Observational Study to Evaluate the Clinical Efficacy of Thermalytix for Detecting Breast Cancer in Symptomatic and Asymptomatic Women

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PURPOSE To evaluate the sensitivity and specificity of Thermalytix, an artificial intelligence–based computer-aided diagnostics (CADx) engine, to detect breast malignancy by comparing the CADx output with the final diagnosis derived using standard screening modalities.

METHODS This multisite observational study included 470 symptomatic and asymptomatic women who presented for a breast health checkup in two centers. Among them, 238 women had symptoms such as breast lump, nipple discharge, or breast pain, and the rest were asymptomatic. All participants underwent a Thermalytix test and one or more standard-of-care tests for breast cancer screening, as recommended by the radiologists. Results from Thermalytix and standard modalities were obtained independently in a blinded fashion for comparison. The ground truth used for analysis (normal or malignant) was the final impression of an expert clinician based on the symptoms and the available reports of standard modalities (mammography, ultrasonography, elastography, biopsy, fine-needle aspiration cytology, and so on).

RESULTS For the 470 women, Thermalytix resulted in a sensitivity of 91.02% (symptomatic, 89.85%; asymptomatic, 100%) and specificity of 82.39% (symptomatic, 69.04%; asymptomatic, 92.41%) in detection of breast malignancy. Thermalytix showed an overall area under the curve (AUC) of 0.90, with an AUC of 0.82 for symptomatic and 0.98 for asymptomatic women.

CONCLUSION High sensitivity and high AUC of Thermalytix in women of all age groups demonstrates the efficacy of the tool for breast cancer screening. Thermalytix, with its automated scoring and image annotations of potential malignancies and vascularity, can assist the clinician in better decision making and improve quality of care in an affordable and radiation-free manner. Thus, we believe Thermalytix is poised to be a promising modality for breast cancer screening.

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INTRODUCTION

The incidence of breast cancer in women has been increasing over recent years. Approximately 2.1 million women were diagnosed with breast cancer in 2018, and more than 600,000 women died as a result.[1,2] Screening mammography has been shown to reduce breast cancer mortality by approximately 20% in high-resource settings.[3,4] However, mammography has low sensitivity in women with high breast density and is not scalable or economical in resource-constrained environments.[4,5] Breast ultrasonography (USG) is effective in symptomatic women and is used as an adjunct to mammography in patients in whom mammography is inconclusive, noncontributory, or contraindicated.[6-8]

Infrared (IR) breast thermography has been considered for detecting early breast cancer in the past.[9] Thermography involves analyzing heat patterns on the skin surface of the breasts to determine focal thermal increase, asymmetry, and other thermal abnormalities. The vascular changes associated with malignancy, facilitated by the release of nitric oxide, lead to an increase in heat in the vicinity of a malignant lesion and depict abnormal warm thermal patterns surrounding the lesion that can be captured using a high-resolution IR camera.[9-11] However, conventional thermography involves manual interpretation of thermal images, which is complex and often results in erroneous results owing to subjectivity. Thermalytix is a computer-aided diagnostic engine intended to detect early-stage breast cancer with automated quantitative analysis of thermal images, eliminating the subjectivity in interpretation. In this article, we evaluate the clinical efficacy of Thermalytix.

ASSOCIATED CONTENT

Data Supplement

Author affiliations and support information (if applicable) appear at the end of this article.

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CONTEXT

Key Objective

We introduce a new screening modality—Thermalytix—a low cost, portable, and radiation-free test—and present the results of a multisite clinical study. Thermalytix is a computer-aided diagnostics engine that detects breast malignancy from thermal variations on the breast surface using artificial intelligence algorithms.

Knowledge Generated

Thermalytix resulted in a sensitivity of 91%, specificity of 82.4%, and area under the curve of 0.9. Thermalytix, with its automated scoring and image annotations of potential malignancies, can be a promising imaging modality to help a clinician make better decisions and improve overall quality of care.

Relevance

Because Thermalytix is a low-cost, noninvasive test and can be conducted by technicians with minimal training, it can be used as the primary screening method in resource-constrained populations for early detection of breast cancer in women of all age groups.

LITERATURE REVIEW

In 1980, Gautherie et al[12] evaluated the performance of thermography in more than 58,000 symptomatic women. Among them, 1,245 women diagnosed as normal or benign by conventional screening modalities exhibited questionable thermal anomaly on thermography. More than a third of these women with thermal abnormality developed cancer in the 5-year follow-up period.[12] This study, along with others, generated a spike in thermography-based breast cancer screening studies, but eventually, there was a lack of enthusiasm from practitioners because interpretations of thermal images suffered from subjectivity.[9] Furthermore, the sensitivity of thermography in multiple studies conducted between 2000 and 2019 ranged from 47% to 100%, showing subjectivity and variability in interpretation.[13-26] This could be attributed to the manual interpretation of thermal images that involves visual analysis of thousands of color pixels, which is a cognitive overload and, hence, error prone.

