Dynamic Angiothermography (DATG)

F. Casali, R. Brancaccio, F.P. Draetta, M.P. Morigi, M. Bettuzzi and G. Baldazzi

Abstract Dynamic Angiothermography (DATG) is a noninvasive technique for the diagnosis of breast cancer. The instrument consists of a thin plate with liquid crystals that changes color due to a change in temperature, consequently offering an image of breast vasculature. DATG is based on the angiogenesis theory on tumor initiation, development, and growth. A tumor needs new vessels. Therefore, by studying the changes in the pattern of vascular blood supply, it is also possible to diagnose neoplasms very early. In particular, it is shown that every human being has his or her own vascular pattern which, in the absence of disease, does not vary throughout the life time. By repeating DATG periodically, an efficient control of the onset of disease is possible, even in its early stages. This is not new but still little-known technique which is a component of the overall diagnostic techniques for the study and prevention of breast cancer that serves to offer a complete clinical picture of the patient. The great advantages of DATG are: it does not use radiation; it is not invasive or painful; it is low-cost and can be repeated periodically and successfully with no drawbacks. The angiothermographic examination thus makes it possible to visualize the breast vascularity pattern without using contrast medium. On the other hand, while highlighting changes in mammary vascularization, DATG is not able to indicate the size or depth of the tumor; even if recent researches (based on the approximated solution of the inverse Fourier heat equation) show the possibility to evaluate the depth of the tumor. This paper, after the introduction in

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Sect. 1, starts with a description of historical context in Sect. 2, and outlines the instrumentation in Sect. 3. Section 4 describes the technique, while a comparison with other diagnostic techniques is provided in Sect. 5. To close, Sect. 6 offers a practical guide on the use of this method.

Keywords Breast cancer · Diagnosis · Dynamic AngioThermoGraphy (DATG) · Liquid crystals · Contactthermography · Angiogenesis

1 Introduction

Despite the numerous diagnostic techniques, according to the WHO (World Health Organization) breast cancer as well as lung cancer and colorectal cancer, is the second leading cause of death in developed countries [1]. In recent years, breast cancer is the leading cause of cancer death among females in developing countries [2]. Each diagnostic technique has advantages and limitations, and only a proper synergy between the different techniques, together with forms of multidisciplinary collaboration, can lead to real progress. To this end, screening is an extremely important tool for prevention which, however, requires an extensive organization and considerable financial resources. There are several efficient diagnostic techniques (such as magnetic resonance imaging MRI) which are very expensive, and the use of which is justified only when there is a high probability of tumor [3]. Mammography is the gold standard in older women, but it is not effective in younger ones [4, 5]. Breast ultrasound is a radiation-free technique, but it is an auxiliary test and its specificity is lower than that of mammography [6–8]. The little-known Dynamic AngioThermoGraphy (DATG) has some attractive features [9–11]. This technique should not be confused with breast thermal imaging (or mammary thermography) [12–14], making use of a tool that shows the blood distribution (blood pattern) in the mammary gland. Any changes in this distribution, due to the presence of new blood vessels (*angiogenesis*), may be related to the presence of malignancy [15, 16]. The basic idea is that every human being has his or her own blood pattern, much like a fingerprint, when the person is healthy, does not change during his or her lifetime [17, 18]. Conversely, the alteration of this pattern might be evidence of a suspected tumoral or pretumoral activity [19, 20].

2 Historical Note

The importance of the influence of the vascular system in tumors was extensively studied and demonstrated by Judah Folkman in 1965. In 1992, he won the Wolf Prize for medicine for his research on angiogenesis. Studies on angiogenesis continued in France where, in the 1970s, J. Tricoire developed the first *contact thermography* technique. To display the temperature distribution on the breast surface,

he developed a kind of plate coated with liquid crystals [21–23]. The captured images by a camera were analyzed by physicians who were experienced in standard diagnostic techniques (usually gynecologists, oncologists, and radiologists). Studies on the vascular pattern showed a correlation between contact plate images and cancer. The method developed by Tricoire was based on the principle that emergent tumors can be detected by recording and mapping the heat generated by them.

The research on contact thermography, initiated by Tricoire, was continued in Bologna at the private "Madre Fortunata Toniolo" hospital by two gynecologists, Dr. Giancarlo Montruccoli and his son, Dr. Daniel Montruccoli. They used and studied contact thermography and found that the original technique gave rise to numerous false positives (low specificity), while the picture had a poor spatial resolution: characteristics confirmed by literature [24–26]. These physicians started to analyze the vascularity pattern and its changes rather than searching directly for the tumor as a heat source. In accordance with the angiogenesis theory, DATG does not use the quantitative measurements of emitted heat as a diagnostic criterion. Instead, it is based on the qualitative interpretation of breast blood flow lines, a feature that is making DATG increasingly more valuable from both a clinical and a scientific standpoint. In more than 30 years of clinical practice, approximately 4000 patients were followed up with a total of over 40,000 tests, of which around 1200 were histological examinations [27–30].

Thanks to the experience of these physicians, new plates were developed and the DATG instrumentation was improved [9, 31].

3 The Instrumentation for Contact Thermography

While in mammary thermography the temperature of the area to be investigated is recorded by an infrared camera, DATG analyzes the vascularization pattern. As an example of mammary thermography, Fig. 1a shows (in "false colors") a healthy breast, while Fig. 1b shows an advanced cancer in the left breast.

In DATG, the examination tool is made of two components: a thermographic sensor placed in contact with the breast, and a digital camera connected to a computer (Fig. 2) [31].

3.1 The Detector (Thermographic Plate)

The detector is a plate covered with cholesteric liquid crystals. Crystals orientate themselves in different ways depending on their temperature. Even though liquid crystals may work in a very broad temperature range (from −30 to 120 °C), for the DATG application their temperature range is designed to be that of the human body skin (32–38 °C). At room temperature only infrared radiation is reflected and

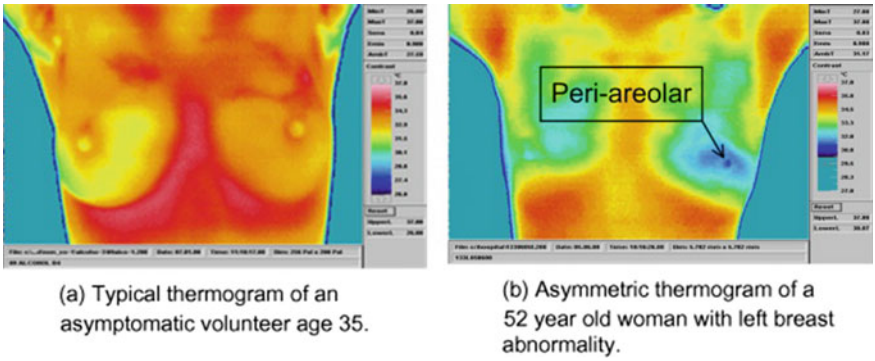

Fig. 1 Typical images of breast thermography (in "false color"): **a** healthy breast, **b** left breast with an advanced cancer [32] (Reprinted from Infrared Physics and Technology, Volume 66, Faust O, Acharya UR, Ng EYK, Hong TJ, Yu W, Application of infrared thermography in computer aided diagnosis, Pages 160–175, September 2014, with permission from Elsevier. doi: 10.1016/j.infrared.2014.06.001)

