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DYNAMIC OPTICAL BREAST IMAGING (DOBI): prospective study on the diagnostic accuracy of ComfortScan IN BREAST CANCER. PRELIMINARY RESULTS.

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INTRODUCTION

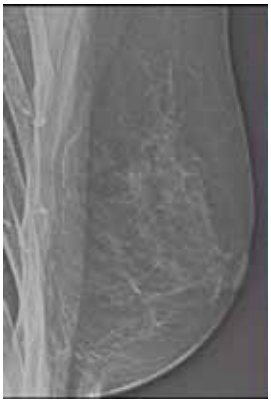
Breast cancer is the most frequent cancer in women and stands as the second leading cause of cancer death in women.

It has an overall incidence of 990,000 new cases per year, with an average annual increase of 2% and a predominant distribution in industrialized countries (Europe and North America) than those in the developing world.

In Italy, every year, more than 31,000 women are sick of this cancer and approximately 11,000 die from it (ISS). Therefore, breast cancer should be considered a medical emergency, which must be counterbalanced by identifying diagnostic methods more and more adherents to the knowledge on biology of this cancer.

In recent years the contribution of research has radically changed the therapeutic approach to breast cancer.

With the improvement of instrumental diagnostic techniques, has in fact occurred so relevant diagnostic anticipation to change profoundly therapeutic paradigms.



Contrary to what happened in pre-mammography when breast lesions are presented as palpable swelling present, in most cases, the base of conservative treatment options, there is the detection of non-palpable mammographic alteration economic.

However, current methods of breast imaging (mammography, ultrasonography and MRI) are burdened with some considerable limitations that affect diagnostic accuracy, since all characterized by a satisfactory sensitivity but variable specificity.

In fact, mammography is strongly influenced by the degree of radiopacity of the breast and exposes patients to ionizing radiation; Ultrasonography provides an in-depth clinical and mammographic findings diagnostic doubts, but has a sensitivity and specificity of operator-dependent imaging methods such as additional MRI (Magnetic

Resonance Imaging) can be expensive and inconclusive, for example in the detection of microcalcifications, and finally the cyto-histology, a diagnosis that in nature highly suspect in the case of images, is not without limits, identified in the most cost greater injury and greater susceptibility to sampling errors.

The international research is currently directed towards technologies that can provide additional diagnostic information in support of the data currently available, to obtain a more complete and accurate diagnosis.

In this sense, the progress of photonic technologies,

mathematical models of light propagation through tissue and the knowledge of the photophysical properties of tissues, has necessitated a reevaluation of the usefulness of transluminescenza in the study of breast diseases.

The DOBI (Dynamic Optical Breast Imaging) is an innovative tool for optical imaging, non-invasive, which exploits the properties of light absorption by breast tissue in order to measure in static and dynamic conditions, the ability to reduce the light signal dependent neoplastic processes in the mammary gland.

The foundation on which medical science has been based technology is to provide DOBI physiological data related to functional tumor-induced neoangiogenesis.

The process of neovascularization associated with tumor growth is characterized by progressive replacement of normal tissue vasculature with numerous arterio-venous shunts that increase the blood volume in the context of the neoplastic process in response to increased metabolic demand.

The angiogenic blood vessels in malignant tissues share several characteristics observed.

Together, these features create a "profile vascular only" or "angiogenic footprint" that can be identified by DOBI in the diagnosis of breast lesions.

The aim of our study is to assess the diagnostic accuracy of DOBI, determining the indications and limitations of the method and, ultimately, identifying the benefits, in order to propose it as a useful tool for integration in the study of breast diseases.

HISTOLOGICAL CLASSIFICATION

The primary malignancies of the breast can be divided into epithelial and non-epithelial.

Malignant epithelial tumors, a very rare finding, usually represented by sarcomas, lymphomas and cutaneous melanomas.

Malignant tumors of the breast epithelial cells, which constitute the area of our interest, are a heterogeneous group of lesions discariocinetiche far more frequent.

On the morphological level and therapeutic the most important distinction is that between infiltrating forms, recognizable for the invasion of the stroma, and forms no infiltrating or in situ, in which proliferation is confined to the epithelium of the mammary gland and there is not exceeded basement membrane.

The development of cancer occurs through a process with multiple stages and, as with other solid tumors, it is likely that invasive breast cancer is preceded by a pre-invasive 37-44.

The molecular genetic studies confirm the theory of a linear progression in the *sequence:-normal epithelium hyperplasia - atypical hyperplasia - carcinoma in situ - invasive carcinoma* [13] -46.

The proliferative lesions that may precede the onset of an invasive carcinoma originating from the terminal duct lobular-(TDLU) 48.

In the current definition, the **ductal intraepithelial neoplasia (DIN)** are classified according to Tavassoli at 117:

Usual hyperplasia (UDH) Stage 1a

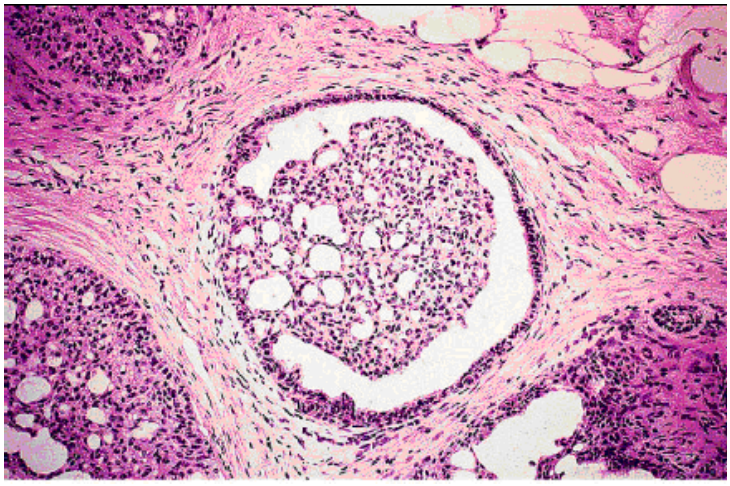
Flat atypia (ADH-Monomorphous Flat Type) Stage 1b

Atypical epithelial hyperplasia / carcinoma in situ low-grade Stage 1c

Carcinoma In Situ of intermediate Stage 2

Carcinoma In Situ Of High Grade /Comedocarcinoma Stage 3

The concept of intraductal proliferative lesions of the spectrum is also the theory of a line of progression with respect to the risk of developing subsequent invasive carcinoma, which is lower than for usual ductal hyperplasia and cancer higher for DCIS 48-49 - 117.