In recent years, with the development of high-resolution thermal sensors coupled with computer-aided diagnostic (CADx) analysis, IR breast thermography is again re-emerging as a modality for detecting breast cancer.[11,14] Borchartt et al[27] conducted a survey of different research efforts that showed the efficacy of machine learning (ML) for automating thermal analysis for breast cancer screening that could help in making the analysis more quantitative and consistent. To the best of our knowledge, no systematic clinical study has been published so far showing the efficacy of automated thermal interpretation compared with standard breast cancer screening modalities.

In this article, we propose a new artificial intelligence (AI)-based CADx solution, called Thermalytix (Niramai, Bangalore, India), for automatic interpretation of thermal images using ML. We present an observational, multisite clinical study evaluating Thermalytix as a screening modality for breast cancer compared with currently accepted screening modalities.

METHODS

Thermalytix Breast Cancer Screening

Thermalytix is computer-aided diagnostic software that uses AI-based techniques to analyze and interpret breast thermal images to generate a breast health report automatically. A thermal image is a representation of temperature variations on the skin captured using a high-resolution IR camera. The Thermalytix engine first determines areas of high thermal activity from captured

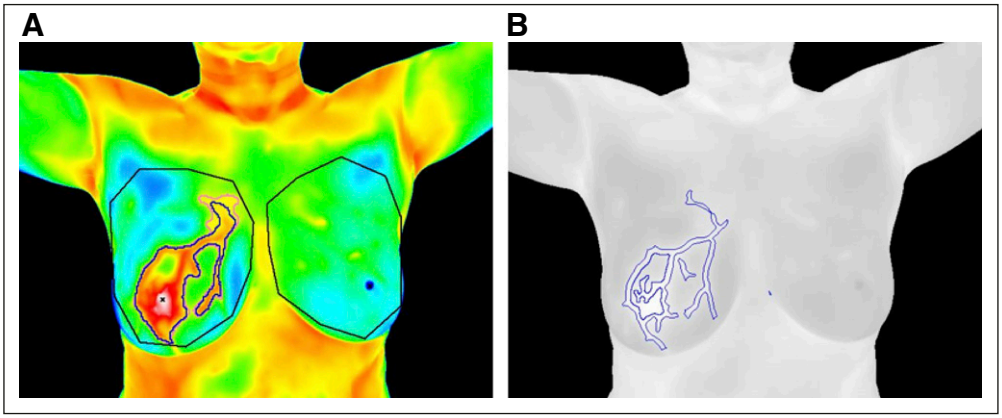


FIG 1. (A) Potential tumor boundaries marked with blue boundaries and (B) automatically extracted vessel regions with blue boundaries in grayscale.

thermal images using relative temperature thresholding to identify hot spots and warm spots.[28] In addition, in high-resolution images, it identifies cylindrical thermal patterns that represent vascular structures using a novel image processing technique.[29.]

These hot spots, warm spots, and vascular patterns are further analyzed to extract a set of features that are provided as input to three pretrained ML models to generate quantitative scores. These scores signify the probability of a malignant breast lesion. The Thermalytix engine also generates a quantitative interpretation report with the scores and annotated thermal images with markings of hot spots indicating malignant lesions and the vascularity network. Figures 1A and 1B show the analyzed images with lesion marking and vascularity, respectively. Additional details of the Thermalytix algorithms are described in our recent technical article [30]

A sample Thermalytix report is provided in the Data Supplement. The report includes three automatically generated quantitative scores, each of which is a real number between

TABLE 1. Distribution of Study Population Characteristics and Imaging Modalities Across Two Age Groups and Associated Cancer Rates