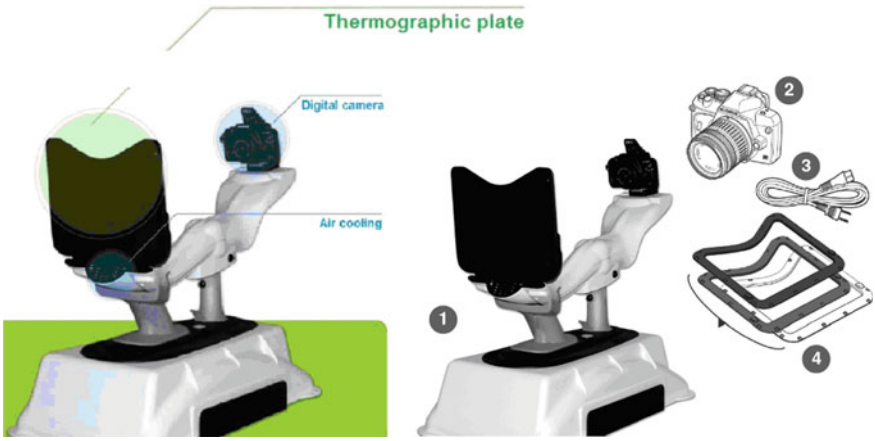

Fig. 2 *Left* Photo of Aura machine, (*Right*) *1* plastic support, *2* digital camera, *3* connecting cables, *4* removable plates, where the three colored frames are indicated in *white*, *gray*, and *black* [31] (Reprinted from http://www.breastlife.it/index.html with permission from BreastLife s.r.l)

crystals appear brown. When the temperature is increased, the crystal structure changes so that the reflected radiation becomes, successively, red, yellow, green and blue, and then returns to brown with the reflection of UV radiation.

When the physician places the plate in contact with the patient's breast, the plate is able to provide false color images of its vascularization. For good results, in order to eliminate superficial vein signals, the breast must be cooled with a current of cold air encapsulated within the plastic support (see Fig. 2).

Three plates with different sensitivities (with white, gray, or black frames, respectively) were available:

- Black frame plate: low sensitivity (34.0–37.5 °C)
- White frame plate: high sensitivity (31.5–34.0 °C)
- Gray frame plate: intermediate sensitivity (32.5–34.5 °C).

The difference in sensitivity is very important. The low-sensitivity plate (black frame) is used for young patients, whereas the high-sensitivity plate (white frame) is used for patients near or going through menopause.

At present, images can be interpreted visually by the doctor and/or evaluated with the aid of digital image enhancement techniques.

3.2 Physical Characteristics of the Plate

The physical characteristics of plates (spatial resolution of the image and its persistence) were measured by means of two Plexiglas phantoms, containing thermoresistors crossed by a current that brought them to a temperature of 37 °C (with a variation of no more than 1 °C). In the first phantom there is a series of thermoresistors with an increasingly close distance and the relative distribution of the temperature acquired from the plate (Fig. 3). With this instrument it was possible to evaluate a spatial resolution of a few tenths of mm. With the second phantom (Fig. 4), it was possible to verify that the time for the proper image formation is around just 3 s while the fade out image took only 1.2 s. Similar measurements were carried out using LCD (liquid crystal display) commercial plates, with much worse results [9].

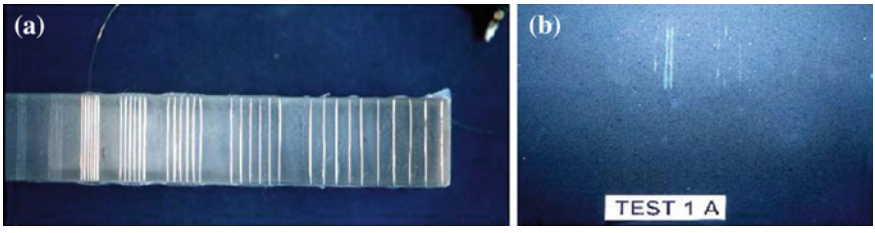

Fig. 3 Sequence of thermoresistors in the Plexiglas phantom (*left*) and the image on the crystal plate (*right*) [9] (Reprinted from Montruccoli et al. [9], with permission from Elsevier. doi: 10.1400/19286)

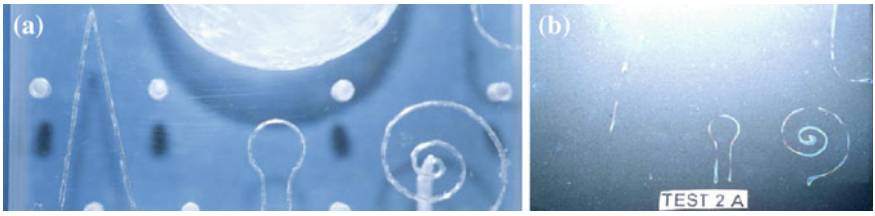

Fig. 4 Plexiglas phantom with thermoresistors to measure the acquisition time of the correct image [9] (Reprinted from Montruccoli GC, Montruccoli Salmi D, Casali F. A new type of breast contact thermography plate: a preliminary and qualitative investigation of its potentiality on phantoms. Phys Medica 2004; XX(1):27–31, with permission from Elsevier. doi: 10.1400/19286)

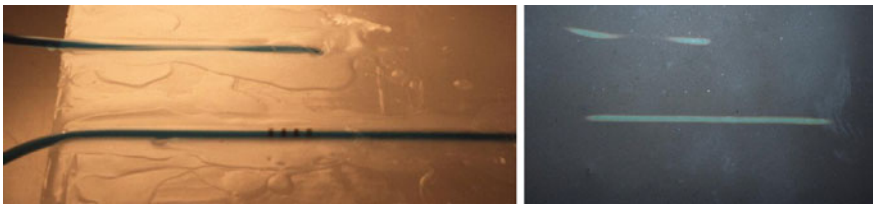

Fig. 5 Block of paraffin with two small hot water pipes (simulation of the breast blood circulation) [9] (Reprinted from Montruccoli et al. [9], with permission from Elsevier. doi: 10.1400/19286)

3.3 Simulation of the Breast Vascular Pattern

In a healthy breast the vascular pattern of a mammary artery is shaped like a small channel which ends with a tip in the direction of the nipple.

A third parallelepiped-shaped phantom made of paraffin was used to simulate the blood distribution in the breast and to assess its correct reproduction by the plate. Paraffin was chosen because of its thermal characteristics which are similar to the human tissues (Fig. 5). Two cannula, of a diameter of about 2 mm, were inserted into the block of paraffin introducing water at about 37 °C. The figure clearly shows that the cannula penetrates into the block, the same way as the vein descends toward the nipple, thus producing an image that ends in a "wedge" mode, indicating a proper blood circulation.