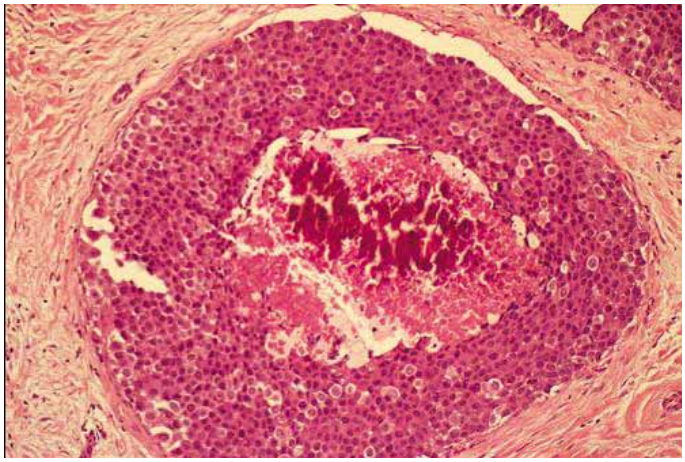
Cancer Ductal in situ (DCIS) represents 20-30% of breast cancers not palpable.

In most cases, is identified as mammographic finding of a cluster of microcalcifications, but can also occur in the form of a palpable nodule.

Are classically distinct forms comedones, with greater malice, and no forms comedones (cribriform, micropapillare, papillary, solid). According to the classification of Van Nuys, the DCIS is further defined **low-grade** (grade **1),** intermediate grade **(grade 2)** and high grade **(grade 3)** based on nuclear grade, necrosis and intraductal polarization functional differentiation understood as Architectural.

The evolution towards forms infiltrating varies depending on the cytological characteristics of neoplastic proliferation. In 20% of cases a concomitant invasive carcinoma

with an in situ component.



In DCIS is reported in the literature an incidence of axillary lymph node metastases from 1% to 4%, which is generally attributed to the presence of unrecognized microinvasive carcinomas.

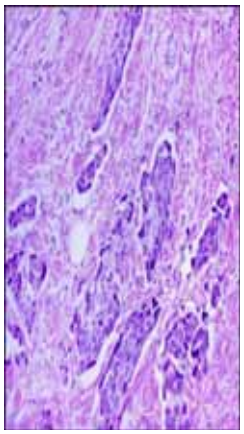
The **lobular carcinoma in situ (LCIS)** is considered the true precursor of invasive cancer [50].

His response, often casual, requires careful follow-up for the risk of developing in both breasts, an invasive carcinoma.

This risk is 8-10 times higher than the healthy population in the first 15 years after diagnosis.

And 'multicentric in 70% of cases and bilateral in 30-40%.

Invasive **cancer,** as defined by the infiltration of the basement membrane and the subsequent invasion of the stroma by tumor cells, is classified according to the architectural and cellular differentiation:



· **Invasive ductal carcinoma,** which represents approximately 70-80% of all malignancies of the breast and includes all those breast cancers that are commonly called ductal carcinomas not otherwise specified (NAS).

A ductal carcinoma infiltrating itself as "a predominantly intraductal component or microinvasive" if it displays a predominant component of DCIS (> 75% of T).

Macroscopically it appears as a lump of hard-wood, or consistent as parenchymal thickening.

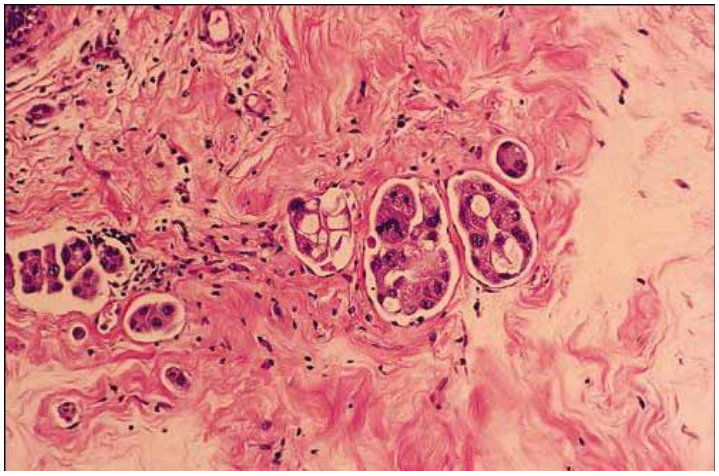
Histologically it is composed of glandular structures together in cords or small clusters surrounded by a fibrous stroma; unfavorable prognostic sign is the finding of a tumor necrosis.

It can manifest itself in the form multifocal (3-5%) and in approximately 10% of cases in multicentric form, sometimes comes in disguised form, with the detection of axillary metastases in the absence of obvious breast lesions;

· **Invasive lobular carcinoma** is the second breast malignancy in frequency (7-20%) and occurs mostly in the form of parenchymal thickening, rarely microcalcifications.

It is' often multicentric and multifocal and in a variable percentage from 6% to 28%, according to published studies, it is bilateral.

Histologically, it consists of individual cells which are arranged in single file around breast ducts but can also provide free facilities, such as solid nests or tubular-alveolar formations. In addition, 50% of cases associated with LCIS, often as a finding independent of tumor infiltrating.



Other rarer forms are represented by infiltrating **medullary carcinoma** (1%) that looks like a well-circumscribed tumor with intense lymphoid stroma and cells with marked atypia in solid form aggregated syncytial virus.

Is prevalent in young women under the age of 35 years, is not associated with formed in situ and has an excellent prognosis.

