INFRARED REGULATION THERMOGRAPHY FOR CANCER

HEALTH TECHNOLOGY ASSESSMENT SECTION
MEDICAL DEVELOPMENT DIVISION
MINISTRY OF HEALTH MALAYSIA
004/2014

DISCLAIMER

Technology review is a brief report, prepared on an urgent basis, which draws on restricted reviews from analysis of pertinent literature, on expert opinion and / or regulatory status where appropriate. It has been subjected to an external review process. While effort has been made to do so, this document may not fully reflect all scientific research available. Additionally, other relevant scientific findings may have been reported since completion of this review.

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DISCLOSURE

The author of this report has no competing interest in this subject and the preparation of this report is totally funded by the Ministry of Health, Malaysia.

EXECUTIVE SUMMARY

Introduction

Thermographic systems use an infrared camera to produce images (thermograms) that show the pattern of heat and blood flow on the surface of the body. Clinical thermography has been used since the 1960s by Dr. Ray Lawson who discovered that the skin temperature over a cancer in the breast was higher than normal tissue. The use of thermography as a means of detecting breast cancer has a substantial history. A nationwide study, Breast Cancer Detection Demonstration Projects (BCDDP) launched in 1973, investigated breast cancer screening by clinical breast examination, mammography and thermography. However, it was dropped at an early stage of the project due to unsatisfactory results.

The advances in both infrared cameras and digital processing of the acquired images have suggested that the systems currently available are not comparable to those that were previously used. Since then it has been used not only adjunctive for breast cancer screening and diagnoses but also for other cancer.

The effectiveness and safety of infrared regulation thermography for screening and diagnosis of cancers still debatable. Hence this technology review was requested by the Director of National Cancer Institute, Ministry of Health Malaysia to review the evidence on Infrared Regulation Thermography to be used in detecting cancer in the MOH hospitals and healthcare facilities following a proposal from a company to introduce them in the MOH facility.

Objectives

To assess the safety, efficacy/effectiveness and cost-effectiveness on Infrared Regulation Thermography in detecting cancer in the MOH hospitals and healthcare facilities.

Results and conclusions

The search strategy yielded five full text articles that consist of three Systematic Reviews (SRs) and two diagnostic studies on the efficacy and effectiveness of infrared regulation thermography for screening and diagnosing of breast cancers. There were no retrievable studies on effectiveness of the other cancer and cost-effectiveness of the technology.

There was limited fair level of evidence to suggest that infrared regulation thermography was not effective as a screening tool for breast cancer. Fair level of evidence showed inconsistent results when infrared regulation thermography was used as a diagnostic tool for breast cancer. There was no retrievable evidence for the effectiveness of infrared regulation thermography for screening and diagnosis of other cancers.

In regards to safety, there was no retrievable evidence for the safety of infrared regulation thermography for screening and diagnosis breast and other cancers. USFDA did not approve the use of thermography for screening or used as diagnostic tool for breast cancer.

Methods

Literature search was done for published articles that assess the safety, efficacy or effectiveness and cost-effectiveness of Infrared Regulation Thermography. The following electronic databases were search: MEDLINE (1946 to 10 March 2014), EBM Reviews-Cochrane Database of Systematic Reviews (2005 to December 2013), EBM Reviews-Cochrane Central Register of Controlled Trials (January 2014), EBM Reviews–Database of Abstracts of Review of Effects (1st Quarter 2014), EBM Reviews-Health Technology Assessment (1st Quarter 2014) NHS economic evaluation database (1st Quarter 2014) via OVID, Pubmed, INAHTA database, HTA database and USFDA database. The last search was run on 10 March 2014. No limits were applied to the search. Detailed search strategy is as in **Appendix 1**. Additional articles were identified from reviewing the references of retrieved articles and hand searching of journals. General search engine was used to get additional web based information.

Infrared Regulation Thermography for Cancer

1. INTRODUCTION

Thermographic systems use an infrared camera to produce images (thermograms) that show the pattern of heat and blood flow on the surface of the body. Clinical thermography has been used since the 1960s by Dr. Ray Lawson who discovered that the skin temperature over a cancer in the breast was higher than normal tissue. The use of thermography as a means of detecting breast cancer has a substantial history. A nationwide study, Breast Cancer Detection Demonstration Projects (BCDDP) launched in 1973, investigated breast cancer screening by clinical breast examination, mammography and thermography. However, it was dropped at an early stage of the project due to unsatisfactory results.[1]

The advances in infrared camera technology over the last decade have been accompanied by progress in computerised image processing systems. It was not until the 1970s that data acquired by infrared cameras was processed by computers into digital images for viewing. Currently more sophisticated modelling programmes can enhance the spatial resolution of images already acquired. The advances in both infrared cameras and digital processing of the acquired images have suggested that the systems currently available are not comparable to those that were previously used.[2-4] Since then it has been used not only adjunctive for breast cancer screening and diagnoses but also for other cancer.

The effectiveness and safety of infrared regulation thermography for screening and diagnosis of cancers still debatable. Hence this technology review was requested by the Director of National Cancer Institute, Ministry of Health Malaysia to review the evidence on Infrared Regulation Thermography to be used in detecting cancer in the MOH hospitals and healthcare facilities following a proposal from a company to introduce them in the MOH facility.

2. OBJECTIVES

To assess the safety, efficacy/effectiveness and cost-effectiveness on Infrared Regulation Thermography in detecting cancer in the MOH hospitals and healthcare facilities.

3. TECHNICAL FEATURES

3.1 Definition Infrared Regulation Thermography

Infrared thermography use an infrared camera to produce images (thermogram) that showed the pattern of heat and blood flow on the surface of the body. It gathers information about the functioning health and integrity of the various tissues and organ.

This approach is based on the idea that the response to the stimulus enhances the diagnostic value and acuteness. These applies to exposure of the patient (disrobed at the room temperature of 19 – 21^{0}C) and measures immediately after the disrobing (comfort temperature) and the second time after adapting the cool ambient (temperature after 10 minutes). It measures the difference between the two temperatures taken before and after the cool air exposure. The reaction to cool stimulus lead to skin temperature decrease to about 1^{0}C within the breast tissue.

3.2 Mechanism of action

There is a well-known relationship between cancer and heat signs. The aggressive and fast growing breast cancers have an exaggerated metabolism causing by high blood supply.

Nitric oxide (NO) is a molecule with potent vasodilating properties. It is a simple highly reactive free radical that readily oxidizes to form nitrite or nitrate ions. It diffuses easily through both hydrophilic and hydrophobic media. Thus, once produced, NO diffuses throughout the surrounding tissues, inside and outside the vascular system, and induces a variety of biochemical changes depending on the specific receptors involved. NO exerts its influence by binding to receptor sites in the endothelium of arteries or arterioles. This causes inhibition of sympathetic vasoconstriction. The end result is NO induced vasodilatation, which in turn may produce an asymmetrical thermovascular pattern.[6-7]

Current understandings of the underlying pathological mechanisms for increased temperature in cancer cells produce nitric oxide (NO). This NO interferes with the normal neuronal (nervous system) control of tissue blood vessel flow by causing regional vasodilation in the early stages of cancerous cell growth, and enhancing angiogenesis (new blood vessel formation) in later stages.[5]

3.3 Procedure

[redacted] Infrared Regulation Thermography is an exact temperature measurement taken with a probe in contact with the skin. The output is displayed as a computerized graph rather than an infra-red image. It also involves a cold stimulus challenge with contact skin temperature measurements taken before and after the thermal stimulus because it measures the regulatory capacity of certain organs, glands and tissues.

