USE OF DIGITAL INFRARED IMAGING IN ENHANCED BREAST CANCER DETECTION AND MONITORING OF THE CLINICAL RESPONSE TO TREATMENT

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ABSTRACT

Infrared imaging of the breast has been primarily hampered by the many factors inherent in its technology. With the use of computer automated digital infrared technology, problems with subjectivity, reproducibility and spatial localization have been eliminated. The Digital Infrared Imaging (DII) discussed herein, has a 98% detection sensitivity in a study of 67 tissue proven cases of breast cancer. It's sensitivity has been successfully demonstrated in lesions as small as 4 mm. Additionally, DII, can now be used in the clinical monitoring of localized breast cancer to access therapeutic response. In conjunction with mammography and ultrasound, DII can be utilized in the early detection of breast cancer.

INTRODUCTION

Mammography is considered to be the "gold standard" technology for the diagnosis of breast cancer. However, serious deficiencies in this regard are well documented in both medical and lay publications. In recent NY Times articles, several focused on the debate over mammography, acknowledging that 20 to 25% of existing cancers are missed in women under age 50 [1]. Even as improved film-screen technology, digital mammography, MRI, high resolution ultrasound , and PET scanning present their cases, the call for additional, more sensitive and more effective methodology, continues unabated.. As reported in Medical Imaging Magazine [2], many of the newest modalities fall short in breast cancer screening. Digital mammography's recent introduction into the breast cancer diagnostic *weapons cache*, while accompanied by considerable fanfare, is not likely to significantly lower the false negative rate in dense breasts. MRI still is not a practical screening tool because of expense, the need to inject a contrast agent, and non-specificity, with similar drawbacks for PET. Ultrasound, although extremely useful for detecting masses in the breast, frequently fails to diagnose ductal carcinoma in situ (DCIS). This neoplasia usually presents as a cluster of minute calcifications rather than a mass, accounts for almost 50% of all malignancies. It is clear that none of these modalities can be used by itself, and any proposed combination has its limitations.

As long as 40 years ago, temperature differences on the breast surface, obtained with infrared hardware, were postulated as having relevance for breast cancer diagnosis [13]. These early studies using primitive technology showed promise as a diagnostic tool, but they were discredited for multiple reasons: Interpretation of the images involved a high degree of expertise and subjectivity; the rate of false positives and false negatives was unacceptably high and certainly no improvement on mammography; and the results were often not repeatable as they required controlled environments and patient thermal stabilization. In spite of the lack of enthusiasm for infrared imaging among mainstream practitioners, a few investigators persisted in acquiring data regarding its utility as an adjunctive diagnostic procedure. Although these data have gone largely unnoticed, they are quite consistent throughout the literature [3,4,5,6,7,8]. The well documented shortcomings of past studies and techniques, have been addressed and eliminated in the current system. The state-of-the-art infrared studies described here, illustrate the benefit of infrared imaging in the detection of even very small early breast cancer.

MATERIALS AND METHODS

Three hundred and fifty one female patients ranging in age from 35 to 80 years were included in this study. They comprised three groups, those believed cancer free, those with newly discovered cancer, and those who previously had a diagnoses of cancer. The first group

consisted of 238 patients with no known cancer (presumed normal). The second group was comprised of 67 patients with newly detected, biopsy proven cancer, and the third group included 46 patients who had lumpectomies for proven malignancy 1 to 10 years previously. Included in the 67 cancer cases, were three cases undetectable by mammography alone and were found only on ultrasound examination. Various types of malignancy were represented in our sample, including, DCIS, LCIS, invasive ductal carcinoma, invasive lobular carcinoma, and inflammatory carcinoma; in some cases with lesions as small as 4 mm..

The patient examination was carried out in a dedicated suite equipped with an ergonomically designed height adjustable chair equipped with infrared reflecting side mirrors An equipment cart with an air cooler , a self viewing video monitor and the infrared camera were located approximately 5 feet in front of the patient. Other major equipment included a state -of -the-art digital infrared camera of the focal plane array type, with an aperture size of 320x240 pixels, a sensitivity to 0.05 degrees C, and an operating spectral range of 7-12 microns, as well as a high speed computer workstation with specialized custom software.

