A Review of Breast Thermography

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The use of thermal imaging in health care is not a recent phenomenon. Its utilization in breast cancer screening, however, is seeing renewed interest. This attention is fueled by research that clearly demonstrates the value of this procedure and the tremendous impact it can have on the mortality of breast cancer.

The following is not a comprehensive review of the literature. Over 30 years of research compiling over 800 studies in the index-medicus exist. What follows is a pertinent sample review of the research concerning the clinical application of diagnostic infrared imaging (thermography) for use in breast cancer screening. All the citations are taken from the index-medicus peer-reviewed research literature or medical textbooks. The authors are either PhD's with their doctorate in a representative field, or physicians primarily in the specialties of oncology, radiology, gynecology, and internal medicine.

The following list is a summary of the informational text that follows:

- In 1982, the FDA approved breast thermography as an adjunctive diagnostic breast cancer screening procedure.
- Breast thermography has undergone extensive research since the late 1950's.
- Over 800 peer-reviewed studies on breast thermography exist in the index-medicus literature.
- In this database, well over 300,000 women have been included as study participants.
- The numbers of participants in many studies are very large -- 10K, 37K, 60K, 85K .....
- Some of these studies have followed patients up to 12 years.
- Strict standardized interpretation protocols have been established for over 15 years.
- Breast thermography has an average sensitivity and specificity of 90%.
- An abnormal thermogram is 10 times more significant as a future risk indicator for breast cancer than a first order family history of the disease.
- A persistent abnormal thermogram caries with it a 22x higher risk of future breast cancer.
- An abnormal infrared image is the single most important marker of high risk for developing breast cancer.
- Breast thermography has the ability to detect the first signs that a cancer may be forming up to 10 years before any other procedure can detect it.
- Extensive clinical trials have shown that breast thermography significantly augments the long-term survival rates of its recipients by as much as 61%.
- When used as part of a multimodal approach (clinical examination + mammography + thermography) 95% of early stage cancers will be detected.

INTRODUCTION

The first recorded use of thermobiological diagnostics can be found in the writings of Hippocrates around 480 B.C. [1]. A mud slurry spread over the patient was observed for areas that would dry first and was thought to indicate underlying organ pathology. Since this time, continued research and clinical observations proved that certain temperatures related to the human body were indeed indicative of normal and abnormal physiologic processes. In the 1950's, military research into infrared monitoring systems for nighttime troop movements ushered in a new era in thermal diagnostics. The first use of diagnostic thermography came in 1957 when R. Lawson discovered that the skin temperature over a cancer in the breast was higher than that of normal tissue [2].

The Department of Health Education and Welfare released a position paper in 1972 in which the director, Thomas Tiernery, wrote, "The medical consultants indicate that thermography, in its present state of development, is beyond the experimental state as a diagnostic procedure in the following 4 areas: (1) Pathology of the female breast. (2).....". On January 29, 1982, the Food and Drug Administration published its approval and classification of thermography as an adjunctive diagnostic screening procedure for the detection of breast cancer. Since the late 1970's, numerous medical centers and independent clinics have used thermography for a variety of diagnostic purposes.

FUNDAMENTALS OF INFRARED IMAGING

Physics – All objects with a temperature above absolute zero (-273 K) emit infrared radiation from their surface. The Stefan-Boltzmann Law defines the relation between radiated energy and temperature by stating that the total radiation emitted by an object is directly proportional to the object's area and emissivity and the fourth power of its absolute temperature. Since the emissivity of human skin is extremely high (within 1% of that of a black body), measurements of infrared radiation emitted by the skin can be converted directly into accurate temperature values.

Equipment Considerations – Infrared rays are found in the electromagnetic spectrum within the wavelengths of 0.75 micron - 1mm. Human skin emits infrared radiation mainly in the 2 - 20 micron wavelength range, with an average peak at 9-10 microns [3]. State-of-the-art infrared radiation detection systems utilize ultra-sensitive infrared cameras and sophisticated computers to detect, analyze, and produce high-resolution diagnostic images of these infrared emissions. The problems encountered with first generation infrared camera systems, such as improper detector sensitivity (low-band), thermal drift, calibration, analog interface, etc. have been solved for almost two decades.

