



Differences in accuracy detecting breast cancer between mammography and stress thermography as determined by breast biopsy
by Bridget Sue Bradshaw

A thesis submitted in partial fulfillment of the requirements for the degree of MASTER IN NURSING
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Abstract:

To determine whether any difference existed in accuracy between mammography and stress thermography in the detection of breast cancer in symptomatic women was the purpose of this study. Therefore, a retrospective review was conducted of 780 records of women who had the stress thermography procedure. This review yielded 72 women with biopsy confirmation of their breast disease. Twenty-four of the subjects had breast malignancies while 48 had benign breast disease.

The mammography procedure performed on 54 subjects yielded 75% sensitivity and 87% specificity to breast cancer with an overall accuracy of 85%. Mammography, tended to be less accurate in detecting cancer in young women. The stress thermography procedure performed on 66 subjects produced a sensitivity of 88%, a specificity of 52% to breast cancer, and an overall accuracy of 65%.

In the subjects with cancer, three out of 24 were negative with the stress thermography while four of 16 were negative with mammography. One cancer was missed by both procedures; the combined procedure specificity was 94%. In the subjects with benign breast disease, five had positive mammograms while 20 had positive stress thermograms. Two subjects were false-positive with both procedures.

The results suggested that neither stress thermography nor mammography discriminated sufficiently to replace biopsy as a diagnostic modality in a disease of so serious a nature with such consequences as breast cancer. Given the retrospective nature of the data, the small sample size, and the current lack of follow-up data on each subject, these results were to be interpreted cautiously.

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DIFFERENCES IN ACCURACY DETECTING BREAST CANCER
BETWEEN MAMMOGRAPHY AND STRESS THERMOGRAPHY
AS DETERMINED BY BREAST BIOPSY

by


BRIDGET SUE BRADSHAW

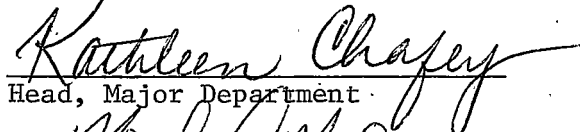
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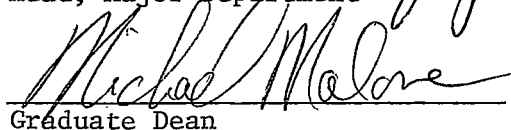
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BSB

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ABSTRACT

To determine whether any difference existed in accuracy between mammography and stress thermography in the detection of breast cancer in symptomatic women was the purpose of this study. Therefore, a retrospective review was conducted of 780 records of women who had the stress thermography procedure. This review yielded 72 women with biopsy confirmation of their breast disease. Twenty-four of the subjects had breast malignancies while 48 had benign breast disease.

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Chapter 1

INTRODUCTION

Breast cancer is among the most dreaded of diseases. Not only is it the major cause of cancer death for women, but the crude incidence rate of cancer of the breast far exceeds that for any other type found in either sex (Cooperman & Esselstyn, 1978; Feig, 1979). In the United States, cancer of the breast is the most frequent malignancy in females with 100,700 new cases and 35,000 deaths annually. Among women who are between 25 and 74 years of age, breast cancer is the leading cause of death from cancer; and in women between 40 and 44 years of age it is the leading cause of all deaths (Graphic Stress Telethermometry System, 1980; Maharry, 1980). Statistics in 1980 indicate that one out of every 11 women, or about 9%, will develop breast cancer in her lifetime (Townsend, 1980).

Over 90% of breast cancer is detected initially by the woman herself (Breast Cancer Digest, 1980; Cooperman & Esselstyn, 1978). A large portion of these women are subjected to further diagnostic examinations before biopsy or mastectomy. Current available methods for aiding in diagnosis are physical examination of the breast, mammography, infrared thermography, and, more recently, stress telethermography. None of these methods, including breast biopsy, are 100% accurate given the nature of the disease.

The use of mammography as a diagnostic technique in evaluating

patients with signs and symptoms of breast disease is well established. At present, mammography is believed to be of benefit in women over the age of 50; but its value in young women is controversial (Azzopardi, 1979; Breast Cancer Digest, 1980; Shapiro, 1977). Mammography is able to detect nonpalpable cancers less than 1 cm. in diameter including about 17% of the clinically occult cancers, but this is primarily restricted to post-menopausal women rather than premenopausal women with denser, more glandular breasts (Cooperman & Esselstyn, 1978; Dodd, 1977; Hicks, Davis, Layton, & Present, 1979; Shapiro, 1977). Fewer occult carcinomas are detected in young age groups (Azzopardi, 1979). A question of radiation hazard to the breast during mammography also exists. Although no direct evidence is available that the low dose of radiation currently used in mammography increases the incidence of breast cancer (Moskowitz, Gartside, Gardilla, de Groot, & Guenther, 1977),* current concerns are based on extrapolation from data on the carcinogenic effects of high doses of radiation. These dose-response relationships are derived from studies which show an increased incidence of breast carcinoma in women who received repeated chest fluoroscopies in tuberculosis clinics, those treated by radiation for post-partum mastitis and other non-neoplastic conditions of the breast, and from atomic bomb survival data (Azzopardi, 1979; Cooperman & Esselstyn, 1978; Dodd, 1977; Feig, 1979; Stark & Way, 1974; Townsend, 1980). The question of radiation hazard to the breast

during mammography is an emotive one and currently the topic of much discussion. The radiation dose required to obtain a good image is greater in younger women than in women over 50, and the sensitivity of the breasts of younger women to radiation may be greater. Since the effects of radiation are cumulative over the years, current guidelines recommend that mammography be used only in patients under 50 years of age who are symptomatic or at high risk of cancer (Breast Cancer Digest, 1980; Cooperman & Esselstyn, 1978; Seidman, 1977; Townsend, 1980).

Thermography of the breast is a newer procedure than mammography and must be developed further before its full potential can be realized. Thermography cannot be considered an adequate prescreening technique to obviate further diagnostic procedures as was once anticipated. Although quantification of thermographic images has been performed, the interpretation depends on subjective analysis of an image and is only as accurate as the degree of expertise of the examiner. Thermographic diagnosis of malignancy has been based on venous pattern and regional temperature variations. Although the constancy and symmetry of the thermal pattern of the breasts has been found to be unchanging over several years (Isard, 1980a, 1980b), it is easily affected by biologically active, but benign, processes such as fibroadenomas, mastitis, medications, stage in ovulatory cycle, and pregnancy. The thermogram also is influenced by the growth rate of a

tumor. Early cancer and rapid-growing cancers may give rise to strong hyperthermias, whereas advanced carcinomas or small carcinomas with unfavorable heat transfer conditions from the tumor to the skin do not give rise to thermographic abnormalities (Gautherie, 1980). As a result, conventional thermography has a false-positive rate of 20-25% and a false-negative rate of 20-30% (Jurist & Myers, 1980). Thermography has fallen into disfavor with the Breast Cancer Detection Demonstration Projects, and the current recommendation for its use is in conjunction with physical examination and mammography to reinforce diagnosis (Dodd, 1977), as a prognostic indicator (women with cancer who have normal thermograms have higher survival rates than those with abnormal thermograms), and as an interim screening tool in young women. Even though thermography is an entirely safe, noninvasive method, its current limitations preclude its use as an isolated diagnostic technique.

Stress thermography, or Graphic Stress Telethermometry (GST), is a variant of thermography which has been under investigation since 1975; but few published studies of this technique are available. No published long-term studies of this procedure and no repetitive studies of the test to determine whether changes in the scores indicate changes in breast pathology exist. Stress thermography is based on two principles. First, increased thermal emission occurs when blood vessels are located near the body surface and when certain

organs have a significant vascularity near the body surface. It also occurs over areas of high metabolic activity such as is found with malignant tumors, infection, or injury which exceeds that of the surrounding normal tissue. Second, temperature measurements after a generalized vasoconstrictive (ice water) stress show that abnormal areas, such as in cancer, do not exhibit the same reduction in temperature from vasoconstriction as do normal areas. This observation presumably is a result of the vessels in the tumor not constricting to the same degree as those in normal tissue in response to the same vasoconstriction stimulus (Snyder, Watson, & Cruz, 1979). The use of the ice-water stress is thought to increase diagnostic sensitivity and specificity. *Snyder et al. (1979) report 37% false-positives and 7% false-negatives, and Jurist and Myers (1980) report a false-positive rate of 28% and a false-negative rate of 10%.

* To note that several factors can affect results such as the ambient room temperature, relaxation of the patient, as well as those variables mentioned under thermography, is important. One researcher even reports that a full bladder can alter the readings (Snyder et al., 1979). Hopefully, however, the physiological contrast between pre- and post-vasoconstrictive stress as well as the objective evaluation offered by computer analysis will more than offset these problems.

The continued evaluation of stress thermography as a diagnostic procedure in breast cancer is essential since it is noninvasive, does

not use ionizing radiation, and "offers the advantages of an objective thermography reading and the potential discriminatory factor of insensitivity of tumor vessels to normal thermo-regulatory mechanisms"

(Snyder et al., 1979, p. 201). The problem centers around the fact that no current diagnostic test exists that is 100% reliable in indicating either "cancer" or "no cancer."

Review of the Literature

Normal human breasts are composed of three types of body tissue: connective, epithelial, and fat. Arranged within each breast are 15-20 lobes or segments which converge on the nipple in a radial fashion. These lobes are subdivided into lobules and end in milk-producing bulbs called acini (ductals). The lobes, lobules, and acini are connected to the nipple by a complex network of ducts that enlarge as they enter the nipple. These enlargements are called the lactiferous sinuses. Though no externally visible or palpable anatomical separation of the segments exists, their ductal and lobular systems are distinct (Azzopardi, 1979; Breast Cancer Digest, 1980).

The lobules are composed of dense glandular tissue and are held together by connective tissues, blood vessels, and by the lactiferous ductules which unite to form the main duct. The lobes are covered and loosely connected by fibrous tissue, but the intervals between lobes are occupied by fatty tissue. A subcutaneous layer of fatty tissue

envelops the breast except under the nipple and areola (Merrill, 1975). Figure 1 shows the anatomical parts of the breast.

Breast cancer begins with neoplastic proliferation of cells in the mammary ducts.