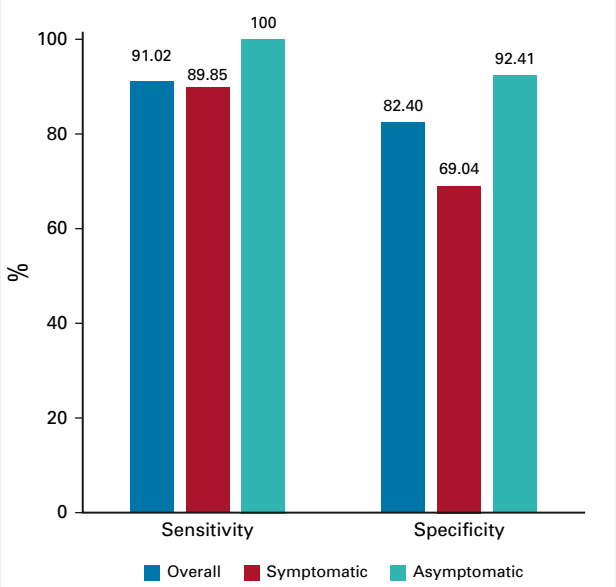
	Age < 40 Years			Age ≥ 40 Years		
Characteristic	**Participants**	**Cancer Detected (No.)**	**Rate[a] (95% CI)**	**Participants**	**Cancer Detected (No.)**	**Rate[a] (95% CI)**
No. of women	(n = 127)	11	8.7 (4.6 to 15.3)	(n = 343)	67	19.5 (15.5 to 24.2)
Symptomatic	75 (59)	11	14.7 (7.9 to 25.2)	163 (48)	58	35.6 (28.3 to 43.5)
Lump	41 (55)	9	21.9 (11.1 to 38.0)	90 (55)	47	52.2 (41.5 to 62.8)
Discharge	6 (8)	1	16.7 (0.9 to 63.5)	11 (7)	3	27.3 (7.3 to 60.7)
Pain	38 (51)	2	5.7 (0.9 to 19)	67 (41)	13	19.4 (11.1 to 31.2)
Asymptomatic	52 (41)	0	0 (0 to 8.6)	180 (52)	9	5 (2.5 to 9.6)
Family cancer history	24 (19)	2	8.3 (1.5 to 2.8)	58 (17)	13	22.4 (12.9 to 35.6)
Breast cancer	15 (63)	1	6.7 (0.3 to 34.0)	34 (58)	4	11.8 (3.8 to 28.4)
Ovarian cancer	1 (4)	0	0 (0 to 94.5)	2 (3)	1	50 (2.7 to 97.3)
Other cancer	8 (33)	1	1.2 (0.7 to 5.3)	23 (40)	8	34.8 (17.2 to 57.2)
No family history	103 (81)	9	8.7 (4.3 to 16.4)	285 (83)	54	18.9 (14.7 to 24.1)
Menopause						
Yes	46 (36)	1	2.2 (0.1 to 13.0)	208 (61)	44	21.2 (15.9 to 27.5)
No	81 (64)	10	12.3 (6.4 to 22.0)	135 (39)	23	17.0 (11.3 to 24.7)
Thermal imager used						
FLIR T650SC (site 1)	16 (13)	2	12.5 (2.2 to 39.6)	40 (11)	9	22.5 (11.4 to 38.9)
FLIR A315 (site 1)	52 (41)	8	15.4 (7.3 to 28.6)	174 (51)	48	27.6 (21.2 to 35.0)
Meditherm (site 2)	59 (46)	1	1.7 (0.1 to 10.3)	129 (38)	10	7.7 (4.0 to 14.2)
Results of different tests						
Thermalytix						
Positive	33 (26)	11	33.3 (18.6 to 51.9)	107 (31)	60	56.1 (46.2 to 65.5)
Negative	94 (74)	0	0 (0 to 4.9)	236 (69)	7	2.97 (1.3 to 6.3)
Mammography						
BIRADS 4,5	11 (23)[b]	6	54.5 (24.6 to 81.9)	49 (25)[b]	43	87.8 (74.5 to 94.9)
BIRADS 1, 2, 3	37 (77)[b]	3	8.1 (2.1 to 23.0)	145 (75)[b]	5	3.5 (1.3 to 8.3)
Not performed	79 (62)	2	2.5 (0.4 to 9.7)	149 (43)	19	12.7 (8.0 to 19.4)
Ultrasound						
BIRADS 4, 5	13 (10)[b]	11	84.6 (53.7 to 97.3)	69 (21)[b]	67	97.1 (88.9 to 99.5)
BIRADS 1, 2, 3	113 (90)[b]	0	0 (0 to 4.1)	263 (79)[b]	0	0 (0 to 1.8)
Not performed	1 (1)	0	0 (0 to 94.5)	11 (3)	0	0 (0 to 3.2)

NOTE. Data presented as No. (%) unless otherwise indicated.
Abbreviation: BIRADS, Breast Imaging and Reporting Data System.
[a]Rate is presented as number of cancers per 100 women.
[b]Percentages excluded women who did not undergo the test.

0 and 1 indicating the probability of malignancy, with 0 being normal and 1 being a high chance of malignancy. Following is a brief description of the three scores:

1. The Thermobiologic Score (TS) is based on the 34 thermal and symmetry features using information regarding boundary and shape of hot spots and warm spots, relative temperature differences, thermal symmetry between breasts, and the presence and extent of both hot-spot and warm-spot regions.[28]
2. The Areolar Score (AS) describes the heat pattern around the areolar region and is derived by extracting 16 features characterizing hot-spot regions near the nipple.
3. The Vascular Score (VS) is based on 21 extracted features derived from the shape and temperature of the blood vessel structures as well as the tortuosity of the vessels, relative increase in temperature, number of vessels, number of branches in the largest vessel, temperature deviation in the vessel, and symmetry of vasculature between the breasts. A novel image processing and deep learning–based algorithm is used to determine the blood vessel structure from the thermal image to obtain the VS from extracted vascular features.[29]

An overall Thermalytix score is derived from a combination of TS, AS, and VS, along with patient risk factors such as age, presence of symptoms, and last menstrual period, using a support vector machine (SVM) ML classifier.



