

# Nondestructive Testing of the Human Breast: The Validity of Dynamic Stress Testing in Medical Infrared Breast Imaging

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**Abstract**—The validity of the autonomic cold challenge for use in screening breast thermography is reviewed. A review of the literature is discussed along with reasoning for the choice of the cold stress method used. Breast thermogram results from 23 patients with histologically confirmed breast cancers are presented demonstrating positive and negative responses to the challenge. Cold challenge responses from 500 patients without breast cancer and with normal and persistent abnormal thermograms are also discussed. The question is posed, should the use of the cold challenge be continued considering that a negative response does not rule out the possibility of neoplasm nor does a positive response guarantee its existence? Conclusions are drawn from the available data that suggest that the use of the cold challenge be left up to the discretion of the interpreting thermologist and not mandated with every breast thermogram. Until further studies are performed and ample evidence can be presented, a review of the available data indicates that infrared imaging of the breast can be performed excluding the cold challenge without any known loss of sensitivity or specificity in the detection of breast cancers.

*Keywords:* thermography, cold challenge, sensitivity, specificity, breast cancer.

## 1. INTRODUCTION

Breast thermography, a graphic display of the infrared radiation from the breast, has been used for approximately 45 years as an adjunctive screening procedure in the evaluation of the breast. Its inception dates to Lawson's observations in 1956-1958 that a breast cancer may be warmer than the surrounding tissue<sup>[1-3]</sup>. He also showed that the venous blood draining the cancer may be warmer than its arterial supply. Since this time, significant advances have been made in the technology itself and the methodology of interpretation.

The incorporation of an external stressor during screening breast thermography was initially designed as a method of visualizing a dynamic temperature response in the breasts to an external cold stimulus. Either direct or indirect cooling methods lower the overall temperature of the breast, theoretically increasing apparent areas of pathological thermovascular emissions by enhancing thermal contrast. Images taken in series have also been incorporated to measure the rates of cooling or re-warming to provide additional data that may increase suspicion.

Different methods have been employed in dynamic thermography. Most notably, air flow directed at the breasts by fans or ice water immersion of the extremities. Less frequently used methods include isopropyl alcohol sprayed on the breasts and ice pack application to the lower thoracic spine (Wexler).

## 2. PHYSIOLOGY OF THE COLD CHALLENGE

Currently, the most common method of applied autonomic challenge involves ice water immersion of the hands or feet. The mechanism is purely neurovascular and involves a primitive survival reflex initiated from peripheral neural receptors and conveyed to the central nervous system. To protect the body from hypothermia, the reflex invokes a sympathetically mediated blood vessel constriction in the periphery in an attempt to maintain a normal core temperature. This stress test is intended to increase the sensitivity of the thermogram by attempting to identify non-responding blood vessels such as those involved in neoangiogenesis associated with neoplasm. Blood vessels produced by cancerous tumors are mere endothelial tubes devoid of a muscular layer and the neural regulation afforded to embryologic vessels. As such, these new vessels should fail to constrict in response to a sympathetic stimulus. The normal breast would display a relative cooling with attenuation of vascular diameter. Consequently, a breast harboring a malignancy would theoretically remain unchanged in temperature or demonstrate hyperthermia with vascular dilation.<sup>[4]</sup>

Past studies have also used thermoconductive methods of stress. Coolants such as alcohol applied to the breasts or fans directing air at the breasts cause rapid cooling of the skin surface. The temperatures of cooler regions fall rapidly while warmer areas resist change. This causes a relative increase in thermal contrast, thus exposing subtle areas of hyperthermia. Also, due to the rapid cooling of the skin surface, an increase in the thermal gradient between the superficial and deeper areas of the breast occurs. This causes increased heat transfer toward the cooler surface tissues (Zeroeth Law of Thermodynamics). Studies have used this thermodynamic effect to monitor re-warming rates with serial imaging. Regions of the breast that are more thermally active would re-warm the surface at a faster rate than less active areas.

Previous studies have been performed using both neurovascular (ice water immersion) and thermoconductive (fans) methods. Authors have discussed the possible merits for using each type. Concerns have been voiced over the

creation of thermal artifacts due to the inherent difficulty in applying an even air flow distribution to a curved surface such as the breast. Consequently, studies have shown clear preference to the use of the ice water challenge when attempting to investigate neoangiogenesis<sup>[5-7]</sup>.

### 3. LITERATURE REVIEW

A review of the literature denotes the use of the cold challenge as a method of increasing the accuracy of breast thermography. In general, the incorporation of the cold challenge was intended to decrease false-negatives and especially false-positives.

#### A. Decreasing false-positives

Early on in the use of thermography for breast cancer screening, opponents to the technology argued that the false-positive rate was too high for the procedure to be used. The incorporation of the cold challenge to decrease suspicion was proposed as a possible solution to the problem. Studies can be found espousing the virtues of a “true” improvement in false-positives<sup>[8-11]</sup>. Some studies have indicated a reduction of up to a 40%<sup>[9]</sup>.