Mucinous carcinoma (1-2%), has a clinical behavior similar to invasive ductal carcinoma, but microscopically looks like a well-defined nodule with a high content of mucin with little cellular component, the prognosis is generally good even in the presence of lymph node metastases .

The **tubular carcinoma** (2%) is generally small and consists of tubules surrounded by a dense stroma sclero-hyaline.

It has a peak incidence between the V IV decade of life, is often multicentric or bilateral but rarely associated with lymph node metastases, and benefits from a favorable prognosis.

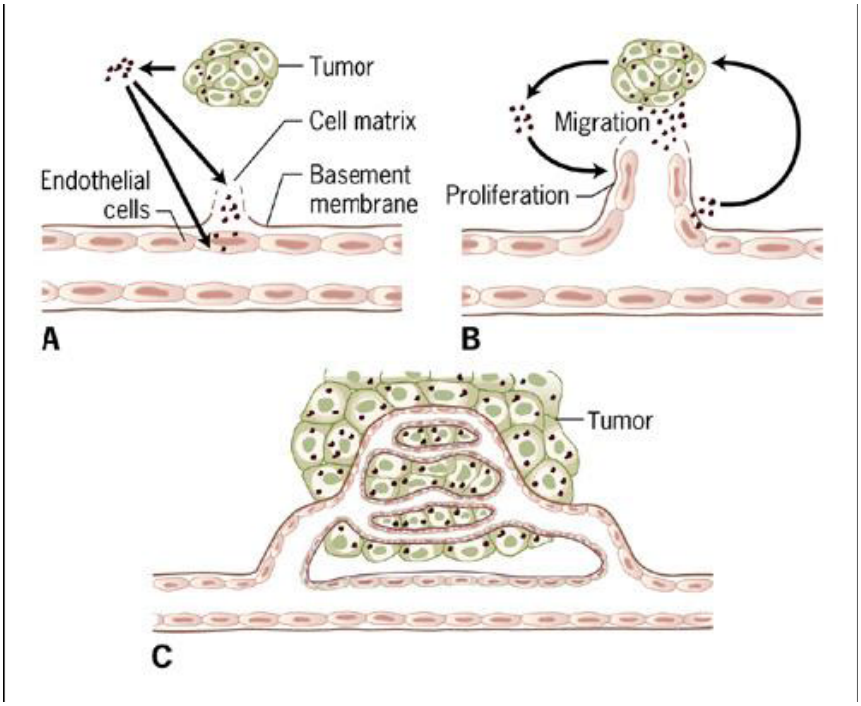
The **papillary carcinoma** (2%) has a tendency to lymph node metastases (8-10%).

Other rare cancers, such as **cribriform carcinoma,** represent occasional events in clinical practice, usually associated with good prognosis, 12-15.

ROLE OF NEOANGIOGENESIS

Angiogenesis is a biological process that stimulates the proliferative activity of endothelial cells, giving rise to the formation of new capillaries.

It takes place in a number of processes both physiological and pathological conditions, such as ovulation, corpus luteum formation, inflammation, the healing process. In the development of solid tumors on angiogenesis is a must.



Pathological angiogenic stimuli produced in the microenvironment promote tumor neovascularization

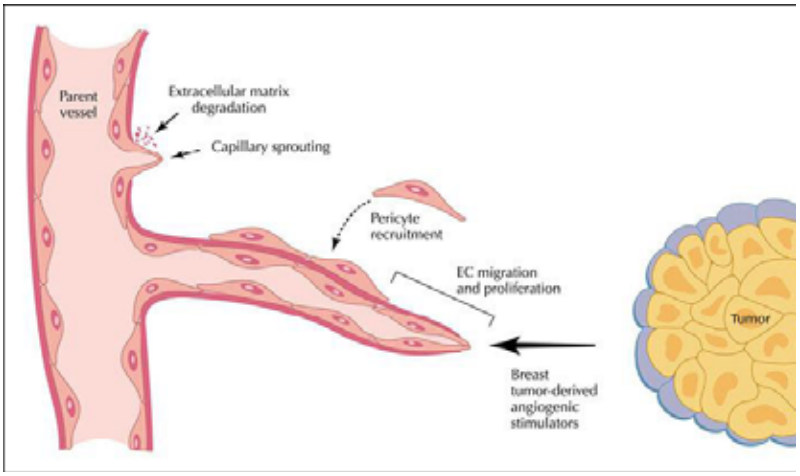
The neoplastic development occurs initially through a phase of so-called *"avascular",* during which the cancer cells receive nutrients and oxygen through a process of diffusion from the interstitial fluid from which they are surrounded.

This phase coincides with the condition of intraepithelial carcinoma or in situ, which consists of a cluster of tumor cells of the maximum diameter of 1-2 mm, in the context indovate epithelium which gave rise to the transformed cell.

The tumor neoangiogenesis begins with the disintegration of the basement membrane and extracellular matrix by enzymes produced in the pathologic microenvironment.

In the natural history of cancer, the onset of angiogenic activity marks the transition from avascular to the vascular neoplastic development.

The vascular phase is characterized by the production of angiogenic factors that act as mitogens on endothelial cells.



Cellular and biochemical processes of a 'tumor angiogenesis

These factors are produced by cells isolated tumor cell lines in which there has been a derepressione of genes encoding angiogenic factors.

Contribute to this production cells infiltrating the tumor tissue such as activated macrophages, mast cells and T cells, amplifying the angiogenic activities performed directly by cancer cells.

The vascular phase is a prerequisite for a more rapid development and increased invasive capacity of cancer suggesting a close correlation between the onset of angiogenic activity and that of the metastatic phenotype.

The existence of abnormal vascularization in the context of malignant breast lesions was supported by Feldman for the first time [13] and [14] watts in a study published in 1967, which took advantage of the use of techniques to identify small groups of vascular tumors the breast.

Wells came to similar results with ultrasound [15, 19] and Weidner found that micro-vascular density (MVD) was greater at the periphery of lesions heteroplastic, identifying the MVD as an element of evaluation of a suspicious lesion.