	True Positives (No.)	False Negatives (No.)	True Negatives (No.)	False Positives (No.)
Overall	71	7	323	69
Symptomatic	62	7	117	52
Asymptomatic	9	0	206	17

FIG 2. Performance of Thermalytix on 470 women compared with standard of care.

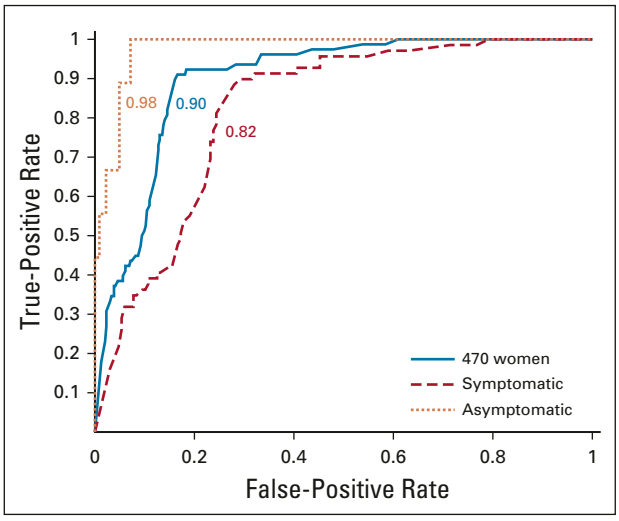


FIG 3. Receiver operating characteristic curves for Thermalytix considering all 470 women, only symptomatic and only asymptomatic population.

Study Protocol

A multisite, cross-sectional, observational study to compare the clinical efficacy of Thermalytix with standard of care was conducted on women ≥ 18 years of age at two sites, namely, Health Care Global, a reputed cancer hospital chain, and Central Diagnostics Research Foundation, a diagnostic center, both in Bangalore, India. All women who visited the two centers between May 6, 2016 and February 2, 2019, were invited to participate in the study. All women between 18 and 82 years of age who gave informed consent and had no previous clinical breast intervention were included in the study. Women who were pregnant, were lactating, had a known history of breast cancer, or had undergone lumpectomy or mastectomy were excluded from this study.

Initially, 587 women provided consent for the study and were recruited. Participant details such as demographic characteristics, symptoms, family cancer history, and menopausal status were obtained using a questionnaire. Based on these data, 15 patients were excluded because of biopsy-proven cancer before recruitment (n = 7), had undergone a mastectomy (n = 4), had undergone a lumpectomy (n = 1), or were lactating (n = 3). The initial 102 participants were used for retraining ML models of the Thermalytix AI engine to include images from all three different thermal camera models available in the current setting. The subsequent 470 participants were included in the prospective study.

All study participants underwent the radiation-free automated Thermalytix test, followed by mammography and/or USG tests, which were interpreted by qualified radiologists and were documented independently. Per clinical practice and at the radiologist's discretion, women > 40 years of age were referred for mammography, followed by USG,

TABLE 2. Summary of Results

Characteristic/Result	Value
Total No. of women included in data analysis	470
No. of women who underwent mammography	242
No. of women who underwent ultrasonography	458
No. of women who also had breast ultrasound elastography	35
Total No. of malignancies	78
Overall sensitivity, %	91.02
Overall specificity, %	82.39
Sensitivity of Thermalytix in asymptomatic patients, %	100
AUC	
Overall	0.90
Symptomatic	0.82
Asymptomatic	0.9

Abbreviation: AUC, area under the curve.

whereas younger women and women with severe pain or swelling underwent only USG. Mammography was performed in 27% of the women < 40 years of age as recommended by a radiologist to reach a final diagnosis. In some patients, USG included elastography at the radiologist's discretion. In patients in whom malignancy was suspected, fine-needle aspiration cytology (FNAC) or biopsy was recommended. Respective radiologists of the institutes arrived at a final diagnosis based on the various test results available (blinded to Thermalytix), which was used as the ground truth for computing sensitivity and specificity of Thermalytix.

