients underwent core biopsy of breast lesions, diagnosed by mammography and/or ultrasound imaging. All the patients had a CTLM examination as an adjunct to mammography (lesions qualified to BIRADS 3,4,5) and/or ultrasound imaging in a time not longer than 12 weeks before the biopsy.

The CTLM exams and biopsies were performed in two following years: 2005 (207 exams) and 2006 (275 exams) in the Department of Radiodiagnosics of the Comprehensive Cancer Centre, Maria Skłodowska-Curie Memorial Institute Branch Gliwice, Poland.

The histopathology was performed in the Department of Tumor Pathology of the Comprehensive Cancer Center, Maria Skłodowska-Curie Memorial Institute, Gliwice Branch, Poland.

CTLM:

CTLM imaging was performed using a CTLM Model 1020. by Imaging Diagnostic Systems Inc. Florida, USA www.imds.com

The examination is carried out with the patient lying prone on the couch. The examined breast is introduced loosely into the scanning chamber. Inside the scanning chamber there is a diode which emits laser light, along with rings of detectors. During the scanning procedure, the beam of laser light performs a 360 degree rotation around the examined breast, from the chest wall towards the nipple. The intensity of the laser light which has penetrated the breast is measured by detectors. The slice thickness is 2 to 4 mm depending on the breast size. The scanning time of one breast approximates 15 minutes.

Slice images in coronal, sagittal and transverse sections along with 3D MIP (maximum intensity projection) and FTB (front to back) images were analyzed on the workstation provided by the manufacturer.

Areas containing significant levels of hemoglobin, i.e. with a high coefficient of laser light absorption are visible as bright (in the color scheme used it is light green or white), whereas areas where few blood vessels are present are visible as dark green or black. Angiogenesis was diagnosed on the basis of the presence of an area of increased absorption of laser light i.e. a bright, commonly irregular shape not corresponding with normal blood vessels. It is worthwhile to mention that a hematoma is characterized by a very high level of laser light absorption.

Table 1. Overall number of cases examined in 2005.

	CTLM +	CTLM -	Total
Benign	57 FP	85 PN	142
Malignant	25 PP	40 FN	65
Total	82	125	207

The examining radiologist was not familiar with the histopathology result, but he/she was familiar with the results of mammography and/or ultrasound exams.

The material for histopathology was extracted from the breast by way of core biopsy or vacuum-assisted core biopsy.

Statistical calculations were performed with the Statistica program.

Results

Histopathological diagnosis:

Out of 207 biopsies performed in 2005, 65 lesions (31.40%) were malignant, whereas 142 (68.59%) were benign.

Out of 275 biopsies performed in 2006, 97 lesions (35.27%) were malignant, whereas 178 (64.73%) were benign.

CTLM:

The results obtained in the year 2005 are presented in Tab. I, those obtained in the year 2006 in Tab. II.

Lesions where an area of increased absorption of laser light was observed were marked as CTLM+, whereas those with no such area as CTLM - (Fig. 1, 2).

In 2005, out of a total of 65 malignant lesions angiogenesis was observed in 25 cases (38.46%), whereas no observation

Table 2. Overall number of cases examined in 2006.

	CTLM +	CTLM -	Total
Benign	46 FP	132 PN	178
Malignant	46 PP	51 FN	97
Total	92	183	275

of increased absorption of laser light was noted in 40 cases (61.54%).

Out of a total of 142 benign lesions, in 57 cases (40.14%) areas of increased laser light absorption were observed, whereas in 85 cases (59.86%) such variations were not observed.

In total, true results accounted for 53% (110/207).

Coefficients calculated for the year 2005 were as follows: sensitivity = 38%, specificity = 60%, positive predictive value (PPV) = 30%, negative predictive value (NPV) = 68%, diagnostic accuracy = 53%.

In 2006, out of a total of 97 malignant lesions, in 46 cases (47.42%) angiogenesis was observed, whereas in 51 (52.57%) an increase in absorption of laser light was not observed.

Out of 178 benign lesions, in 46 cases (25.84%) an increase in laser light absorption was observed, whereas in 132 (74.16%) such variations were not observed.

In total, true results accounted for 65% (178 of 275).

Coefficients calculated for the year 2006 were as follows: sensitivity = 47%, specificity = 74%, positive predictive value (PPV) = 50%, negative predictive value (NPV) = 72%, diagnostic accuracy = 65%.