From studies showed that the newly formed vessels of the tumor processes have the following features:

- **increased resistance to blood flow** than normal vessels;

- **greater ability to collapse** of newly formed vessels, when subjected to external pressure;

- a **'high vascular permeability,** responsible for an increased interstitial fluid pressure (IFP), approximately 20 mmHg compared to normal tissues;

- a **high oxygen consumption,** resulting in increased metabolic demand of tumor process which implies the presence of high concentrations of **deoxyhemoglobin** in the newly formed **vessels.**

These characteristics identify a particular profile of blood vessels that has a micro-vascular density (MVD) susceptible to measurement.

The imprint is different from simple *tumor angiogenic* inflammatory processes because of its high density and high blood volume. Numerous studies have documented a significant correlation between MVD and invasiveness in breast cancer, so that it considered a potential predictor of cancer in the preclinical phase.

The new methods of optical imaging, focusing on molecular processes and vascular changes that accompany the development of cancer, have the potential to improve both the sensitivity and specificity of diagnosis of breast cancer.

THE DOBI TECHNOLOGY

The DOBI ComfortScan optical imaging is a method of studying the vascularity of the breast through the analysis of transmission properties-that the light undergoes attenuation through the breast tissue, both in static and dynamic conditions. The DOBI displays these angiogenic effect creating an impression of the breast, whose constituent elements are given by the variation of blood volume and the concentration of deoxy-hemoglobin in the blood vessels.

The elements that make up the DOBI are:

· a platform tilted 30 ° with 127 LEDs (light emitting diodes) that emit a red monochromatic light of wavelength 640 nm,
capable of

ensure high sensitivity optical absorption of deoxyhemoglobin;

· electro-mechanical arm equipped with an air chamber that performs a delicate silicone breast compression on the platform;

· a CCD (charged coupled device) camera with a resolution of 12 bits;

· a computerized system that controls the LEDs, captures images, processes the information obtained and stored in a database.

During the examination, the patient's breast is placed in direct contact with the surface of the platform containing the LEDs, obtaining images in the craniocaudal projection.

The transmitted light is recorded by a CCD camera for about 45 seconds.

As part of the process, the machine exerts a slight pressure on the breast uniform, varying from 5 mmHg (base) to 10 mmHg (analysis) for about 30 seconds.

The entire procedure takes about 10 minutes.

The dynamic response to the modulation of the sinus pressure is recorded in the form of a sequence of images of different intensities obtained before, during and after application of the embossing pressure.

The system measures the DOBI incremental changes, related to the redistribution of blood to the collapse of capillary and venous blood oxygenation over time, by subtraction techniques using magnification and contrast in order to produce a functional diagnostics.

When the LED light meets the tissue surrounding the tumor angiogenesis, hemoglobin trapped in the capillaries absorbs red light more complete than a normal benign tissue.

After each cantilever pressure, the system keeps track of the changes in light transmission and wavelength 42.

When compared with areas with normal vascularity, blood volume and oxygen saturation levels decrease with a different rate.

The dynamics are obtained fingerprints from each pixel of the recorded images. Since the dynamic responses

pathological areas of influence are somewhat different from those of normal regions, it is possible to recognize the differences in the "fingerprint".

To facilitate viewing and pathological classification, it is an image built functional, using a cross-correlation algorithm.

In this process, is selected from the mammary region in accordance with a "reference mark".

Then applies a process of cross-correlation between the dynamics of fingerprints from all regions of the breast with a mark of reference.

Since the dynamic fingerprint of all the regions are similar to physiological 'imprint of reference for these regions we obtain a very high level of correlation.

On the other hand, the dynamics of fingerprints iinfluenza pathological areas are different from those of reference: from these regions will result in a low level of correlation.

This function produces an image with high contrast. Functional image, the light intensity

are normal areas, while the intensities have dark areas of influence *pathological.*

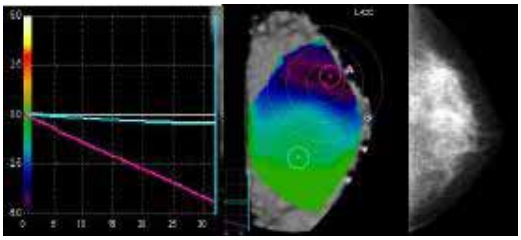
To process the recorded images, the DOBI ComfortScan uses computer algorithms to generate a graph for spectral-temporal values of attenuation of the light produced during the mechanical perturbation for each point.

The interpretation of images obtained by DOBI method is based on two parameters: a *quantity,* namely the number of pixels that reconstruct the areas of interest, and *quality,* ie the evaluation of the dynamic curves.

The *quantitative* parameter coincides with the evaluation of **spatial characteristics** of suspicious areas (intensity of color, location, margins).

Regarding *the intensity of color,* a focal area of intense blue color is characteristic of a malignant lesion is likely, on the contrary, a popular area of green-yellow is a sign of kindness. Reassessing the dynamic images in sequence, the presence of a focal area in a stable *location*

is a sign of malignancy. Finally, the more obvious are the *margins* of a focal suspect, compared to the surrounding areas, the more this issue argues for a diagnosis of malignancy.



The *quality* parameter coincides with the evaluation of **dynamic curves,** half sophisticated calculation of the patterns of vascularization.

The physiological explanation for these curves is based on the influence of heart rate and breathing on the normal vasculature and the significant role of capillaries in ensuring the resilience of blood flow.

In neoplastic processes, areas of neovascularization are typically characterized

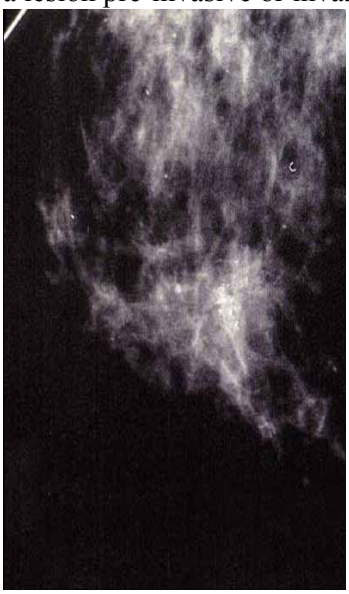
by the replacement of the capillary-venous shunt with abnormal showing anomalous elasticity.