Imaging for Thermalytix was performed on site by a trained technician per protocol as described in the Data Supplement. Thermal images of the participant captured in five views were uploaded to the Thermalytix software. The Thermalytix AI engine performed automated quantitative interpretation in real time and generated a detailed Thermal Analysis report. The following definitions were used for positive tests:

- Thermalytix: Thermalytix result was considered positive if the overall Thermalytix SVM score was ≥ 0.5.
- Mammography and USG: The results were scored by trained expert radiologists according to the American College of Radiology Breast Imaging and Reporting Data System (BIRADS). BIRADS 4 and 5 were considered positive.
- FNAC and biopsy: Lesions detected as positive for malignancy included both in situ and invasive cancers. All other benign findings were documented.
- Disease positive: The final diagnosis of malignancy was decided by radiologists after reviewing the reports from standard breast cancer screening modalities per clinical practice. A patient found positive for malignancy (BIRADS 4 or 5) by mammography was further validated by breast USG. If conventional USG was inconclusive, the radiologists used USG elastography for confirmation. For women who underwent a biopsy or FNAC, the result of the biopsy or FNAC test was considered final diagnosis.

RESULTS

Study Data

A total of 470 women who satisfied the inclusion criteria and consented to the study were included in the data analysis. Of these, 127 women were < 40 years of age, and 343 were ≥ 40 years of age. A study participant was categorized as symptomatic if she had a breast lump, breast pain, nipple discharge, nipple inversion, or skin changes in the breast. In the study population, 238 women were symptomatic and the remaining 232 women were asymptomatic. Among the symptomatic women, 55% had a breast lump. Table 1 provides the distribution of different characteristics of this study population along with the cancer rate for the two age groups.

All 470 women who were included in the analysis underwent the Thermalytix test. Mammography was performed on 242 women, and 458 underwent USG. Of the 470 women, 78 women (16.6%) were considered disease positive based on the final impression of the expert radiologist using one or more of the available reports of mammography, USG, elastography, FNAC, or biopsy tests. Four women who were radiologically positive were found to be benign on full excision biopsy and were therefore considered disease negative. All biopsy-confirmed malignancies were invasive ductal carcinoma, except one, which was invasive lobular carcinoma.

Performance of Thermalytix

The overall sensitivity of Thermalytix was found to be 91.02% (95% CI, 81.8% to 96%). The specificity was 82.39% (95% CI, 78.2% to 86%). Although positive predictive value was 50.71%, Thermalytix showed a high negative predictive value of 97.88%. Detailed sensitivity and specificity results of Thermalytix for the symptomatic and asymptomatic populations are provided in Figure 2. It is interesting to note that Thermalytix showed 100% sensitivity in the asymptomatic population. Thermalytix resulted in an area under the curve (AUC) of 0.90 for all 470 women, with an AUC of 0.82 in symptomatic and 0.98 in asymptomatic women, as shown in Figure 3 and Table 2. The correlation of Thermalytix true positives, false positives, true negatives, and false negatives with mammography and USG imaging tests are shown in Figure 4.

Thermalytix Compared With Mammography

In the subset of the study population who underwent both Thermalytix and mammography (n = 242), Thermalytix showed higher sensitivity (91.23%) compared with mammography (85.96%), whereas mammography demonstrated higher specificity (94.05%) than Thermalytix (68.65%). However, because none of the Thermalytix-positive patients who were negative on mammography and USG had confirmatory magnetic resonance imaging

