

Dynamic optical breast imaging: A new technique to visualise breast vessels: Comparison with breast MRI and preliminary results

Alexandra Athanasiou^a, Daniel Vanel^{a,*}, Corinne Balleyguier^a, Laure Fournier^a,
Marie Christine Mathieu^b, Suzette Delalogue^c, Clarisse Dromain^a

^a Department of Radiology, Institut Gustave Roussy, Villejuif, France

^b Department of Pathology, Institut Gustave Roussy, Villejuif, France

^c Department of Clinical Oncology, Institut Gustave Roussy, Villejuif, France

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Abstract

The purpose of our study was to explore and evaluate an innovative imaging approach, which consists on imaging the breast parenchyma by means of photoluminescence detectors (LED) and analysis of dynamic data. Breast magnetic resonance imaging (MRI) was chosen as the reference imaging method, as this is considered to be nowadays the gold standard for breast vascularisation evaluation. Preliminary results reveal a good correlation between breast MRI findings and light images.

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1. Introduction

Breast cancers are very frequent. Palpation is not sensitive, mammography not specific, hence the need of other imaging techniques. MRI detects tumor vessels around malignant lesions. The technique we evaluate combines light, focused at the methemoglobin frequency, thus detecting blood, and a moderate compression during the acquisitions, visualising blood trapped in the tortuous tumor vessels only.

2. Material

The system illuminates and senses light absorption properties of the breast tissue during both static and dynamic conditions. In the dynamic acquisition phase, the scan compresses and decompresses the breast tissue, similar to the process available during conventional mammography, but with very low pressure.

The system analyzes and compares light absorption across the static as well as multiple dynamic images for regions of extraordinary light absorption. Such regions are then more closely examined through a battery of digital processing techniques, and displayed as both scans and waveforms for the practitioner. These techniques involve digital subtraction of two or more of the images frames, spectral and temporal comparisons and intensity amplifications of the organized regions of the scans.

It is today intended for use on patients who have inconclusive diagnosis by mammography or other imaging tests or physical examination. The use of this device could provide the physician with dynamic functional information regarding abnormal vascularisation in an area of interest in the breast. The dynamic functional information will be used to better characterize the lesion.

The system was not tried under the following circumstances:

Patients who were:

- 1 18 years of age or younger.
- 2 Pregnant or lactating.

* Corresponding author. Tel.: +33 142 114873; fax: +33 142 115279.
E-mail address: vanel@igr.fr (D. Vanel).

Patients who had:

- (1) An open wound in the ipsilateral breast.
- (2) Lesions outside of BI-RADS categories 3–5.
- (3) Tattoos on the region of interest.
- (4) Body piercing of the nipple that could not be removed.
- (5) Breast surgery in the ipsilateral breast (e.g. augmentation/reduction/cancer/trauma) within a year of the potential scan date.
- (6) A core or excisional biopsy of the ipsilateral breast within 3 months.
- (7) Small, firm breasts which in the judgment of technologist performing the scan could not be properly illuminated.
- (8) Non-submuscular breast implants.
- (9) Surgical clips or scarring on the ipsilateral breast.
- (10) Internal/external device preventing adequate positioning.

The Scan system is made of three physical assemblies (Fig. 1):

- The patient interface or C-arm assembly.
- The controller.
- The computer system.

The C-arm consists of a breast support platform and a soft holder assembly. The breast support platform is attached to the bottom of C-arm and houses the LED Illuminator. The Illuminator consists of 127 red LED and emits light in the range of 640 nm.

The soft holder assembly consists of an air chamber, a CCD camera and an electromechanical brake. The soft holder assembly is manually lowered onto the breast and provides the means of applying compression to the breast. The air chamber has one surface that comes in contact with the breast, this surface is made from a thin silicon membrane. When the

pressure is increased in the air chamber, the silicon membrane expands and conforms to the breast surface to apply a uniform pressure to the breast.

The CCD camera is operated synchronously with the LED illumination and pressure control system to acquire digital images of the breast during the scanning process. The electromechanical brake locks the soft holder assembly in place during positioning and during the scan.

The controller is an electronic assembly that interfaces with the LED illuminator, the computer, the soft holder assembly and pressure reservoirs located in the bottom of the base unit. Housed in the controller are circuit boards for lighting the LED, operating the pneumatic pump, sensing the pressure in the air chamber and interfacing with the computer. It houses also a microcomputer and a programmable read-only memory.

The computer system provides the main user interface, sending commands to the controller and LED illuminator. Images are read from the CCD camera, processed and displayed. Data are stored and retrieved. The computer system also monitors operation and alerts the operator to fault conditions.