4 The Scientific Basis of Contact Thermography

Up until now, breast thermography was based on the evaluation of the cutaneous heat level and the research on its isotherms. This approach is very different from DATG for which, conversely, the morphological criterion is the diagnostic principle: knowing the normal perfusion of the healthy breast, any change in its shape is

an indication of some pathology. In fact, DATG studies the change in the blood perfusion both within the whole breast and within a well-defined area of it. In particular, a relationship between interpretative patterns and corresponding histological findings has been demonstrated, both for precancerous states and for in situ carcinomas or invasive cancers [29, 33–35].

4.1 Images of the Breast by Contact Thermography

The well-known characteristics of healthy mammary vascularity are a constant blood perfusion pattern for many years, its sudden change in a histologically demonstrated disease, its intense activity in the pubertal period versus its evident reduction in the postmenopausal period, the expansion of perfusion lines during pregnancy and lactation and, in the case of diseases, their focus within a single point corresponding to the tumor [17, 18]. These vascular behaviors suggest the opportuneness of using this method to study the pathophysiology of mammary gland also through its blood supply. Moreover, this approach has already been adopted by other methods, such as MRI and Doppler ultrasound to study precisely the various pathological aspects of the blood circulation within the gland.

Reading DATG results means to study the images created by currents of functional flow in relation to certain areas of the mammary gland, more than real blood vessels, where an indeterminate quantity of microvessels (capillaries and precapillaries) are present. This functional current, passing thorough a given area, is able to increase the tissue temperature just enough to distinguish it from the surrounding one. By conduction and by convection, precisely this temperature difference is transmitted through the skin to the plate that registers it. Thus, on the plate, we see some drawings that represent the path of prevalent blood flows and not others which are not visible because they are below the thermal detection threshold of the plate.

On the one hand the new interpretation of the thermographic pattern, on a functional basis, completely overlooks the quantitative aspect of the recorded temperature, moving increasingly away from the concept of "thermography" while, on the other, making it possible to highlight certain aspects of the blood circulation in the mammary gland which are so important that they become its basic diagnostic criterion.

These aspects are:

1. The angiothermographic pattern is unique and typical of each woman. In practice, this is the best explanation for the impossibility of developing a diagnostic–interpretative classification based on standard patterns, as had erroneously been done in the past.
2. In the absence of a disease this pattern remains identical, even for many years, during child-bearing age, up until menopause. This feature has a great predictive value and is one of the proofs of the technique's reproducibility.

3. There is no direct proportion between the detected pattern and the volume of the tumor, supporting in each case a clear sign of malignancy even in the presence of subclinical tumors. The latter aspect is of great importance for early diagnosis, and it is in relation to the phenomenon, presently well known, of angiogenesis whence the absolute need for an increased blood supply caused by the tumor, even in the earliest stage of carcinogenesis.

Figure 6 above on the left shows a scheme of the normal vascular pattern of the left mammary gland and the figure above on the right shows some cutaneous

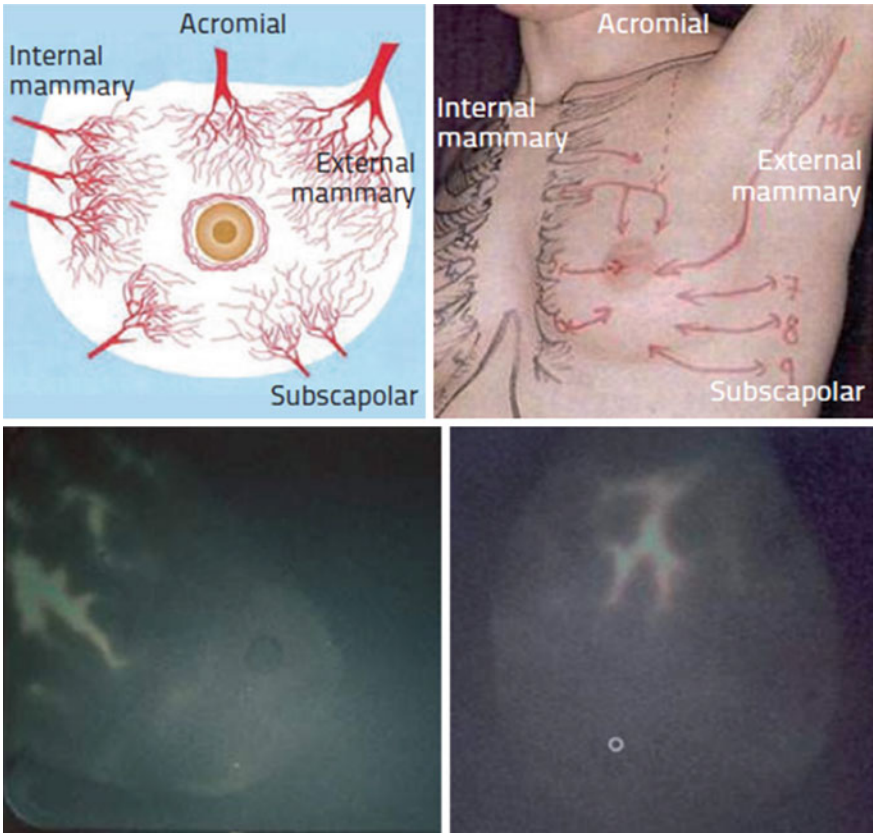

Fig. 6 *Above* (Reprinted from http://www.breastlife.it/index.html with permission from BreastLife s.r.l): *left* normal vascular pattern of the left mammary gland and (on the *right*) cutaneous projections of the main arteries in the mammary gland [31]. *Below* (Reprinted from http://www.breastlife.it/index.html with permission from BreastLife s.r.l): *left* angiothermographic image of the external mammary artery, perfectly representing the blood circulation in a healthy breast; *right* angiothermographic image of the acromial artery: there are lines of normal currents that follow the anatomy of the breast and head toward the nipple without leaving their quadrant of reference [31]

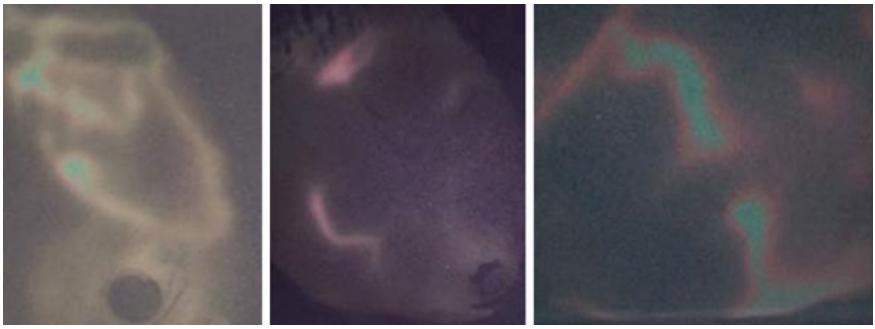

Fig. 7 Sample angiothermographic images of suspected cases. The current lines appear diverted, not speculated and pointing outward or toward a different quadrant from their own [31] (Reprinted from http://www.breastlife.it/index.html with permission from BreastLife s.r.l)