Breast cancer is a disease of the mammary epithelium. The entirety of the mammary system is embryologically derived from ectodermal down growths into the mammary fat pad, thus the ducts and their terminal expansions are . . . epithelial surface (Gallagher, 1980, p. 905).

Carcinoma may affect any part of the ductal system, but evidence shows that the smaller ducts are more often involved than the larger ducts. Lobules also may be affected by either carcinoma or epitheliosis, but more commonly by carcinoma (Azzopardi, 1979).

Figure 2, page 9, illustrates the sites affected by breast disease.

Cancers are classified by the specific tissue from which they originate. Most breast cancers arise in the glandular tissue and are called adenocarcinomas; adeno refers to glandular tissue; carcinomas arise from epithelial tissue. The earliest recognizable breast cancers are noninvasive intraductal carcinoma and lobular carcinoma in situ. Once neoplastic transformation is established, growth proceeds within the epithelium of origin. As the neoplastic cells proliferate in the lumen of the ducts, they tend to break through the basement membrane and invade periductal tissues where they incite a proliferation reaction (Brennan, 1973). To this point the evolution of breast carcinoma is a fairly uniform process. Little is known about

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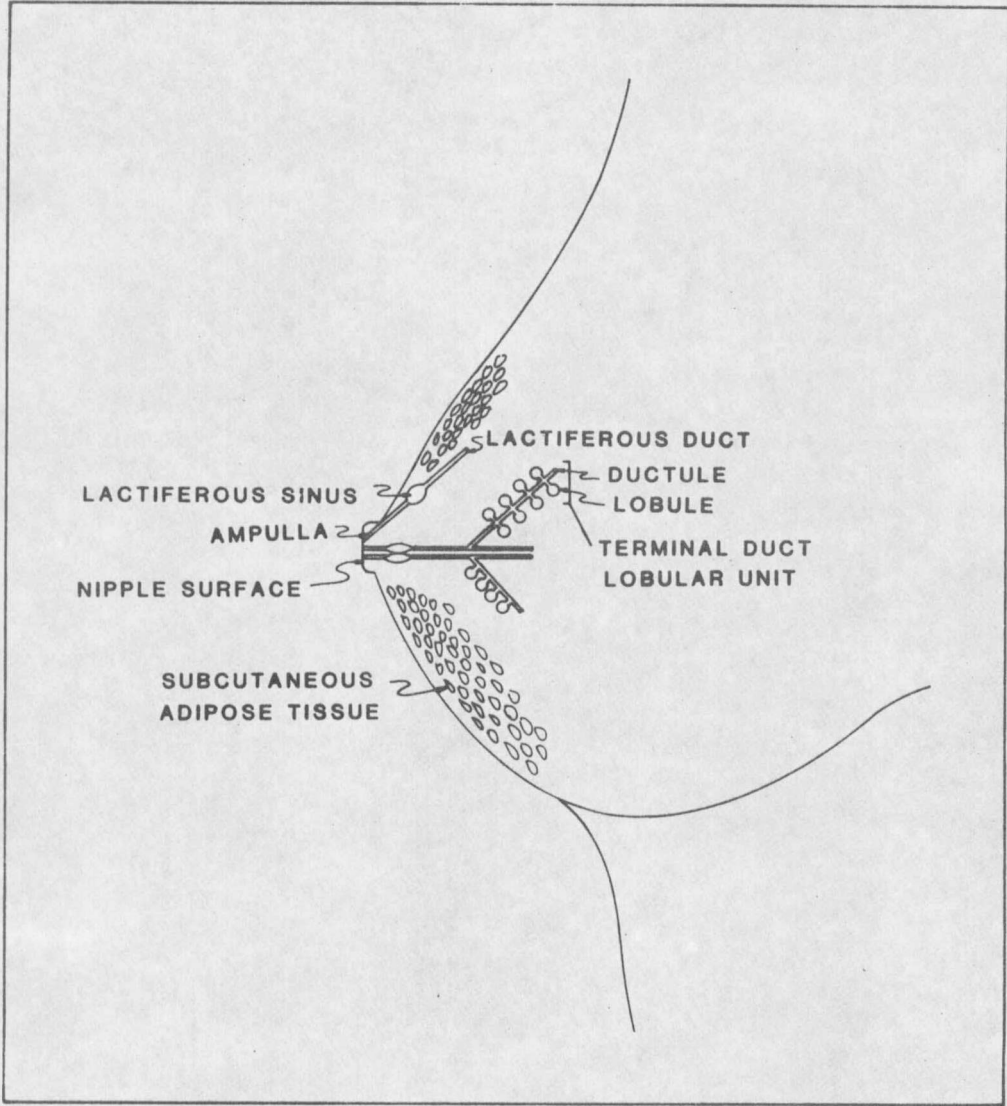


Figure 1. Anatomical parts of the breast. (Adapted from Azzopardi, 1979, p. 9).

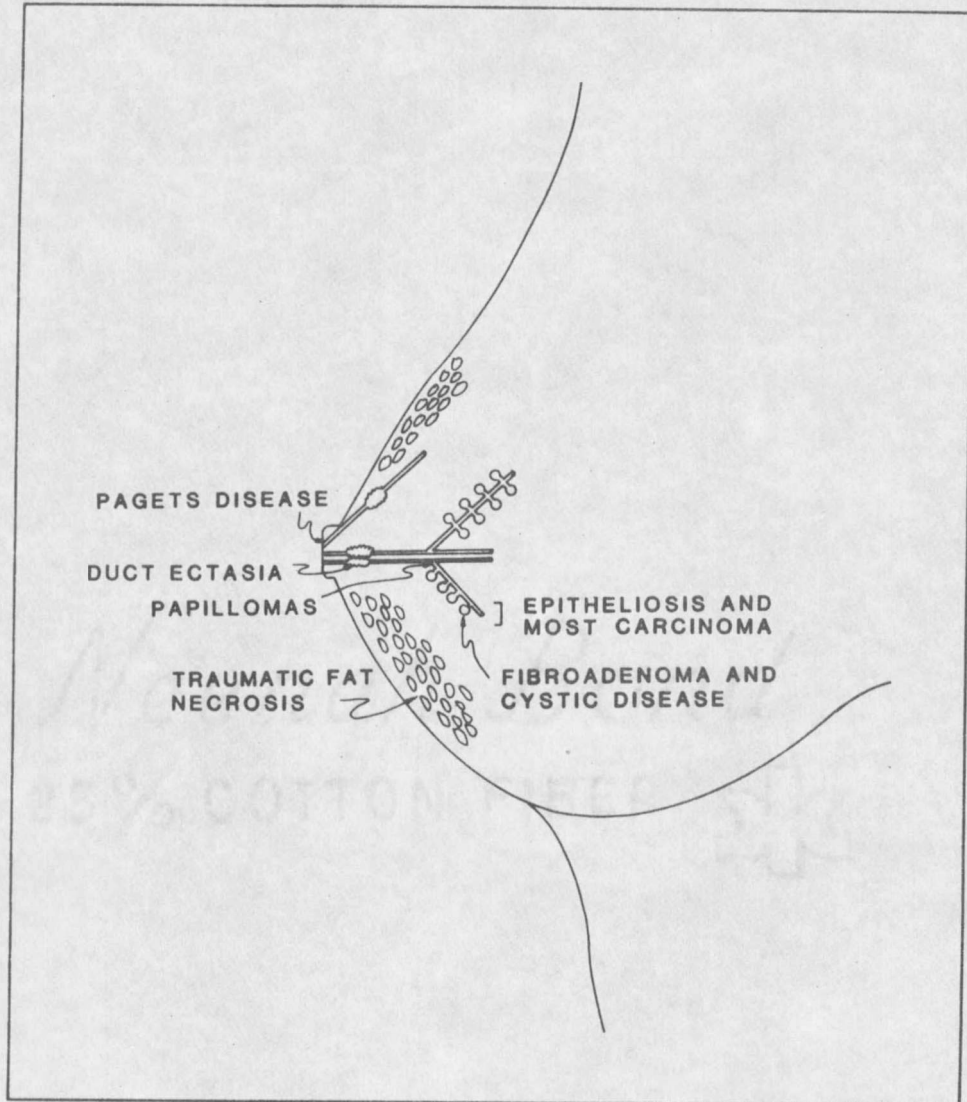


Figure 2. Sites affected by breast disease.
(Adapted from Azzopardi, 1979, p. 10).

the time required for the progression of breast carcinoma from epithelial inception to mass formation; but, in most cases, several years are involved.

As the neoplasm grows and begins to become invasive, diversity begins to appear. Rapidly dividing, highly anaplastic cells are scattered in small groups and rows, and form multinodular masses by coalescence. These undifferentiated cells spread into and along periductal lymphatics, veins, nerves, and tissue planes. Metastasis to the lymphatics may be abundant even when the primary lesion is very small. Less active cells ooze through duct walls into fibrotic periductal tissue and produce stellate masses. The gross texture of the breast may be modified by metaplasia, accumulation of cell products, or reticuloendothelial cell proliferation related to host response.

As the cancer invades the breast parenchyma, it may extend toward the areola and also along the deep lymphatics to the thoracic wall. The fibrosis accompanying cancerous invasion induces contractions along the fascial structures and planes of the breast. In advanced cancers, these fix the neoplasm to the skin and chest wall, retract the nipple, and produce skin dimpling. Lymphatic permeation causes restriction of lymph flow and skin edema. This condition often is associated with superficial vasodilatation which results in heat and redness over the lesion (Brennan, 1973; Gallagher, 1980).

The continued growth of the tumor cells stimulates angiogenesis from the vascular network of the host tissue. This condition results in local proliferation of blood vessels and permits the "feeding" of the growing tumor cell mass (Guillino, 1980; Isselbacher, Adams, Braunwald, Petersdorf, & Wilson, 1980). The tumor cell mass is metabolically active; consequently, local changes in temperature are caused by metabolic heat production and reduction in pH by release of acid catabolites (Gautherie, 1980). Blood which leaves the metabolically active neoplasm is warmer than that from normal breast tissue (Brennan, 1973). Further tumor development is diverse. One type of breast cancer fills the larger mammary ducts with solid cords of tumor cells. Other types may grow in a circumscribed rather than a stellate form or as a globular, well-delineated mass.