3. Scanning acquisition

The breast is positioned in a craniocaudal view (CC), similar to the mammographic one. The soft holder pressure is set to negative pressure to facilitate positioning. The breast should be centered on the breast support platform. The camera will begin acquiring images in a preset rate. These images will be shown in both grayscale and color scale. The LED illuminator controls are now active. A region of interest is defined, by drawing a circle by means of the cursor. This region corresponds to the suspicious areas as been determined by prior clinical or mammography findings. LED are selected according to breast size. The intensity adjustment can be optimized either manually or automatically, to obtain the maximum intensity in the region of interest.

After the complete scan acquisition, three images are being displayed in the diagnostic screen (Fig. 2c):

- (1) The left image is the superior (cranial) image.
- (2) The central image is the inferior (caudal) image.
- (3) The right image is the reference image, it is constant and it is used for positional references for both the breast outline and the blood vessels. A breast icon displays the breast orientation.

By means of region of interest (ROI) select, the curves corresponding to the dynamic signatures of each area selected can be displayed (Fig 2d). The curves of dynamic signatures are considered to represent the vascularisation modifications over time, thus permitting an qualitative approach of neovascularisation in suspicious breast lesions.

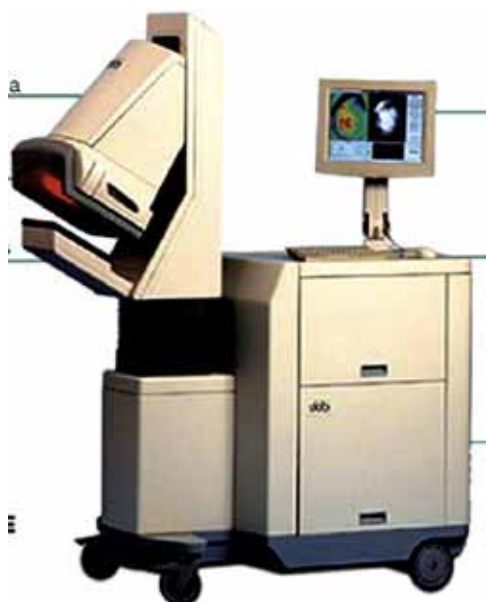


Fig. 1. The optical unit.