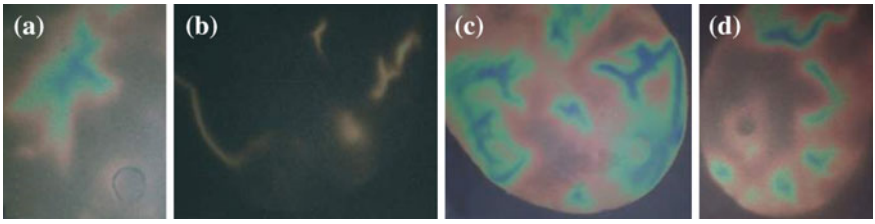

Fig. 8 Sample angiothermographic images of evidently malignant cases: **a** current lines that intersect to form a "malignant star"; **b** current lines that converge toward a "hotspot"; **c** and **d** current lines that converge from different points [31] (Reprinted from http://www.breastlife.it/index.html with permission from BreastLife s.r.l)

projections of the main arteries in the mammary gland [31]. Figure 6 below shows two images of healthy breasts. If a cancer or precancerous lesion is present, the image on the sensor either has a rounded shape or is the result of several converging channels for the tumor feeding. Figures 7 and 8, respectively, show some images of suspected and malignant cases.

4.2 The Role of Skin Cooling

To decrease the noise from superficial veins, the breast skin is cooled by a flow of fresh air. Figure 9 shows the venous network before and after cooling. These images of the superficial vein network before and after cooling show how DATG plates are able to record even minimum differences in blood flow. Moreover, the anatomical layout corresponds completely, both before and after cooling.

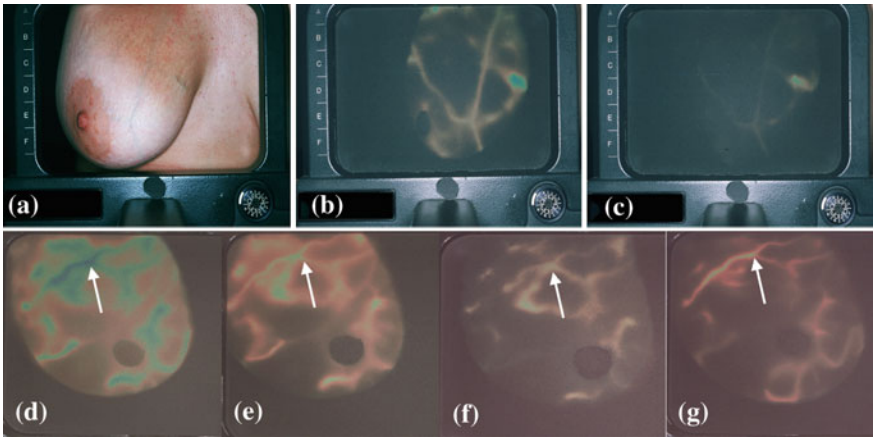

Fig. 9 Examples of skin cooling. In the first case the problem is generated by superficial veins. **a** Photo of the breast with evidence of superficial veins, **b** angiothermographic image without skin cooling, **c** angiothermographic image after skin cooling. In the second case the progressive cooling makes correct image interpretation possible: **d** first image, **e** the same after cooling, **f** after more cooling, **g** diagnostic image [31] (Reprinted from http://www.breastlife.it/index.html with permission from BreastLife s.r.l)

Like all diagnostic imaging techniques, DATG can present interpretation problems. An example is in Fig. 9e, where a quick interpretation of this highly congested breast is difficult. It is necessary to isolate the DATG signs by progressively cooling the breast and carefully selecting plates with appropriate sensitivity. In particular, at first glance, a possible malignant cross (white arrow) is indicated. In the second image (e), photographed after more cooling, the "cross" is indicated to be formed by an acromial flow line intersecting with an external mammary one. In the third image (f), taken after still more cooling, one of the two flow lines that seemed to form the "cross," is disappeared altogether. The fourth image (g) solves the problem: in a true "malignant cross," the two flow lines always have a similar intensity, but this is not the case here.

4.3 Persistence of the Vasculature in a Healthy Breast

As previously stated, in a healthy breast the vascular pattern remains unchanged over time, as shown by two images of the same patient acquired after 16 years, 20 years, and 33 years (Fig. 10). The reproducibility of the technique makes a long follow-up possible without pattern changes. Given the total lack of invasiveness of the DATG technique, tests can also be performed very close together in time, which is extremely useful in follow-ups after breast surgery.

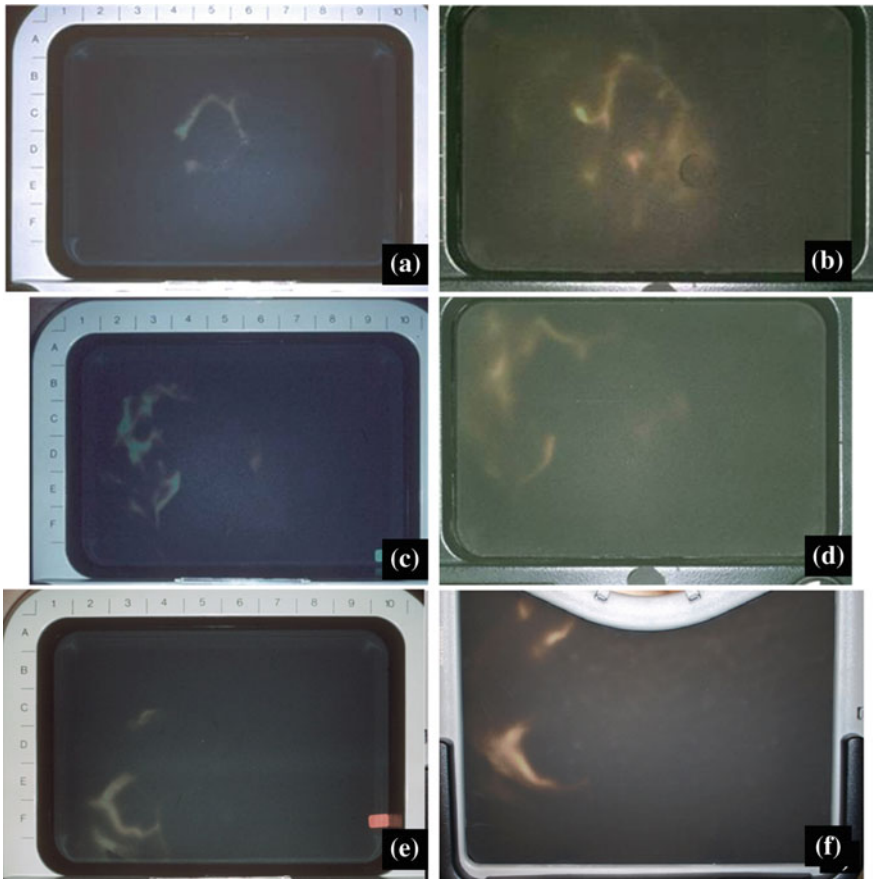

Fig. 10 Three examples of the long-lasting persistence of the shape of the blood pattern: DATG pattern remains the same over time in the absence of a disease. First woman: **a** angiothermographic test in 1979 and **b** in 1995 (after 16 years). Second woman: **c** angiothermographic image in 1979 and **d** in 1999 (after 20 years). Third woman: **e** angiothermographic image in 1978 and **f** in 2011 (after 33 years). It is evident that images represent, in all cases, the same blood diagram [31] (Reprinted from http://www.breastlife.it/index.html with permission from BreastLife s.r.l)

On the one hand, the pattern remains identical throughout life in the absence of malignancy, on the other hand, it can be more or less apparent in the various stages of a woman's life. During pregnancy and breastfeeding, an intensification of flow lines is expected, while after menopause they are gradually reduced (see Figs. 11, 12, and 13). It should be noted that, under any circumstances, these natural changes in a healthy woman involve the creation of new blood–vessels (angiogenesis).