The process is based on a double measurement of the skin temperature at 120 locations (specific points) on the surface of the body. The patient first sits fully clothed in a slight cool room 20°C to 23° C for 10 to 15 minutes while the body temperature acclimates. The technician begins the measurements by gently touching a temperature probe on specific points on the face and neck. The patient is then asked to remove their clothes from the waist up, so that the

remainder of the measurements on the arms, chest, upper and lower abdomen, back and breast can be taken. After that, the patient is asked to disrobe from the waist down and stands unclothed in their underwear, with arms by their side, exposed to the cool room air for 10 minutes. The exposure provides a challenge to the body's temperature regulation processes.

Then the device analyzes the input data and provides both a graphic representation of the thermal measurements and an interpretation based on the combined data. The computer program also analyzes and prints out a variety of interpretive indices. **(see Appendix 1)**

It does not entail the use of ionizing radiation, venous access, radioactive dyes, or any other invasive procedures. It is safe and simple. The examination process of touching a temperature probe to the body poses no harm or discomfort to the patient.

Figure 1: [redacted] Thermometry Scan System

4. METHODS

4.1. Searching

Literature search was done for published articles that assess the safety, efficacy or effectiveness and cost-effectiveness of Infrared Regulation Thermography. The following electronic databases were search: MEDLINE (1946 to 10 March 2014), EBM Reviews-Cochrane Database of Systematic Reviews (2005 to December 2013), EBM Reviews-Cochrane Central Register of Controlled Trials (January 2014), EBM Reviews–Database of Abstracts of Review of Effects (1st Quarter 2014), EBM Reviews-Health Technology Assessment (1st Quarter 2014) NHS economic evaluation database (1st Quarter 2014) via OVID, Pubmed, INAHTA database, HTA database and USFDA database. The last search was run on 10 March 2014. No limits were applied to the search. Detailed search strategy is as in **Appendix 1**. Additional articles were identified from reviewing

the references of retrieved articles and hand searching of journals. General search engine was used to get additional web based information.

4.2. Selection

Based on the inclusion and exclusion criteria, study selection were carried out. The titles and abstracts of all studies were assessed for the eligibility criteria. Following the inclusion and exclusion as stated below:

Inclusion criteria

Population	Patients with cancer
Interventions	Infrared Regulation Thermography
Comparators	Conventional diagnostic procedure such as mammography, ultrasound, Histological, CT and MRI imaging
Outcomes	Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). Detection rate, mortality rate, survival rate, quality of life (QOL), and quality adjusted life years gained (QALY) gained. Cost, cost-benefit, cost-effectiveness, cost utility, and economic evaluation
Study design	Systematic review, Health Technology Assessment (HTA), randomised controlled trial (RCT), cohort, cross sectional study and case control

Exclusion criteria

i) Animal study
ii) Narrative review
iii) Non English full text articles

5. RESULTS

The search strategy yielded five full text articles that consist of three Systematic Reviews (SRs) and two diagnostic studies on the efficacy and effectiveness of infrared regulation thermography for screening and diagnosing of breast cancers. There were no retrievable studies on effectiveness of the other cancer and cost-effectiveness of the technology.

5.1. SAFETY

There was no adverse effect of the devices were reported in the included studies. The United State Food Drug Administration (USFDA) did not approve the use of thermography on its own as effective screening or diagnosing tools for breast cancer.

5.2 EFFICACY/EFFECTIVENESS

5.2.1 Breast cancer (Screening)

There were two systematic reviews (SRs) that appraised the same study done by Williams et al. (1990). The study was a prospective cohort done among 10,229 women aged 40–65 and attended a breast screening clinic at Royal United Hospital. Among the participants 229 were symptomatic of breast cancer. The aim of the study to determine the diagnostic accuracy of thermography as a screening test for breast cancer, and to show whether or not it could be used to identify women at high-risk for developing the disease over five years. Once enrolled, each woman gave medical history, underwent infrared thermography and physical examination. If either infrared thermography or physical examination (PE) was classified as positive at initial visit, then them woman referred for mammography and other diagnostic test to confirm the diagnosis. Documentary follow-up conducted of each woman five years later through general practitioner (GP) records to identify those who developed breast cancer. The result showed that in 2681 patients with positive infrared thermography 36 developed breast cancer and among 7548 patient with negative infrared thermography 23 had breast cancer. At initial screening infrared thermography had sensitivity of 61% (95%, CI 49 to 73), specificity 74% (95% CI 73 to 75), positive predictive value (PPV) 1% (95% CI 0 to 2) and negative predictive value (NPV) 99.7% (95% CI 99.6 to 99.8). After five years following initial screening, infrared imaging reported a sensitivity of 28%, specificity of 74%, PPV of 1% and a NPV of 99%. However there were limitation, as the population studied included both symptomatic and asymptomatic women, without presenting a breakdown of the data that allowed for these sub-groups to be considered separately, which limited the generalisability of these results to a population screening situation. The authors concluded that thermography is not sufficiently sensitive to be used as a screening test for breast cancer, nor it is useful as an indicator of risk developing within 5 years.[10, level I: 11, level I]

5.2.2 Breast Cancer (Diagnosis)

Vreugdenburg TD et al. (2013) in their SR with meta-analysis evaluated the effectiveness and diagnostic accuracy of three emerging classes of technology such as Digital Infrared Thermal Imaging (DITI), electrical impedance scanning (EIS) and elastography for diagnosing breast cancer in women with suspicious symptoms either presented with a breast lump or nipple discharge. Meta-analysis on the use of DITI from the total eight studies on diagnostic cohort study showed sensitivities between 25% and 96.7% (median 82%), and specificities between 11.8% and 84.9% (median 55%). However, there was significant heterogeneity observed among studies due to high levels of variation among study results, and the large degree of variation among the methods and devices used for imaging.[12, level I]

In 2004 National Screening Unit (NSU) of the New Zealand Ministry of Health conducted Health Technology Assessment (HTA) report to evaluate the effectiveness of infrared thermography in the early detection and diagnosis of breast cancer. The search strategy involved searching MEDLINE and other electronic databases between January 1985 and March 2004 and only two articles were included in this review. A case control study, a total of 200 women aged between 31 -84 years old (mean=53) in which 100 of them had either DCIS, stage I, or stage II and another 100 women had benign breast following open surgical breast biopsy. Infrared thermography alone showed sensitivity of 83% (95% CI 76 to 90), specificity 81% (95% CI 73 to 89), PPV 81% (95% CI 74 to 89) and NPV 83% (95% CI 75 to 90). For mammography alone, the was sensitivity 85% (95% CI 78 to 92), specificity 70% (95% CI 61 to 78), PPV 74% (95% CI 66 to 82) and NPV 82% (95% CI 74 to 90). In combination of mammography and infrared imaging there was incremental increase in sensitivity from 85% to 95%. Another study conducted by Parisky et al. (2003) of 4-year multicentre clinical trial conducted at five institutions to determine the efficacy of a dynamic computerised infrared thermography for distinguishing between benign and malignant lesions in patients undergoing biopsy on the basis of mammographic findings in 769 women aged between 40-60 years old. The recruitment of patients to undergone breast biopsy was recommended on basis of abnormal mammography, abnormal PE, or both. Patients then had infrared thermography imaging, followed by surgery. Each subject's infrared thermography images were analysed by three evaluators (875 lesions produced 2299 infrared imaging results) and evaluators were blinded to biopsy result, but knew certain PE and mammography details. The results showed sensitivity of 97% (95% CI 96 to 99) specificity 14% (95% CI 13 to 16), PPV 24% (95% CI 22 to 26) and NPV 95% (95% CI 93 to 98). The authors' concluded that infrared thermography imaging has a high NPV and it is non-invasive and safe procedure. Therefore it has an adjunctive role in determining whether immediate biopsy is warranted. However there was limitation in this study because it was sponsored by manufacturers of BSC2100® (Computerized Thermal Imaging®).[10, level I]

Another SR conducted by Fitzgerald A. et al in 2012 to review the evidence for the effectiveness of infrared thermography for population screening and diagnostic testing of breast cancer. The results of the five studies included are shown in below. **(Table 1)**.