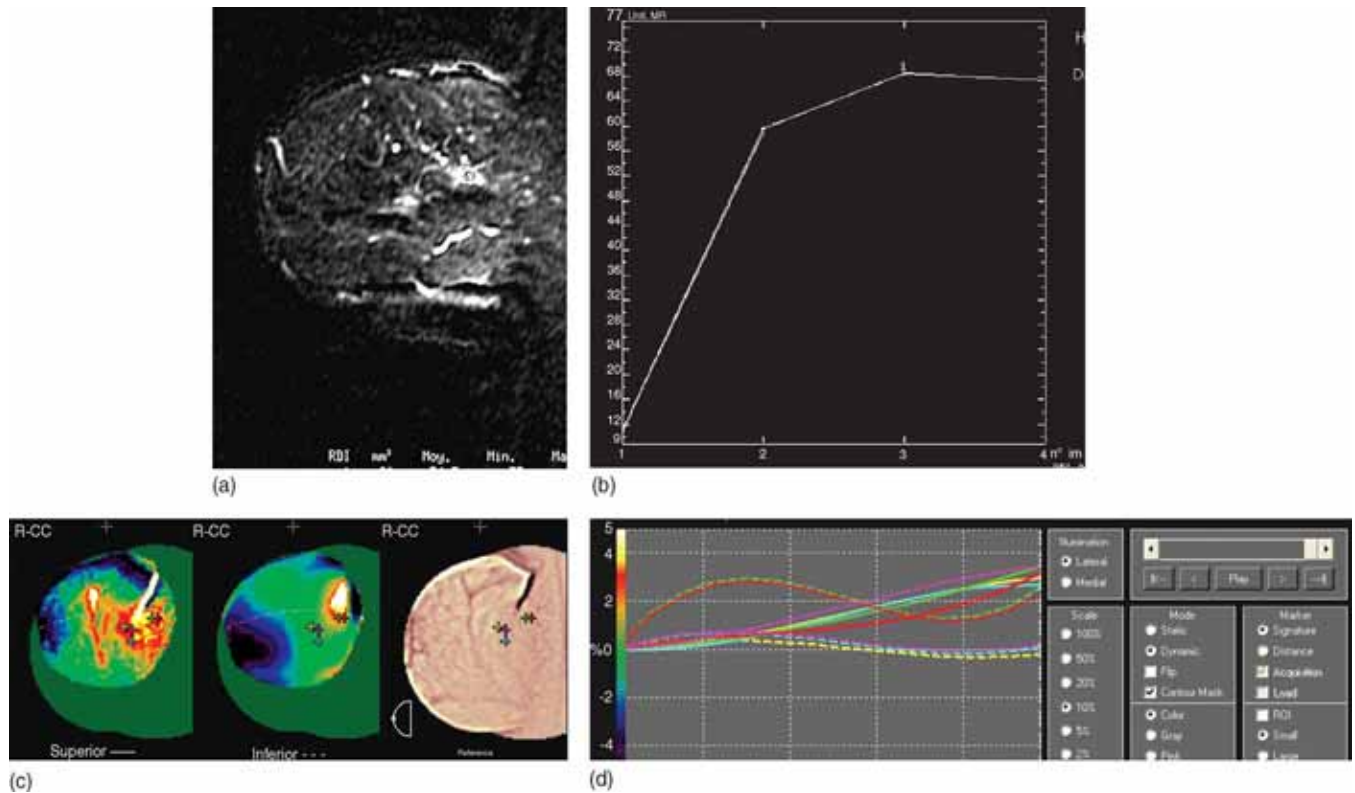


Fig. 2. Patient under chemotherapy for a T3 breast tumour. Breast MRI for evaluation of tumor response to therapy. Dynamic images after i.v. gadolinium (a) and digital imaging subtraction (b) showing an area of abnormal enhancement; the patient being under chemotherapy, the curve analysis is rather progressive, with a late washout. Corresponding light images showing an area of increased red pixels corresponding well to the tumor area depicted on MRI (c). The dynamic curves are of mixed, fluctuating and progressive type (d). This finding could be due to chemotherapy modifications of tumor vasculature.

The interpretation of images is based on two separate parameters:

- (1) The color range in color window and
- (2) The dynamic curves corresponding to each area selected.

The red color corresponds to areas of increased vascularisation, as this is estimated by analyzing the signal of LED emission by means of imaging functional programs incorporated into the computer system. The dynamic curves offer a more sophisticated means of calculating the patterns of increased vascularisation, optimally permitting to predict the areas of neovascularisation. There are two types of curves registered:

- the progressive one that is correlated so far with the areas of increased, abnormal vascularisation (Fig. 2) and
- the fluctuating one that correlates with areas of benign increased vascularisation (Figs. 3–6).

The proposed physiological explanation for these curves is based in the fluctuating rate of normal vascularisation, which is influenced by cardiac and respiratory rate, thus presenting smoothly curved up and down lines, in accordance with inspiration–expiration and systolic–diastolic rates. Capillary vessels permit an ‘elasticity’ of hematogenous flow. On the contrary, areas of neovascularisation are typically char-

acterised by the absence of capillary trichoid vessels, and blood is ‘pooling’ into abnormal arteriovenous shunts, not following the fluctuating cardiac and respiratory rate. This is represented by a progressive curve, without ‘elasticity’.

For our preliminary study, we have chosen to compare the results with the findings of the considered-to-be the gold standard method for breast vascularisation, breast MRI imaging with dynamic i.v. injection of gadolinium. The physical basis of breast MRI is also based on abnormal tumor vessels, especially arteriovenous shunts, responsible for the rapid enhancement and the “wash-out” of malignant lesions.

4. Patients and methods

This prospective study includes 25 patients that underwent both breast MRI and light scans, additionally to their standard mammography and ultrasonography.

All patients fulfilled the selection criteria: no recent trauma, breast surgery or biopsy.

Breast MRI was performed either to clarify a mammography–ultrasonography image that necessitated further imaging exploration or in the protocol of control of BRCA positive patients (these one who have a proven genetic mutation of BRCA 1 or 2 genes, responsible for the hereditary form of breast and ovary cancer).