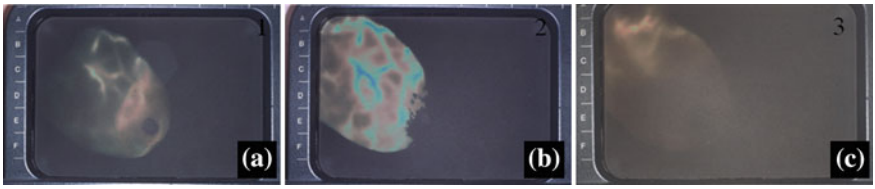

Fig. 11 Example of a DATG pattern change during pregnancy: 29-year-old woman: **a** before pregnancy, the test shows regular external mammary flow lines, mainly in the right breast, while the venous circulation is visible; **b** seven months later, during pregnancy, the functional blood circulation is much stronger; however, no completely new or abnormal flow lines have appeared; **c** sixteen months later the pattern has returned to its original appearance [31] (Reprinted from http://www.breastlife.it/index.html with permission from BreastLife s.r.l)

Fig. 12 Example of a DATG pattern change during breastfeeding: **a** DATG baseline; **b** after 2 years of breastfeeding; **c** after another 4 years, return to baseline pattern. It should be noted that during breastfeeding superficial veins are more congested, but there is no breast neoangiogenesis [31] (Reprinted from http://www.breastlife.it/index.html with permission from BreastLife s.r.l)

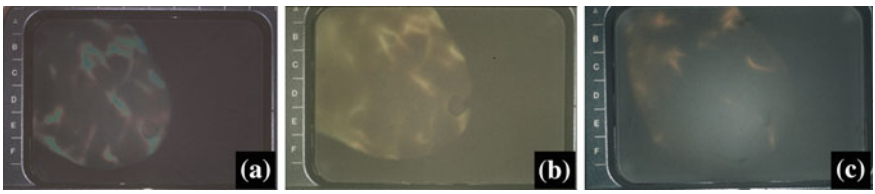

Fig. 13 Example of normal involution of flow lines with the onset of menopause: DATG images **a** at the onset of menopause; **b** after 6 years; **c** after 8 years [31] (Reprinted from http://www.breastlife.it/index.html with permission from BreastLife s.r.l)

5 DATG and Other Diagnostic Methods: Integrated Diagnosis

The comparison of DATG images with other previous acquired images or images acquired in the same laboratory via other methods (e.g. ultrasound, mammography, DOBI, MRI) is very important.

In the words of Doctor Daniele Montruccoli: "While DATG may be a useful diagnostic tool, I have always been mindful of the fact that with science in general, and medicine in particular, absolute certainty does not exist. As noted before, we used all three techniques together—mammography, ultrasound, and DATG—in our work, we aimed to arrive to the most accurate diagnosis possible, what we call it an *integrated diagnosis*."

There are many diagnostic techniques for breast cancer (with their advantages and disadvantages) including: mammography, tomosynthesis, ultrasound, MRI with contrast medium, positron emission tomography (PET), dynamic optical breast imaging (DOBI), and breast thermography. No single instrumental technique by itself, except in glaring clinical cases, offers an absolute certainty of the value of the histopathological examination. In most cases, it is precisely the set of information from various diagnostic techniques that makes it possible to isolate the cases to be submitted to histological examination, while differentiating them from the benign cases or the ones to be monitored during their lifetime; an integrated diagnosis is certainly the best way to tackle the diagnosis of breast cancer. In this context DATG, with its peculiarities, is a further aid to the combined efforts of other techniques for the study of breast cancer.

5.1 Mammography

Mammography is still considered the reference screening technique ("gold standard") for breast cancer, even though some recent publications claim that annual mammograms do not reduce breast cancer mortality in women and new screening programs should be stopped [36, 37]. Mammography highlights the different density of breast tissues. Modern mammography allows digital acquisitions with low- and high-energy X-rays (dual energy) after the administration of iodine-containing contrast media. This method offers a good resolution of the tissue density and is useful for identifying lesions in breasts characterized by high density [38]. A further improvement of mammography is the CT (Computed Tomography) of the breast [39]. This technique shows the tumor in 3D and avoids the compression of the breast. The radiation imparted to the breast is about twice that of a conventional mammography [40]. A new, very interesting, X-ray diagnostic technique for the breast is Digital Tomosynthesis (DTS). This is a sort of computed tomography of the breast done with a smaller number of acquisition angles. The breast image is reproduced in slices that are processed by a software program. For DTS, minimal pressure is needed, just enough to hold the breast in place. The results seem to be much better than for standard mammography [41, 42].

Figures 14 and 15 show an angiothermographic analysis in comparison with a mammogram of the same breast.

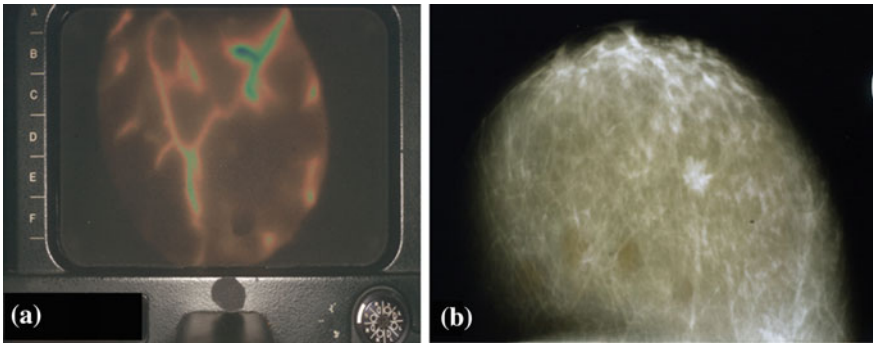

Fig. 14 Integrated diagnosis of DATG and mammography: **a** angiothermographic image and **b** mammography [31] (Reprinted from http://www.breastlife.it/index.html with permission from BreastLife s.r.l)

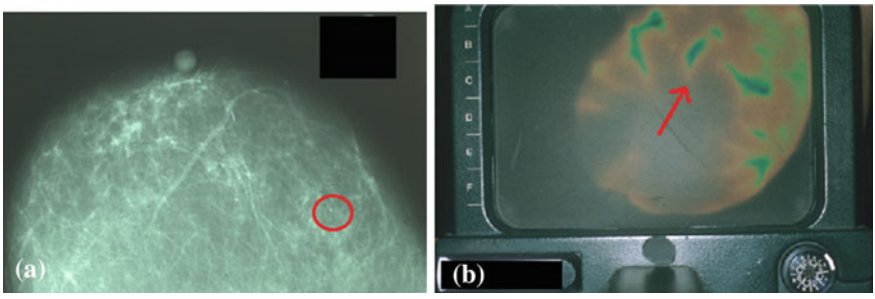

Fig. 15 Integrated diagnosis of DATG and mammography: **a** mammography, **b** DATG image [31] (Reprinted from http://www.breastlife.it/index.html with permission from BreastLife s.r.l)

The density of breast tissues in patients younger than 40 years of age degrades the radiographic image [40]. To acquire a good 2D mammogram, it is necessary to compress the breast, with a resulting discomfort for the patient. The risk of inducing breast cancer—small but not zero—is offset by the benefit of a possible early diagnosis [43, 44].