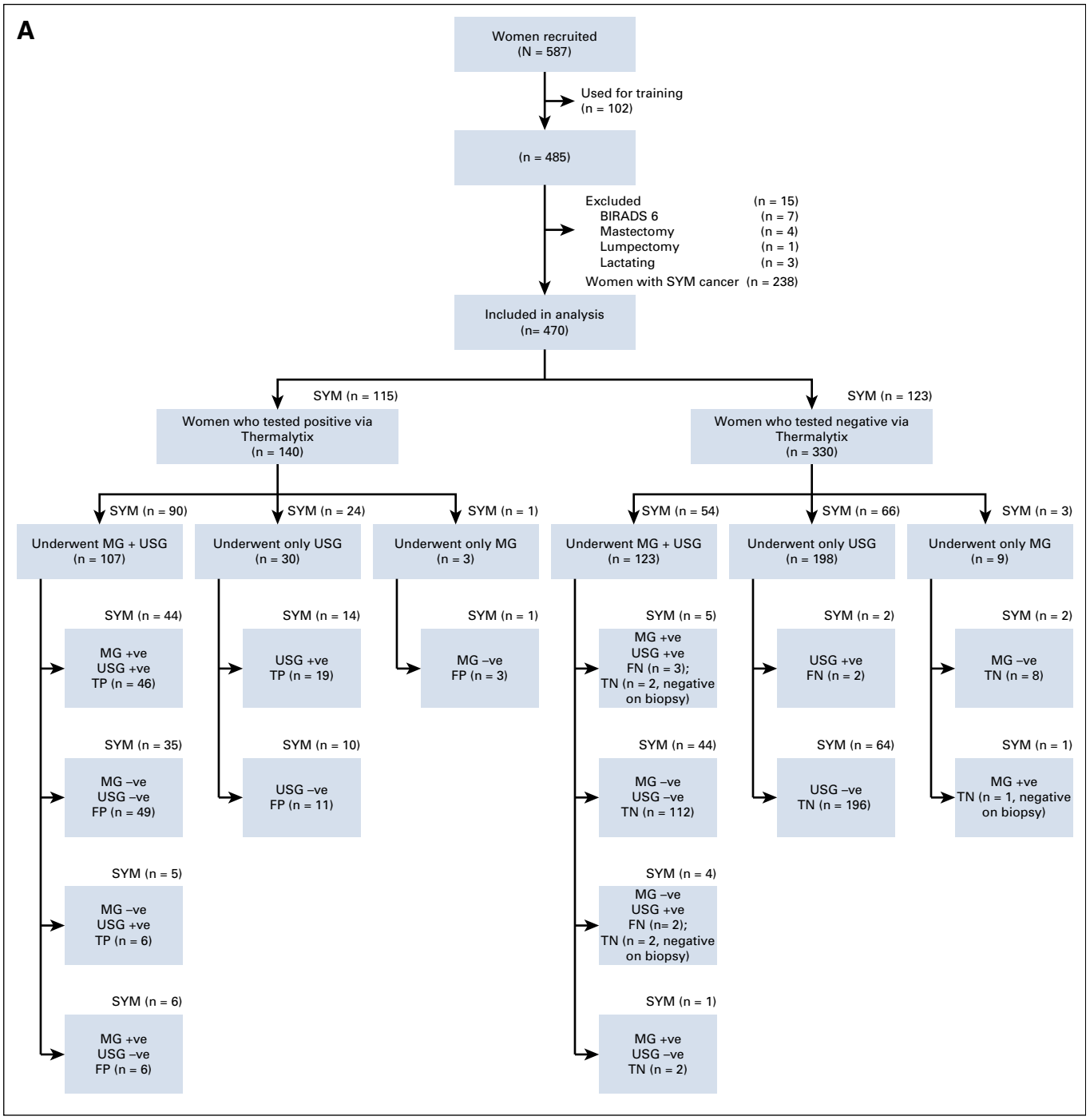


FIG 4. Flow diagram of women enrolled in the trial. BIRADS, Breast Imaging and Reporting Data System; FN, false negatives; FP, false positives; MG, mammography; SYM; women with symptomatic cancer; TN, true negatives; TP, true positives; USG, ultrasonography.

(MRI) or biopsy, final diagnosis of disease negative was biased toward mammography. In the asymptomatic group who underwent both tests (n = 95), four cancers were detected, and Thermalytix demonstrated superior sensitivity of 100% compared with the 50% sensitivity obtained with mammography. This is consistent with other studies, which also found missed cancers during routine screening mammography.[31]

Among the 470 women in the study population, mammography scans were not recommended for 228 women because of dense breasts, younger age, or other clinical reasons as decided by radiologists. In this subset of women (n = 228), Thermalytix showed a high sensitivity and specificity of 90.48% and 94.69%, respectively. Thermalytix detected 19 of the 21 patients diagnosed as having malignancy in this subset of patients who did not

TABLE 3. Results Across Different Camera Models

Camera Model	Thermal Resolution	Thermal Sensitivity (°C)	Sensitivity of Thermalytix (%)	Specificity of Thermalytix (%)
Meditherm IRIS 2000 (TIFF)	320 × 240	0.5	90.1	100
FLIR T650sc	640 × 480	0.02	90.1	42
FLIR A315	320 × 240	0.05	91.1	74.7

undergo mammography. Furthermore, 11 women (9%) who were < 40 years of age (not typically in the screening age group for mammography) were found to have a malignancy and all of the 11 participants were detected by Thermalytix.

Detection of Malignant Lesions < 2 cm

One of the concerns of manual interpretation of thermal images is difficulty in detection of deep tumors, because the metabolic activity of small tumors may not traverse to the breast surface to appear as hot spots. However, automated AI-based analysis in Thermalytix uses vascularity to complement hot-spot detection and can analyze abnormal warm areas, and hence, is capable of detecting small lesions.

In our study, 24 malignant tumors were < 2 cm (T1), and Thermalytix correctly identified 17 of these as positive (71% sensitivity for T1 tumors). Mammography, however, showed 68% sensitivity in detecting T1 malignancies. For tumors > 2 cm, sensitivity of Thermalytix was 94.59% and that of mammography was 93.55%.