In the studies that claim reductions in the number of false-positive thermograms, the data collected is suspect. The patients selected were taken from a study group found without a cancerous tumor in the breast, but with suspicious thermograms (possible false-positives). This group was subjected to the cold challenge. If the challenge was negative, the patients’ TH grading was reduced to normal. This methodology is understandable, but with a false premise. How many of these patients are at future risk? This author agrees with the notation in one of the studies [9] that future research would be needed to observe whether or not the cold challenge effects future risk. As of this time, we are not aware of any long-term studies that have been done to follow patients who have TH3-5 thermograms and negative responses to the cold challenge.

Considering the known status of thermography as the single greatest indicator of future breast cancer risk<sup>[12-14]</sup>, use of the cold challenge to decrease “false positives” could have a seriously poor impact with deadly consequences. Isard stated that, “Thermography is an innocuous examination that can be utilized for preliminary screening of asymptomatic women to focus attention upon those who should be examined more intensively because of greater risk of breast cancer<sup>[5]</sup>.” It is known that a patient with a persistent abnormal thermogram has a greater than 40% chance of discovering breast cancer within 8 years<sup>[14]</sup>. We need to be careful not to use the cold challenge to decrease a TH rating to the detriment of risking women’s lives by not classifying them at high risk. Using the cold challenge in this way could be a fatal mistake.

#### B. Decreasing false-negatives

The most accepted use of the cold challenge is to increase suspicion in a particular study by attempting to discern neoangiogenesis associated with neoplasm. With this in mind, a positive response should make a difference in the thermal grading and subsequent clinical follow up. However, thermograms graded from TH3 and up are routinely sent for follow up structural imaging as a matter of course. As such, a positive cold challenge does not change the clinical decision making process in TH3 and up thermograms.

When a review of the available studies is averaged, the specificity (true-positives) for breast thermography is 90%. Thus, only 10% of breast cancers are devoid of suspicious thermovascular emissions. According to the literature, in the average dispersion of cancers 37% will be found in the TH5 category, 32% in the TH4, 21% in TH3, and 10% in the TH1 and 2 grades<sup>[15, 16]</sup>. The 10% of thermograms without suspicious thermovascular features (TH1 or 2) have been shown to have the highest positive prognosis among the thermographic grades<sup>[17, 18]</sup>. The reason for a lack of thermovascular evidence lies in the biological aggressiveness of the tumor. The majority of these cancers are slow growing and non-aggressive. This type of tumor biology shows very little neoangiogenesis. As such, there is a normal thermographic signal.

Since a positive cold challenge will not change the clinical follow up in TH3-5 thermograms, where would it help? Could the challenge be used to detect the cancers in the TH1 or 2 categories? This selected use of the cold challenge seems to have merit on the surface, but a further analysis is in order. In the baseline images, cancerous tumors in the TH1 or 2 categories have very little angiogenesis or chemical vasodilatory effects on the breast. If the tumor did, the effects would be seen and the grading would be increased proportionately. As such, how much of an effect would a cold challenge have on the thermogram when there is little angiogenesis present? Some may speculate that in this particular TH category the cold challenge may have some benefit. However, this is theoretical and without any known studies to provide evidence of benefit. Personal communication with the preeminent expert in this field in the U.S., William Hobbins, noted that he has failed to produce a single cancer using this methodology in over 35 years of imaging, a personal published study of over 37,000 women, and over 300,000 interpreted thermograms<sup>[19, 20]</sup>. This would stand to reason considering that there is literally no thermovascular evidence of angiogenesis in the baseline images to which a cold challenge would have an effect.

## 4. METHODS

Patients in this study were imaged using a 4th generation high-resolution infrared camera (FLIR) with a spectral

bandwidth of 7-13 microns. Real-time digital capture was facilitated via high-speed computer interface and digital processing software (InfraSoft). Each patient was subjected to 15 minutes of nude acclimation from the waist up in a seated position with arms away from the body. During the last 5 minutes, each patient was instructed to place their hands on top of their head to facilitate improved positioning of the breasts. A special carpeted imaging room was used to facilitate a draft free environment isolated from external infrared sources and held steady between 19-20 degrees C.

Seven baseline images of the breasts were taken to include a bilateral frontal, right and left obliques, and right and left single breast close-up views. Once the baseline images were taken, an autonomic cold challenge was performed. Each patient was instructed to submerge their hands in 6 inches of water with floating ice (approx. 5 degrees C.) for 1 minute. The close-up images of each breast were then repeated at the same distance from the detector as the baseline images.