They can be of two types: *floating,* related to areas of normal vasculature and *progressive,* related to areas of pathological vascularization.

The images are interpreted as positive in all cases the regions of red-blue with the number of pixels greater than 2000 and the concomitant presence of a dynamic curve of the progressive type.

PATIENTS AND METHODS

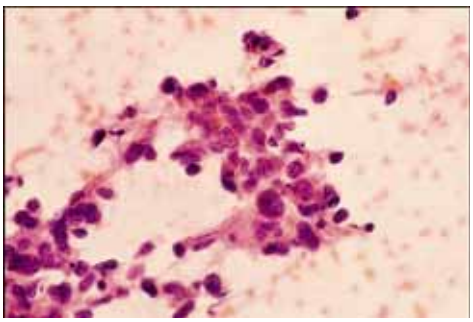
Between June and September 2009, 69 female patients, aged between 23 and 75 years, have come to our attention after finding eco-mammography, uncertain or suspicious of a lesion pre-invasive or invasive breast cancer. Of these, 32 patients were selected for our study and subjected to DOBI and MRI.



To complete diagnosis, all patients selected were under investigation or cytological microistologica.

The data from these patients were collected in a database and subjected to statistical analysis.

Object of our study were patients whose mammographic findings had shown the presence of opacity, parenchymal distortion or microcalcifications suggestive of malignancy.



Needle aspiration of breast glandular tissue

Each radiological doubt has been assigned a rating (B1-B5) as classified BI-RADS (Breast Imaging Reporting and Data System)

American College of Radiology. Were included in the study of micro-calcification clusters classified as suspicious (M3-M5).

The results of the DOBI were compared with those obtained with

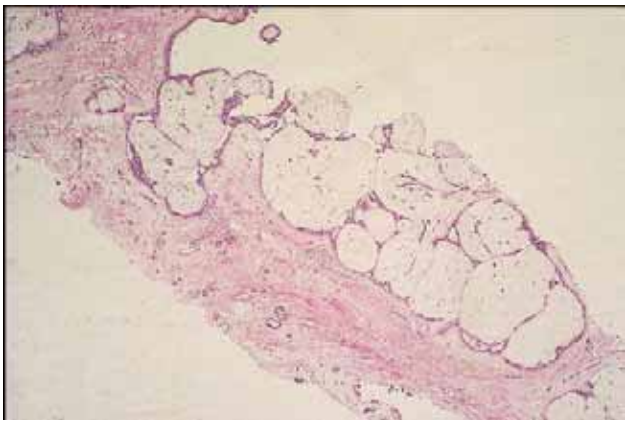
the MRI.

Were taken into account only those positive results, ie, characterized by areas of increased enhancement in an early pathological.

The fine needle aspiration cytology was assessed by fine needle (FNAB) and the result was assigned using standard categories: acellular / inadequate, benign, atypical, suspicious and malignant (C1-C5).

Alternatively, the Mammotome procedure (VACB) has provided a diagnosis microistologica through the taking of multiple chips of tissue.

The criteria for exclusion from the study were:



· patients being investigated biopsy or surgery within 3 months of the ipsilateral breast;

· the presence of tattoos or piercings;

· the presence of inflammatory skin diseases (psoriasis, eczema, etc.).

· the state of pregnancy or lactation;

· allergy to silicone.

All patients signed an informed consent to the study.

RESULTS

Characteristics of patients

Based on inclusion criteria, 32 female patients and mean age of 50.5 years (range 25-76) were selected for our study and submitted to the DOBI.

55% of patients were premenopausal at diagnosis, while 45% post-menopausal.

23% of patients reported a family history of breast cancer in 16% of cases reporting a history of breast cancer occurred in first degree relatives.

The age of menarche was on average 12.8 years (standard deviation 1.8, range 9-18) and that of menopause of 49.7 years (standard deviation 5.7, range 40-60).

Previous pregnancies were reported in 77.5% of patients recruited (mean age at first pregnancy: 25 years, SD 7.9; pregnancies on average 1.71, range 0.7).

Hormone replacement therapy was reported in 6.7% of women in post-menopausal women and 7.6% had taken oral contraceptives for more than six months in the ten years prior to diagnosis.

Table I

Characteristics of patients at diagnosis

Variable	**N = 32**
Average Age	50.5
Range	25-76
Pre-menopausal	55%
Post-menopausal	45%
Familiarity	23%
Family history in first degree relatives	16%
Menarche	12.8 + / - 1.8
Range	9-18
Menopause	49.7 + / - 5.7
Range	40-60
Previous Pregnancies	77.5%
Hormone Replacement Therapy	6.7%
Oral Contraception	7.6%

Characteristics of injury

In this study, a total of 32 lesions were detected on mammography and explored with the technique DOBI.

At mammography, 87% of the studied lesions appeared as nodules or masses, 10% as

microcalcifications and 3% as a parenchymal distortion.

6% of these lesions were classified BIRADS 3, BIRADS 4 33%, 61% BIRADS 5.

The average size of tumors detected was 15 mm (range, 0.6-25 mm).

The incidence of multifocality was 19%.

In 93.75% (n = 30) of cases there was a tumor. The final histology showed in 75% of invasive ductal carcinoma, carcinoma in 12.5% and 3,125% Lubulari infiltrating ductal intraepithelial neoplasia.

Finally, the 6.25% of the lesions is benign (granuloma, fibroadenoma).

Table II

Histopathological features of 32 cases

Histotype	**Malignant lesions**		**Benign Lesions**	
	(N)	**(%)**	**(N)**	**(%)**
DCIS	1	3,125%	-	-
LCIS	1	3,125%	-	-
Infiltrating ductal	24	75%	-	-
Infiltrating lobular	4	12.5%	-	-
More	-	-	2	6.25%

Optical Imaging

All patients selected for the study were submitted to the DOBI.

The image analysis was performed by two specialists in breast pathology.