During the examination procedure the patient sat disrobed from the waist up and appropriately positioned in the ergonomic chair with her arms supported at eye level. Temperature controlled air flow was then directed at the breasts for a 4 minute interval while the infrared camera recorded surface cool down at 250 frames per minute. The stored images were fed into proprietary computer software designed to extract specific thermal parameters, including various temperature differences and thermal symmetry measurements. Additionally, the software was instructed to focus on that singular area of the breasts which showed the greatest difference in temperature between itself and its immediate surroundings, as well as two additional, more sensitive temperature difference settings. The program then produced a color coded, post processed image of the breasts showing one or more these foci, and the result of all measured parameters being evaluated for risk, in a weighted "evaluation" algorithm.

RESULTS AND DISCUSSION

The results of our study are shown in **Table 1**. The most striking result is that the computer generated "risk evaluation" was able to show that 98% of cancer patients have a positive score , while 45% of presumed normal patients have a positive score. Two patients that presented with either an abnormal mammogram or ultrasound and had an abnormal infrared, were later found to have biopsy proven atypical hyperplasia. Thus far only one of 67 cancer patients has tested negative. Clearly, if a patient has a negative result in the "evaluation algorithm", the likelihood of her having cancer is very small. This would have far reaching implications for the 40% of the female population with dense breasts where mammography has limited sensitivity, finding only 68% of breast cancer at best[2,12]. Focusing for a moment on the 55% of presumed normal patients that have a negative score it is quite possible that with further refinement of the algorithm, we will be able to reassure these women that they definitely do not have breast cancer . A positive result signifies that the patient is in a possible risk category, and at first glance, a group comprising 45% of presumed normal patients may seem high. If you consider that about 30% of patients with an abnormal infrared will get cancer within 5 years, as reported by Gauthrie and Gros [6], this number takes on a new perspective. Taking 30% of the positive risk group (of 45%), we arrive at 13.5% of normal "positive" patients will get cancer. Clearly, this is a number that correlates fairly well with the known lifetime risk of 1 in 8, or 12.5% [9].

Table 1

Evaluation Algorithm Results		
Patient Group	**Negative**	**Positive**
Normal	55%	45%
Cancer	2%	**98%**
Post-Op	6%	94%

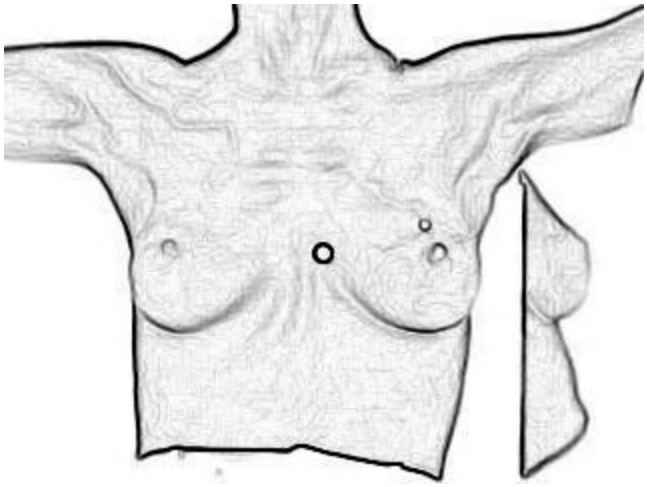
The results shown in **Table 1** are generated by the evaluation of several computer measurable, and quantifiable, parameters. These specific parameters, shown in **Table 2**, are combined in a weighted algorithm which generates either the positive or a negative evaluation result, as well as a post processed image showing the previously discussed foci (note that the algorithm value for these foci is the "Threshold" parameter in Table 2).

An equally important area of our study, focused on the use of serial infrared imaging of patients with locally advanced or inflammatory breast cancer. Selected patients were observed on multiple occasions with the infrared system. The main objective was to monitor the clinical response to chemotherapy and hormonal manipulation. The results of patients in serial infrared imaging, showed

that infrared is highly sensitive, and highly correlated with actual clinical findings [10]. It is obvious from the results we have obtained, that this new tool will benefit not only radiologists, but oncologists as well.