A qualitative and quantitative thermovascular analysis was performed (Hobbins protocol). All patients were assigned a TH rating based on the combined analysis of the vascular patterning and thermal emissions. The cold challenge images were digitally processed and compared to the baseline set. The close-up views were carefully analyzed for minute changes in vascularity and temperatures to denote a response to the cold challenge. A response was considered positive if a breast would remain unchanged in temperature and vascular caliber or demonstrate an increase in temperature and vascular dilation along with cooling and vascular attenuation of the contralateral breast. Any amount of temperature decrease and vascular attenuation in one breast with greater cooling in the contralateral breast must be considered a negative response since there is no known database from which numerical temperatures can be used to determine the minimum amount of temperature change needed to consider a thermogram positive for a cold challenge in one breast when there is cooling of both breasts.

## 5. RESULTS

In this study, 23 patients with histologically confirmed breast cancers were discovered. 500 patients without breast cancer were chosen at random from our clinic's database. This group was composed of normal (TH1 or 2) or persistent equivocal or abnormal (TH3-5) thermograms.

Observations in our clinic agree with Hobbins' data on normal patient responses to a cold challenge: in the group of 500 patients without cancer approximately 70% responded with vasoconstriction, 6% responded with bilateral warming as a Lewis hunting reaction, and 24% showed no change in the breasts. We have also noted that on occasion patients with a TH3, 4, or 5 thermogram may show a positive cold

challenge yet no suspicious signs of cancer can be detected on structural imaging.

Of the 23 patients with histologically confirmed breast malignancies 2 were graded TH3, 8 TH4, and 13 TH5. In the group of 500 patients without breast cancer, normals were graded either TH1 or TH2. Patients in this group that were graded as persistent equivocal or abnormal (TH3-5) had to maintain this grading level for at least 1 year to substantiate the persistent nature of their respective grading. Both the normal and persistent equivocal and abnormal groups were found to have no suspicious findings for cancer on follow up structural imaging. The patients with persistent TH3-5 thermograms are being closely monitored due to their level of increased risk.

The results of the cold challenge showed that of the 23 patients with confirmed malignancies, only 12 (52%) responded with a positive reaction (increased heat, vascularity, or no change in temperature with a contralateral cooling of the normal breast). However, the reaction to the challenge had no bearing on the decision making process for further work-up. Each patient was followed up with either a mammogram, ultrasound, or biopsy depending on what type of tests were recently performed prior to infrared imaging. Ultimately, all 23 patients were tracked until a biopsy confirmed the findings.

In the normal thermogram group (TH1 or 2) none of the images showed a positive response to the cold challenge. As with Hobbins, we have not yet uncovered a single breast malignancy using the cold challenge in the TH1 or 2 grades. We are also not aware of any studies showing efficacy of detecting cancers using the cold challenge in patients with TH1 or 2 thermograms.

## 6. CLINICAL RESPONSES TO THE COLD CHALLENGE

The varying responses to the challenge are dependent on the state of the physiology of the breast. In an attempt to understand specific reactions to a cold stressor, the following hypotheses are offered.

### A. *Negative challenge response with a malignancy present*

The reason for a lack of a response to the cold challenge may lie in the amount of open vasculature in the breast. If a carcinoma is placing a large demand on the overall vasculature of the breast, there is less room for a vasoconstrictive display. This would be especially noticeable in the breast with global hyperthermia.

Another reason may also be in the amount of neoangiogenesis present in a particular tumor. The biological virulence, or activity, of these tumors is very low. As in the rare tumors found in TH1 or 2 thermograms, the amount of

angiogenesis present is too small to elicit a response to the cold challenge.

*B. Positive challenge response with no malignancy present*

In this scenario the cancer is either too small or homogeneous to be detected with current structural imaging technologies. The images demonstrate a positive response, but the patient will have to be closely monitored to find the cancer at a later date. As previously mentioned, in this study all patients with this reaction presented in the TH3-5 category. Consequently, the cold challenge did not change the clinical follow up.

## 7. DISCUSSION

Should the use of the cold challenge be continued considering that a negative response does not rule out the possibility of neoplasm nor does a positive response guarantee its existence? At this time there is a certain amount of discussion amongst thermologists whether or not the cold challenge should be mandatory with all breast thermograms. From the results of this study, and a review of the literature, there seems to be no evidence to support the continued use of the cold challenge in breast thermography. Personal communication with experts in this field reveals that only a very small minority have continued to use this test. It is felt that individual disputes on this topic should be placed in the context of discussion unless significant data can be provided to support the continued use of this test.

Considering the current state-of-the-art in infrared breast imaging, more studies will need to be performed to provide data that would show a true benefit from using the cold challenge. There is insufficient evidence to warrant its use as a mandated test with all women undergoing breast thermography. Considering the available data, the use of the cold challenge would best be left up to the discretion of the interpreting thermologist. However, it would be incorrect to consider a breast thermogram "substandard" if a cold challenge was not included. Until further studies are performed and ample evidence can be presented to the contrary, a review of the available data indicates that infrared imaging of the breast can be performed excluding the cold challenge without any known loss of sensitivity or specificity in the detection of breast cancers.

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