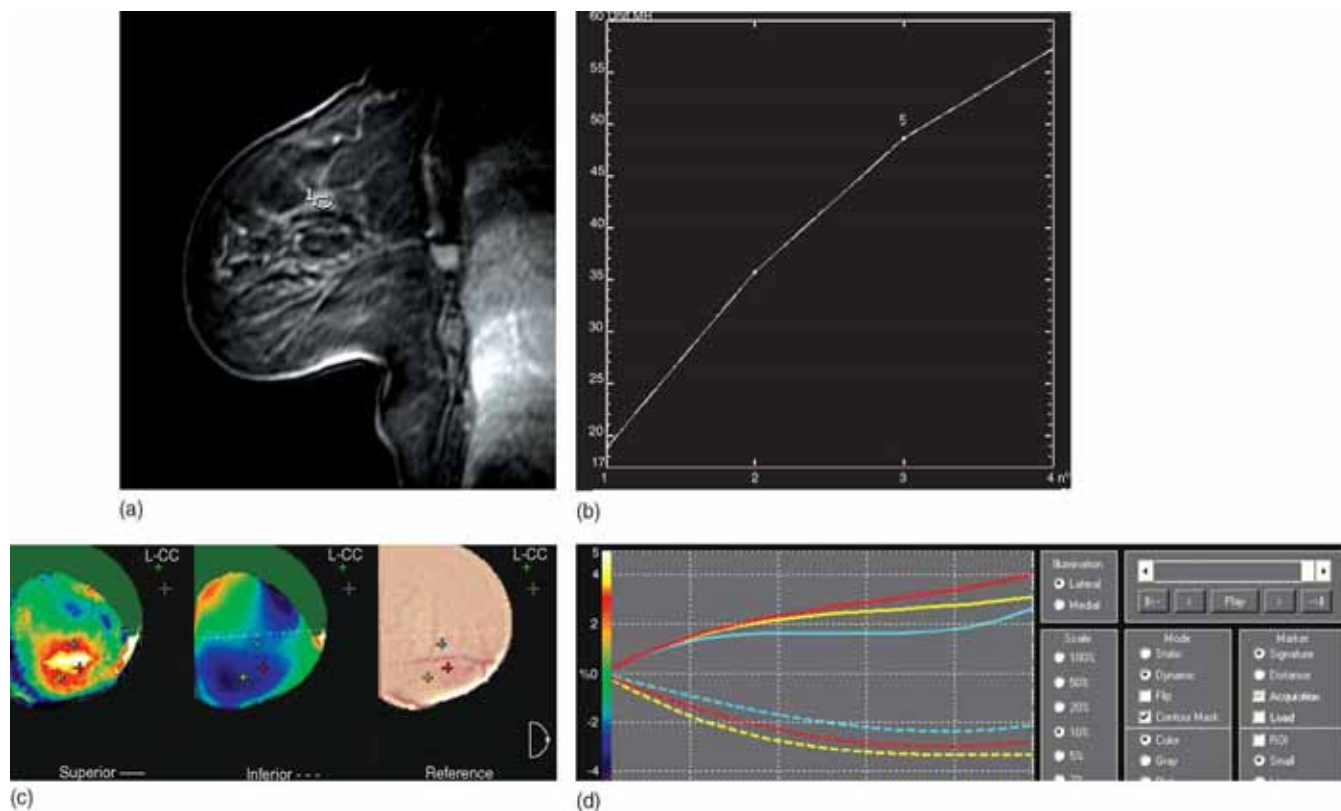


Fig. 3. Corresponding MRI and light findings in a case of benign fibrokystic disease showing a good correlation between the typical progressive curve of benign MRI enhancement (a and b) and the fluctuating curve of light dynamic signals (c and d). The total number of red pixels encountered in the area of interest is <1800 and all dynamic curves are fluctuating.

Written agreement was given by all patients, who were previously informed in detail of the study.

The patients age varied between 28 and 76 years (mean age 50 ± 2 y).

Five patients were BRCA positive, they underwent a bilateral MRI and light scan.

Twenty patients were referred for further control of a image depicted on mammography–ultrasonography. All but one of these 20 patients had already undergone a conservative breast treatment in our institution, and were under regular clinical and radiological follow-up. Only one patient was sent for further exploration of an abnormal image depicted on her annual mammography, without clinical associated findings and without previous history of malignant breast disease.

Breast MRI were performed on a 1.5 T magnet (Sigma Horizon, GEMS, Milwaukee). All examinations were performed with a bilateral dedicated breast coil, with the patient imaged in a prone position. They included sagittal T1-weighted spin-echo (500/14 [repetition time ms/echo time ms]) and T2-weighted, fast spin-echo (4000/120) sequences with fat suppression. The contrast-enhanced sequence was a three-dimensional, dynamic, fast spoiled gradient-echo sequence (minimum repetition time ms/minimum echo time ms, $30\text{--}90^\circ$ flip angle, 28 sections obtained in a minimum of 1 min 30 s, field of view [180–240 mm], large matrix

[512 × 256], and thin sections [2–3 mm, with no intersection gap]). Contrast material (0.1 mmol per kilogram of body weight gadopentate dimeglumine [Dotarem; Guerbet, Roissy, France]) was injected intravenously during approximately 10 s and was followed by a normal saline flush; image acquisition began immediately. Postprocessing image subtraction was performed on a workstation with dedicated software (Functool, GEMS).