Table 1: Results of the four studies included in this reviews.

Study	Participant	Sens	Spec	PPV	NPV	LR+	LR-
Arora (2008) Cohort study	N=92	97%	26%	70%	82%	1.31 (1.07-1.62)	0.28 (0.05–1.47)
Kontos (2011) Cohort study	N=63 (126 breast lesions)	25%	85%	24%	82%	1.67 (0.68–4.09)	0.89 (0.69–1.14)
Wishart (2010) Cohort study	N=100 (106 breast lesions)	78%	48%	69%	59%	1.49 (1.09–2.05)	0.46 (0.26–0.81)
Parisky (2003) Cohort study	N=875 breast lesion	97%	14%	24%	95%	1.14 (1.11–1.17)	0.18 (0.11–0.32)

Overall, most studies showed high sensitivity of over 78% and the generally low specificity, between 14% and 85% however, there were two studies with conflicting results. One study by Kontos (2011) reported that low sensitivity (25%) and a high specificity (85%) and another study by Keyserlingk (1998) showed high sensitivity (83%) and specificity (81%). The authors concluded that, there was insufficient evidence and inconsistent result to show that thermography provided benefit to patients as an adjunctive tool to mammography in diagnosing breast cancer. This SR was of good quality as extensive systematic literature searches were conducted, study quality was carefully assessed using a validated tool and the authors attempted to maximise available data by deriving accuracy data from those studies where not all diagnostic measures were reported.[11, level I]

Kolarić D. et al (2013) conducted a prospective cohort study among a total of 26 consecutive female patients who were scheduled for breast surgery. The preoperative inclusion criteria included age above 35 and all of them had undergone diagnostic work up of mammography, ultrasound examination and fine-needle aspiration (FNA) before the surgery. All eligible patients were then examined by thermography prior to surgery with histological examination as a reference standard. All the collected data were statistically reviewed and showed that mammography sensitivity of 85%, specificity 84% and PPV 85%, while using thermographic results showed sensitivity of 100%, specificity 79% and PPV results 92%. The authors concluded that the results indicate that it would be

prudent to use thermography as a primary screening method in detection of breast carcinoma. However there were limitation in the review such as small sample size and possible selection bias because blinding of the histological assessor was not clear.[13, level II-2]

Keyserlingk et al. conducted study to assess the potential contribution of currently available high-resolutiondigital IR as an adjuvant imaging technique in the detection of breast cancer. Retrospective chart review from August 1995 onwards to identify 100 consecutive cases (post-operative patients having initial diagnosis of breast cancer, with final staging as either DCIS, stage I, or stage II) and 100 controls (post-operative patients with benign breast histology following open surgical breast biopsy). For infrared regulation thermography alone sensitivity 83% (95% CI =76 to 90), specificity 81% (95% CI 73 to 89), PPV 81% (95% CI 74 to 89) and NPV 83% (95% CI 75 to 90) and for mammography alone result showed sensitivity 85% (95% CI 78 to 92), specificity 70% (95% CI 61 to 78), PPV 74% (95% CI 66 to 82) and NPV 82% (95% CI 74 to 90). However, there was incremental increase from 85% to 93% sensitivity in combination of infrared regulation thermography and mammography.[14, level III]

5.2.3 Other cancer

There was no retrievable evidence from the scientific databases on the use of infrared regulation thermography for other cancer other than breast cancer.

5.3 LIMITATIONS

This technology review has several limitations. The selection of studies was done by one reviewer. Although there was no restriction in language during the search but only English full text articles were included in this report. Any abstracts without a full text articles were also excluded.

6. CONCLUSION

6.1 EFFICACY/EFFECTIVENESS

There was limited fair level of evidence to suggest that infrared regulation thermography was not effective as a screening tool for breast cancer. Fair level of evidence showed inconsistent results when infrared regulation thermography was used as a diagnostic tool for breast cancer. There was no retrievable evidence for the effectiveness of infrared regulation thermography for screening and diagnosis of other cancers.

6.2 SAFETY

In regards to safety, there was no retrievable evidence for the safety of infrared regulation thermography for screening and diagnosis breast and other cancers.

USFDA did not approve the use of thermography for screening or used as diagnostic tool for breast cancer.

6.3 COST-EFFECTIVENESS

There was no retrievable evidence from the scientific database but the estimated cost of the [redacted]

7. REFERENCES

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8. APPENDIX

8.1. Appendix 1: LITERATURE SEARCH STRATEGY

Ovid MEDLINE® In-process & other Non-Indexed citations and OvidMEDLINE® 1948 to present

1. Thermography/
2. Thermometry/
3. thermology.tw.
4. (thermal imaging or thermography or thermometry or thermology).tw.
5. (infra-red imag$ or infrared imag$).tw.
6. 1 or 2 or 3 or 4 or 5
7. Carcinoma
8. (carcinoma or malignan$ or neoplas$ or cancer$).tw.
9. 7 or 9
10. 6 and 9

OTHER DATABASES	
EBM Reviews - Cochrane Central Register of Controlled Trials	Same MeSH, keywords, limits used as per MEDLINE search
EBM Reviews - Database of Abstracts of Review of Effects	
EBM Reviews - Cochrane database of systematic reviews	
EBM Reviews - Health Technology Assessment	
PubMed	
NHS economic evaluation database	
FDA	thermography

8.2. Appendix 2

HIERARCHY OF EVIDENCE FOR EFFECTIVENESS STUDIES

DESIGNATION OF LEVELS OF EVIDENCE

I Evidence obtained from at least one properly designed randomized controlled trial.

II-I Evidence obtained from well-designed controlled trials without randomization.

II-2 Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or research group.

II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.

III Opinions or respected authorities, based on clinical experience; descriptive studies and case reports; or reports of expert committees.

SOURCE: US/CANADIAN PREVENTIVE SERVICES TASK FORCE (Harris 2001)

8.3 Appendix 3

HIERARCHY OF EVIDENCE FOR TEST ACCURACY STUDIES

Level	Description	
1.	A blind comparison with reference standard among an appropriate sample of consecutive patients	
2.	Any one of the following	Narrow population spectrum
3.	Any two of the following	Differential use of reference standard
4.	Any three or more of the following	Reference standard not blind Case control study
5.	Expert opinion with no explicit critical appraisal, based on physiology, bench research or first principles.	

SOURCE: NHS Centre for Reviews and Dissemination (CRD) University of York, Report Number 4 (2nd Edition)

8.4 APPENDIX 4

EXAMPLE OF INFRARED REGULATION THERMOMETRY REPORT

alfa THERMODIAGNOSTICS

INFRARED REGULATION THERMOMETRY REPORT

PATIENT INFORMATION

Report Number: R-000002299
Patient Name: Female Age 57
CRT Date Performed: 05-Oct-2012 01:41 PM
Algorithm Version: 1
Practitioner: Jackie Bell
Report Generation Date: 05-Oct-2012 12:42 PM
Chief Complaints and Objective Findings: L breast calcifications; R SI joint; L scapula; abcess tooth #18; chest cold; headaches