The images obtained by the method were compared with the results of mammography and MRI.

Table III

Instrumental methods under study (suspicious of malignancy)

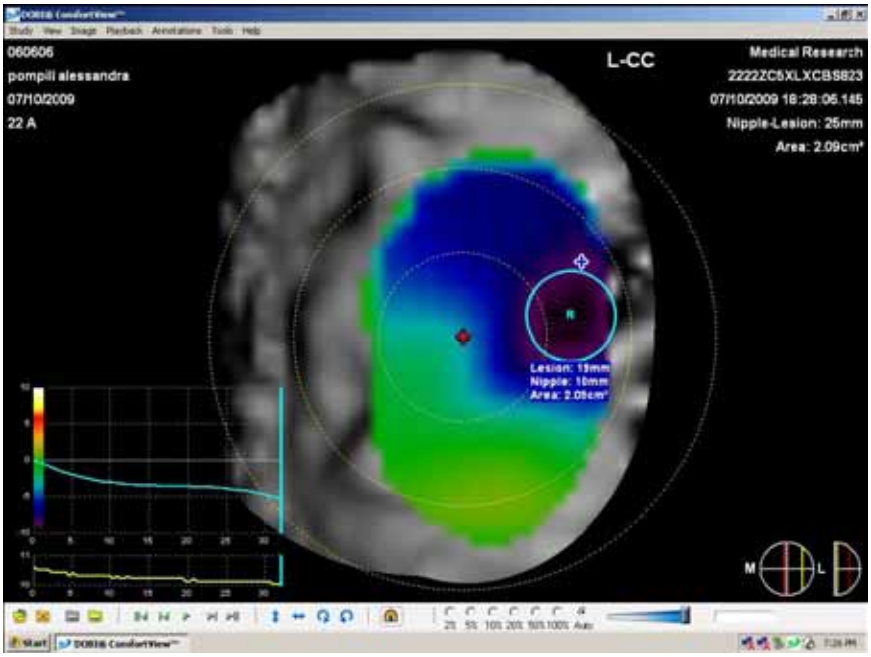
Instrumental method	**Malignant lesions (N) (%)**	**Benign Lesions (N) (%)**
X-ray Mammography	93.75% 30	6.25% 2
MRI	84.37% 27	15,625% 5
DOBI	81% 26	18.75% 6

No side effects or adverse reactions were observed during or after the acquisition of optical images.

In contrast, all patients have enjoyed the comfort and speed of execution diagnostic survey.

The scans were interpreted on the basis of quantitative values (number of pixels in the area of interest) and qualitative (dynamic curves of the signal).

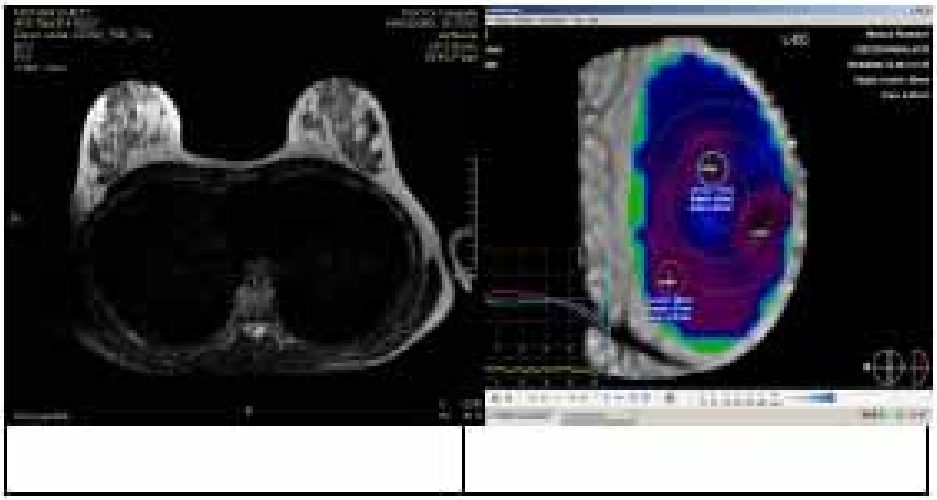
Were interpreted as positive all cases of *focal abnormalities in red-blue* with *the number of pixels greater than 2050* and concurrent *dynamic curve* of the *progressive type.*



With this method have been identified in 26 tumors

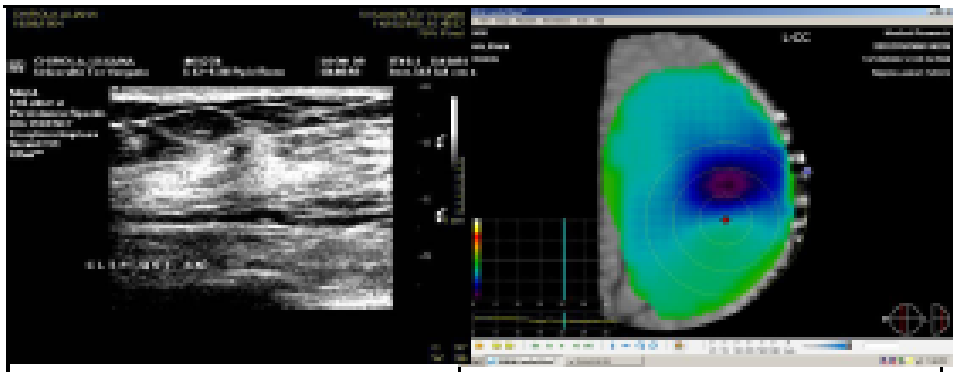
(VP = 81%).

In all cases of abnormal vascular pattern, there was a full agreement with the results obtained by MRI.



Were recorded 3 cases of false negatives **(FN = 9%):** in one case the investigation was hampered by the location of the tumor, which was adherent to the chest wall, in another case the size of the breast (A cup) made difficult to image acquisition.