The light scans were performed the same day as breast MRI.

Image analysis and interpretation were made by two senior radiologists. First interpretation of light images was made independently of MRI findings, followed right after by a correlative analysis of both imaging modalities.

5. Results

Breast MRI exams were considered positive in cases of areas of abnormally increased early enhancement and as negative in all other cases.

For the interpretation of light scans, quantitative and qualitative ratios were calculated based, respectively, on the number of depicted photoluminescence signals (red pixels) passing through the areas of interest and dynamic signal curves evaluation.

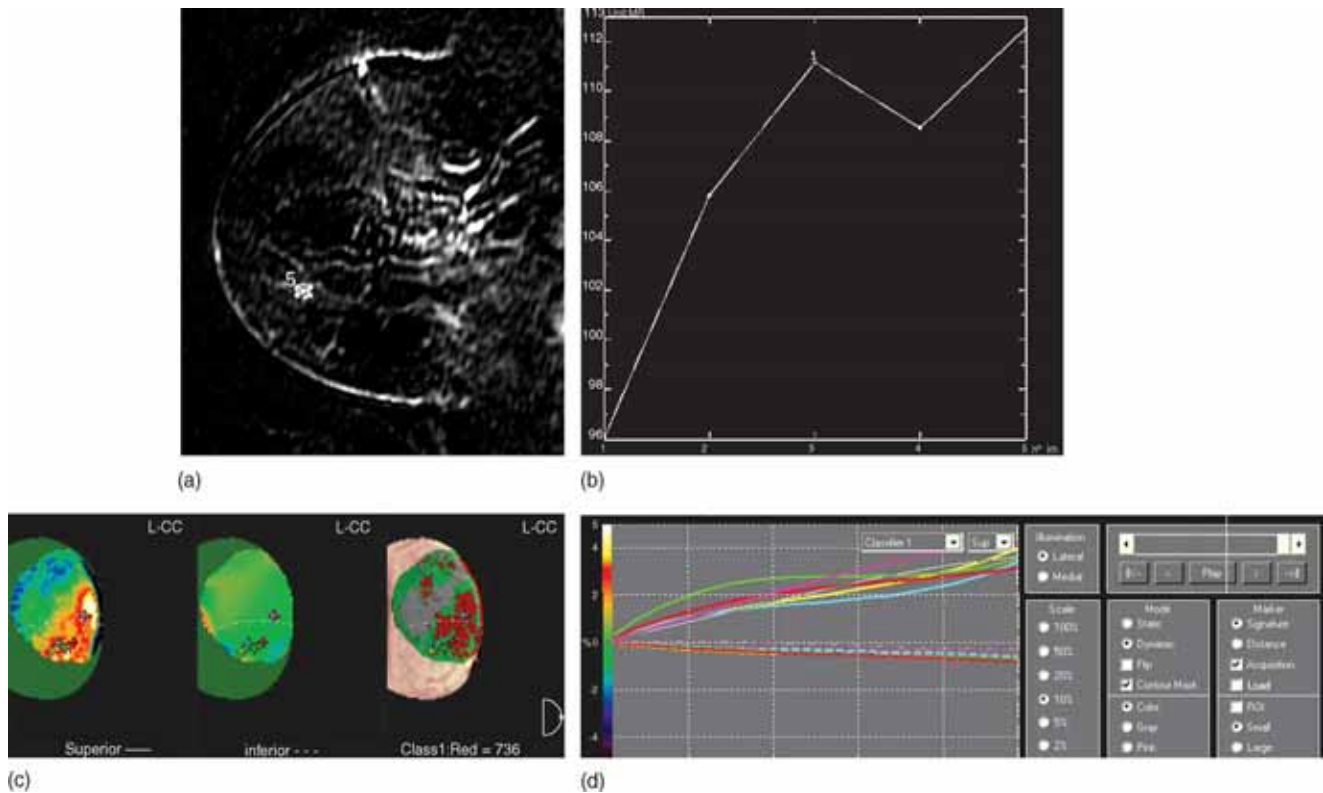


Fig. 4. MRI punctiform focal enhancement (a and b) with a non-specific curve analysis, due to the small size of the lesion (foci). Small foci are difficult to analyze on MR images, mostly because the curve analysis is not specific. No corresponding area of increased red pixels was registered on the light scan (c). All dynamic curves were of benign type (d). MRI guided US was negative. Follow-up after 3 months by MRI was unremarkable proving that it was a focal inflammation in the retroareolar region.