A single mutant tumor cell repeatedly divides, as do its descendants, thereby establishing a colony. After a certain number of divisions, or doublings, the neoplasm attains such a size that it is discovered. One centimeter is stated generally to be the smallest diameter at which tumors are detected clinically (Cooperman & Esselstyn, 1978). This measurement roughly equals one billion cells or 30 doubling passages (Breast Cancer Digest, 1980; Kirch and Klein, 1978; Townsend, 1980). Estimations reveal that the average doubling time of breast cancer is four months; however, doubling times measured by mammography showed these times to range from 23-209 days. Tumor cells

could have been present for 2-17 years before discovery (Baum, 1976; Breast Cancer Digest, 1980; Cooperman & Esselstyn, 1978; Gullino, 1977; Hutter, 1976; Kirch & Klein, 1978).

Breast tissue is a tissue that is far from static.

Under the influence of a number of stimuli (and particularly the endocrine system), it grows rapidly around the time of menarche, fluctuates with the menstrual cycle throughout reproductive life, undergoes physiologic hyperplasia and regression during pregnancy, lactation and the puerperium, and atrophies gradually after menopause. In such an active cell population opportunities for the genetic mutation that produces cells capable of neoplastic proliferation must be abundant (Gallagher, 1980, p. 905).

This concept leads to the belief that the initial event in the development of breast cancer often may take place premenopausally, even though clinical manifestation is long delayed. Such an idea is supported by studies of growth rates of human mammary carcinomas and by epidemiologic data that have shown an increase in incidence in women under 50, an increase that has paralleled the intensification of detection efforts, and the increasing sensitivity of detection techniques (Copeland, 1978; Gallagher, 1980).

Mammography and Thermography

Most prominent among the ancillary methods of examining the breast for cancer are mammography and thermography. In contrast to physical examination of the breast, they have the important attribute

of transforming physical data directly into a permanent image that can serve as a basis for serial comparison. Mammography depends upon differential radiographic density of tissues for image contrast. Pathologic conditions which lack this feature remain undetected. The detection of abnormal temperature is the basis of thermography. Conditions with an undistinguished metabolic rate or those that fail to transfer surplus heat to the surface of the breast remain thermographically obscure. While both modalities have demonstrated the capacity to detect abnormalities that include neoplasia, neither technique is specific for cancer.

Mammography and thermography do not have equal status at present. The vast experience with mammography has established this detection method as a useful addition to clinical practice. Thermography is still in evolutionary stages as a clinical tool and should be considered as largely investigational (Blackwell & Farrell, 1979). In the following sections the merits and the liabilities of mammography and thermography are discussed along with the addition of stress thermography which is a modification of traditional thermography that is still in investigational stages.

Mammography

Mammography is a process of x-raying the breast. All mammographic examinations are performed with an x-ray machine which gives

views of the breast as either a negative image on film or as a positive image on paper. The technique utilizes low-energy x-rays that enhance soft tissue detail due to the differential radiation absorption by fat and fibroglandular tissue. Generally, two views of each breast are obtained: one craniocaudal view and one mediolateral view. When a lesion is seen, it can be localized to a specific quadrant of the breast. The images must be of excellent quality to allow for subtle diagnostic signs to be visualized. The entire breast must be seen from the nipple to the chest wall and from the axilla to the inframammary crease.

"The radiodensity of the breast varies according to the amount of fibroglandular tissue and fat. The contrast required for tissue differentialization depends upon the amount of fatty (radioparent) tissue occupying the interlobular spaces" (Merrill, 1975, p. 822). The nulliparous and the premenopausal breasts are more glandular and radiopaque than are the parous, menopausal, and postmenopausal breasts. The young breast is composed largely of connective tissue and only a small amount of fat. Because of this condition, it casts a homogenous radiographic shadow with little or no tissue differentiation. To project the young breast on film is difficult because of the scant fatty tissue and firm tone of the suspensory ligaments which hold the breast close to the chest wall. Breasts become atrophic with aging. The dense glandular tissue is replaced with

enough fatty infiltration to afford intrastructural detail. After menopause, the glandular elements of breast tissue atrophy and suspensory ligament tone deteriorates, and the breast becomes pendulous. This aids in complete visualization of breast tissue. Abnormalities are more likely to be evident in the partially or completely atrophic breast and may be less evident or even entirely obscured in the more radiodense breast. Mammography is of little, if any, value in screening asymptomatic young adult. It is more reliable and useful in women over 35 years of age (Blackwell & Farrell, 1979; Merrill, 1975).

Mammography may demonstrate many clinically occult cancers at a potentially curable stage (Dodd, 1977), but it does have certain limitations. Not all cancers, including some clinically obvious lesions, may be seen with mammography. They may be missed because of:

- * 1. Poor x-ray technique
2. Not being included on the film because they are too close to the chest wall or in the axillary tail of the breast
3. Being obscured by dense overlying breast tissue
4. Being misinterpreted or simply not recognized

There are two types of abnormalities that are used to differentiate breast tissue; these are primary and secondary. The primary abnormalities that assist in the differential diagnosis of lesions

are:

1. masses
2. calcifications
3. distorted architecture
4. abnormal or dilated ducts (Blackwell & Farrell, 1979; Snyder et al., 1979; Wolfe, 1977a, 1977b)

Benign masses such as cysts or fibroadenomas are round or slightly oval-shaped with smooth well-defined margins. Malignant masses are classically irregular, knobby, or stellate in shape and have spiculated or ill-defined margins. The spiculated border is characteristic of malignant tumors (Azzopardi, 1979; Blackwell & Farrell, 1979). Occasionally, a carcinoma may stimulate a benign density which makes important the comparison of the image of one breast with the opposite breast. Any asymmetry or nonspecific density seen in one breast that is not seen in a similar location in the opposite is suspicious.

Although calcifications are radiographically present in some benign breast diseases, a specific pattern of calcification that can be diagnosed as being in malignant tumor with a high degree of confidence is possible. This calcification pattern is characterized by the presence of multiple punctate calcifications resembling fine grains of sand and generally clustered in a region of the breast even without the existence of a palpable tumor. Any group of five or more

of these calcifications should be regarded as suspicious of malignancy. Punctate calcifications are an important sign of malignancy and are the most frequent indicator of clinically occult carcinomas (Azzopardi, 1979; Blackwell & Farrell, 1979; Leborgne, 1951; Snyder, 1980; Wolfe, 1977b).

Architectural changes typically form small "star-burst," "puckered," or "pinwheel" patterns, or may appear like a "purse string" has been pulled retracting the breast tissue toward a small focus. This radiographic change can occur before a mass is seen (Blackwell & Farrell, 1979; Wolfe, 1977a).

Normally individual ducts are not demonstrated by mammography. Suspicion of malignancy is aroused by a single duct or a segment of breast with prominent linear duct-like structures. Ductal dilatation may occur in some benign breast disease, but ducts that become packed with carcinoma also may become prominent; therefore, masses associated with a prominent duct pattern are more suspect (Azzopardi, 1979; Blackwell & Farrell, 1979; Wolfe, 1977a).

The secondary signs of breast cancer are nonspecific alone, but when found in conjunction with one or more primary signs, give more clues in the differential diagnosis of cancer. *The secondary signs are increased vascularity, skin thickening, nipple retraction, and enlarged axillary nodes. Increased vascularity is not considered as a specific sign when differentiating benign from malignant disease.

When focal and generalized increases in venous diameter of 50% or more relative to comparable veins in the opposite breast are present, the possibility of cancer is considered. Skin thickening may or may not include skin retraction and is usually a late sign. Skin thickening over an area of density or distortion would be considered as a presumptive sign of carcinoma. Nipple retraction may result from benign disease or malignant disease, and when present in the subareolar region, is screened for cause. Large axillary nodes are important only if the nodes are greater than 2.5 cm. in diameter, numerous, and homogenous in density. Most other types of nodes observed on the mammogram are normal and not significant (Azzopardi, 1979; Blackwell & Farrell, 1979; Wolfe, 1977a).

Mammography of the symptomatic woman is indicated because of the varied expertise of physicians in physical examination of the breast and the desire to detect small lesions. As a screening tool, mammography can detect nonpalpable cancers less than 1 cm. in diameter while they are still localized and potentially curable (Cooperman & Esselstyn, 1978; Dodd, 1977; Hicks et al., 1979).

The reported accuracy of mammography ranges from 66-98% (see Table 18-3, Azzopardi, 1979, p. 443, for complete data; Lapayowker, Salen, Ziskin, & Rosemond, 1973). The accuracy that can be achieved depends on the method of selection of the population that is examined, the procedure used, and the experience and expertise of the

interpreter. To obtain a reasonable balance between the percentages of false-negative and false-positive reports is important in order to avoid subjecting large numbers of women to unnecessary biopsies and to avoid delaying needed treatment in a patient with breast cancer.

The mammographic results from the Breast Cancer Detection Demonstration Projects (BCDDP) report cancer detection rates of 1.6 and 19.3 per 1000 women (see Table 18-3, Azzopardi, 1979, p. 454, for complete data) and an overall accuracy of 93%, a false-negative rate of 12.8% and a false-positive rate of 14.9% (Azzopardi, 1979; Dodd, 1977), although some studies report false-negative rates of 21% to 27% (Maharry, 1980; Niloff & Sheiner, 1981). Mammography picked up 17% of the clinically occult cancers (Dodd, 1977). The false-positive rates are highest in those series with highest true-positive rates.

Benign lesions which can be misinterpreted as carcinoma include:

1. the cystic disease complex, particularly sclerosis
adenosis
2. duct ectasia
3. postoperative scarring
4. skin lesions
5. breast abscesses
6. fat necrosis

Failure to identify a malignant tumor may occur because the

lesion is either not visualized or mistaken for a benign lesion. The density of the breast surrounding the lesion or an adjacent benign lesion may obscure the carcinoma. This happens most frequently in young women with small, dense breasts or in the presence of extensive fibrocystic disease. Diffusely infiltrated tumors may produce little density and may be missed. In situ carcinomas often produce little density and will not be visualized unless calcifications are present. Occasionally a peripheral lesion or one close to the chest wall may be missed by technical errors (Azzopardi, 1979).

Since mammography is not 100% accurate and the interpretation is subjective, it does not replace other diagnostic modalities in detection of breast cancer. Negative findings in one modality should not preempt positive findings in another (Cooperman & Esselstyn, 1978; Townsend, 1980).