In conclusion, standard 2D mammography is a cheap, quick, and well-known technique, widely used for screening, albeit with the above-mentioned contraindications. In this field a better diagnostic technique is tomosynthesis [42] and, even better, breast CT [39].

5.2 Ultrasounds

With the development of modern probes, ultrasound has made significant strides forward. This technique has been proven to be very useful in the context of other

techniques; such as mammography, DATG, or clinical palpation that measure different physical parameters [45]. In particular, the DATG examination in combination with the ultrasound test can be very useful: in fact, the DATG can be a guide, highlighting the areas to be examined by ultrasound [46]. This is an example of the advantages of integrated diagnosis in breast examination [47]. Ultrasounds are able to measure the size of the tumor and to distinguish its liquid or solid nature within the breast tissue. The difficulty of distinguishing the acoustic impedance of various structures of the breast may produce some false positives. In some cases the cancer is manifested with characteristics of a benign nodule having a homogeneous structure and regular contours (such as in colloid, mucinous, and intracystic carcinomas). Also, when a tumor has poor cellularity, the answer is negative and we will have false negatives [48].

The technique requires considerable skills on the part of the operator, thus making it extremely "operator-dependent" [49].

In conclusion, ultrasound can be performed on women (and men!) of all ages and is totally non-invasive. The possibility of detecting a tumor remains high regardless of its size. A disadvantage of ultrasound scans is that they are admittedly unable to detect non-palpable tumors, such as microcalcifications [50].

5.3 Magnetic Resonance Imaging (MRI)

If Magnetic Resonance Imaging (MRI) performed with a suitable material to increase the contrast (for example, gadolinium), it can measure the distribution of blood within the breast in 3D. MRI can be performed on women of all ages (even those with dense breasts). It is recommended for women (also young ones) who have a family history of breast or ovarian cancer [51]. MRI sensitivity and specificity are very high [52]. Before surgery, an MRI test is very much appreciated by the surgeon for the good indications (spatial distribution) on the part of the tissue to be excised. Figure 16 shows the comparison between DATG and MRI.

MRI may be considered the best diagnostic technique for invasive cancer [53].

The disadvantages of MRI are that it is laborious (taking a long time) and requires expensive equipment. In order to produce good diagnostic images, contrast media that may cause allergic reactions must be used. There are several limitations to its performance [46]. Absolute contraindications regard the bearers of metal implants and cochlear implants, plates, screws or nails, mechanical valve prosthesis, neuroenhancers, cardiac pacemakers, tissue expanders (breast), and tattoos done less than six months earlier.

Among the relative contraindications are pregnancy in the first quarter and the possibility of claustrophobia during the test [54], even if the new MR equipment is designed for overcoming this problem.

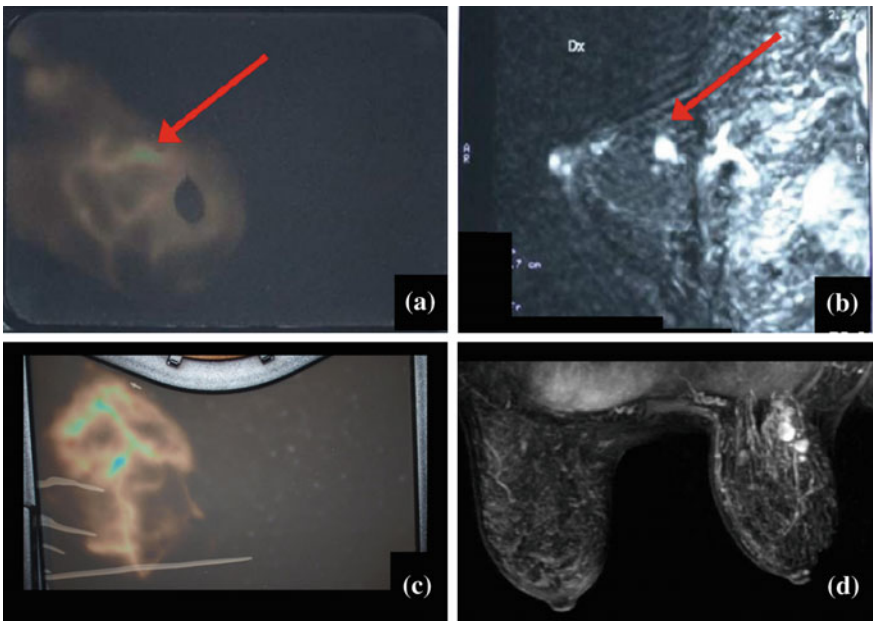

Fig. 16 Two examples of consistency between DATG and MRI tests. First woman: **a** angiothermographic image, and **b** resonance image. Second woman: **c** angiothermographic image, and **d** resonance image. MRI shows a local recurrence confirmed by DATG [31] (Reprinted from http://www.breastlife.it/index.html with permission from BreastLife s.r.l)

5.4 Positron Emission Tomography (PET)

Another way to highlight the bloodstream is the technique called Positron Emission Tomography (PET). A radioisotope, which emits positrons (positive electrons, β+), is injected into the blood. The emitted positron interacts with an electron, giving rise to the emission of two 511 keV photons (gamma rays) that exit the body in opposite directions. The two photons are detected by a series of counters that surround the organ on which the PET is performed. A specific software program reconstructs the digital images of the area of blood where the reaction takes place, thus creating a map of the vasculature as for MRI [55, 56].

The radiation dose, issued to the body from the beta + and by the two gamma rays, is much higher than that released in a mammographic test. The spatial resolution of the image is not too good [57].

5.5 DOBI (Dynamic Optical Breast Imaging)

Dynamic Optical Breast Imaging (DOBI) is a technique of optical mammography where, instead of X-rays, a light in the near-infrared spectrum is used. An array of Light Emitting Diodes (LEDs) illuminates the slightly compressed breast. A system with a fast digital camera, providing many images per second, records the light through the breast tissue; the amount of light depends on the ratio between hemoglobin and deoxyhemoglobin. A mathematical procedure reconstructs the 3D concentration of deoxyhaemoglobin in the breast tissues, thus making possible an evaluation of the vasculature [58]. This test can be performed on women of all ages (even those with dense breasts), and its cost is not very high and has a good tolerability [59, 60].