After exclusion of papilloma (4 cases), DCIS (8 cases), atypical ductal hyperplasia (ADH -12 cases), inflammations

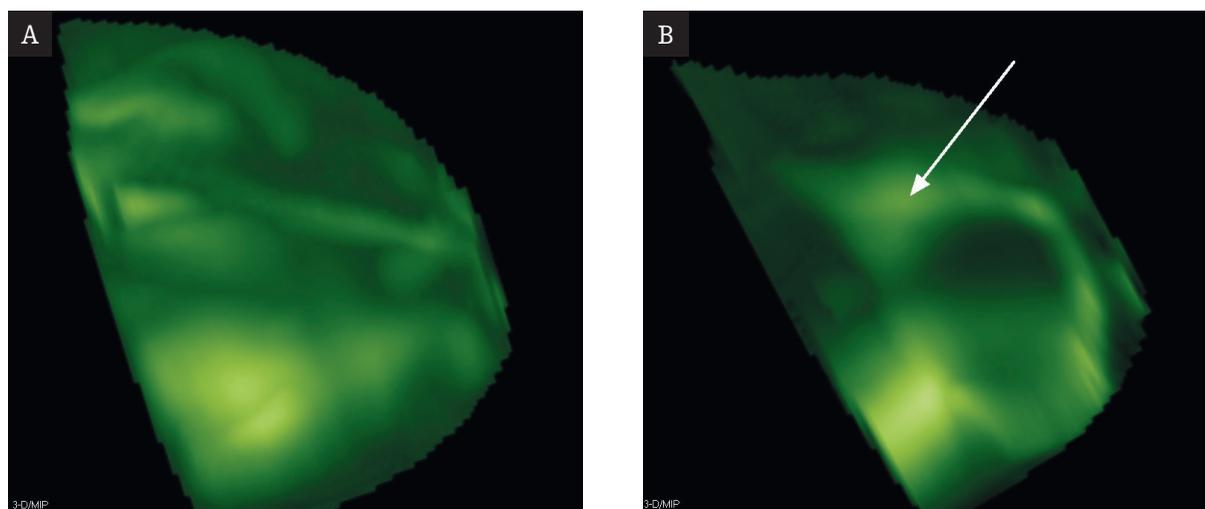


Figure 1. A 67-year old woman. CTLM examination of left (A) and right (B) breast. A. no evidence for increased laser light absorption. CTLM classified as negative. B. area of increased laser light absorption (arrow). CTLM was classified as positive. Histopathologic diagnosis: carcinoma ductale infiltrans.

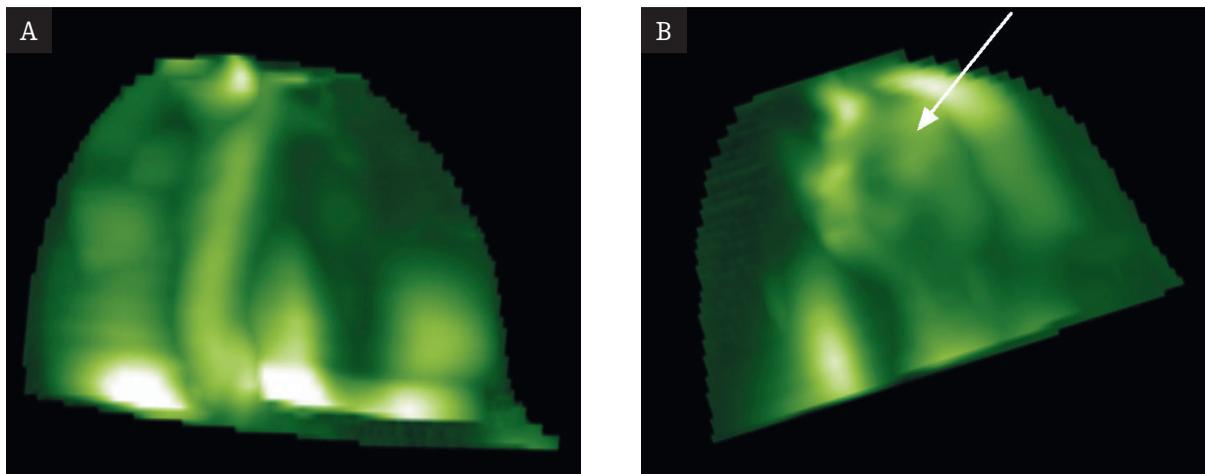


Figure 2. A 58-year old woman. CTLM examination of left (A) and right (B) breast. A. no evidence for increased laser light absorption. CTLM classified as negative. B. area of increased laser light absorption (arrow). CTLM was classified as positive. Histopathologic diagnosis: carcinoma ductale invasivum.

