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Can the application of computed tomography laser mammography (CTLM) in dense breast (category 3,4 according to ACR) examinations combined with x-ray mammography enhance the detection of breast cancer?

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Summary

Background: The aim of this study was an attempt to answer the question whether laser mammography in dense breast (classified as category 3,4 according to ACR) examination together with x-ray mammography can enhance the detection of breast cancer.

Material/Method: 248 women who had undergone a CTLM examination and mammography in the Department of Radiology of Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology in the years 2005–2007 were analyzed retrospectively. In these examinations, x-ray mammography did not reveal lesions (BIRADS 1, category 3 and 4 according to ACR). An interval between CTLM and mammography did not exceed 30 days. The examination result was verified by cytology/histopathology or observation after a minimum of 12 months provided a regular result. CTLM visualizes normal and pathological blood vessels and tissues which are rich in blood, because laser rays used in CTLM (808nm) are more absorbable by hemoglobin than by the surrounding tissue, making it possible to show a malignant tumor by its accompanying angiogenesis. The result of CTLM mammography was qualified either as the presence (+) or absence (–) of angiogenesis.

Results: Among 248 women, angiogenesis was discovered by CTLM in 48 cases, in the CTLM (+) Group 13/48 women were diagnosed with breast cancer, whereas 35/48 were diagnosed with benign lesions.

Angiogenesis was not identified in 200 women, in the CTLM (-) group 13/200 were diagnosed finally with cancer, with 187/200 patients having no malignancy.

Ultimately, in the group of 248 women (with dense breast, category 3 and 4 according to ACR), in whom x-ray mammography did not reveal malignant processes (BIRADS 1), 26 cancers were detected out of which 13 were revealed with CTLM

Conclusions: Computed Tomography Laser Mammography, when used as an adjunct to x-ray mammography, enhances the detection of breast cancer in women with dense breast tissue.

Key words: CTLM • breast cancer • laser technique • dense breast

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Background

Breast cancer is the most common malignant tumor among women, accounting for 18.4% of womens' cancers in Poland and 22% internationally [1]. Nearly 50% of breast cancer cases diagnosed in Poland are advanced stages, with bad prognoses [2].

The fundamental method of detecting breast cancer is mammography. This method, although having many advantages, suffers from two substantial limitations: 1. ionizing radiation, limiting the possibilities of frequent usage and application in young or pregnant women. 2. problems with cancer visualization in dense breast tissue.

A mammography image depends upon the quantity ratio of adipose tissue versus glandular and connective tissues. The breast composition is described by a four-degree scale introduced by the ACR (American College of Radiology). The more adipose tissue (category 1,2 according to ACR) is in the breast, the easier it is to visualize cancer infiltration and the smaller changes are visible. On the other hand, breast composition characterized by high percentage of glandular tissue (category 3,4 according to ACR) is associated with significant diagnostic problems with location of the pathologic foci, which leads to impaired detection of early-stage cancer. The mammography symptoms of breast cancer include: nodules, microcalcifications, asymmetry, breast architecture distortion The sensitivity of cancer detection in dense breasts approximates 75–80% [3–6] In such cases, we regularly apply other available examination modalities such as ultrasound and MRI. Ultrasound imaging is a commonly used modality, with no known contraindications. Because of intensive progress of ultrasonography in the recent years, sensitivity increase has been observed and ultrasonography can evaluate those areas where masses undetectable by a mammogram may occur [7]. Elastosonography is applied for evaluation of lesions pictured in presentation B and it enhances specificity of ultrasonography [8]. The sensitivity of MRI in malignant disease detection ranges from 80 to nearly 100% in invasive cancer, but the specificity is much lower (37–97%) [9–11]. The cost of the examination, its availability but first of all a high number of false positives are all limitations of this modality; therefore, it is not recommended as a routine examination in dense breast cases. Taking into account the limitations of currently applied modalities, it is reasonable to search for other breast imaging techniques. One alternative solution is Computed Tomography Laser Mammography (CTLM).This method of imaging acquires a 3D breast image by detecting absorption of laser light (808 nm wavelength). Laser light of this particular wavelength is strongly absorbed by the hemoglobin. This approach makes it possible to visualize blood vessels: healthy, pathologic (angiogenesis) and also areas containing blood such as hematomas. A neoplasm, and in particular a malignant cancer, stimulates the development of new blood vessels (angiogenesis). The vessels developed in neoplastic lesions are of irregular build, and generally more numerous per unit of volume than in healthy tissue. Because of this, a neoplastic lesion and its immediate vicinity contains a large amount of hemoglobin – higher than in healthy breast tissue [11,12]. The postulate of CTLM is therefore visualisation of angiogenesis accompanying the neoplasm. Laser mammography is a safe and non-compressing examination using non-ionizing radiation, lending itself to women of all ages and to multiple repetitions. Contraindications are relative and few:

- oozing wounds of the breast,
- less than 3 months following a surgical intervention.