Thermography

The term thermography is used to designate the process of recording temperature images of the surfaces of objects under study and should not be confused with conventional infrared photography. Thermography is a passive process and depends entirely upon the fact that all objects whose temperatures are above absolute zero emit infrared energy as a function of their temperatures and absorb some portion of the energy emitted by every other object in the

line-of-sight environment as a function of their temperatures.

For example, the temperature of a person's hands and face is about 32°C. rather than 37°C., the normal core body temperature. The reduced temperatures represent equilibrium conditions between core and environmental temperatures. Since the body core is a higher temperature than the environment, skin emits more infrared radiation than it absorbs and assumes a somewhat reduced equilibrium temperature.

Normal thermography is concerned with this self-emitted energy. For a given complex object in a given environment, a certain normal thermal pattern will exist. If any parts of the object are warmer or cooler than normal, a correspondingly abnormal thermal pattern will exist. In forming the thermal images, the infrared-sensitive instrument records the amounts of emitted energy from the various parts of the object and is not at all concerned with the sources of the heat or infrared energy.

Clinically it appears that thermal abnormalities of the order of $\pm 1^{\circ}\text{C}$. may be significant. The human body normally exhibits a high degree of right-left thermal symmetry. If a person is placed in a cool, draft-free room, the skin quickly will come to thermal equilibrium with the room, and the thermal patterns which exist on the skin will be characteristic of the individual. The patterns will be largely determined by localized vascularities and by body heat conducted to the skin from discrete areas deep within the body

(Barnes, 1967).

Medical thermography, and in particular breast thermography, started in 1956 in Canada when Lawson (1956) reported an area of heat in a breast harboring cancer. His article stated that, "one of the important biological characteristics of malignant tumors is the increased rate of growth as compared to that of the surrounding tissue. The malignant propensities are directly related to the speed of cell division" (Lawson, 1956, p. 309). This, in turn, is reflected by local metabolism which is supported adequately by increased blood and lymphatic vascularity (Breast Cancer Digest, 1980; Guillino, 1977; Lawson, 1956). Rapidly growing tumors induce an increased blood supply giving increased venous drainage and a higher surface temperature. The elevated temperatures thus result in increased infrared radiation from the skin (Barash, Pasternak, Venet, & Wolfe, 1973; Breast Cancer Digest, 1980; Gautherie, 1980; Gautherie & Gros, 1976; Guillino, 1980; Isard, 1972; Lapayowker et al., 1973).

In breast thermography the main steps involved in the formation of the thermographic signal are important.

* These steps are:

1. Heat is generated by cancer tissue as a result of the increased metabolism of its cells. This metabolic heat is transferred from the tumor to the surrounding tissue by conduction and capillary convection.

2. This heat is transported within the surrounding tissues, especially to the skin, principally by blood convection by the large vessels. This gives rise to a local increase in skin temperature.
3. Metabolites of cancer growth produce vascular changes, morphological as well as dynamic, giving rise to modification of the cutaneous thermal pattern.
4. The breast exchanges heat with the environment by conduction, convection, and radiation. Thus, part of the "cancer heat" is radiated into the environment as infrared radiation in accordance with Planck's Law (the quantity of heat radiated is a function of emissivity and temperature of the cutaneous surfaces). Infrared thermography is based on measurements of this infrared energy (Gautherie & Gros, 1976; Stolwijk, 1980).

Figure 3 illustrates the formation of the thermographic signal.

A person having a breast thermogram first equilibrates with the surrounding environment by disrobing to the waist with arms above the head in a draft-free room held to 20-21° C. After 10-15 minutes, the breasts are scanned by an infrared detector. The detector displays skin surface temperatures which then may be photographed (Breast Cancer Digest, 1980; Gautherie & Gros, 1976; Isard, Becker, Shilo, & Ostrum, 1972). "The person has to be thermally adapted in order to

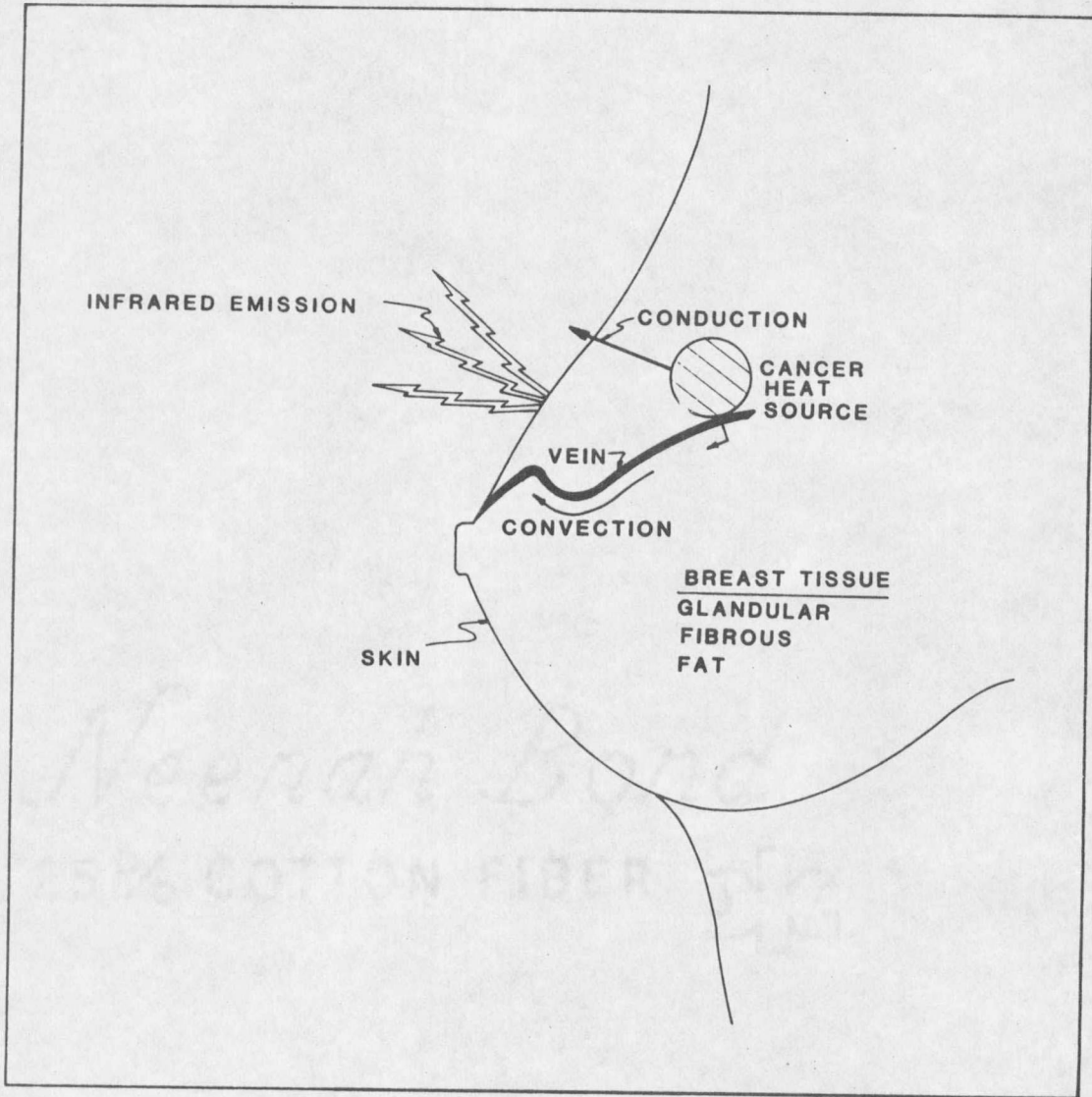


Figure 3. Formation of the thermographic signal.

take advantage of the differential cooling rates of the normal and pathological skin areas called physiopathological contrast enhancement" (Gautherie & Gros, 1976, p. 135).

Many investigators have contributed to the classification of the normal and abnormal female breast thermographic patterns. In the normal breast the cutaneous thermal pattern is remarkably constant in any given patient (Dodd, 1977; Gautherie & Gros, 1976; Isard, 1980a, 1980b; Isard et al., 1972).

Seventy-three percent of normal healthy females have unchanging patterns, 19% have some change, and 9% have thermal changes that could be due to benign disease, hormonal intake or oral contraceptives. The breasts have increased thermal changes during ovulation, lactation and pregnancy and are coldest following menstruation (Blackwell & Farrell, 1979, p. 135).

Isard (1980a) reported: "The constancy of a thermal pattern is unchanging, and observations over a decade and longer have shown that a woman's thermal pattern never changes, provided that her breasts remain normal" (p. 10).

Another hallmark of the normal thermogram is symmetry (Isard, 1976, 1980; Isard et al., 1973). The thermal pattern is not identical in the two breasts but there is approximate bilateral symmetry. The two parameters of increased heat emission and asymmetry are the basis for detecting and evaluating breast abnormalities.

Thermographic diagnosis have been based on venous pattern (which will not be discussed in this study) and differences in

temperature. Several investigators have defined the presence of malignant tumors associated with increased temperatures relative to surrounding or contralateral tissue (Barash et al., 1973; Blackwell & Farrell, 1979; Guillino, 1980). They have indicated that about one third of the cancers are 1-2° C. hotter, another third 2-3°C., and a final third are over 3° C. hotter than the corresponding contralateral areas, while 10% of the cancers are not more than 1°C. warmer than the corresponding contralateral area (Barash et al., 1973). From a diagnostic point of view, the essence of thermography lies in the detection of differences in the bilateral thermal symmetry, corresponding to localized or generalized increases in temperature level since temperature and thermal conductivity of cancerous tissues are higher than that of healthy tissues (Barash et al., 1973; Gautherie, 1980; Guillino, 1980; Isard, 1976; Isard et al., 1972). Thermal asymmetry may be apparent as hyperthermia of either the entire breast, a peri-areolar hyperthermia, or focal hot spot (Blackwell & Farrell, 1979; Isard, 1980a).

Thermography is not a totally definitive procedure. Benign, but biologically active processes, may produce positive thermograms (Cooperman & Esselstyn, 1978; Dodd, 1977). Thermography is, therefore, not a specific indicator of cancer, but it does alert to the possibility of the disease. It exploits indirect thermal

consequences of biological processes and does not provide etiological information.