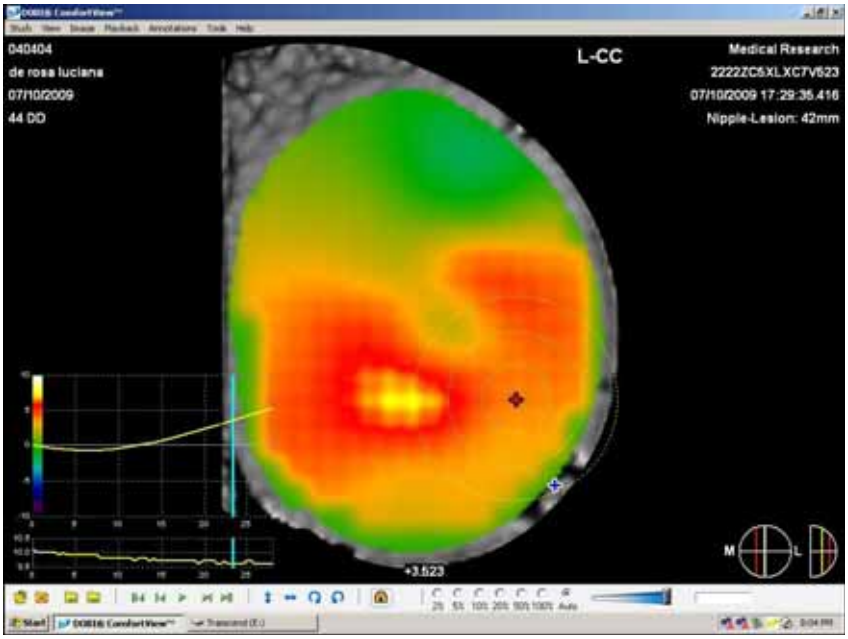
The DOBI was also negative in a case of diagnosis of microistologica DIN1B (Flat Atypia).



The usefulness of the method, in this specific case, was to exclude the presence of neovascularization areas are suggestive of microleakage, confirming the treatment plan established for the patient.

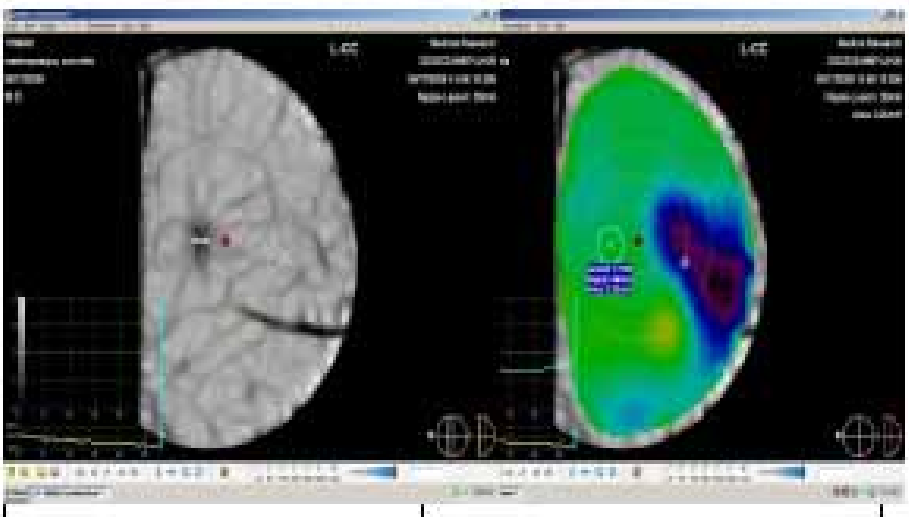
In two cases **(FP = 6%),** the DOBI has given a positive result in the absence of abnormalities detected on MRI. In one case, this result was interpreted as a consequence of the hormonal status of the patient during image acquisition.

In fact, during the 2 nd phase of the menstrual cycle there is a physiological phenomenon hypervascularization of the gland, to which the DOBI was susceptible.



In the other case, the positive outcome of the survey was attributed to the asymmetric distribution of the glandular component in the context of the breast.

Finally, the DOBI was invalidating in one case **(NV = 3%)** in which the instrumental tests (ultrasound and mammography) gives evidence of a lesion discariocinetica and cytology gave an indeterminate result.



The optical images have shown a pattern of homogeneous illumination of the breast, in the absence of areas of neovascularization. The histological diagnosis

final then confirmed the benignity of the lesion (granuloma).

Overall, were excluded from our study 37 patients (53%). Of these, 20 patients (30%) were submitted to DOBI and subsequently excluded for technical reasons of failure in the acquisition of images, confirming the existence of a learning curve in using the technique.

Statistical analysis of the data showed significant differences in mean values of the number of pixels of benign lesions (1325 + / - 984) than malignant (3590 + / - 2861) (P = 0.002), identifying the c *ut-off* to 2050 pixels.

Optical images of intensity greater than the value reported in this study, a sensitivity of 72%, a specificity of 92%, positive predictive value of 93%, negative predictive value of 61% and a diagnostic accuracy of 79%.

Table IV

Optical Imaging Results DOBI (number of pixels suspicion for malignancy)

Optical Imaging Results	**Malignant**	**Benign**	**-**
N ° Pixels> 2050	VP = 26	FP = 2	PPV = 93%
N ° Pixels> 2050	FN = 3	NV = 1	VPN = 61%
-	If = 72%	Sp = 92%	Total = 32

DISCUSSION

Breast cancer is one of the most complex and traumatic disorders of the human race has always been studied by the most eminent physicians of all time, as shown by historical research.

Approach to breast diseases, the use of mammography has marked a historic transition, as it has allowed the diagnosis earlier and earlier, increasing the percentage of detection of non-palpable lesions.

This has resulted as a consequence, the evolution toward minimally invasive surgical approaches, capable of guaranteeing the radical cancer treatment, compared with less impact on the quality of life of patients.

In the last two decades, technological innovations, the acquisition of specific skills by a team of specialists and a better knowledge of the natural history of breast cancer have

resulted in a significant improvement in the management of this disease.

In fact, an accurate diagnosis and preoperative staging are, to date, the assumption upon which the subsequent choice of therapeutic strategy.