I. THERMOGRAPHIC BIO-REGULATION RESULTS

General Identifier patterns	There appears to be a minimal deficit in detoxification capability (There are hints to metabolically challenged hepatic, renal filtration or other metabolic functions). There appears to be a severe signature for heavy metal toxicity. The adrenal function is moderately stressed. There is a severe global immune stress apparent. There is a minimal suspicion of a circulatory or cardiovascular (hypo/hyper tension) signature.
Head	The disorder decreased. There is a minimal cerebrovascular/carotid circulatory deficit pattern identified. A minimal temporomandibular joint or neck disorder pattern identified. There is a minimal degree of viral hint signature identified.
Neck	The disorder increased. There is a minimal lymph block apparent. Investigate major source in the head region.
Chest	The disorder increased. The sternum moderately appears blocked, -see chest and breast sections. There appears a moderate chest block indication.
Upper Abdomen	The disorder decreased. There is a minimal level of apparent enzyme dysfunction/deficiency present. There appears a severe indication for an insulin-resistance pattern.
Lower Abdomen	The disorder decreased. There appears a severe food intolerance or allergy. There appears a severe general dysbiosis (mycosis, bacterial imbalance) indication.
Kidney/Back	The disorder increased. There appears a moderate degree of stress vertebral column.
Cubital Fossae	The disorder increased. There appears identified a problem residing on the right side of the body. Investigate further.
Dental	The disorder increased in left upper jaw and decreased in right upper jaw, right lower jaw, and left lower jaw. There appears to be a dental focus. There is a severe indication for the right upper jaw quadrant(s). Recommend dental examination for hidden focal infection. There appears to be a moderate degree of dental toxicity in the left lower jaw quadrant(s). A minimal temporomandibular joint or neck disorder pattern identified.
Breast	The disorder decreased in right breast. The disorder remained high in left breast. There appears 15 blocked spot(s) in the R/L breast. this may be benign. There appears a severe side-to-side difference (R-L).
Prognostic Index (PI)	1.

II. PRIORITY FOR TREATMENT

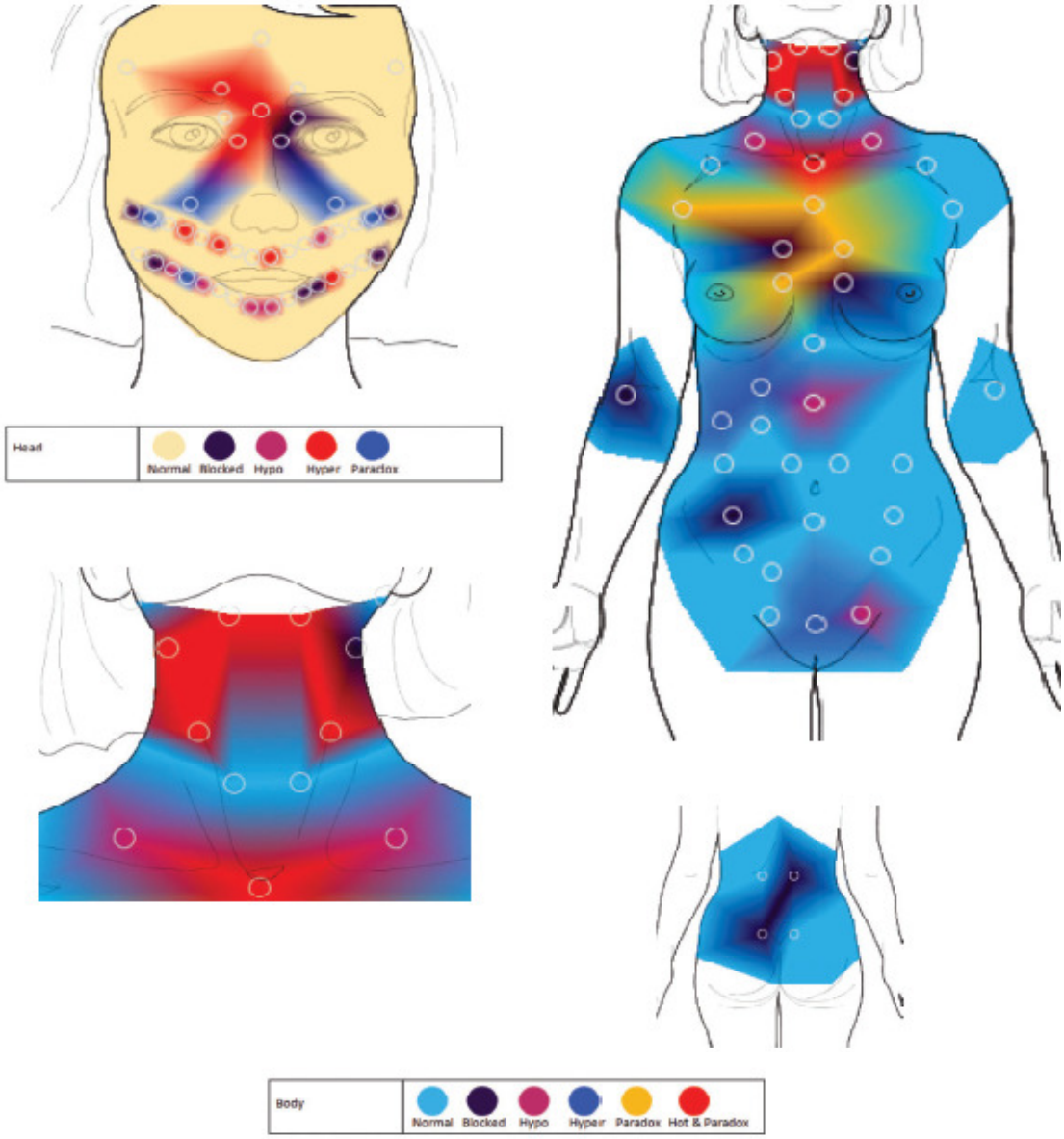
By placing disorder highest priority, blocked regulation second, and proximal radical differences (within the same region) third, priority for treatment can be established with providing the best strategies and patient benefits.

1. Heavy Metal Signature
2. Dental Focus
3. Insulin Resistance Apparent
4. Food Intolerance, Sensitivity
5. Dysbiosis (Mycosis or Bacterial Infection)
6. Side Alert

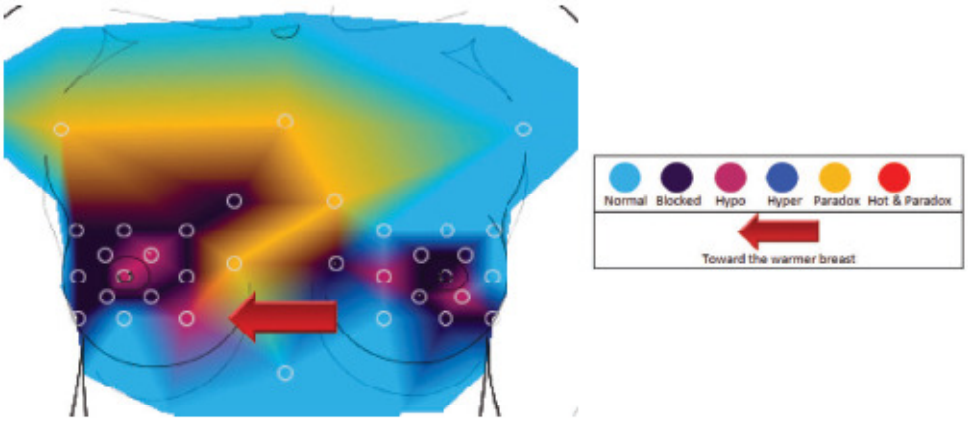
RECOMMENDATIONS

1. Consider chronic toxic metal or environmental chemical exposures such as mercury poisoning (long term); Consider chelation therapy, dietary restriction, Urinary challenge or hair element testing.
2. Investigate for occult infection; X-Ray, root canal assessment; Additionally panoramic x-Ray, assessment of dental metals, interactivity, correlation to stressed organs, galvanism.
3. Consider A1-c, glucose and further pre diabetes as well as diabetes II testing; Supplements may include bitter melon, chromium. In addition, exercise, sugar restriction, raw food diet.
4. Refer to test for celiac and other food sensitivities; Consider l-glutamine, probiotics, elimination diet.
5. Stool analysis for yeast, bacterial, parasitic infection; Alkalization, antifungals, probiotics, dietary restriction of carbohydrates.
6. Investigate problems e.g. teeth, tonsil, sinus, organ on applicable side.