The initial enthusiasm for breast thermography has waned. Since 1973 data pertinent to the overall accuracy of thermography have accumulated from 27 Breast Cancer Detection Demonstration Programs in the United States as well as from England and other European countries (Isard, 1980b). Reported true-positive rates vary from 75% to 85%, and false-positive rates from 15% to 40% depending upon the population studied and criteria of the interpreter (Dodd, 1977; Isard, 1980a; Libshitz, 1977). Unfortunately, the false-negative rate, as high as 49.5% in one study (Byrd, 1977), has been reported to be unacceptably high; and when compared to histological results, indicates that perhaps 15%-25% of cancers are thermographically inactive (Blackwell & Farrell, 1979). Although very small tumors occasionally will produce a positive thermogram, the thermal response would seem to be a function of the size as well as the biological nature of the tumor. Varying metabolic activity of breast cancers may account for variations in their thermographic detectability (Blackwell & Farrell, 1979; Dodd, 1977; Gautherie, 1980).

Currently, thermography is being used as an ancillary technique in combination with physical examination and mammography to enhance yields in screening programs for detection of early breast cancer in healthy, asymptomatic women (Blackwell & Farrell, 1979; Stark & Way,

1974). Breast thermography is not recommended as an isolated technique for diagnostic purposes, but may prove useful when physical findings are questionable and the mammogram is not decisive (Cooperman & Esselstyn, 1978; Isard, 1980a). It is also useful in follow-up examinations of patients with primary or recurrent cancer, as an indicator for mirror-image biopsy, and as a tool for breast examination of women under 50 years of age if the concern of radiation hazard continues (Blackwell & Farrell, 1979).

Stress Thermography

Stress thermography is also known as Graphic Stress Telethermometry (GST). This experimental method can be used in conjunction with physical examination and mammography as a breast cancer risk indicator. It is based on the same biological principles as conventional thermography, that any warm spot in the breast may indicate the presence of an abnormal condition, especially cancer. It differs from conventional thermography in that an image display of the converted infrared signal is not used. Instead the infrared detector or probe is connected directly to a computer for numerical processing.

In 1975 Schwamm of West Germany developed a system for thermography using an infrared probe (Thermophil M202). He coupled this with a stress test to cause cutaneous vasoconstriction, first using injections or topical application of Novocaine and later substituting

ice water. The rationale for the ice-water stress procedure is that certain parts of the body, namely the volar surfaces of the hands, feet, lips, nose and ears, serve as sensor regions for afferent signals to the thermoregulatory areas in the posterior hypothalamus and spinal cord (Guyton, 1980). The principal method of regulating heat loss is by varying the volume of blood flowing to the skin. When a need for conservation of heat exists, adrenergic (norepinephrine) autonomic stimuli cause cutaneous vasoconstriction and a sharp reduction to the blood flow to the surface. This in effect transforms the skin and subcutaneous tissue into layers of insulation (Isselbacher et al., 1980). The skin is an effective radiator system, and the flow of blood to the skin is a most effective mechanism of heat transfer from the body core to the skin. If blood flow from the internal structures to the skin is depressed, internally produced heat is lost to the exterior, more by conduction through the insulator tissues of the skin and subcutaneous areas, and less by circulatory convection (Guyton, 1980). The skin cools as a result. Abnormal areas such as those involved in breast cancer do not show this same temperature reduction following vasoconstrictive stress, presumably because the blood vessels in the tumor do not respond to the same degree as do those in normal tissue under the same stimulation (Schwamm, 1975; Snyder et al., 1979). Measurement of infrared radiation before and after the ice-water stress demonstrates a failure to

cool around areas that harbor a biologically active process such as cancer.

Graphic stress telethermometry was developed by Phillips (Snyder et al., 1979) as an extension of Schwamm's work. It utilizes the infrared probe, stress temperature differential, and a computer program to assign a score, placing the patient into a low, intermediate, or high-risk category (Snyder et al., 1979). The procedure followed is to have the subject disrobe to the waist and equilibrate with the environment for 15 minutes. The infrared probe then is used to measure the forehead temperature to provide an individualized reference. The probe then is passed over nine regions of each breast to measure the peak temperature emission from each region. After the baseline thermographic results are obtained, the subject then places the hands into ice water for 15 seconds. Physiological reaction to the stress causes peripheral vasoconstriction and a subsequent drop in temperature for all segments of normal breasts. A second set of temperature measurements then is obtained in precisely the same manner as performed prior to the induced vasoconstriction stress. A comparison of temperatures is made pre- and post-stress, noting those areas, either contralaterally or ipsilaterally, that showed no response to the stress. If no response or asymmetry is shown in any segment or segments, an abnormality is suspected.

To date few published studies have been done regarding this

detection modality. The results from the original study by Snyder, Watson, and Cruz (1978) at the Memorial Sloan-Kettering Institute showed that, of 127 patients undergoing biopsy that had stress telethermometry prior to surgery, 66% had biopsy-proven cancer, and according to the scoring method devised by these researchers, all had increased risk scores. A subsequent publication in 1979 by Snyder on 315 symptomatic women with biopsy-proven diagnoses showed that 93% of the women with cancer were detected (true-positives), 7% were not (false-negatives). Snyder, Watson, and Cruz (1979) found, however, that only when scores were greater than 70 (high-risk 62% of the sample) could it be said that a patient was more likely to have cancer than an atypical or benign condition. Size of the tumor seemed to make little difference in this study (Snyder et al., 1979).

In 1980 Jurist and Myers published a study of 659 subjects which included 10 biopsy-proven cancers. In this study nine out of 10 breast cancers were determined correctly using an algorithm which may be adjusted as the number of patients increases. The most significant parameter for discriminating cancerous from normal breasts was the asymmetry measurement of the breasts following the ice-water stress (Jurist & Myers, 1980).

In a follow-up study using the same algorithm, Jurist and Myers found false-negatives in two out of 19 breast cancers with an associated false-positive rate of 30% in 140 normal women (Jurist &

Myers, 1981). Their data then were evaluated blindly with an algorithm developed at another facility. This algorithm yielded a false-positive rate of 17.3% with a false-negative rate of 11% (Jurist & Myers, 1981). Both Jurist and Myers (1980) and Snyder et al. (1979) concluded that stress thermography was worthy of further investigation.

Two studies have been published recently which describe clinical application of the test (Brooks, 1979; Morese, Sullivan, Dugan, & Gaudio, 1979). Both studies are preliminary, with low biopsy confirmation (Brooks, 1% and Morese et al., 2%), but both studies enthusiastically support the use of the GST tool and recommend additional study of the instrument. One additional study by Brooks (Brooks, Gart, Heldford, Margolin, & Allen, 1981) utilizes the stress thermography procedure in evaluating the effect of caffeine restriction on fibrocystic breast disease. The study is significant as it is a longitudinal study over a six-month period objectively monitoring changes in the subjects' scores with the prescribed treatment regime.

Purpose of the Study

The review of current literature about mammography, stress thermography, and conventional thermography reveals that mammography is the most accurate and reliable method of detecting breast cancer as

proven by biopsy. The use of conventional thermography is on the decline because of its high false-positive and false-negative rates. Stress thermometry is a new procedure, and its usefulness has been established tentatively by limited research. This study is intended to answer the following question: Is there a difference in accuracy in differentiating benign from malignant breast disease in symptomatic women between stress thermometry and mammography as determined by breast biopsy? It is assumed that stress thermometry ultimately will prove to be at least as accurate as mammography in detecting malignant breast disease given the constancy and symmetry of each individual's thermographic pattern and the employment of objective numerical scores rather than the subjective criteria used for mammographic interpretation.

Chapter 2

MATERIAL AND METHODS

Subjects

The subjects in this investigation were selected from 780 women who had participated in stress thermography studies which were conducted in Jurist's laboratory in Billings, Montana. The subjects were included in the investigation if they had experienced a biopsy for breast pathology within a year of the stress thermogram and mammogram studies. This group of women was a purposive sample selected because the experiment was to test not only the sensitivity but also the specificity of the stress telethermometry tool and mammogram for the presence of cancer in symptomatic women. All of the women who participated in the study had demonstrated symptomatic breast disease; however, not all of the women had experienced both of the diagnostic modalities.

The subjects were selected without reference to age, to race, or to ethnic background but solely on the fact that they had undergone biopsy confirmation of their disease. The range was from 17 years of age to 86 years of age. The mean age for the group was 48 years. The total number of participants in the investigation was 72. The breakdown by age group is noted in Table 1.

Table 1

Age Distribution of Subjects

Subjects	Biopsy Proven		
	Malignant	Benign	Total
Under 40 years	2	22	24
40-60 years	10	24	34
Over 60 years	12	2	14
Mean age	61	42	48
		Total	72

Procedure

The charts of the 780 women who had the stress thermography procedure between June, 1978, and June, 1981, were reviewed for indication of mammography procedure and breast biopsy. From this group, subjects who had biopsy confirmation of their breast disease were selected. As a follow-up, letters in which permission was requested to investigate their medical records were sent to two Billings hospitals (see Appendix A and Appendix B). Within a week permission was granted (see Appendix C and Appendix D).

The mammography procedure needed to have been performed within one year of the stress thermography procedure and both needed

to be performed within one year prior to biopsy. The biopsy results were reviewed for each subject, and the diagnosis of benign or malignant disease was established. Following this, the mammography results were reviewed. A diagnosis of benign disease included such diagnoses as mammary dysplasia, benign adenoma, fibrocystic disease, and no evidence of malignant disease. If the mammogram was interpreted as slightly suspicious with recommendation for follow-up mammogram in 3-6 months and no recommendation for biopsy, or interpreted as no evidence of malignant disease, it was considered negative. If the mammogram was interpreted as suspicious or included a recommendation for biopsy, or a positive diagnosis of malignancy, it was considered to be positive.

The algorithm devised by Jurist and Myers (1980), which is adjusted as the numbers of patients change, was used to discriminate malignant from nonmalignant scores. Zero (0) is designated as the discriminant threshold between malignant and normal thermograms. Those women having scores above zero were considered to have positive stress thermogram and those having scores below zero were considered to be negative.

The two diagnostic modalities of stress thermography and mammography were evaluated by detection sensitivity, specificity, and overall accuracy. They are:

1. Detection sensitivity (true-positive rate) refers to the

probability of a test being called positive when malignancy is present. In this study it represents the percentage of positive test results when malignancy is proven by biopsy.