Light images were considered positive in all cases of red color regions with total number of red pixels >1800 , with more emphasis given to the concomitant presence of progressive type dynamic curves.

In 20 out of 25 (80%) patients, breast MRI was negative. Light images showed in 12 cases an homogeneous illumination pattern, predominating in the upper outer quadrants, according to the normal distribution of glandular elements in the breast (Fig. 5). We did experience red color signals in the upper outer quadrants, but quantitative ratio was <1800 and the dynamic curves were smoothly fluctuating, representing normal vessel blood flow (Fig. 3). In eight cases, light scans gave positive results without abnormal MRI findings. We attributed these images to the asymmetric distribution and predominance of glandular elements in certain areas inside the breast, as well as normal hypervascularisation phenomenon (e.g. second phase of menstrual cycle, or hormonal replacement therapy).

In the remaining five patients (20%), breast MRI was positive, depicting, respectively, two lesions in the upper outer quadrants, two lesions in the upper quadrant union (one behind the nipple) and one lesion in the lower quadrant union. Further diagnostic and imaging investigations comprised an MRI focused ultrasonographic examination followed by biopsy in cases of positive U/S findings, and this was the case for four out of five patients. Histology revealed

one infiltrating ductal adenocarcinoma and three fibrokystic disease changes. No corresponding U/S findings were found for the fifth patient, whose mammography and physical examination were unremarkable, so a new MRI follow-up was performed after a 3-month interval, which was negative. The gadolinium enhancement was attributed to focal inflammation changes (lesion just behind the nipple) (Fig. 4).

Light imaging was characterised as positive in four out of these five patients, giving rates of red color areas >1800 . The patient with negative U/S findings had also a light scan within the normal limits, thus permitting to estimate the possible significant negative predictive value of the method.

6. Discussion

Breast cancer is the most common cancer in women. One in nine women will develop breast cancer during her lifetime [1,2]. With breast cancer incidence rates showing no signs of abating, there is interest in expanding the breast imaging arsenal. Mammography remains the standard imaging procedure of control and all recent studies [3–5] support its value as a screening tool. However, our “gold standard” it is not an ideal screening tool. Even when performed optimally the