III. GENERALIZED OVERVIEW OF SUSPICIOUS REGIONS



V. BREAST ANALYSIS

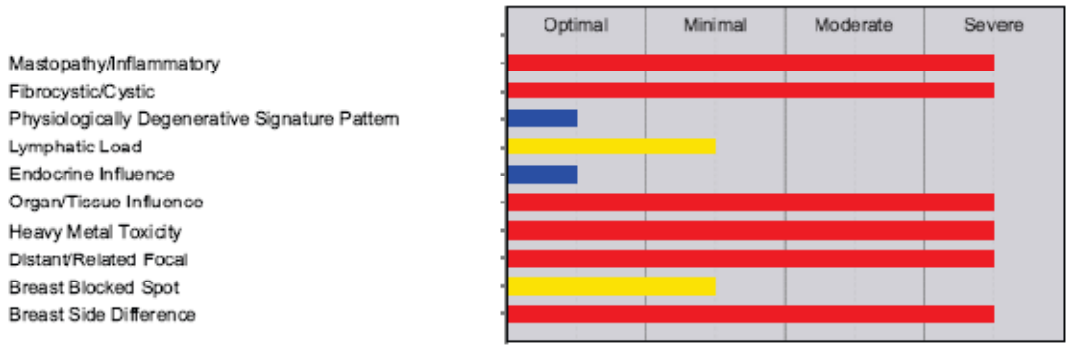


Breast Suspicion Criteria

Sternum Block	X	Breast blocked spot	X	Breast R-L asymmetry	X (R/Warm)
Liver warm/block		Opp. Ovary Dysregulation		Lyl and Terrain Index high	
Tonsil/lymph block	X	Chest disorder elevated	X	2nd Molar possible	X
Lymphatic Index high	X	Breast disorder elevated		Stomach cold/blocked	X

Result: 8/12 criteria met for suspicion (X) (0-5 normal)

Signature & Gradings for Breast Dysfunction



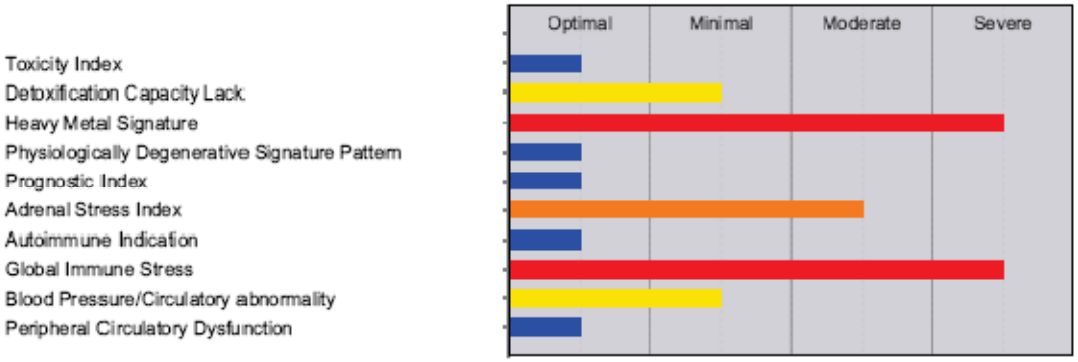
NOTE: Signatures for breast dysfunction can be summarized from a series of 31 criteria based on confirmed case studies. Although Computerized Regulation Thermometry is an adjunct diagnostic device, thousands of patients' lives have been saved by its surveillance of the terrain, possible causal infections distantly involved, and local immune events such as lymphatic influences or hormone receptor abnormalities. The three main categories pertaining to breast diseases and conditions are mastopathy, fibrocystic, and suspicion for a neoplastic tendency.

Breast Analysis Summary

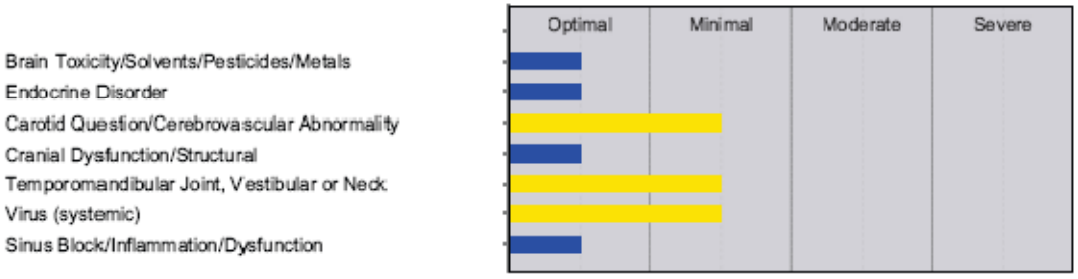
- This 57 year old woman was referred to Jackie Bell. The overview appears as a/an Mastopathy/Inflammatory, Fibrocystic/Cystic, and Organ/Tissue Influence stress patient.
- There is Breast blocked spot and Breast R-L asymmetry apparent.
- According to the established 12 breast criteria 8/12 were indicated. This leaves moderate concerns for breast problems.
- Another thermogram should follow within 3 months in regards to the status after appropriate treatment and investigation. There is also a possibility an elevated suspicion may be due to hormonal cycles and therefore should be repeated at another phase of the menstrual cycle.
- These contributing organs and tissues are given in priority of severity of stress and form the basis for treatment or further tests:
  1. Breast blocked spot
  2. Breast R-L asymmetry
  3. Tonsil/lymph block

VI. DYSREGULATIVE PATTERN SIGNATURES AND RECOGNITION

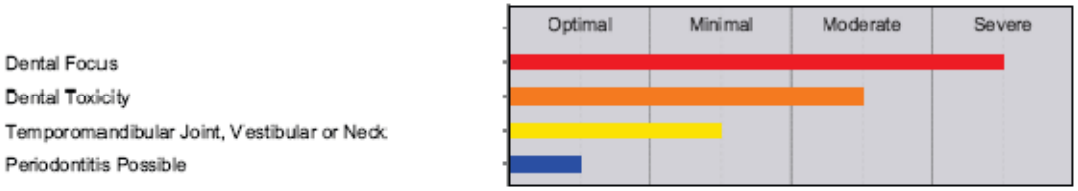
Whole Body Identifier Patterns



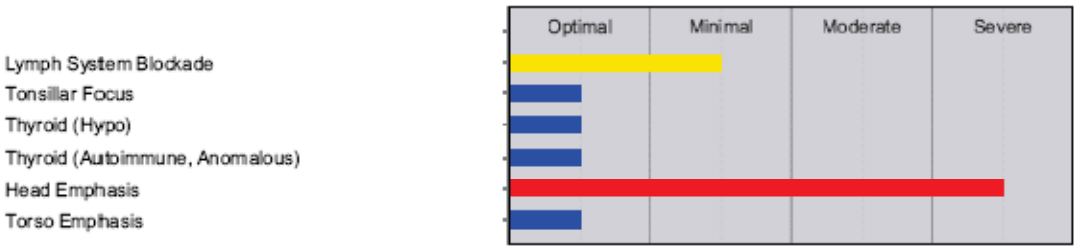
Head/Cranial Disturbances



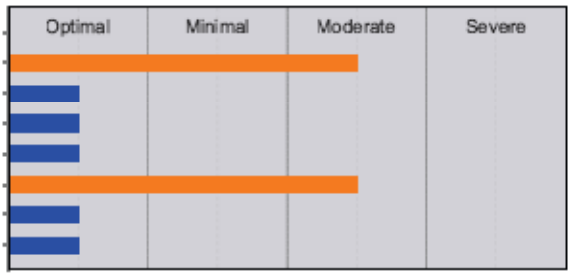
Dental



Neck Region



Chest Region



Sternum Block
Cardiac Function Abnormality
Cardiac Conduction
Myocardium Danger
Lung/Bronchi Suspicion
Pericardium/Extracardial Stress
Axilliary Lymph