Comparing Results Across Different Thermal Cameras

Per Food and Drug Administration clinical guidelines, to test generalizability of Thermalytix across imaging hardware, our study involved the use of three different models of thermal cameras with different thermal resolutions.[32] Of the 470 women in the study, 56 women were captured using an FLIR T650SC camera (FLIR Systems, Wilsonville, OR), 226 women were captured using an FLIR A315 camera, and the remaining 188 women were captured using a Meditherm camera (Meditherm, Cheyenne, WY). These were captured by three different technicians at the two study sites. Table 3 lists the results for each model of thermal camera used. High-resolution and high-sensitivity cameras seem to introduce more noise in the data. Table 3 lists a summary of the results.

DISCUSSION

In our study of 470 asymptomatic and symptomatic women aged 18 to 82 years, Thermalytix demonstrated an overall high sensitivity of 91.02% and specificity of 82.4% in detecting breast malignancy. It also correctly identified all disease-positive patients in the asymptomatic population. Thus, Thermalytix could be a potential primary screening method for breast cancer.

Among the 140 participants identified as positive by Thermalytix, 71 (50.71%) were also positive with the standard breast cancer screening modalities. However, the remaining 69 participants with a positive Thermalytix test (but who were radiologically negative) did not undergo a confirmatory test of either MRI or biopsy, and hence were not proven negative. Among these 69 false positives, 50 patients had a benign radiologic finding, such as fibroadenoma, abscess, duct ectasia, or fibrocystic change, and were in the BIRADS 2 or 3 categories. Furthermore, among the 69 patients with Thermalytix false positives, 52 (75%) corresponded to women with symptoms, such as lump, discharge, or pain, who were considered the diagnostic population. Of the 232 asymptomatic participants, only 17 (7.62%) false positives were observed, which led to a specificity of 92.41% (Fig 2).

Of the seven breast cancer patients whose Thermalytix test results were false-negative and were determined to be positive by a clinician based on standard modalities, only three had a confirmatory biopsy test. All seven patients were symptomatic: two had nipple discharge, three had palpable lumps, and two had persistent breast pain.

In low- and middle-income countries (LMICs), organized mammography screening is not feasible because of high cost, population demography, and lack of skilled technicians.[33] In the absence of mammography-based screening, clinical breast examination (CBE) is used for community screening in these countries. CBE, however, only detects palpable lumps (size ≥ 2 cm). As discussed in the previous section, Thermalytix showed promising results in detecting T1 lesions (size ≤ 2cm) in this study cohort. Additionally, Thermalytix correctly identified 17 of 18 malignancies in women < 45 years of age and in all the 11 malignancies in women < 40 years of age, which is another significant need in Asian countries, where the incidence of breast cancer in the younger population is high.[2,4] Hence, Thermalytix demonstrated its potential role as a prescreening solution for breast cancer detection over CBE in LMICs.

Given that Thermalytix is a low-cost automated test that can be conducted by technicians with minimal training, it would be suitable for resource-constrained environments for early detection of breast cancer in women of all age groups. Because Thermalytix is a portable, noninvasive, radiation-free test that has shown promising results in this preliminary study, it can be an affordable and scalable method of

screening in remote areas. To validate this further, we plan to conduct a large-scale prospective study to evaluate the effectiveness of Thermalytix for its definitive role in routine screenings in LMICs.

In this study, patients who tested positive with Thermalytix, but who were radiologically negative did not undergo a confirmatory test of either MRI or biopsy, and hence, were not proven negative. Therefore, the ground truth was biased toward standard of care and clinical practice. In future such studies, we would like to refer every Thermalytix-positive patient for MRI correlation. We are also preparing for a large-scale multicountry trial to evaluate the benefits of Thermalytix in women with dense breasts.

In conclusion, Thermalytix showed high sensitivity for breast cancer detection in both symptomatic and asymptomatic women. The high AUC of 0.90 and ability to detect T1 lesions (size $\leq$ 2 cm) shows the efficacy of Thermalytix for early-stage breast cancer screening. Furthermore, Thermalytix detected two more cancers than mammography in asymptomatic women $<$ 40 years of age, showing its complementarity to screening mammography. Thermalytix AI software can reduce the need for highly skilled imaging technicians, thus making it more affordable for emerging market countries. A large-scale study needs to be conducted to evaluate the potential role of Thermalytix as a standard-of-care breast cancer screening modality. Overall, we believe that Thermalytix—with its automated scoring, annotations of potential malignant lesions, and high accuracy of interpretation—is poised to be a promising modality for breast cancer screening.