DOBI is a totally non-invasive technique, takes little time, and requires only a slight compression of the breast. This test can also be performed on women who have breast implants. It is a good test for monitoring recurrences, adjuvant chemotherapy, and hormone replacement therapy.

Its disadvantages are the multi-scattering of the light, with the wavelength of the near-infrared spectrum, and the poor spatial resolution in the image of blood distribution. Sometimes DOBI does not provide reliable results for: a) women who have undergone surgery less than one year before; b) after either less than three months from biopsy or less than one year after irradiation; c) lactating women (sometimes pregnant) due to the density of the milk secretion. Other causes of disturbance in the measurement can be the hyperpigmentation and inflammation of the skin [61].

5.6 Thermography (Or Tele-thermography)

The human body emits infrared radiation whose wavelength depends on the body's temperature. The distribution of the body's surface temperatures may be acquired by means of photo cameras with infrared sensors. Modern infrared cameras can detect variations in temperature of about 0.025 °C. For a better interpretation of the image, some temperature ranges are associated with different colors ("false color" images). Tumor tissues with high vascularization have a higher temperature than healthy ones. Figure 1a shows a thermal image of healthy breasts, while Fig. 1b shows the left breast affected by cancer at an advanced stage. In 1956, thermography started being considered as a method for breast screening; it obtained FDA approval in the U.S. and was well accepted by physicians. In 1977, a study gave less credit to thermography, stating that it produced too many false positives [62]. This study, which was partially rebutted [63], left a "stain" of unreliability on thermography. Today, with the development of new thermal imaging cameras, breast thermography has regained its credibility [64].

Thermography is an easy and inexpensive test. It is totally non-invasive and can be performed on women (and men) of all ages. Its best contribution is offered by its ability to report abnormalities in young patients in whom mammography does not provide reliable results.

Drawbacks are that the image does not properly define the place where biopsy should be performed. The majority of false negatives derive from microcalcifications, abnormalities that are not identified by thermography. The accuracy of measurements depends on environmental conditions (e.g., constant temperature in the location where measurements are performed). To perform these tests, patients must remain bare-chested in a room kept at a somewhat low temperature, for a relatively long time (about 15 min).

6 Other Interesting Applications of DATG

There are many other clinical cases other than breast cancer diagnosis in which DATG can be useful; for example: therapy monitoring, and diagnosis of other clinical cases. Here we will briefly explain some of the latter one. However, one should remember that, because of the physical conformation of plates (the sensors of DATG), this technique can provide diagnostic information only when the medical problem is generated, more or less, superficially in the body and in areas where the plate can be easily placed. In any case, it should be noted that it is not possible to diagnose a problem, for example, in the pancreas, which is located deep inside the abdomen.

6.1 DATG in a Child

DATG examination in a child of 29 months: early left breast development (Fig. 17a). Possible cause is the breastfeeding prolonged for over 24 months (maternal estrogens). After the abdomen ultrasound check of ovaries for pituitary adrenal stimulation, with negative results, breastfeeding was discontinued. The DATG examination after 7 months shows that the problem has been solved (Fig. 17b).

6.2 Checking and Monitoring Therapies

DATG can be very useful to check the efficacy of various therapies. Figure 18 shows an example of preoperative chemotherapy. Figure 19 shows the effect of antibiotic therapy in a case of mastitis. A third example is the monitoring of oral contraception therapy (see Fig. 20).

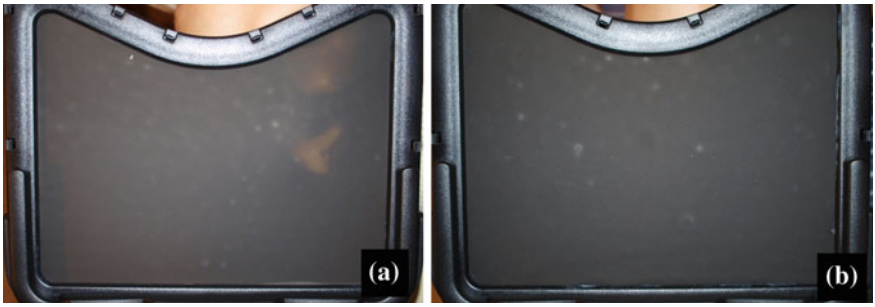

Fig. 17 DATG examination in a child of 29 months: **a** early left breast development; **b** normal pattern 7 months after the suspension of breastfeeding [31] (Reprinted from http://www.breastlife.it/index.html with permission from BreastLife s.r.l)

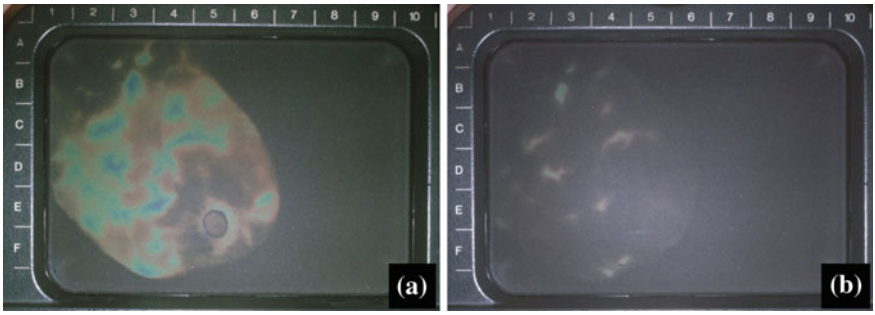

Fig. 18 Example of DATG applied to check the efficacy of a therapy: **a** at diagnosis, the external upper quadrant of the right breast shows an incomplete malignant ring made of numerous short flow lines in the external mammary gland, of acromial and internal mammary origin, all ending in spatula terminations; **b** after two months and two cycles of preoperative chemotherapy, the DATG pattern has become negative and all the abnormal flow lines have largely disappeared [31] (Reprinted from http://www.breastlife.it/index.html with permission from BreastLife s.r.l)

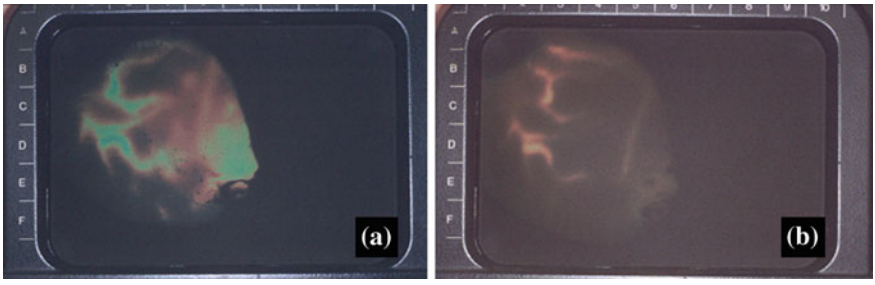

Fig. 19 Uncertain differential diagnosis between purulent and carcinomatous mastitis: **a** initial DATG examination; **b** after 14 days of antibiotics therapy the DATG pattern was completely negative [31] (Reprinted from http://www.breastlife.it/index.html with permission from BreastLife s.r.l)