The combination of *early diagnosis - healing* inspired the international search, directing it towards the identification of technologies can provide highly sensitive and specific diagnostic information.

In light of the achievements in the field of medicine, the use of transluminescenza has found application in the study of malignant disease.

The DOBI (Dynamic Optical Breast Imaging) is a noninvasive optical imaging instrument, easy to capture and well tolerated studying the vascularity of the breast through the analysis of transmission properties-that the light undergoes attenuation through the breast tissue, both in static and dynamic conditions.

The purpose of this study was to assess the diagnostic accuracy of DOBI, determining indications, advantages and limitations.

In order to propose it as a useful tool for integration in the study of breast diseases, the results obtained with this method were compared with those of mammography and MRI.

In line with those reported in the literature, our study was conducted on a population of patients with suspicious mammographic images (B3-B5).

In full agreement with the results observed with MRI, the DOBI was able to differentiate benign from malignant lesions based on their fingerprints angiogenic, showing a sensitivity of 72%, specificity and diagnostic accuracy of dell'92% 79%.

The DOBI proves a useful investigative tool in the analysis of the angiogenic component typical of malignant proliferative lesions.

The performance of the method is suitable for integrating digital mammography examination limits when affected by the degree of opacity in dense breasts.

In addition, optical imaging is a useful adjunct in the diagnostic study of young patients symptomatic.

Some of the main advantages found in the use of the method, were: the ability to capture real-time dynamic functional images, the cost of the survey contained moderately, and not using ionizing radiation.

In our experience, a limit of the method has been found in breast size or the location of the lesion, which sometimes made it difficult to carry out the survey.

The study of small breasts has been problematic for the conduct of the examination in relation to the structural characteristics of the machine.

The same difficulty was found in the analysis of large breasts, it is impossible to adjust the

plane of light to the surface of the gland (limit of 127 LEDs).

In the study, the diagnostic accuracy in the localization of the disease was limited when lesions at the chest wall or nipple-areola complex (NAC).

When the optical imaging scans glandular abnormalities near the chest wall, the difficulty in the study of the lesion depends on centering problems related to the rigidity of the panel analysis.

When studying morphological changes in the glandular region located para and retro-areolar, the problems involved in settling the nature of the injury arises from photo-absorption features typical of the NAC, whose intense vascularization any dark areas of pathological neo-angiogenesis.

In clinical practice, the NAC is marked with black, resulting in its exclusion functional optical imaging.

The selection of patients is therefore a key moment to optimize the diagnostic potential of the DOBI.

This method revealed a poor correlation with mammography as regards the definition and dimensional topography of lesions found.

The explanation of this phenomenon must be sought in 'intense absorption of light by tissue pathology, which appears as a broad area of optical attenuation sull'imaging final.

In the series, most of the lesions tested positive for infiltrating ComfortScan through focal abnormalities of red-blue with the number of pixels greater than 2050 and concurrent dynamic curve of the progressive type.

The finding of a normal vascular pattern in only one case of ductal carcinoma in situ (DCIS grade 2) observed in the study, raises questions about the potential of the method in the differentiation

Histological between invasive carcinoma and a pre-invasive disease.

The preoperative planning of a correct surgical treatment addresses the need for adequate treatment to the "gold standard cancer."

Define a phase infiltrating a neoplasm can ensure the proper execution of a staging lymph node surgery on the component (N) following the treatment guidelines (LNSB / Axillary Dissection).

Further application methods in the study of cancer in situ will be useful in the diagnostic definition of this disease with important clinical and therapeutic implications if the method proves able to establish accurately the nature.

Subsequent studies will be needed in order to optimize the technique, defining the optical aspects of the breasts are not pathological; evaluating sensitivity and specificity of the method on a larger population of patients, and, ultimately, improving the knowledge about its potential applications.

CONCLUSIONS AND OUTLOOK

In a context of knowledge, development and technology have been major changes in the quality of services linked to breast pathology.

The correct approach to multidisciplinary treatment, timing of treatment, planning studies and clinical research are essential prerequisites for surgery suitable for a "gold standard" of cancer.

The implementation of diagnostic and therapeutic skills with the aggregation function is the basis of a draft continuity of care to achieve high quality standards.

Joint activities, operating consistency and expert assistance have dramatically changed the therapeutic approach to breast cancer.

The incidence is increasing in nearly every country in the world, while the opposite trend is observed for the relation-specific mortality.

The diffusion of screening programs along with new paradigms for early diagnosis have increased the diagnosis of subclinical cancers, providing substantial benefits in terms of overall survival and disease-free.

Among the technological innovations in imaging, the DOBI (Dynamic Optical Breast Imaging) is proposed as a useful tool for integrating diagnosis, capable of providing functional information about the angiogenic characteristics of malignant proliferative lesions.

As a further examination, its use provides the opportunity to study and monitoring of breast lesions, when integrated digital mammography and MRI.

In the study, the method has found correlation with radiological suspicion of malignancy, defining footprints typical of angiogenic lesions infiltrating.

In cases where traditional examinations have not provided an accurate definition of nature, ComfortScan offered a characterization of risk, in full

correlation with the data assessed by functional MRI.

However, unlike what is reported in the literature, non-functional optical imaging has proved sensitive in identifying the only case of cancer ductal carcinoma in situ (DCIS) present in the study.

It 'likely that the lack of detection of suspected vascular pattern constitutes the defect of the method in the diagnosis of a malignant disease in pre-invasive.

Require further studies on large series of population to determine the boundary between the limits and potential disease-related diagnostic pre-invasive.

However, in the case studies presented optical analysis of the lesions proved to be sensitive and specific than the histopathological characterization of tumor tissue in most cases (30/32).

ComfortScan would thus be a promising imaging technique and its potential to define and establish an invasive stage disease represents a major challenge in implementing

diagnostic pathways, which are useful to implement modern application methods in surgery of invasive breast cancer.

Today, advances in diagnostic tools and substantial changes in surgical practice have been shown to affect the local and remote control of neoplastic disease.

It is believed that further improvement may result from the discussion of literature in clinical practice guidelines and the use of continuous monitoring data of follow-up.

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