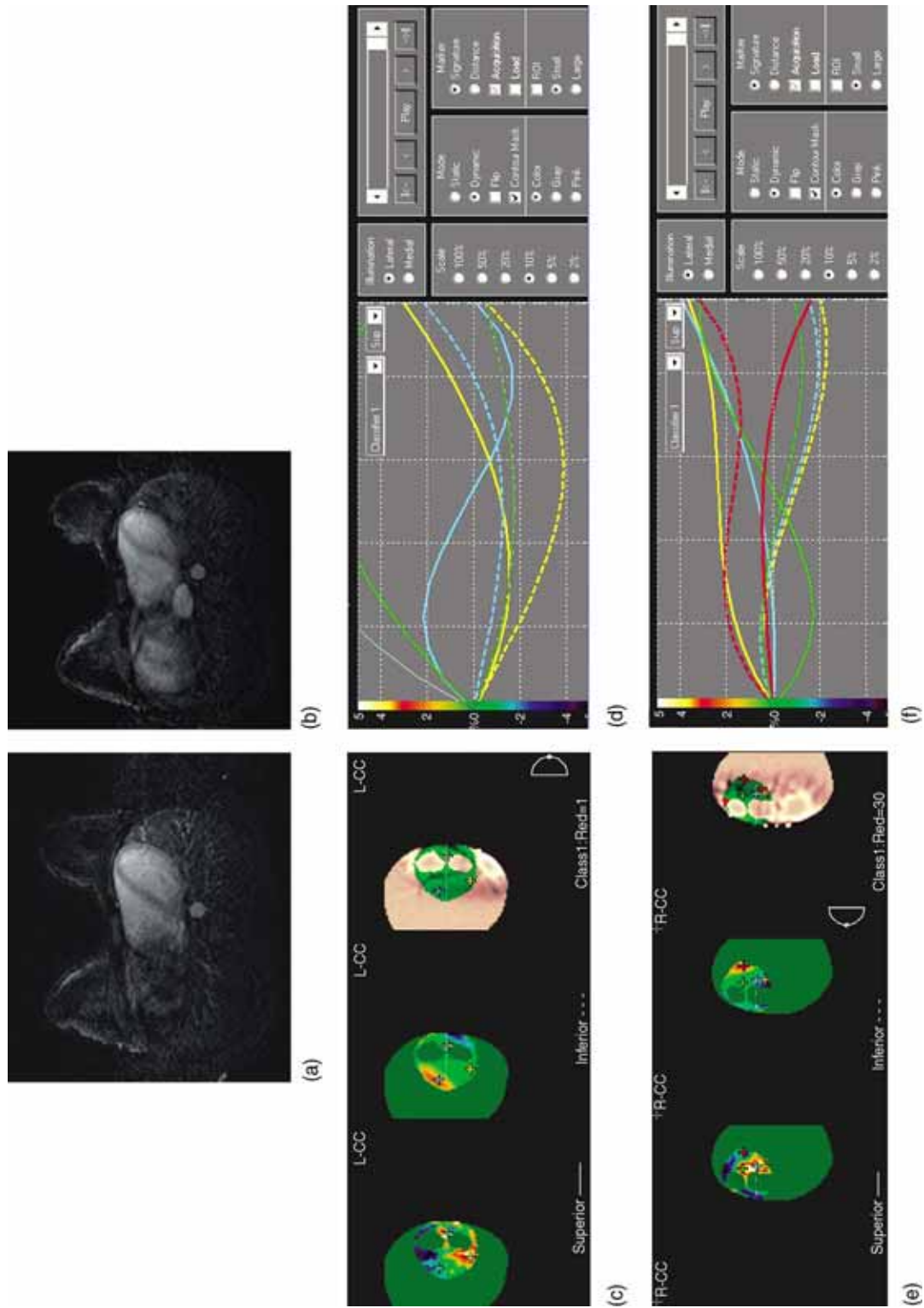


Fig. 5. Bilateral normal breast MRI (a and b) in a positive BRCA 1 patient and normal light scans (c–f).

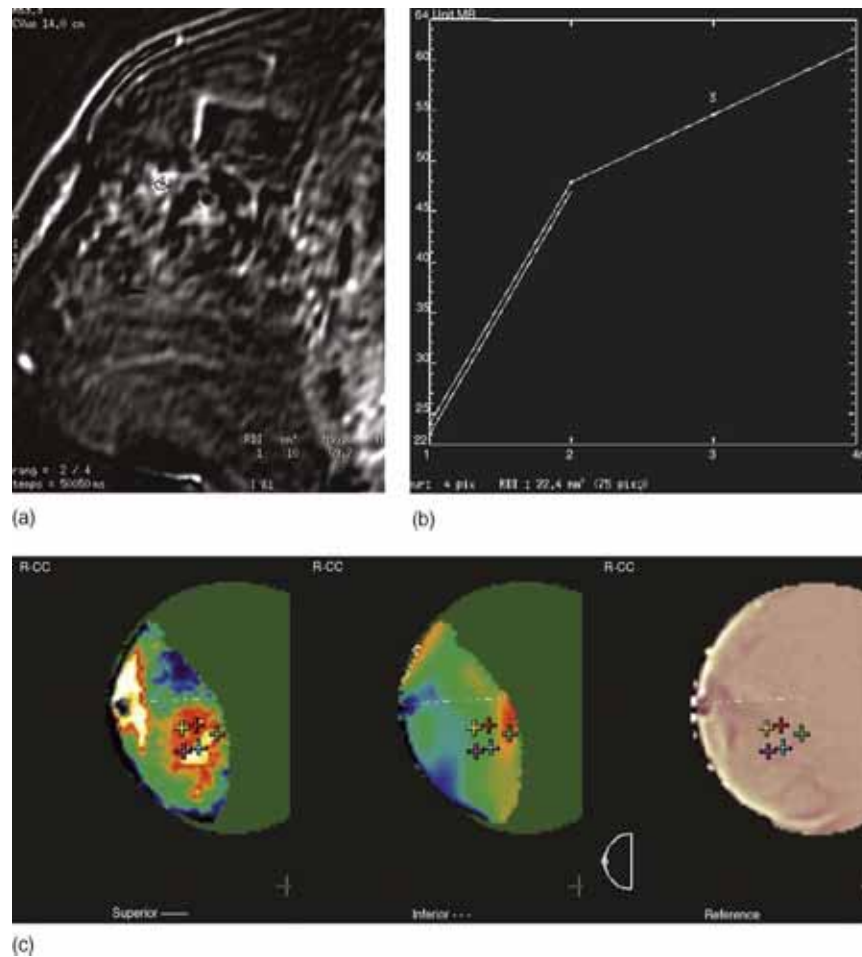


Fig. 6. Breast MRI typical scar enhancement (a) with progressive curve (b) in a patient treated conservatively for an adenocarcinoma 5 years ago. Light scan depicted the treated area as a region of high red pixels signal (c), but all curves were of benign fluctuating type (d).