Past researchers have reported the relatively high sensitivity of infrared in the detection of the signs of breast cancer. In 100 cases of cancer, Dr. J. Keyserlink [11] reported that infrared demonstrates an 83% sensitivity, compared to 66% for a positive mammography alone (cases include DCIS, and infiltrating Stage 1 and Stage 2 cancers). Combining mammography with clinical exam, improves the sensitivity to 83%. When infrared, mammography, and clinical are combined together, the sensitivity is reported at 98% [11]. In this study we show the tremendous potential of computer evaluation and infrared together; wherein the combination is highly sensitive, 98% without the benefit of any patient mammographic or clinical information in the automated evaluation process.

When a patient's infrared image sequence, which recorded during the four minute acquisition period, is subjected to post processing by computer, a resultant image is created, an example (a line drawing for this publication) of which is shown below. In this example, the single dot above the left breast nipple, indicates the focus of maximum temperature difference between a small central area and its neighbors (note that the dot in the sternum area is an infrared target used during the recording phase). The lesion later proved to be a 3 mm x 4 mm cancer, detectable only by ultrasound (due to the patient's very dense breasts) in the precise location of the dot. It is believed that these foci, represent areas of angiogenesis, in agreement with that which is well documented by many researchers. Gamagami [8] states, that infrared "telethermography can show angiogenesis in the preneoplastic or neoplastic stage..".



Infrared imaging is an FDA approved procedure when used as an adjunctive modality in breast cancer detection. Our intended use of this technology is to enhance the awareness of both, the clinician when evaluating a patient, and the radiologist when reading the accompanying mammogram or performing the accompanying ultrasound, by providing a guide to those sites where cancer is most likely to be found. In this regard it is noteworthy that although our cancer group is small, virtually every malignancy we have encountered, thus far, has correlated well with these foci.

As mentioned in the previous section, our automated algorithm gathers various temperature and thermal characteristics of the breast, and tests them with an empirically determined "best fit" value that was selected specifically for each parameter. If one or more of a patient's parameters fell above this selected value, she was categorized as being at risk. Observing **Table 2**, one can see that all of these parameters show substantial discrimination ratios between the cancer patients and the patients presumed normal. These data are similar to those reported by numerous other investigators [3,4,8]. Additionally, some investigators have presented evidence indicating positive infrared findings may have predictive value regarding future development of malignancy. Gautherie and Gros [6] reported that of 1200 women with positive infrared signs about one third developed malignancies over the following 5 years. Our own, relatively short term study, includes three patients with results relevant to this possibility. There were two patients that proved to have atypical hyperplasia—a pre-cancerous condition. A third patient that had a normal annual mammogram and a suspicious infrared in February 2000, and in February 2001, had a very small cancer at the site identified by the infrared test from the previous year. The fact that this current study, which only evaluates objective parameters, is consistent with previous studies, serves to further validate these past studies.

CONCLUSION

With our automated digital infrared system, no longer are just a few highly experienced practitioners able to use infrared to its fullest potential. We have addressed the shortcomings of the past use of the technology in this system. The interpretation of infrared data is no longer subjective, irreproducible, and insensitive. As a result, the infrared system as described herein, opens the doors to a very valuable technology that clearly has utility in early detection and monitoring of breast cancer. We believe

that digital infrared imaging, when used in conjunction with mammography and ultrasound can enhance our ability to diagnose early breast cancer and pre-cancerous conditions and may help minimize procedures related to false positives. We further believe that therapeutic modalities can be evaluated by oncologists in patients with breast cancer in a new and exciting way.

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Table 2

"Risk" Parameter Distribution

	Percent of Patient Group that exceeds algorithm "risk" value					
Patient Group	**Threshold**	**Nipple**	**Areolar**	**Global**	**Asymmetry**	**Hot Spot**
Normal	31%	18%	8%	12%	1%	1%
Cancer	73%	43%	22%	33%	4%	4%
Post-Op	46%	59%	49%	49%	12%	2%
Ratio Ca/Norm	2.4	2.4	2.8	2.8	4.0	4.0
Ratio PO/norm	1.5	3.3	6.1	4.1	12.0	2.0