Laboratory Considerations – Thermographic examinations must be performed in a controlled environment. The primary reason for this is the nature of human physiology. Changes from a different external (non-clinical controlled room) environment, clothing, etc. produce thermal artifacts. Refraining from sun exposure, stimulation or treatment of the breasts, and cosmetics and lotions before the exam, along with 15 minutes of nude acclimation in a florescent lit, draft and sunlight-free, temperature and humidity-controlled room maintained between 18-23 degree C, and kept to within 1 degree C of change during the examination, is necessary to produce a physiologically neutral image free from artifact.

CORRELATION BETWEEN PATHOLOGY AND INFRARED IMAGING

The empirical evidence that underlying breast cancer alters regional skin surface temperatures was investigated early on. In 1963, Lawson and Chughtai, two McGill University surgeons, published an elegant intra-operative study demonstrating that the increase in regional skin surface temperature associated with breast cancer was related to venous convection [4]. This early quantitative experiment added credence to previous research suggesting that infrared findings were related to both increased vascular flow and increased metabolism.

Infrared imaging of the breast may have critical prognostic significance since it may correlate with a variety of pathologic prognostic features such as tumor size, tumor grade, lymph node status and markers of tumor growth [5]. The pathologic basis for these infrared findings, however, is uncertain. One possibility is increased blood flow due to vascular proliferation (assessed by quantifying the microvascular density (MVD)) as a result of tumor associated angiogenesis. Although in one study [6], the MVD did not correlate with abnormal infrared findings. However, the imaging method used in that study consisted of contact plate technology (liquid crystal thermography (LCT)), which is not capable of modern computerized infrared analysis. Consequently, LCT does not possess the discrimination and digital processing necessary to begin to correlate histological and discrete vascular changes [7].

In 1993, Head and Elliott reported that improved images from second generation infrared systems allowed more objective and quantitative analysis [5], and indicated that growth-rate related prognostic indicators were strongly associated with the infrared image interpretation.

In a 1994 detailed review of the potential of infrared imaging [8], Anbar suggested, using an elegant biochemical and immunological cascade, that the previous empirical observation that small tumors were capable of producing notable infrared changes could be due to enhanced perfusion over a substantial area of the breast surface via regional tumor induced nitric oxide vasodilatation. Nitric oxide is a molecule with potent vasodilating properties. It is synthesized by nitric oxide synthase (NOS), found both as a constitutive form of nitric oxide synthase (c-NOS), especially in endothelial cells, and as an inducible form of nitric oxide synthase (i-NOS), especially in macrophages [9]. NOS has been demonstrated in breast carcinoma [10] using tissue immunohistochemistry, and is associated with a high tumor grade. There have been, however, no previous studies correlating tissue NOS levels with infrared imaging. Given the correlation between infrared imaging and tumor grade, as well as NOS levels and tumor grade, it is possible that infrared findings may correlate with tumor NOS content. Future studies are planned to investigate these possible associations.

The concept of angiogenesis, as an integral part of early breast cancer, was emphasized in 1996 by Guido and Schnitt. Their observations suggested that it is an early event in the development of breast cancer and may occur before tumor cells acquire the ability to invade the surrounding stroma and even before there is morphologic evidence of an in-situ carcinoma [11]. Anti-angiogenesis therapy is now one of the most promising therapeutic strategies and has been found to be pivotal in the new paradigm for consideration of breast cancer development and treatment [12]. In 1996, in his highly reviewed

textbook entitled Atlas of Mammography - New Early Signs in Breast Cancer, Gamagami studied angiogenesis by infrared imaging and reported that hypervascularity and hyperthermia could be shown in 86% of non-palpable breast cancers. He also noted that in 15% of these cases infrared imaging helped to detect cancers that were not visible on mammography [13].

The underlying principle by which thermography (infrared imaging) detects pre-cancerous growths and cancerous tumors surrounds the well documented recruitment of existing vascularity and neoangiogenesis which is necessary to maintain the increased metabolism of cellular growth and multiplication. The biomedical engineering evidence of thermography's value, both in model in-vitro and clinically in-vivo studies of various tissue growths, normal and neoplastic, has been established [14-20].