Upper Abdomen

Stomach Block
Liver Stress
Biliary Stress
Enzyme Dysfunction
Insulin Resistance Apparent
Pancreatitis Suspicion

Lower Abdomen

Food Intolerance, Sensitivity
Dysbiosis (Mycosis or Bacterial Infection)
Putrification Apparent
Diverticulitis/osis
Appendix Focus
Pelvic Toxicity
Uterine Hypo-function
Uterine Inflammation Indication
Ovarian Hypo-function

Kidney/Back

Kidney Toxicity
Kidney Hypo-function
Back Problem

Cubital Fossae

Side Alert

Approved by Dr. Daniel Beilin, O.M.D., Certified IMAT Thermographic Interpreter

Note: Medical opinions expressed in this report in no way replace the level of pertinence met by the patient's physician when clinical examination and investigation may reveal permutations or reframing of the outcomes and results, leading to variance of conclusion. Thermometry reporting is intended as future and present guidance that reveals trends and suspicions, rather than being an 'absolute' diagnostic test. It functions best when corroborated with laboratory findings and normal imaging methods.

Patient: Female · Age 51 Date: 05-Oct-2015 Page 7

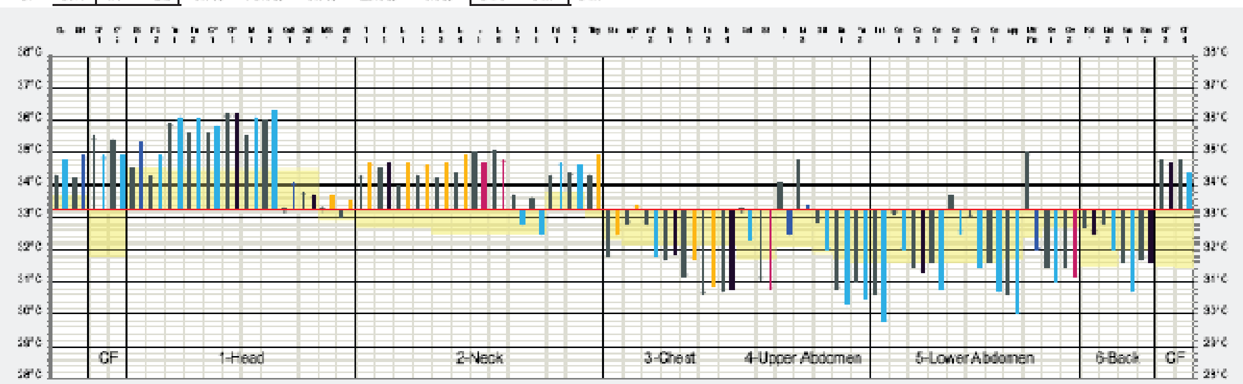
Body

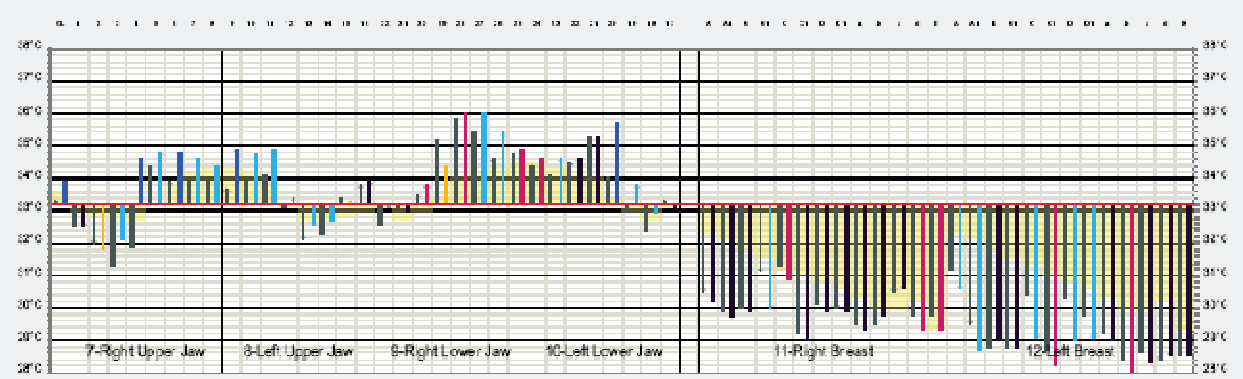
Area	T-xA	DI-A		DI-B	Hyper	Normal	Hypo	Rigid	Paradox	T-Rb	T-Lb	T-xB
1	34.7°	6.1	→	5.5	16.7%	50.0%	0.0%	16.7%	16.7%	35.2°	35.1°	35.2°
2	34.3°	5.5	→	8.2	0.0%	30.8%	15.4%	7.7%	46.2%	34.4°	34.4°	34.4°
3	31.7°	5.0	→	5.7	0.0%	14.3%	0.0%	28.6%	57.1%	32.1°	31.4°	31.9°
4	32.6°	6.2	→	6.5	28.6%	57.1%	14.3%	0.0%	0.0%	32.1°	30.6°	31.7°
5	32.2°	6.9	→	5.9	9.1%	72.7%	9.1%	9.1%	0.0%	31.0°	31.5°	31.2°
6	32.2°	5.7	→	8.0	0.0%	50.0%	0.0%	50.0%	0.0%	31.6°	31.8°	31.7°
1-6	33.0°	6.6	→	6.7	9.1%	45.8%	6.5%	18.7%	20.0%	32.7°	32.5°	32.7°
CF	35.1°	1.0	→	2.9	0.0%	75.0%	0.0%	25.0%	0.0%	34.8°	34.7°	34.7°

Dental/Breast

Area	T-xA	DI-A		DI-B	Hyper	Normal	Hypo	Rigid	Paradox	T-Rb	T-Lb	T-xB
7	33.0°	8.0	→	7.8	25.0%	50.0%	0.0%	12.5%	12.5%	N/A	N/A	33.7°
8	33.3°	6.5	→	8.2	12.5%	50.0%	12.5%	12.5%	12.5%	N/A	N/A	33.8°
9	34.4°	8.2	→	7.8	0.0%	37.5%	37.5%	12.5%	12.5%	N/A	N/A	34.6°
10	33.9°	7.5	→	7.3	12.5%	37.5%	12.5%	37.5%	0.0%	N/A	N/A	34.3°
11	30.1°	7.5	→	8.6	0.0%	7.7%	23.1%	69.2%	0.0%	N/A	N/A	28.8°
12	29.3°	9.7	→	9.1	0.0%	38.5%	15.4%	46.2%	0.0%	N/A	N/A	28.8°

Normal Blocked Hypo Hyper Paradox





Evidence Table : Effectiveness
Question : Is thermography effective in screening and diagnosing breast cancer?