sensitivity is between 69% and 89% [6–12]. Potential radiation risk and diminished sensitivity in radiographically dense breasts represent the two main disadvantages of the technique, thus limiting its usefulness in high-risk young women. It is well documented in the study carried out by Kuhl et al. [13] that gene carriers BRCA 1 and BRCA 2 are susceptible to have an increased radiosensitivity of breast parenchyma. Other clinical areas in which mammography is of limited diagnostic value are: detection of lobular cancer, detection of ductal carcinoma in situ without associated microcalcifications, diagnostic work up of unknown primary presenting as axillary lymphadenopathy (these are usually small high grade lesions lodged in dense breast tissue), evaluation of multifocal disease and of locally advanced disease, and diminished sensitivity in post-treatment breasts [14].

The addition of ultrasound to mammography can improve overall sensitivity, as this is an excellent method for differentiating solid from cystic lesions and for characterizing lesions depicted on screening mammograms. However, it is not recommended as a first-line imaging method because of a vari-

able false-negative rate, ranging between 3% and 47% [14] as this is a highly operator dependant examination [15].

Breast magnetic resonance imaging is gaining popularity, as this method demonstrates an excellent sensitivity, with a very low false-negative rate.

The abnormal vascularity patterns of malignant lesions have been already well studied, with emphasis on the absence of normal capillaries and their replacement by the arteriovenous shunts pathologic basis, presented without exception in all cases of infiltrating tumors regardless of their histology, representing the physiological explanation of suspicious MRI enhancement. Our preliminary results of light scans showed that it may be also responsible for the progressive type of curve, which theoretically could enable to distinguish between red color areas of abundant gland tissue or benign fibrokystic changes and hypervascularised suspicious breast lesions. Light imaging is showing to have an increased sensitivity, depicting all areas of increased blood flow in the breast and correlated well with the gold standard method of breast MRI in all true positive cases. The most remarkable obser-

vation was not only the high number of red pixels associated with the MRI hypervascularised lesions (the higher the number of pixels the more pronounced the vascularisation) but also the type of dynamic curve. In the only case of infiltrating adenocarcinoma that we experienced the total red pixel number was >2900 and the dynamic curve was progressive (images 2a–d).

Two out of true positive MRI-true positive light images referred to fibrokystic disease areas. In these cases the total number of red pixels was <2500 and the dynamic curves were smoothly fluctuating (images 3a–d).

In the only false positive MRI case, for which light examination was considered as normal, as shown in images 4a–d, a focal punctiform enhancement was depicted by MRI in the retroareolar region, without clinical, mammographic or MRI focused U/S findings. Corresponding light images were considered as negative. We chose a 3-month follow-up by breast MRI, which became negative, so the punctiform enhancement area was attributed to focal inflammatory changes in the retroareolar region. The patient was under regular follow-up for the next 12 months without any abnormality noticed so far.

A full concordance was noted between negative MRI and normal light scans. This could be of special interest in cases of patients who are BRCA 1 or 2 positive, as shown in the case 5 (Fig. 5), as well as in cases of treated breast (Fig. 6) eventually opting in an additional screening method for the high-risk patients. Case 6 is referring to a patient having undergone a QSE lumpectomy and complementary irradiation 5 years ago. Recent mammography was equivocal, showing an increased density in the treated area. MRI was performed to exclude or verify a local recurrence, and it was proved to be negative, showing the typical scar type of enhancement. Light images were also in the low range of red pixel total number and dynamic signal curve was fluctuating.

However, we had a high rate (32%, eight out twenty five patients) of false-positive light scans, with negative MRI control, so the specificity of the method is to be further evaluated, with eventually the development of more specific parameters.

Potential advantages of the method include the facility of patient positioning, the fastness of the examination (about 60 s of acquisition), a good tolerance, the absence of ionizing radiation and a probable high sensitivity. All patients showed very well breast compression, which is lower than the compression during a classical mammography. Light imaging could also be of theoretical value in cases of claustrophobic patients or in any other case of MRI contra-indication.

Method limitations include a possible low specificity, which should improve with new improvements and a relative high cost as the system is always under experimentation.

Many parameters need to be further defined and explored in order to achieve a full knowledge of this modality limits.

7. Conclusion

Dynamic optical breast imaging can be a promising complementary imaging modality in women with inconclusive mammography and/or physical examination.

Our study includes a small number of patients, but the preliminary results are encouraging enough. However, further evaluation with a larger number of patients should be carried out.

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