THE ROLE OF INFRARED IMAGING IN THE DETECTION OF CANCER

In order to evaluate the value of thermography, two viewpoints must be considered: first, the sensitivity of thermograms taken preoperatively in patients with known breast carcinoma, and second, the incidence of normal and abnormal thermograms in asymptomatic populations (specificity) and the presence or absence of carcinoma in each of these groups.

In 1965, Gershon-Cohen, a radiologist and researcher from the Albert Einstein Medical Center, introduced infrared imaging to the United States [21]. Using a Barnes thermograph, he reported on 4,000 cases with a sensitivity of 94% and a false-positive rate of 6%. This data was included in a review of the then current status of infrared imaging published in 1968 in CA - A Cancer Journal for Physicians [22].

In prospective studies, Hoffman first reported on thermography in a gynecologic practice. He detected 23 carcinomas in 1,924 patients (a detection rate of 12.5 per 1,000), with an 8.4% false-negative (91.6% sensitivity) and a 7.4% false-positive (92.6% specificity) rate [23].

Stark and Way screened 4,621 asymptomatic women, 35% of whom were under 35 years of age, and detected 24 cancers (detection rate of 7.6 per 1,000), with a sensitivity and specificity of 98.3% and 93.5% respectively [24].

In a mobile unit examination of rural Wisconsin, Hobbins screened 37,506 women using thermography. He reported the detection of 5.7 cancers per 1,000 women screened with a 12% false-negative and 14% false-positive rate. His findings also corroborated with others that thermography is the sole early initial signal in 10% of breast cancers [25-26].

Reporting his Radiology division's experience with 10,000 thermographic studies done concomitantly with mammography over a 3 year period, Isard reiterated a number of important concepts including the remarkable thermal and vascular stability of the infrared image from year to year in the otherwise healthy patient and the importance of recognizing any significant change [27]. In his experience, combining these modalities increased the sensitivity rate of detection by approximately 10%; thus, underlining the complementarity of these procedures since each one did not always suspect the same lesion. It was Isard's conclusion that, had there been a preliminary selection of his group of 4,393 asymptomatic patients by infrared imaging, mammographic examination would have been restricted to the 1,028 patients with abnormal infrared imaging, or 23% of this cohort. This would have resulted in a cancer detection rate of 24.1 per 1000 combined infrared and mammographic examinations as contrasted to the expected 7 per 1000 by mammographic screening alone. He concluded that since infrared imaging is an innocuous examination, it could be utilized to focus attention upon asymptomatic women who should be examined more intensely. Isard emphasized that, like mammography and other breast imaging techniques, infrared imaging does not diagnose cancer, but merely indicates the presence of an abnormality.

Spitalier and associates screened 61,000 women using thermography over a 10 year period. The false-negative and positive rate was found to be 11% (89% sensitivity and specificity). 91% of the nonpalpable cancers (T0 rating) were detected by thermography. Of all the patients with cancer, thermography alone was the first alarm in 60% of the cases. The authors also noted that "in patients having no clinical or radiographic suspicion of malignancy, a persistently abnormal breast thermogram represents the highest known risk factor for the future development of breast cancer" [28].

Two small-scale studies by Moskowitz (150 patients) [29] and Treatt (515 patients) [30] reported on the sensitivity and reliability of infrared imaging. Both used unknown "experts" to review the images of breast cancer patients. While Moskowitz excluded unreadable images, data from Threatt's study indicated that less than 30% of the images produced were considered good, the rest being substandard. Both of these studies produced poor results; however, this could be expected from the fact alone that both used such a small patient base. However, the greatest error in these studies is found in the methods used to analyze the images. The type of image analysis consisted of the sole use of abnormal vascular pattern recognition. At the time these studies were performed, the most recognized method of infrared image

analysis used a combination of abnormal vascular patterns with a quantitative analysis of temperature variations across the breasts. Consequently, the data obtained from these studies is highly questionable. Their findings were also inconsistent with numerous previous large-scale multi-center trials. The authors suggested that for infrared imaging to be truly effective as a screening tool, there needed to be a more objective means of interpretation and proposed that this would be facilitated by computerized evaluation. This statement is interesting considering that the use of recognized quantitative and qualitative reading protocols (including computer analysis) was available at the time.