(8 cases) coefficients for 2005 are: sensitivity = 40%, specificity = 65%, PPV = 36%, NPV = 69%, diagnostic accuracy = 57%, and for 2006 – sensitivity = 49%, specificity = 75%, PPV = 51%, NPV = 73%, diagnostic accuracy = 66%.

In all cases, 100% (4/4) papilloma, 67% (8/12) ADH and 75% (6/8) inflammations angiogenesis was detected in CTLM. Only in 12.5% (1/8 DCIS) increased absorption of laser light was revealed.

Discussion

Core biopsy, and in particular vacuum-assisted biopsy is a low-invasive and effective method of histopathological verification of breast lesions. Unfortunately, it is a rather costly method. A diagnostic imaging method, differentiating between malignant and benign lesions would certainly allow for a reduced number of benign lesion biopsies, resulting in both economic and psychological improvement.

Compared with other techniques of breast imaging, CTLM is a technique with many advantages. It is safe, it does not utilize ionizing radiation and does not involve breast compression, which is an important factor for the patient's comfort. This examination may be carried out multiple times and independently of the patient's age. It is accepted that indications for CTLM would be the following: dense breast tissue, equivocal result of classic mammography, the presence of implants, differentiating between the relapse of cancer and changes after treatment. Counter-indications are relative and few: exuding wounds of the breast, or a time of less than 3 months after surgery.

In fact, CTLM produces a „hemoglobin angiogram“ of the breast. Tissue with high hemoglobin content has a high absorption coefficient, whereas tissue with little Hb content has a low or very low coefficient. This is why healthy tissue demonstrates low absorption of laser light, whereas malignant lesions, in particular those with a diameter above 1 cm, are characterized by a high coefficient of laser light absorption [25, 26].

The presented data reveal that an increase of laser light absorption was observed by us more often in cases of malignant lesions than of benign ones (47.42% vs. 25.84%, $p < 0.001$, data from 2006). These results are in accordance with those reported by other authors [26, 27]. This is linked to high diagnosed angiogenesis and increased concentration of hemoglobin in invasive tumors of the breast [7, 21, 24, 26], although there are exceptions to this and that is why increased laser light absorption in CTLM images is also observed in benign lesions such as: fibroadenoma, papilloma, and atypical ductal hyperplasia [7, 24]. This fact is also visible in our studies, because nearly 1/3 of benign lesions manifested an increase in laser light absorption (103/320). The features of angiogenesis (increased absorption of laser light) were manifested in our material by 100% papillomas, 67% ADH, 78% inflammatory cases and 13% DCIS.

On the other hand, some malignant lesions (around 30%) do not manifest increased absorption of laser light in CTLM and these lesions could be overlooked if the diagnostics were to be based solely on CTLM. [27]. In our material, the percentage of malignant lesions where no increase of laser light absorption was observed was much higher and in the year 2006 exceeded 50% (51 / 97). According to our material, the sensitivity of the method is lower than that quoted by Floery et al. [27] and it is similar to that of classic x-ray mammography [28, 29, 30]. Athanasiou et al. [31] found a sensitivity of 73%, utilizing laser light of a wavelength of 640 nm. According to individual reports, the sensitivities of experimental methods of breast imaging are: 58% for transillumination light scanning [19] and diaphanography [18], 83.1% for time-domain mammography [11], 77.3% for electrical impedance scanning [10]. The sensitivity of MR mammography exceeds 95% [12], however, this method is costly and burdened by a relatively high percentage of false positive results.

The specificity index of 74% is slightly lower than specificity indexes of classic mammography which are usually in the range of 75-76% [29], to 88% [30], it is also lower than specificity indexes of sestamibi scintigraphy (80.5%) [7] and electrical impedance scanning (82.3%) [10] but it is higher

than that (67%) quoted by Floery et al. [27]. It is clearly higher than the specificity of laser mammography which utilizes laser light of 640nm wavelength, which, as quoted by Athanasiou et al., is 38% [31].

The comparison of calculated coefficients demonstrates their rise in 2006 as compared to 2005 (sensitivity 47% vs. 38%, specificity: 74% vs. 60%, PPV: 50% vs. 30%, NPV: 72% vs. 68%, diagnostic accuracy 65% vs. 53%). This points to the fact that experience of the radiologist in interpretation of

CTLM images is important, as well as the radiological and anatomopathological correlations of previous examinations.

Conclusions

The results obtained point to the fact that a positive CTLM reading is indeed diagnosed more often in malignant lesions than in benign ones and that this examination is a valuable method adjunct to classic x-ray mammography.

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