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
Kerr J. Review of the effectiveness of infrared thermal imaging (thermography) for population screening and diagnostic testing of breast cancer. Christchurch: New Zealand Health Technology Assessment (NZHTA), 2004:49.	**Systematic Review** **<u>Method</u>** The NZHTA Core Search was employed and included major bibliographic databases (Medline, Embase etc.) and review databases (EBM reviews, Cochrane, DARE etc). The literature search for this evaluation was not limited by publication date or language. **Objective** To review the evidence for the effectiveness of infrared thermography for population screening and diagnostic testing of breast cancer **Publication type** Studies published between 1985 and 20 May 2004 (inclusive) in the English language, including primary (original) research (published as full original reports) and secondary research (systematic reviews and meta-	I	**Population** **Screening** Asymptomatic women at (any) risk for breast cancer. Women aged 30 to 50 years, women with small breasts, and women with breast implants **Diagnostic** Patients symptomatic for breast cancer (e.g., presenting with a breast lump, thickening, asymmetrical glandular prominence, pain, or nipple discharge) or who have had an abnormal mammogram.	Thermography	Mammography, clinical breast examination ultrasound including infrared thermography compared with the same approaches without infrared thermography.	-	**Outcomes** • significant differences in estimates of sensitivity (Se), specificity (Sp), positive predictive value (PPV) or negative predictive value (NPV), detection of disease at an earlier stage between comparators in the detection of cancer • quality of life (including psychological costs) • health care costs • safety outcomes • reduction in breast cancer mortality. **Results** **Screening** One retrieved article was eligible for review and was appraised for the screening. (prospective cohort) **Diagnostic** Two retrieved article was eligible for review and was appraised for the diagnostic (case-control) **Conclusion** The evidence that is currently available does not provide enough support for the role of infrared thermography for either population screening or adjuvant diagnostic testing of breast cancer. The major gaps in knowledge at this time can only be addressed by large-scale, prospective randomised trials. More	Good Methodological

	analyses). **Appraisal Methodology** Summaries of appraisal results are shown in tabular form (known as Evidence Tables) **Quality of primary paper** categorise studies of diagnostic methods according to susceptibility for bias						robust research on the effectiveness and costs of technologically advanced infrared thermography devices for population screening and diagnostic testing of breast cancer is needed, and the conclusions of this review should be revisited in the face of additional reliable evidence.	

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Fitzgerald A, Berentson-Shaw J. Thermography as a screening and diagnostic tool: a systematic review. N Z Med J. 2012 Mar 9;125(1351):80-91. Review.	**Study design** Systematic review **Method** A comprehensive search of electronic databases together with a search of international websites was conducted. Diagnostic studies comparing thermography with mammography for screening in asymptomatic populations; or comparing thermography with histology in women with suspected breast cancer; were eligible for inclusion. The literature was systematically searched for English language articles that fitted the inclusion criteria from 1984 to the end of April 2011. **Quality of primary**	I	**Participants** For studies investigating thermography for screening, asymptomatic women with unknown disease status were eligible for inclusion. For studies investigating thermography for diagnosis, women with suspicious symptoms (e.g. presenting with a breast lump or nipple discharge), women with suspicious findings on clinical examination or women with an abnormal mammogram were eligible for inclusion. Studies of patients younger than 16 years, animal studies, and studies with fewer than ten	Digital infrared thermography	Screening tool-mammogram or clinical diagnosis As a diagnostic tool-histology.	-	**Results** **Breast thermography for screening** One study was identified (Williams and colleagues in 1990) However, the quality of the included study was poor. Verification bias occurs when not all of the study group receive confirmation of the diagnosis by the reference standard (partial verification bias) A prospective single-gated (diagnostic cohort) study aimed to determine whether thermography could be used to identify women with breast cancer during screening, or identify women at risk of developing breast cancer within 5 years.10,229 women aged 40–65 were invited and attended a breast screening clinic. At the time of screening, infrared imaging reported a sensitivity of 61%, specificity of 74%, PPV of 0.01%, NPV of 1.00% ,+LR of 2.35 (95% CI 1.91 to 2.88) and –LR 0.53 (95% CI 0.38 to 0.73). Five years following initial screening, infrared imaging reported a sensitivity of 28%, specificity of 74%, PPV of 0.01%, NPV of 0.99%, +LR 1.09 (95% CI 0.73 to 1.63) and –LR 0.97 (CI 95% CI 0.83 to 1.14). **Breast thermography for diagnosis** Five studies were identified assessing the	

	paper included studies was appraised using the QUADAS criteria. Extensive systematic literature searches were conducted, study quality was carefully assessed using a validated tool,7 and the authors attempted to maximise available data by deriving accuracy data from those studies where not all diagnostic measures were reported.		participants were excluded.				use of thermography as a diagnostic tool in women with suspicious symptoms. Overall the included studies were of average quality. All studies reported a high risk of bias for at least one item on the QUADAS checklist. A limited number of studies were identified comparing digital infrared thermography to histology in women with symptoms, suspicious clinical findings, or abnormal mammogram. Four studies used adiagnostic Cohort design, while one study used a case-controldesign. While most studies were able to show sensitivity over 70% for at least one mode of digital infrared thermography, the specificity of thermography for diagnosting breast cancer was generally low, between 12% and 85% for most studies (Table 2). One study reported results that conflicted with other studies, showing low sensitivity (25%) and a high specificity (85%)14 and another study showed high (83%) sensitivity and high 81% specificity (81%)13. In the studies presented in this review, low specificities are due to a high number of false-positive results. For example, the study by Parisky15 reported a false-positive rate of 1544 and a false-negative rate of 13 out of the 2299 patients tested. This means that for 68% of the patients in this study thermography provided an incorrect diagnosis. Another study by Arora12 that showed a higher specificity reported a false positive rate of 19 and a false-negative rate of 6 in a study of 92 participants. This means that for 27% of the patients in the study, thermography provided an incorrect diagnosis.	

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Vreugdenburg TD, Willis CD, Mundy L, Hiller JE. A systematic review of elastography, electrical impedance scanning, and digital infrared thermography for breast cancer screening and diagnosis. Breast Cancer Res Treat. 2013 Feb;137(3):665-76.	**Study Design** Systematic Review with Meta analysis **Objective** The objective of this study aimed to systematically identify and evaluate all the available evidence of safety, effectiveness and diagnostic accuracy for three emerging classes of technology promoted for breast cancer screening and diagnosis. **Search strategy** A systematic search of seven biomedical databases (EMBASE, PubMed, Web of Science, CRD, CINAHL, Cochrane Library, Current Contents Connect) was conducted through March 2011, along with a manual search of reference lists from relevant studies. **Study selection** Search results were	I	Studies were eligible for inclusion if they investigated the use of a relevant index test for the detection of breast lesions in human participants The principal outcomes of interest included measures of diagnostic and screening effectiveness (a reduction in breast cancer mortality attributable to imaging), safety and diagnostic accuracy.	DITI	Histology	-	**Results** Significant heterogeneity was observed among studies with a prospective study design, and those that did not blind the index test to the results of the reference standard. DITI studies were also highly variable, reporting sensitivities between 25.0 and 96.7 % (median 82 %), and specificities between 11.8 and 84.9 % (median 55 %). Due to high levels of variation among study results, and the large degree of variation among the methods and devices used for imaging, it was deemed inappropriate to produce pooled estimates of diagnostic accuracy for any of he three classes as a whole. DITI studies reporting diagnostic accuracy parameters in symptomatic populations only **Conclusion** Due to the lack of available data evaluating the use of these devices in asymptomatic women, these devices cannot be recommended for safe use in healthy, screening populations at this time. It is recommended that future	

	initially screened by title and abstract by the principal author using selection criteria that were determined a priori. Inclusion of full-text articles was decided by consensus with secondary authors. Quality appraisal was conducted by the principal author using a standardised scoring sheet and **validated by coauthors.** Diagnostic accuracy studies were appraised using the **Quality Assessment of Diagnostic Accuracy Studies (QUADAS)** tool.						research should aim to determine the performance of these devices in asymptomatic populations before they are adopted more widely into practice as a screening tool or diagnostic tools.	