2. Detection specificity (true-negative rate) is the probability of a test being called normal or benign given the absence of malignancy. It represents the percentage of negative test results when biopsy revealed a benign lesion.
3. Overall accuracy represents the probability of obtaining a correct test result. It is the sum of true-positives and true-negatives divided by the total number of biopsy-proven cases. Detection error rates, false-positive and false-negative, are correlated also with histological diagnosis. Appendix E shows the table of formulas used.

Chapter 3

RESULTS

A review of 780 stress thermograms done in Jurist's laboratory revealed that 82 women had breast biopsies within a year of their stress thermograms. One subject had two stress thermography procedures with corresponding biopsies for a total of 83 procedures. Nine subjects had no record of biopsy. Eight stress thermograms were eliminated for technical errors, and 20 subjects had no mammogram. A total of 66 subjects were in the stress thermography group while 54 subjects were in the mammography group. Table 2 identifies the number of subjects having each procedure.

Table 2

Procedure Distribution of Subjects

Procedure	Number of Subjects
Thermogram and Mammogram	48
Thermogram only	18
Mammogram only	6
Total	72

Twenty-four malignancies in this study represented 33% of the total subjects.

The overall detection sensitivity, the "true positive" rate of

correct malignant diagnosis in patients with malignant disease, was 75% for mammography and 88% for stress thermography. There were insufficient numbers for chi-square analysis. Binomial expansion failed to establish a significant difference in detecting cancer (true-positive) between the two procedures at the .05 level of confidence. Figure 4 demonstrates these figures in comparison with biopsy results. Table 3 indicates the age-related detection sensitivity of both procedures. The percentages in Table 3 refer to correct diagnoses of malignancy in the defined group. One cancer was missed by both the stress thermography and mammography procedures.

Table 3
Age-Related Detection Sensitivity
of Both Procedures

Age	Mammography	Stress Thermography
17-40	0/1 (0%)	2/2 (100%)
41-60	6/8 (75%)	9/10 (90%)
61-86	6/7 (86%)	10/12 (83%)

The detection specificity, the "true negative" rate of correct benign diagnosis in patients with benign disease, was 87% for mammography and 52% for thermography. Chi-square analysis indicates a significant difference in the specificity (true-negative) between the

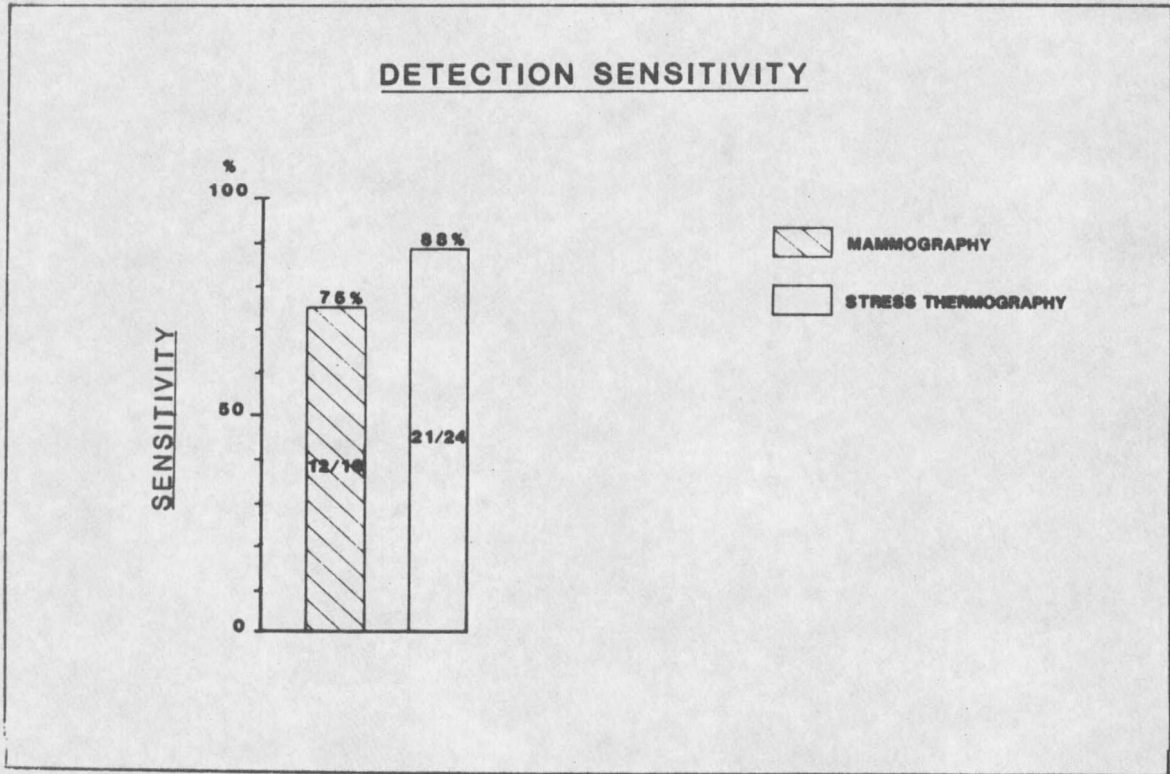


Figure 4. Detection sensitivity.

two procedures at the .001 level of confidence. Figure 5 demonstrates the biopsy-proven true negatives. Table 4 indicates the detection specificity by age.

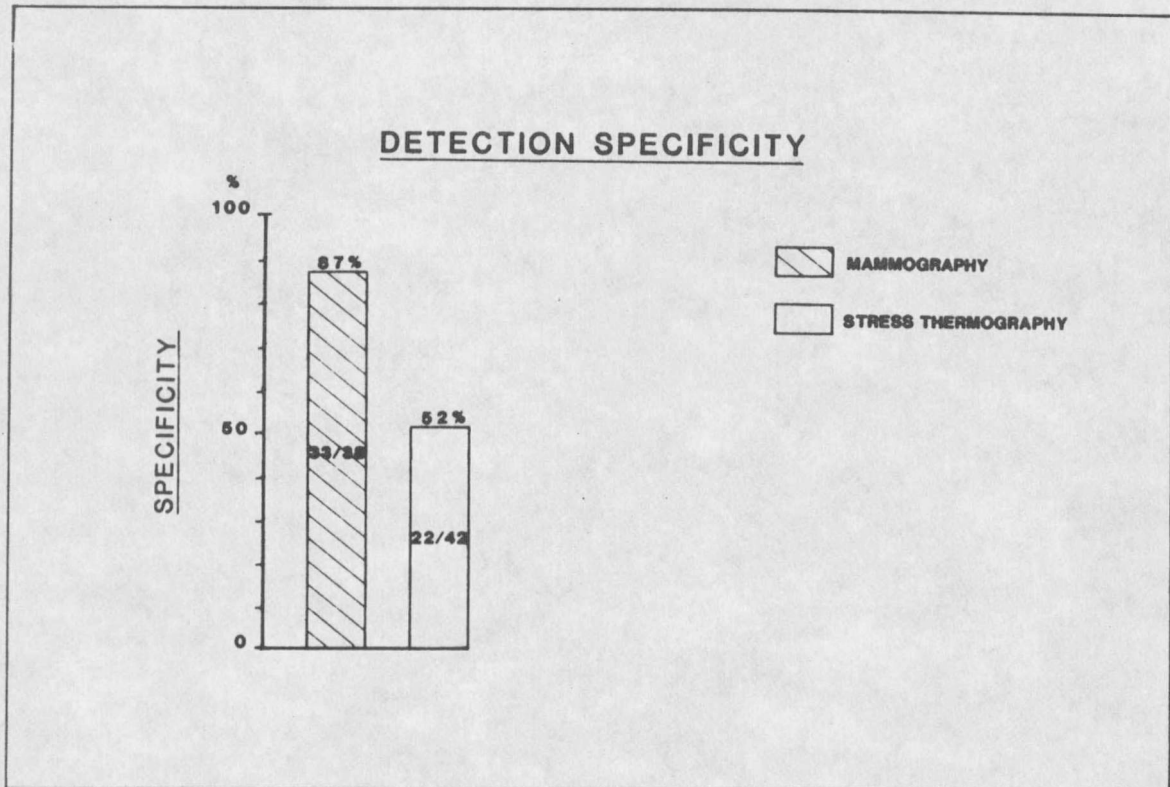
Table 4
Age-Related Detection Specificity for Mammography
and Stress Thermography

Age	Mammography	Stress Thermography
19-40	13/16 (81%)	9/20 (45%)
41-60	20/22 (91%)	12/20 (60%)
61-86	no subjects in this category had negative mammograms	1/2 (50%)
	n=54	n=66

Detection error rates are indicated in Figure 6, page 43.

False-positives were obtained in five out of 38 subjects who were examined by mammography, and 20 out of 42 subjects who were examined by stress thermography. The false-negative rate was four out of 16 for mammography and three out of 24 for thermography.

The records were reviewed on those subjects with false-positive or false-negative results. Nineteen subjects who had positive stress thermograms but negative biopsies were below the age of



df = 1
p = .001

Critical $\chi^2 = 10.827$
Calculated $\chi^2 = 11.0276$

Figure 5. Detection specificity.