In a unique study comprising 39,802 women screened over a 3 year period, Haberman and associates used thermography and physical examination to determine if mammography was recommended. They reported an 85% sensitivity and 70% specificity for thermography. Haberman cautioned that the findings of thermographic specificity could not be extrapolated from this study as it was well documented that long term observation (8-10 years or more) is necessary to determine a true false-positive rate. The authors noted that 30% of the cancers found would not have been detected if it were not for thermography [31].

Gros and Gautherie reported on 85,000 patients screened with a resultant 90% sensitivity and 88% specificity. In order to investigate a method of increasing the sensitivity of the test, 10,834 patients were examined with the addition of a cold-challenge (two types: fan and ice water) in order to elicit an autonomic response. This form of dynamic thermography decreased the false-positive rate to 3.5% (96.5% sensitivity) [32-35].

In a large scale multi-center review of nearly 70,000 women screened, Jones reported a false-negative and false-positive rate of 13% (87% sensitivity) and 15% (85% sensitivity) respectively for thermography [36].

In a study performed in 1986, Usuki reported on the relation of thermographic findings in breast cancer diagnosis. He noted an 88% sensitivity for thermography in the detection of breast cancers [37].

In a study comparing clinical examination, mammography, and thermography in the diagnosis of breast cancer, three groups of patients were used: 4,716 patients with confirmed carcinoma, 3,305 patients with histologically diagnosed benign breast disease, and 8,757 general patients (16,778 total participants). This paper also compared clinical examination and mammography to other well known studies in the literature including the NCI-sponsored Breast Cancer Detection Demonstration Projects. In this study, clinical examination had an average sensitivity of 75% in detecting all tumors and 50% in cancers less than 2 cm in size. This rate is exceptionally good when compared to many other studies at between 35-66% sensitivity. Mammography was found to have an average 80% sensitivity and 73% specificity. Thermography had an average sensitivity of 88% (85% in tumors less than 1 cm in size) and a specificity of 85%. An abnormal thermogram was found to have a 94% predictive value. From the findings in this study, the authors suggested that “none of the techniques available for screening for breast carcinoma and evaluating patients with breast related symptoms is sufficiently accurate to be used alone. For the best results, a multimodal approach should be used” [38].

In a series of 4,000 confirmed breast cancers, Thomassin and associates observed 130 sub-clinical carcinomas ranging in diameter of 3-5 mm. Both mammography and thermography were used alone and in combination. Of the 130 cancers, 10% were detected by mammography only, 50% by thermography alone, and 40% by both techniques. Thus, there was a thermal alarm in 90% of the patients and the only sign in 50% of the cases [39].

In a study by Gautherie and associates, the effectiveness of thermography in terms of survival benefit was discussed. The authors analyzed the survival rates of 106 patients in whom the diagnosis of breast cancer was established as a result of the follow-up of thermographic abnormalities found on the initial examination when the breasts were apparently healthy (negative physical and mammographic findings). The control group consisted of 372 breast cancer patients. The patients in both groups were subjected to identical treatment and followed for 5 years. A 61% increase in survival was noted in the patients who were followed-up due to initial thermographic abnormalities. The authors summarized the study by stating that “the findings clearly establish that the early identification of women at high risk of breast cancer based on the objective thermal assessment of breast health results in a dramatic survival benefit” [40-41].

In a simple review of over 15 studies from 1967 - 1998, breast thermography has showed an average sensitivity and specificity of 90%. With continued technological advances in infrared imaging in the past decade, some studies are showing even higher sensitivity and specificity values. However, until further large scale studies are performed, these findings remain in question.

BREAST CANCER DETECTION AND DEMONSTRATION PROJECTS

The Breast Cancer Detection and Demonstration Project (BCDDP) is the most frequently quoted reason for the decreased use of infrared imaging. The BCDDP was a large-scale study performed from 1973 through 1979 which collected data from many centers around the United States. Three methods of breast cancer detection were studied: physical examination, mammography, and infrared imaging (breast thermography).