The aim of this study is an attempt to answer the question whether the application of laser mammography in dense breast (category 3,4 according to ACR) examinations in combination with x-ray mammography can enhance the detection of breast cancer.

Material and Methods

Material

248 women who had undergone a CTLM examination and mammography in the Department of Radiology of Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology in the years 2005–2007 were analyzed retrospectively. The criteria for inclusion into the study group included:

- identification of dense breast tissue in x-ray mammography -category 3, 4 according to ACR,
- x-ray mammography result BIRADS 1,
- laser mammography of good quality, without artefacts, performed maximum 30 days after the x-ray examination,
- examination result verified by a cytology/histopathology examination or observation – mammography performed after a minimum of 12 months provided a regular result.

Method

The CTLM examinations were performed using a CTLM device Model 1020 (Imaging Diagnostic Systems, Florida, USA) During the examination, the patients were lying prone and the scanned breast was positioned loosely in the scanning chamber. The reading of one breast takes around 10–15 minutes, depending on the breast size. The scanning chamber consists of a ring, on the inner circumference of which there are two rows of detectors (each row containing 84 detectors). On the ring there is also a diode emitting laser light of 808 nm wavelength. Absorbed light is registered by the detectors after passing through the imaged object. This is the basis for creating axial slices that picture the absorption of laser light by the tissue present in the slice (of 1–4 mm thickness). Subsequently, a 3D image is reconstructed. Both bright areas of the CTLM images and dark parts were analysed. The former indicated high degree of laser light absorption, while the latter indicated weak absorption of laser light. For visualization purposes, areas appearing dark in CTLM images were considered as containing few vessels and/or avascular. Such areas include adipose tissue, cysts, fibrous tissue. Areas appearing bright in CTLM images were considered as containing many vessels. Such areas can represent glandular tissue, neoplasms, inflammation processes.

In a CTLM exam, a blood vessel appears as a bright, linear or strand structure. Blood vessels were considered healthy if they appeared in a CTLM image as regularly shaped and forming a „pyramid" with its base toward the chest wall,

Table. 1 CTLM and x-ray mammography results.

	BIRADS 1
CTLM +	48
CTLM –	200
Total	**248**

Table 2. CTLM results.

	CTLM + (48/248)	CTLM – (200/248)
BIRADS 1	48	200
TP (true positive)	13	
FP (false positive)	35	
TN (true negative)		187
FN(false negative)		13

and pointed toward the nipple. The presence of angiogenesis was defined as an area of amorphic, irregular shape and intermediate brightness. The identification of such an area was classified as CTLM (+).

The result of CTLM mammography was qualified either as the presence (+) or absence (–) of angiogenesis.

All women who had undergone CTLM had also x-ray mammography (in cranio-caudal and oblique projection) at an interval not exceeding 30 days.

Results

Among 248 women, angiogenesis was detected by CTLM in 48 cases (Table 1).

In the CTLM (+) group [48 patients]:
- 13/48 women were diagnosed with breast cancer,
- 35/48 women were diagnosed with benign lesions (in 27 cases, the diagnosis was established on the basis of core or regular biopsy, or a surgical procedure, in the last 8 cases the final result was obtained from a control mammography performed min. 1 year after the CTLM examination.

Angiogenesis was not identified in 200 women (CTLM (–).

In the CTLM (–) group [200 patients]:
- 13/200 women diagnosed finally with cancer,
- 187/165 women were found clear of malignant disease (Table 2).

Ultimately, in the group of 248 women with dense breast (category 3 and 4 according to ACR), in whom x-ray mammography did not reveal malignant processes (BIRADS 1), 26 cancers were detected out of which 13 were revealed with CTLM.

Therefore, the addition of CTLM to x-ray mammography increased the detectability of cancer in the examined group (category 3,4 according to ACR).

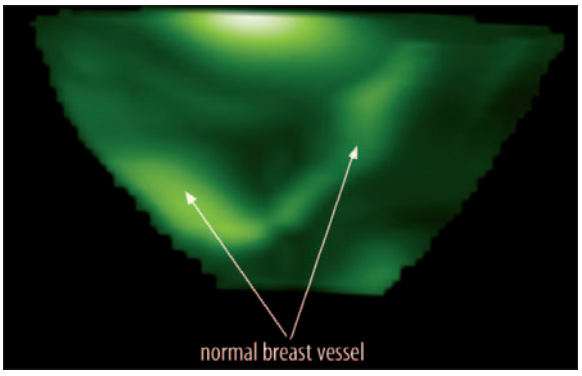

Figure 1. CTLM image – normal breast vessel. No evidence for increased laser light absorption – CTLM classified as negative.