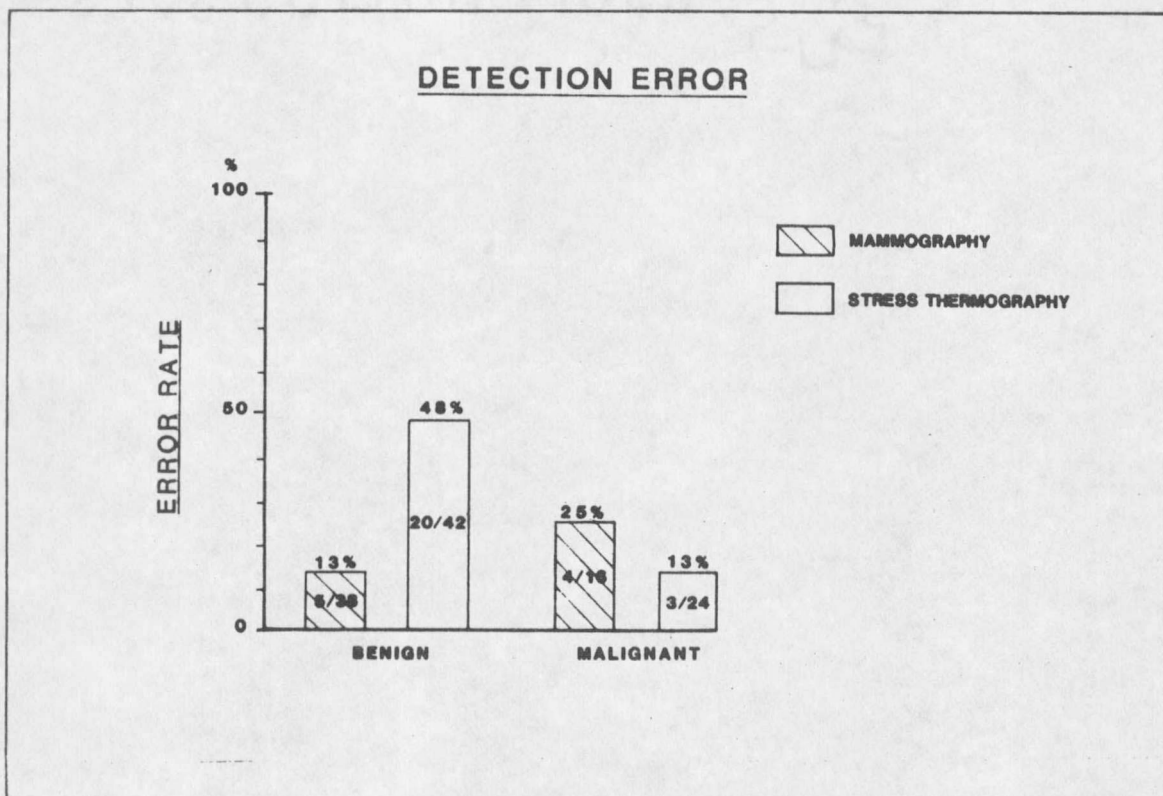


Figure 6. Detection error.

60, with ten below the age of 40. Three of the subjects in the 41-60 group had conditions which are known to be associated with abnormal thermographic activity. Inflammation, fibroadenoma, and some hormonal influences may have contributed to the thermographic activity, though this is just supposition since stage-in-ovulatory cycle is not incorporated into the current scoring system. One false-positive with negative biopsy was in a 79-year-old subject whose stress thermogram three years later with subsequent biopsy revealed a diagnosis of papillary intraductal carcinoma. Those subjects with cancer who had thermographically negative scores were reviewed. Two subjects had infiltrating ductal carcinoma with metastasis to nodes, indicating these may have been advanced cancers. The remaining subject also had an infiltrating ductal carcinoma, but with no metastasis. Gautherie (1980) offers an explanation of this phenomenon. He suggests that certain cancers, although markedly heat producing, do not produce an appreciable increase in the skin temperature due to poor conditions for heat transfer between the tumor and the skin.

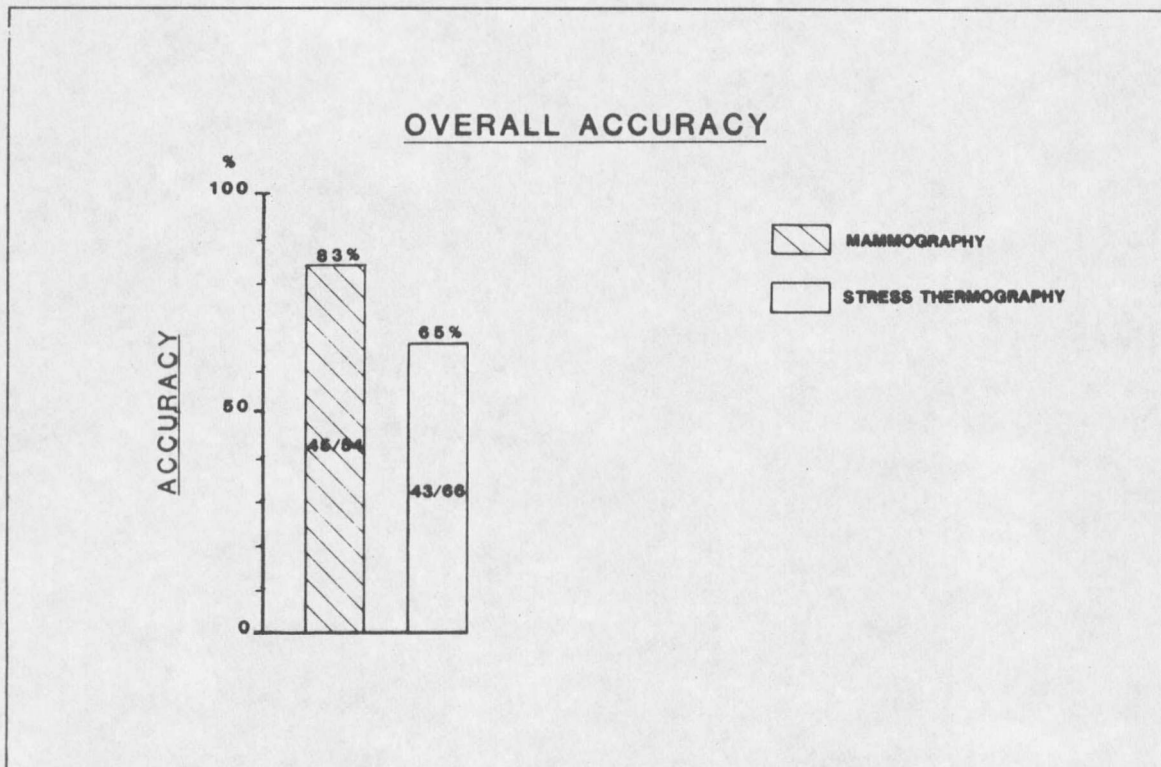
The false-positives that were noted on mammography were considered suspicious due to calcification pattern (three), breast asymmetry (one), and a mass which on biopsy was a fibroadenoma (one). Two of these false-positives were also false-positives with the stress thermogram. Four false-negatives were on mammography, two with metastasis at time of mastectomy. Three of the subjects were below

the age of 45 years, when mammographic evidence of cancer may be obscured by dense breast tissue. The fourth was 71 years of age; no obvious reason can be offered why this subject was missed.

Evaluation of the usefulness of these two procedures in differentiating cancers from benign diseases was determined by the application of the chi-square test. This established significance at the .001 level of confidence for mammography and at the .005 level of confidence for stress thermography. The usefulness of mammography was, $df = 1$ with a calculated X^2 at 19.962; the usefulness of stress thermography was, $df = 1$ with a calculated X^2 at 10.323. The overall biopsy-proven accuracy rate in Figure 7 indicates mammography with accuracy of 83% and stress thermography 65%. Chi-square analysis shows a significant difference exists in the overall accuracy between procedures at the .05 level of confidence. Table 5 summarizes the age-related accuracy of detection.

Table 5
Overall Accuracy of Detection by Age

Age	Mammography	Stress Thermography
19-40	13/17 (77%)	11/20 (55%)
41-60	26/30 (87%)	21/32 (66%)
61-86	6/7 (86%)	11/14 (79%)



df = 1
p = .05

Critical $\chi^2 = 3.841$
Calculated $\chi^2 = 5.020$

Figure 7. Overall accuracy.

That age of the subject influences diagnostic accuracy is shown in Table 5 and in Table 6. Both the mammogram and the stress thermogram demonstrated improved accuracy in cancer patients with advancing age of the patient. Analysis of benign patients incorrectly diagnosed (that is, false-positives) was similar.

Table 6
Correct Diagnosis by Age

Procedure (by age)	Malignant (true-positive)	Benign (false-positive)
Mammogram		
17-49	3/6 (50%)	4/29 (14%)
50-86	9/10 (90%)	1/9 (11%)
Thermogram		
17-49	6/7 (86%)	16/33 (48%)
50-86	15/17 (88%)	4/9 (44%)

In an attempt to discriminate cancer from benign disease with the stress thermography procedure, the investigator reviewed the scores of the 24 subjects with diagnosed cancer. When the discriminate threshold of zero was used to differentiate cancer from benign disease, the results showed three subjects with negative scores.

The first negative number was -0.170 with the next two at

-4.760 and -4.950. The score of -0.170 then was used as the number to discriminate benign from malignant disease. The use of this score also included 19 subjects with diagnosed benign disease. Using this negative score increased the number of cancers detected by one for 92% sensitivity, decreased the false-negative rate to 8%, increased the false-positive rate to 55%, and decreased the specificity to 45%. The overall accuracy of the procedure which used the negative score decreased from 65% to 62%. Clearly, no benefit exists in this study in altering the threshold which discriminates benign from malignant disease.

Chapter 4

DISCUSSION

As far as is known, no case of breast cancer was missed in this study. Local referring physicians have been conscientious in reporting back those patients who have positive diagnosis of cancer.

Considering the highly selected population sample of symptomatic women either referred by a physician or by self-referral because of a breast problem, the detection results of 75% by mammography are less than expected, though in concert with other studies (Niloff & Sheiner, 1981; Stark & Way, 1974). This is in view of the fact that a broad definition of accuracy was used: any opinion from slightly suspicious to definite cancer was included as true-positive in malignant cases. The false-negative rate means that one out of every four women with a proven carcinoma of the breast had no mammographic evidence of malignant disease. This result suggests that a negative mammogram may give a false sense of assurance to both the physician and the subject and could delay appropriate treatment, even though this did not occur with subjects in this study.

This study also confirms the findings of others that mammography is less accurate when performed on young women. The denser, more glandular breasts that are found generally in young women make mammographic interpretation of carcinomas less accurate than in the fatty breasts found in older women. Three of the four subjects with

false-negative mammograms had positive stress thermograms. The fourth subject with a negative mammogram also had a negative stress thermogram and no nodal metastasis. This cancer was not an early one.

It is important with any diagnostic procedure to exhibit some clinical judgment so as not to be all-inclusive, and as with mammograms, to expose the patient to additional expensive and hazardous procedures. In this study, the false-positive rate of 13% seems justified in view of the fact that all five subjects exhibited one of the primary signs of malignancy on the mammogram. A detection specificity of 87% is comparable to the other research studies.