Inflated Expectations -- Just before the onset of the BCDDP, two important papers appeared in the literature. In 1972, Gerald D. Dodd of the University of Texas Department of Diagnostic Radiology presented an update on infrared imaging in breast cancer diagnosis at the 7th National Cancer Conference sponsored by the National Cancer Society and the National Cancer Institute [42]. In his presentation, he suggested that infrared imaging would be best employed as a screening agent for mammography. He proposed that in any general survey of the female population age 40 and over, 15 to 20% of these subjects would have positive infrared imaging and would require mammograms. Of these, approximately 5% would be recommended for biopsy. He concluded that infrared imaging would serve to eliminate 80 to 85% of the potential mammograms. Dodd also reiterated that the procedure was not competitive with mammography and, reporting the Texas Medical School's experience with infrared imaging, noted that it was capable of detecting approximately 85% of all breast cancers. Dodd's ideas would later help to fuel the premise and attitudes incorporated into the BCDDP. Three years later, J.D. Wallace presented to another Cancer Conference, sponsored by the American College of Radiology, the American Cancer Society and the Cancer Control Program of the National Cancer Institute, an update on infrared imaging of the breast [43]. The author's analysis suggested that the incidence of breast cancer detection per 1000 patients screened could increase from 2.72 when using mammography to 19 when using infrared imaging. He then underlined that infrared imaging poses no radiation burden on the patient, requires no physical contact and, being an innocuous technique, could concentrate the sought population by a significant factor selecting those patients that required further investigation. He concluded that, "the resulting infrared image contains only a small amount of information as compared to the mammogram, so that the reading of the infrared image is a substantially simpler task".

Faulty Premise -- Unfortunately, this rather simplistic and cavalier attitude toward the generation and interpretation of infrared imaging was prevalent when it was hastily added and then prematurely dismissed from the BCDDP which was just getting underway. Exaggerated expectations led to the ill-founded premise that infrared imaging might replace mammography rather than complement it. A detailed review of the Report of the Working Group of the BCDDP, published in 1979, is essential to understand the subsequent evolution of infrared imaging [44]. The work scope of this project was issued by the NCI on the 26th of March 1973 with six objectives, the second being to determine if a negative infrared image was sufficient to preclude the use of clinical examination and mammography in the detection of breast cancer. The Working Group, reporting on results of the first four years of this project, gave a short history regarding infrared imaging in breast cancer detection. They wrote that as of the sixties, there was intense interest in determining the suitability of infrared imaging for large-scale applications, and mass screening was one possibility. The need for technological improvement was recognized and the authors stated that efforts had been made to refine the technique. One of the important objectives behind these efforts had been to achieve a sufficiently high sensitivity and specificity for infrared imaging under screening conditions to make it useful as a pre-screening device in selecting patients for referral for mammographic examination. It was thought that if successful, this technology would result in a relatively small proportion of women having mammography (a technique that had caused concern at that time because of the carcinogenic effects of radiation). The Working Group indicated that the sensitivity and specificity of infrared imaging readings, with clinical data emanating from inter-institutional studies, were close to the corresponding results for physical examination and mammography. They noted that these three modalities selected different sub-groups of breast cancers, and for this reason further evaluation of infrared imaging as a screening device in a controlled clinical trial was recommended.

Poor Study Design -- While this report describes in detail the importance of quality control of mammography, the entire protocol for infrared imaging was summarized in one paragraph and simply indicated that infrared imaging was conducted by a BCDDP trained technician. The detailed extensive results from this report, consisting of over 50 tables, included only one that referred to infrared imaging showing that it had detected only 41% of the breast cancers during the first screening while the residual were either normal or unknown. There is no breakdown as far as these two latter groups were concerned. Since 28% of the first screening and 32% of the second screening were picked up by mammography alone, infrared imaging was dropped from any further evaluation and consideration. The report stated that it was impossible to determine whether abnormal infrared imaging could be predictive of interval cancers (cancers developing between screenings) since they did not collect this data. By the same token, the Working Group was unable to conclude, with their limited experience, whether the findings were related to the then available technology of infrared imaging or with its application. They did, however, conclude that the decision to dismiss infrared imaging should not be taken as a determination of the future of this technique, rather that the procedure continued to be of interest because it does not entail the risk of radiation exposure. In the Working Group's final recommendation, they state that "infrared imaging does not appear to be suitable as a substitute for mammography for routine screening in the BCDDP." The report admitted that several individual programs of the BCDDP