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Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
Parisky et al. (2003)	**Study setting** Multicentre. Clinical sites in Los Angeles, Baltimore, Washington DC, Boston and Miami. **Design** Non-controlled clinical trial (analysed like a case-control). **Study aim** To determine the efficacy of a dynamic computerised IR imaging system for distinguishing between benign and malignant lesions in patients undergoing biopsy on the basis of mammographic findings. **Methods** Recruited patients for whom breast biopsy was recommended on basis of abnormal M, abnormal PE, or both. Patients then had IR imaging, then surgery. Each subject's IR images analysed by 3 evaluators (so 875 lesions produced 2625 IRI results) Evaluators were **blinded to biopsy result, but knew certain PE and M**	III	Participants Patients recruited n = 1293 (Exclusions n = 524) Patients whose data remained in study for evaluation n = 769 **Gender** female (766), male (3). **Age** <40 years (68), 40-60 years (433), > 60 years (268). No age range, median or mean reported (although median age must have been between 40-60 years). **Ethnicity** white (463), black (207), hispanic (81), asian (13), other (5). A subset analysis	**Index test** **Infrared imaging (IR).** Dynamic imaging process (breast cooling).	**Other diagnostic tests** All subjects had **mammography (M)**. No technical details, nor result categories specified. All subjects had **physical examination (PE).** No details specified. 45% subjects had ultrasound (US). No technical details, nor result categories given. **Reference standard** Histological diagnosis (core or	-	**Results** Of the total 875 lesions analysed, 187 were malignant and 688 were benign. So, for these lesions, the PPV for standard work-up (M +/- PE, +/- US) is 21% (95% CI= 19 to 24). From 875 lesions 2625 IR results were reported. 326 IR results were then excluded (because evaluators could not concur IR area with M or PE area of suspicion), leaving 2299 IR results for analysis. Se 97% (95%CI =96, 99) Sp 14% (13, 16) PPV 24% (22, 26) NPV 95% (93, 98). From these 2299 results, the PPV for standard work-up can be calculated and is 22% (20, 23)*. The subset analysis of 479 lesions produced 1437 IR results, (206 excluded because of same reasons as above) leaving 1231 IR results: Se 100% (95%CI =99, 100), Sp 18% (16, 21), PPV 27% (25, 30), NPV 99% (98, 100). From these 1231 results, the PPV for standard work-up can be calculated, and is 24% (21, 26)*.	

	details. Inclusion criteria None specified. Exclusion criteria Breast surgery in last year Breast implants Breast reduction surgery Radiation or histologically proven cancer in breast of interest Pregnancy Weight more than 135kg.		excluded lesions defined as microcalcifications on M. This subset therefore left for analysis 479 lesions from 448 patients.		surgical biopsy).			

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Bibliographic citation	**Study Type / Methods**	**LE**	**Number of patients and patient characteristics**	**Intervention**	**Comparison**	**Length of follow up (if applicable)**	**Outcome measures/ Effect size**	**General comments**
Kolarić D, Herceg Z, Nola IA, Ramljak V, Kulis T, Holjevac JK, Deutsch JA, Antonini S. Thermography--a feasible method for screening breast cancer? Coll Antropol. 2013 Jun;37(2):583-8.	**Study Design** **Co**hort study **Study Aim** Our study analyzed the ability of mammography and thermography to accurately detect breast carcinoma. **Method** All subject undergone diagnostic work up of performed mammography, ultrasound examination and fine-needle aspiration (FNA). Who had scheduled breast surgery **Index Test** Thermography imaging using a new generation of digital infrared camera According to standardized protocol, the patients raised their arms above the head and 5 images were taken: front, right semi-oblique, right oblique, left-semi oblique and left oblique, in order to obtain the images of complete breast skin area.	I	26 consecutive female patients who had scheduled breast surgery at the University Hospital for tumors, Zagreb in 2009 The average age of patients was 49.42 years **Inclusion criteria** age above 35 years, diagnostic work up of performed mammography, ultrasound examination and fine-needle aspiration (FNA).	Thermography	Histological examination	-	**Results** While mammography detected 31 changes in 26 patients, thermography was more sensitive and detected 6 more changes. **Cytological Examination** All 37 changes were subjected to the cytological analysis and it was found that in 16 (43.24%) samples malignant alterations 8 (21.62%) samples were suspected malignant 11 (29.73%) were benign with atypia/ proliferation 2 (5.4%) samples had benign findings. **Histological examination** Found 75.7% malignant changes. All collected data were statistically reviewed and showed that **mammography** sensitivity was 85% and specificity 84%, and proportion of PPV results were 85%, while **thermographic** results showed sensitivity of 100% specificity 79% and proportion of PPV results 92% (at confidence interval CI 95%) **Conclusion** Authors conclude that their »results indicate that it would be prudent to use thermography as a primary screening method in detection of breast carcinoma«	Not mentioned whether the histological assessor were blinded Small sample size No CI were given Selection bias Symptomatic or asymptomatic patients nor were they compared in a fashion blinded to the results of mammography and ultrasound preventing from any

	They are graded using Marseille and Hoekstra protocol standardized reading protocols. It was considered that breast lesions finding was positive if both TH2–TH5 Marseille scores and positive finding on Hoekstra descriptive protocol were present. **Other Diagnostic Test** **Ultrasound exams** No result categories specified. **Mammography imaging** Had technical detail and result categories specified Fine Needle Aspiration (FNA) Had technical detail and result categories specified **Reference Standard** Histological biopsy							possibility to analyze results from thermography alone, but only from thermography as an adjunct to mammography and/or ultrasound No method so far was described to accurately transpose the thermographic location of the lesion to the mammogram or ultrasound and to surgical specimen.

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Keyserlingk et al. (1998) Montreal, Canada	**Study setting** Ville Marie Breast and Oncology Center. **Study design** Case Control. **Study aim** To assess the potential contribution of currently available high-resolution digital IR as an adjuvant imaging technique in the early detection of breast cancer **Methods** Retrospective chart review from August 1995 onwards (end date not specified) to identify consecutive cases (post-operative patients having initial diagnosis of breast cancer, with final staging as either DCIS, stage I, or stage II) and controls (post-operative patients with benign breast histology following open surgical breast biopsy). **Inclusion criteria** Patient pre-operative evaluation included	III	**Participants** n = 200 Clinical reason for referral to breast centre not specified. **Cases** n=100 (from 128 charts reviewed) Age range 31-84 years (mean= 53). Final staging of breast cancer DCIS (n=4), stage I (n=42) stage II (n=54). Mean tumour size 2.5cm. **Controls** n = 100 (from unknown number of charts reviewed) No further demographics provided for this group. No pathological diagnostic details supplied for this patient group. No statistical	Index test Infrared imaging (IR) (Bales Scientific®*). High-resolution, scanning, electronically cooled system. Four images. Computer reading graded by examining physician. Final results categorised as 'normal' or 'abnormal'.	Comparators Mammography (M). At least four standard-view images. Interpreted by examining physician and radiologist. Graded as 'suspicious', 'equivocal' or 'non-specific'. Physical examination (PE) Details not specified. Graded as 'suspicious', 'equivocal' or 'nonspecific'. Reference standard Histological diagnosis (surgical	-	IR alone Se 83% (95%CI=76, 90) Sp=81% (73, 89) PPV=81% (74, 89) NPV=83% (75, 90). M* alone Se=85% (78,92) Sp=70% (61,78) PPV=74% (66, 82) NPV=82% (74, 90). Cases Incremental difference between M (66%) and IR +M (93%) Exact McNemars ^{2} value=27 (1d.f.), p<0.0001. **Reviewer conclusions** Although the sensitivity results present highly significant data suggesting an additive benefit of IR to M, there is inadequate data reported, specifically the proportion of false positive results, to fully confirm a beneficial role of IR as an adjuvant diagnostic modality for breast cancer	

	clinical exam, mammography and IR imaging. Definitive surgical management as first therapeutic modality.		analyses presented comparing demographics of patient groups at baseline.					