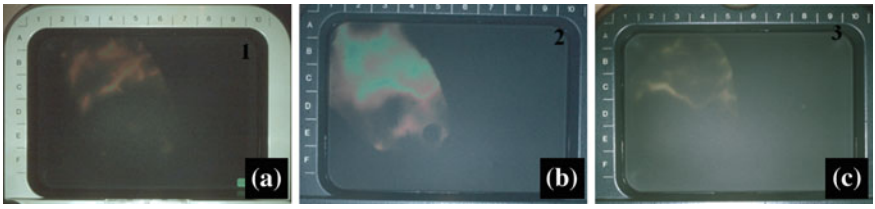

Fig. 20 Oral contraception in a 25-year-old woman. The initial DATG pattern **a** is almost completely normal. The only irregularity is the direction of an acromial flow line in the right breast, which runs toward the external upper quadrant. After 3 years of oral contraception, the DATG pattern **b**) shows a marked increase in the functional blood flow without any appearance of suspicious signs. Two years after suspension of the hormonal therapy, the DATG pattern **c** has returned to its initial appearance. Lastly, note that the initial abnormality of the acromial flow line, which was directed toward the external upper quadrant, has now completely disappeared. This was probably due to the presence of cysts, which may have disappeared because of the efficacy of the hormonal therapy [31] (Reprinted from http://www.breastlife.it/index.html with permission from BreastLife s.r.l)

Fig. 21 Example of a male breast cancer diagnosis. In a 74-year-old man, the left breast shows short abnormal flow lines with nonpointed terminations. These flow lines, covering nearly all the external upper quadrant, almost form an incomplete malignant ring around a hotspot. Note also the hot nipple. The histological test detected infiltrating ductal carcinoma [31] (Reprinted from http://www.breastlife.it/index.html with permission from BreastLife s.r.l)

6.3 Male Breast Cancer

Male breast cancer is a very rare event. Its annual prevalence in Europe and in the USA is of 1 or fewer in 100,000 and fewer than 1% of all breast cancer patients, while male breast cancer in Japan totals fewer than five per million [65]. Jewish men are the only racial group with higher incidence, two or three per hundred thousand. The main problem in diagnostic approaches and treatments for men is that techniques and therapy are generally extrapolated from those designed for women, due to inadequate research in male patients [66]. It is apparent that mammography is unfeasible for a man, while there are no contraindications or issues against the use of DATG. An example of a male breast cancer diagnosis is in Fig. 21.

7 Advantages and Disadvantages of DATG

Like all other diagnostic methods, DATG has advantages and disadvantages.

7.1 Advantages

DATG is non-invasive, does not require a contrast medium, and can be repeated as often as desired.

This technique is totally non-invasive (no ionizing radiation or contrast agents) and free from the painful compression of the breast. It can also be used in cases of acute or chronic mastitis, when other diagnostics tools cause great pain. Thanks to its total lack of side effects, it is particularly useful for monitoring patients at risk of familiarity and/or undergoing contraceptive and hormone replacement therapy, or estrogen–progestin ovarian stimulation for in vitro fertilization: all cases where a periodic examination is crucial.

As for the patient's age and conditions, DATG is also very useful for young patients or women with dense breasts, because its result is independent of the age and condition of menopausal or fertile status. Therefore it is not affected by glandularity or mammary fat. Dermatological diseases such as: herpes zoster, cutaneous hemangiomas, Recklinghausen do not affect the result. Pregnancy is not a limiting factor for diagnosis. Moreover, breast implants, plastic surgery procedures such as breast lifts, reductions, etc., are not absolute contraindications for exclusion.

The medical examination's run time is very fast: the entire procedure, which is called "angio test" includes taking the patient's history and a clinical examination, usually takes no longer than 15 min. Moreover, the test requires inexpensive and easy-to-move tools, if any. This rapid and inexpensive technique also makes possible a high number of angio tests per working day, and is matched by the immediate response, which is another big advantage.

As for diseases, the DATG examination provides signs of suspicious or malignant tissues that are independent of the size and shape of the lesion which also appear in cases of non-solid carcinomas. This technique is useful for screening, and it is also able to detect precancerous lesions where these have been highlighted by clinical examination (palpation) or other instrumental methods. DATG plays an important role in the differential diagnosis of lipoma and liposarcoma (showing the total absence of vascularization in the first, and vice versa in the second), and it is suitable for checking on therapy or following up: antiblastic chemotherapy when it would be useful to have presurgical DATG images. Certainly, it is also very useful in the difficult diagnosis of lobular, medullary, and colloidal carcinomas. The diagnostics of cutaneous melanoma is another interesting application of this technique. In fact, its DATG image is characteristic of cutaneous melanoma. Further studies will be carried out in the future.

Lastly, this technique—thanks to its low cost and ease of use—is indicated in screening programs, especially in "developing" countries.

7.2 Disadvantages

DATG shows the 2D vascular distribution, and not the 3D distribution, as with MRI, PET, and DOBI. It consequently provides no in-depth information and is therefore prone to errors caused by overlapping blood vessels and other vascularized structures. However, recent researches (based on the solution of the inverse Fourier heat equation) show the possibility to evaluate the depth of the tumor [67]. In fact, the temporal formation of the image on the plate can be processed to obtain information about the depth of the heat source (vasculature).

Moreover, DATG is not able to determine the size of a tumor, but indicates the presence of a suspicious lesion and points of the area looking at by using, for example, magnetic resonance imaging. Indeed, the intensity and size of the features in the image acquired by DATG, are not related to the shape and size of the tumor, but rather to the biological activity of its base.

Body lotion and ultrasound gel, when applied shortly before the test, can have a filter effect and cause an incorrect diagnosis, especially false negatives.

The existing blood flow lines immediately increase in diameter in early in pregnancy, and almost always new ones are generated, which do not, however, provide other predictive signs of disease. This gestational pattern remains more or less constant throughout pregnancy. Breastfeeding, instead, causes the maximum expression of flow lines: they become numerous, intersecting, almost indistinguishable from each other. During breastfeeding, DATG is not contraindicated but must be accompanied by other techniques.

Menopausal and postmenopausal conditions are characterized by a constant, very slow decrease in diameter and number of flow lines. But the situation differs greatly from woman to woman, as there are women who have a pattern corresponding to that of the reproductive age and others with an entirely quiescent one. Therefore, in many cases, the ovarian menopausal situation does not correspond to a "menopausal" breast. Consequently, each case should be evaluated independently.

8 Concluding Remarks

As happens with a work of art, observation from different points of view provides a greater chance of a better understanding; the same is true for DATG. This diagnostic technique, in fact, is not replacing with other techniques; but can combine with them in order to add information to the clinical picture from another viewpoint: that of the variation of blood distribution (angiography) which is linked to the

development of tumors. This technique is easy to learn for gynecologists, radiologists, sonographers, and oncologists. If they appropriately trained, they all can make correct diagnoses. It is affordable from the economic standpoint: thus it can play a very important role especially for young women and for those applicants who need frequent checks (follow-ups).

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Lastly, we fondly remember Dr. Daniele Montruccoli, who died prematurely during the course of our research; he was the greatest world expert in DATG and introduced this technique even to the poorest countries.

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