had results that were more favorable than what was reported for the BCDDP as a whole. They encouraged investment in the development and testing of infrared imaging under carefully controlled study conditions and suggested that high priority be given to these studies. They noted that a few suitable sites appeared to be available within the BCDDP participants and proposed that developmental studies should be solicited from sites with sufficient experience.

Untrained Personnel and Protocol Violations – JoAnn Haberman, who was a participant in this project [45], provided further insight into the relatively simplistic regard assigned to infrared imaging during this program. The author reiterated that expertise in mammography was an absolute requirement for the awarding of a contract to establish a Screening Center. However, the situation was just the opposite with regard to infrared imaging – no experience was required at all. When the 27 demonstration project centers opened their doors, only 5 had any pre-existing expertise in infrared imaging. Of the remaining screening centers, there was no experience at all in this technology. Finally, more than 18 months after the project had begun, the NCI established centers where radiologists and their technicians could obtain sufficient training in infrared imaging. Unfortunately, only 11 of the demonstration project directors considered this training of sufficient importance to send their technologists to learn proper infrared technique. The imaging sites also disregarded environmental controls. Many of the project sites were mobile imaging vans which had poor heating and cooling capabilities and often kept their doors open in the front and rear to permit an easy flow of patients. This, combined with a lack of pre-imaging patient acclimation, lead to unreadable images.

In summary, with regard to thermography, the BCDDP was plagued with problems and seriously flawed in four critical areas: (1) Completely untrained technicians were used to perform the scans, (2) The study used radiologists who had no experience or knowledge in reading infrared images, (3) Proper laboratory environmental controls were completely ignored. In fact, many of the research sites were mobile trailers with extreme variations in internal temperatures, (4) No standardized reading protocol had yet been established for infrared imaging. The BCDDP was also initiated with an incorrect premise that thermography might replace mammography. From a purely scientific point, an anatomical imaging procedure (mammography) cannot be replaced by a physiological one. Last of all, and of considerable concern, was the reading of the images. It wasn't until the early 1980's that established and standardized reading protocols were introduced. Considering these facts, the BCDDP could not have properly evaluated infrared imaging. With the advent of known laboratory environmental controls, established reading protocols, and state-of-the-art infrared technology, a poorly performed 20-year-old study cannot be used to determine the appropriateness of thermography.

THERMOGRAPHY AS A RISK INDICATOR

As early as 1976, at the Third International Symposium on Detection and Prevention of Cancer in New York, thermography was established by consensus as the highest risk marker for the possibility of the presence of an undetected breast cancer. It had also been shown to predict such a subsequent occurrence [46-48]. The Wisconsin Breast Cancer Detection Foundation presented a summary of its findings in this area, which has remained undisputed [49]. This, combined with other reports, has confirmed that thermography is the highest risk indicator for the future development of breast cancer and is 10 times as significant as a first order family history of the disease [50].

In a study of 10,000 women screened, Gautherie found that, when applied to asymptomatic women, thermography was very useful in assessing the risk of cancer by dividing patients into low- and high-risk categories. This was based on an objective evaluation of each patient's thermograms using an improved reading protocol that incorporated 20 thermopathological factors [51].

From a patient base of 58,000 women screened with thermography, Gros and associates followed 1,527 patients with initially healthy breasts and abnormal thermograms for 12 years. Of this group, 40% developed malignancies within 5 years. The study concluded that "an abnormal thermogram is the single most important marker of high risk for the future development of breast cancer" [35].