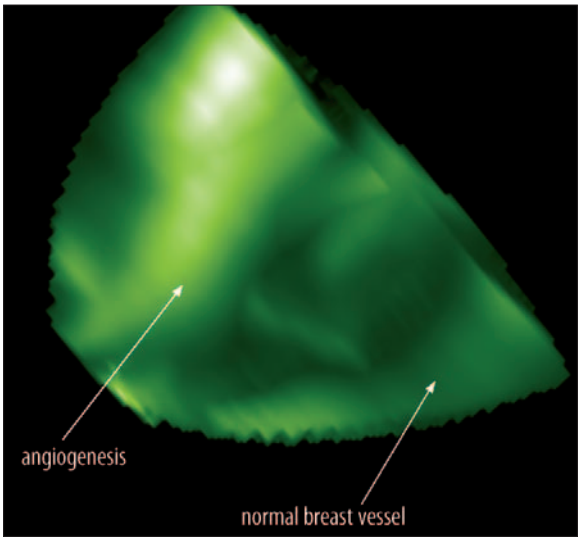

Figure 2. CTLM image – area of neovascularization, CTLM classified as positive. Histopathologic diagnosis; carcinoma ductal invasium.

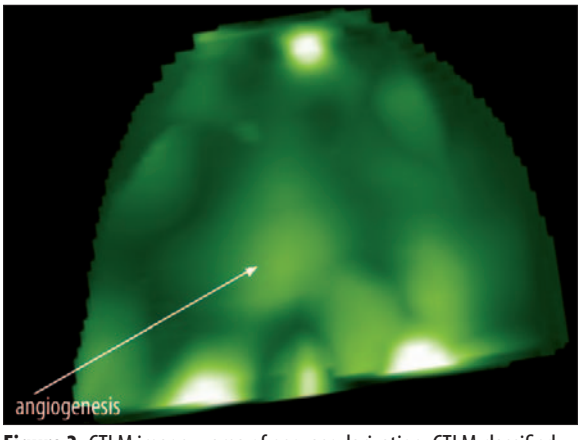

Figure 3. CTLM image – area of neovascularization, CTLM classified as positive. Histopathologic diagnosis; carcinoma ductal invasium.

In the examined group, CTLM sensitivity was 50%. Specificity 85%, PPV 30%, NPV 90%

Discussion

The aim of this analysis was to check whether the addition of CTLM to x-ray mammography would enhance the rate of detection of breast cancers in women with dense breast tissue.

CTLM is a non-invasive examination with no ionising radiation and no breast compression. The examination can be performed many times, irrespective of the patients' age or pregnancy. Absolute contraindications to this examination are practically not known.

The relevant literature and our experience [13,14] show that CTLM does not allow the character of a lesion visible in other modalities to be determined. For this reason, we have resolved to determine the value of this examination as an adjunct for women with dense breast tissue, for whom x-ray mammography has limited sensitivity.

According to the authors' knowledge, no work analyzing the value of CTLM in cancer diagnosis of dense breast cases has been published. We have conducted a retrospective analysis of 248 womens' examinations, where x-ray mammography did not reveal lesions (BIRADS 1, category 3 and 4 according to ACR). All patients underwent a CTLM examination at an interval not longer than 30 days since their x-ray scan, and the concluding diagnosis was established either on the basis of a cyto/histopathological investigation or by observation. In this group of 248 patients, cancer was ultimately diagnosed in 26 women (10.5%), and none of these cancers was detectable by x-ray mammography. Laser mammography revealed 50% (13/26) of cancers in the group which were invisible in mammography examination.

In the examined group, the CTLM sensitivity was 50%, specificity 85%, PPV 30%, NPV 90% – these results are slightly higher compared to the results we published in the previous article [14], (sensitivity 47%, specificity 74%, PPV 50%, NP. 72%), and this surely has to do with the radiologists' learning curve. The advantage of the method is high NPV and specificity [14], a negative examination result precludes with a high degree of probability the existence of a malignant growth process, which may suggest the application of this method in prophylactic examination of young women with a genetic mutation (BRCA 1 and BRCA 2) [15] There still remains the problem of false negative results – the problems with diagnosing angiogenesis arise when the growth process is localized under the nipple (on the account of the subareolar plexus, where a physiologically large number of vessels is present in a constraint area). In the presented group, 13/26 cases were false positives, out of which 2/13 patients had a growth process localised under the nipple. In the group of true positives there were no growths in that localization. Also in the case of rapidly growing tumors with central necrosis, angiogenesis may be weakly visible only on the circumference. There are also problematic artefacts, caused mainly by the physical properties of laser light (eg. its absorption while penetrating the tissue), in large breasts, laser radiation may be absorbed to a very large degree, or even completely before it reaches the cancer and/or may not reach the detector at all. Unfortunately, angiogenesis is not uniquely characteristic of malignant lesions, it may also manifest itself in benign lesions such as fibroadenoma, atypical ductal hyperplasia, papilloma and/or foci of glandular hyperplasia. In our previously published material, angiogenesis in benign cases was present in 100% of papillomas, 67% of ductal atypical hyperplasia, 78% of inflammations [14].

Conclusions

Computed Tomography Laser Mammography when used as an adjunct to x-ray mammography enhances the detection of breast cancer in women with dense breast tissue.

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