The sensitivity of the stress thermographic procedure at 88% in this study compares favorably with published data for mammography and conventional thermography. The high false-positive rate may be too "all-inclusive" at this time to make the instrument medically acceptable without further refinement of the scoring system. The fact that 15 out of 20 subjects with positive scores were age 50 or less could imply that hormonal levels associated with the menstrual cycle, which are known to affect thermographic results, may have influenced the scores in this study. A review of the biopsy reports of the subjects with positive stress thermogram scores revealed that 13 scores were clean misses. The remaining seven subjects had biopsy diagnosis of conditions that are reported in the literature to be of significant risk for breast cancer or are premalignant conditions.

Two of the subjects had biopsy diagnoses of papilloma, a breast disease which was cited by Moskowitz, Pemmaraju, Russel, Gardella, Gartside, and De Groot (1977) and Azzopardi (1979) as having an increased risk for malignancy, 3.51 per thousand. In fact one of the subjects in the investigation subsequently had a repeat thermogram and biopsy diagnosis two years later of papillary intraductal carcinoma. The assumption is reasonable that this original false-positive may have been a prevalent cancer rather than an incident cancer which was discovered two years later. The other subject with papilloma also was a false-positive on mammography. Three of these subjects had moderate to severe hyperplasia while two subjects had severe fibrocystic disease. Both diseases are considered by some investigators to carry an increased risk of cancer (Azzopardi, 1978; Moskowitz et al., 1977).

The overall accuracy of the stress thermography procedure of 65% is affected adversely by the high rate of false-positive in this study. Several investigations have shown that the efficacy of the thermogram and the mammogram procedures is increased when they are used in combination with each other or with clinical examination. This study corroborates those findings. Table 7 demonstrates specificity to cancer when results of both the stress thermogram and the mammogram procedures are combined.

Table 7

Combined Mammogram and Stress Thermogram Results

Results	Cancer	Benign
Both tests positive	10 (63%)	2 (6%)
Negative stress thermogram/ Positive Mammogram	2 (13%)	2 (6%)
Positive stress thermogram/ Negative Mammogram	3 (19%)	15 (47%)
Both tests negative	1 (6%)	13 (41%)

When one or both procedures were positive, there was a 94% specificity for cancer and a 6% false-negative rate. When both tests were negative, there is a 41% specificity rate with a corresponding false-positive rate of 59%. Hicks et al. (1979) indicate that the predictive value of a test, the percentage of positive results that are true-positive, is a useful parameter when interpreting an abnormal finding. They state that,

screening tests should ideally detect all persons with disease, i.e., 100% sensitivity or no false negative results. Therefore, sensitivity is the most important parameter to evaluate a test. This implies that lower degrees of specificity may be acceptable (Hicks et al., 1979, p. 2083).

In this study the combination of the two procedures allows for a high degree of predictability for cancer when both tests are positive. Since it has been established that both procedures are

useful in differentiating cancer from benign breast disease, the high false-positive rate could be acceptable for establishing a high risk group. The true-positive rates are good; and when combined with clinical examination and judgment, they could perhaps eliminate biopsy in selected cases of symptomatic women.

Chapter 5

CONCLUSION

From this study the conclusion might be drawn that neither the mammography nor the stress thermography procedure is currently at a state of the art where either could be used as a sole diagnostic modality. The results of this study certainly correlate with other previous studies and indicate that these procedures are an adjunct to clinical examination and biopsy.

The sensitivity of the mammographic procedure may have been affected adversely by the small sample size of 16 cancers in this study but did show a high rate of specificity for the disease. This study also reconfirms the limitation of mammography in diagnosing clinically palpable breast masses in young women and should not be used as a substitute for physical examination or biopsy in subjects with clinically suspicious lesions of the breast. On the other hand, mammography does have a use in the older woman with a clinically palpable breast mass and should be used to search for an occult carcinoma in the ipsilateral or contralateral breast.

The sensitivity of the stress thermographic test was certainly much better than expected but does not demonstrate any difference over mammography. Interestingly in conventional thermography an abnormal thermogram is considered a high risk factor, and those subjects are followed up who exhibit an abnormal thermogram. Gautherie

(1980) reports 38% of the subjects who had an abnormal thermogram subsequently developed breast cancer within a four-year retrospective study. Gautherie (1981) also maintains that an abnormal thermogram is a "ten times better marker" (p. 4) than a family history for the risk of breast cancer.

Since the sensitivity of stress thermography to cancer is greater than mammography in the young woman, a possible use for the stress thermography procedure would be to establish baseline studies in the young woman; and changes in the established thermal pattern could serve as indicators for further diagnostic tests. This could eliminate the use of mammography in these subjects and the attendant exposure to radiation. "Stability of the thermal pattern may be an adequate substitute for mammography" (Dodd, 1977, p. 2797). The false-positive rate is excessive but could be acceptable for establishing a high-risk group when the true-positive rates are improved. For now, the use of stress thermography should be as an adjunct and not the sole modality.

One of the limitations of the study was the small sample size and the fact that it was limited to symptomatic women. The results are not applicable to the population at risk for breast cancer as a whole. Another limitation was in the interpretation of mammographic results. It is believed that if a similar future study were conducted, a clinician outside of the study would be employed to

evaluate the mammographic findings.

The purpose of this study was to determine if there was a difference in accuracy between mammography and stress thermography procedures. It is clear that thermography showed a greater sensitivity for the disease, but mammography showed a greater specificity and overall accuracy. The information revealed in this study is encouraging, and by no means precludes further study of the stress thermography procedure. It would be advantageous to develop a more effective discriminant algorithm to differentiate benign from malignant disease. This possibly could be done by incorporating into the scoring system some factors which adversely affect the thermogram such as stage in ovulatory cycle, medications, and circadian rhythm. The fact that the results of the stress thermography procedure are totally objective is a desirable factor in future use as a screening tool.

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APPENDICES

APPENDIX A

COPY OF LETTER SENT TO SAINT VINCENT HOSPITAL

May 15, 1981

Sr. Therese Zimmerman, RN
Director of Nursing Service
Saint Vincent Hospital
Billings, Montana 59101

Dear Sr. Therese:

As a requirement for a Master's Degree in Nursing, I am investigating the diagnostic accuracy of mammography and stress thermography as proven by breast biopsy. I would appreciate your permission to review the records of a selected group of patients who had mammography or breast biopsy at your facility.

You have my assurance that at no time will the confidentiality of the patient be violated and only the age and the results of the procedure will be used. No other person will have access to the raw data and only summarized data will be published in the thesis.

This study hopefully will contribute to the knowledge of the most effective noninvasive procedure to diagnosing breast cancer in women. It will serve as a foundation study in the continuing effort to provide improvement in health care delivery to the consumer.

Sincerely,

Sue Bradshaw
Graduate Student in Nursing
Montana State University

APPENDIX B

COPY OF LETTER SENT TO DEACONESS HOSPITAL

May 15, 1981

Ms. Joanne Dodd
Director of Nursing
Billings Deaconess Hospital
Billings, Montana 59101

Dear Ms. Dodd:

As a requirement for a Master's Degree in Nursing, I am investigating the diagnostic accuracy of mammography and stress thermography as proven by breast biopsy. I would appreciate your permission to review the records of a selected group of patients who had mammography or breast biopsy at your facility.

You have my assurance that at no time will the confidentiality of the patient be violated and only the age and the results of the procedure will be used. No other person will have access to the raw data and only summarized data will be published in the thesis.

This study hopefully will contribute to the knowledge of the most effective non-invasive procedure to diagnosing breast cancer in women. It will serve as a foundation study in the continuing effort to provide improvement in health care delivery to the consumer.

Sincerely,

Sue Bradshaw
Graduate Student in Nursing
Montana State University

APPENDIX C

LETTER OF PERMISSION TO USE MEDICAL RECORDS
AT SAINT VINCENT HOSPITAL



Saint Vincent Hospital
1233 North 30th Street
Billings, Montana 59103

TO: Sue Bradshaw
FROM: Sister Therese, DNS *SR*
RE: Use of patients' medical records in Master's Thesis
DATE: May 15, 1981

In reply to your letter requesting permission to review mammographic and biopsy reports, the policy of St. Vincent Hospital is to ensure total confidentiality of patients' medical records. Providing that this policy is maintained by you, you may use data from the medical records of patients you select for inclusion in your Master's Thesis in Nursing.

APPENDIX D

LETTER OF PERMISSION TO USE MEDICAL RECORDS
AT DEACONESS HOSPITAL



BILLINGS DEACONESS HOSPITAL

May 22, 1981

Sue Bradshaw
802 Clark
Billings, Mt. 59102

Dear Sue,

Permission is granted for you to review a selected group
of patient's laboratory and radiology records, for the purpose
of your thesis.

We trust that the rule of confidentiality will be followed
by you with this information.

Sincerely,

Joanne Dodd

Joanne Dodd
Vice President for Nursing Service

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APPENDIX E

TABLE OF FORMULAS

Demonstration of Method to Evaluate the Accuracy
of Stress Telethermometry and Mammography:
Sensitivity and Specificity

Test or Examination	Disease Present	Disease Absent
Positive (indicating disease is probably present)	A (true-positive)	B (false-positive)
Negative (indicating disease is probably absent)	D (false-negative)	C (true-negative)
Totals	A+D	B+C
Sensitivity:	$\frac{\text{True Positive (A)}}{\text{True Positive (A) + False Negative (D)}} \times 100$	
Specificity:	$\frac{\text{True Negative (C)}}{\text{True Negative (C) + False Positive (B)}} \times 100$	
Accuracy:	$\frac{\text{True Positive} + \text{True Negative}}{\text{True Positive} + \text{False Positive} + \text{True Negative} + \text{False Negative}} \times 100$	

- A. True positive: indicates mammogram interpretation of malignant or suspicious or a stress thermogram score above zero (0) with biopsy-proven cancer.
- B. False positive: indicates mammogram interpretation of suspicious or malignant or a stress thermogram

APPENDIX E (continued)

score above zero (0) with biopsy-proven benign disease.

- C. True negative: indicates mammogram interpretation of benign disease or no evidence of malignancy or stress thermogram score below zero (0) with biopsy-proven benign disease.
- D. False negative: indicates mammogram interpretation of benign or no evidence of malignancy or a stress thermogram score below zero (0) with biopsy-proven cancer.

False positive: $\frac{\text{test indicated positive/biopsy negative}}{\text{total number of negatives}}$

False negative: $\frac{\text{test indicated negative/biopsy positive}}{\text{total number of positives}}$