Spitalier and associates followed 1,416 patients with isolated abnormal breast thermograms. It was found that a persistently abnormal thermogram, as an isolated phenomenon, is associated with an actuarial breast cancer risk of 26% at 5 years. Within this study, 165 patients with non-palpable cancers were observed. In 53% of these patients, thermography was the only test which was positive at the time of initial evaluation. It was concluded that: (1) A persistently abnormal thermogram, even in the absence of any other sign of malignancy, is associated with a high risk of developing cancer, (2) This isolated abnormal also carries with it a high risk of developing interval cancer, and as such the patient should be examined more frequently than the customary 12 months, (3) Most patients diagnosed as having minimal breast cancer have abnormal thermograms as the first warning sign [52-53].

CURRENT STATUS OF DETECTION

Current first-line breast cancer detection strategy still depends essentially on clinical examination and mammography. The limitations of the former, with its reported sensitivity rate often below 65% [54] is well-recognized, and even the proposed value of self-breast examination is now being contested [55]. While mammography is accepted as the most reliable and cost-effective imaging modality, its contribution continues to be challenged with persistent false-negative rates ranging up to 30% [56-57]; with decreasing sensitivity in patients on estrogen replacement therapy [58]. In addition, there is recent data suggesting that denser and less informative mammography images are precisely those associated with an increased cancer risk [59]. Echoing some of the shortcomings of the BCDDP concerning their study design and infrared imaging, Moskowitz indicated that mammography is also not a procedure to be performed by the untutored [60].

With the current emphasis on earlier detection, there is now renewed interest in the parallel development of complimentary imaging techniques that can also exploit the precocious metabolic, immunological and vascular changes associated with early tumor growth. While promising, techniques such as scintimammography [61], doppler ultrasound [62], and MRI [63], are associated with a number of disadvantages that include exam duration, limited accessibility, need of intravenous access, patient discomfort, restricted imaging area, difficult interpretation and limited availability of the technology. Like ultrasound, they are more suited to use as second-line options to pursue the already abnormal clinical or mammographic evaluation. While practical, this step-wise approach currently results in the non-recognition, and thus delayed utilization of second-line technology in approximately 10% of established breast cancers [60]. This is consistent with a study published by Keyserlingk et al [64].

Because of thermography's unique ability to image the thermovascular aspects of the breast, extremely early warning signals (from 8-10 years before any other detection method) have been observed in long-term studies. Consequently, thermography is the earliest known indicator for the future development of breast cancer. It is for this reason that an abnormal infrared image is the single most important marker of high risk for developing breast cancer. Thus, thermography has a significant place as one of the major front-line methods of breast cancer detection.

CONCLUSION

The large patient populations and long survey periods in many of the above clinical studies yields a high significance to the various statistical data obtained. This is especially true for the contribution of thermography to early cancer diagnosis, as an invaluable marker of high-risk populations, and therapeutic decision making (a contribution that has been established and justified by the unequivocal relationship between heat production and tumor doubling time).

Currently available high-resolution digital infrared imaging (Thermography) technology benefits greatly from enhanced image production, standardized image interpretation protocols, computerized comparison and storage, and sophisticated image enhancement and analysis. Over 30 years of research and 800 peer-reviewed studies encompassing well over 300,000 women participants has demonstrated thermography's abilities in the early detection of breast cancer. Ongoing research into the thermal characteristics of breast pathologies will continue to investigate the relationships between neoangiogenesis, chemical mediators, and the neoplastic process.

It is unfortunate, but many physicians still hesitate to consider thermography as a useful tool in clinical practice in spite of the considerable research database, continued improvements in both thermographic technology and image analysis, and continued efforts on the part of the thermographic societies. This attitude may be due to the fact that the physical and biological bases of thermography are not familiar to most physicians. The other methods of cancer investigations refer directly to topics of medical teaching. For instance, radiography and ultrasonography refer to anatomy. Thermography, however, is based on thermodynamics and thermokinetics, which are unfamiliar to most physicians; though man is experiencing heat production and exchange in every situation he undergoes or creates.

Considering the contribution that thermography has demonstrated thus far in the field of early cancer detection, all possibilities should be considered for promoting further technical, biological, and clinical research in this procedure.

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