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REFERENCES

1. WHO: Cancer. https://www.who.int/cancer/prevention/diagnosis-screening/breast-cancer/en/
2. International Agency for Research on Cancer: Cancer. https://publications.iarc.fr/Databases/Iarc-Cancerbases/Cancer-Today-Powered-By-GLOBOCAN-2018–2018
3. WHO: WHO position paper on mammography screening. https://www.ncbi.nlm.nih.gov/books/NBK269545/
4. Rajaraman P, Anderson BO, Basu P, et al: Recommendations for screening and early detection of common cancers in India. Lancet Oncol 16:e352-e361, 2015
5. Bakker MF, de Lange SV, Pijnappel RM, et al: Supplemental MRI screening for women with extremely dense breast tissue. N Engl J Med 381:2091-2102, 2019
6. Evans A, Trimboli RM, Athanasiou A, et al: Breast ultrasound: Recommendations for information to women and referring physicians by the European Society of Breast Imaging. Insights Imaging 9:449-461, 2018
7. Indian Council of Medical Research: Consensus document for management of breast cancer. http://cancerindia.org.in/wp-content/uploads/2017/11/Breast_Cancer.pdf
8. Kelly KM, Dean J, Comulada WS, et al: Breast cancer detection using automated whole breast ultrasound and mammography in radiographically dense breasts. Eur Radiol 20:734-742, 2010
9. Kennedy DA, Lee T, Seely D: A comparative review of thermography as a breast cancer screening technique. Integr Cancer Ther 8:9-16, 2009
10. Keyserlingk JR, Ahlgren PD, Yu E, et al: Functional infrared imaging of the breast. IEEE Eng Med Biol Mag 19:30-41, 2000
11. Kakileti ST, Manjunath G, Madhu H, et al: Advances in breast thermography in Malik AM (ed): Breast Imaging: New Perspectives. Rijeka, Croatia, IntechOpen, 2017, p 91
12. Gautherie M, Gros CM: Breast thermography and cancer risk prediction. Cancer 45:51-56, 1980
13. Arora N, Martins D, Ruggerio D, et al: Effectiveness of a noninvasive digital infrared thermal imaging system in the detection of breast cancer. Am J Surg 196:523-526, 2008
14. Ghobadi H, Thainimit S, Sugino N, et al: Comparative accuracy of digital infra-red thermal imaging (DITI) in breast cancer diagnosing. J Chem Pharm 8:577-583, 2016
15. Wishart GC, Campisi M, Boswell M, et al: The accuracy of digital infrared imaging for breast cancer detection in women undergoing breast biopsy. Eur J Surg Oncol 36:535-540, 2010
16. Kolarić D, Herceg Z, Nola IA, et al: Thermography--a feasible method for screening breast cancer? Coll Antropol 37:583-588, 2013
17. Yao X, Wei W, Li J, et al: A comparison of mammography, ultrasonography, and far-infrared thermography with pathological results in screening and early diagnosis of breast cancer. Asian Biomed 8:11-19, 2014
18. Parisky YR, Sardi A, Hamm R, et al: Efficacy of computerized infrared imaging analysis to evaluate mammographically suspicious lesions. AJR Am J Roentgenol 180:263-269, 2003
19. Head JF, Wang F, Lipari CA, et al: The important role of infrared imaging in breast cancer. IEEE Eng Med Biol Mag 19:52-57, 2000
20. Arena F, Barone C, DiCicco T: Use of digital infrared imaging in enhanced breast cancer detection and monitoring of the clinical response to treatment. Proceedings of the 25th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (IEEE Cat. No.03CH37439) 2: 1129-1132, 2003
21. Sella T, Sklair-Levy M, Cohen M, et al: A novel functional infrared imaging system coupled with multiparametric computerised analysis for risk assessment of breast cancer. Eur Radiol 23:1191-1198, 2013
22. Prasad SS, Ramachandra L, Kumar V, et al: Evaluation of efficacy of thermographic breast imaging in breast cancer: A pilot study. Breast Dis 36:143-147, 2016
23. Wu LA, Kuo WH, Chen CY, et al: The association of infrared imaging findings of the breast with prognosis in breast cancer patients: An observational cohort study. BMC Cancer 16:541, 2016
24. Rassiwala M, Mathur P, Mathur R, et al: Evaluation of digital infra-red thermal imaging as an adjunctive screening method for breast carcinoma: A pilot study. Int J Surg 12:1439-1443, 2014
25. Sarigoz T, Ertan T, Topuz O, et al: Role of digital infrared thermal imaging in the diagnosis of breast mass: A pilot study: Diagnosis of breast mass by thermography. Infrared Phys Technol 91:214-219, 2018
26. Omranipour R, Kazemian A, Alipour S, et al: Comparison of the accuracy of thermography and mammography in the detection of breast cancer. Breast Care (Basel) 11:260-264, 2016
27. Borchartt TB, Conci A, Lima RCF, et al: Breast thermography from an image processing viewpoint: A survey. Signal Processing 93:2785-2803, 2013
28. Madhu H, Kakileti ST, Venkataramani K, et al: Extraction of medically interpretable features for classification of malignancy in breast thermography. Presented at the 38th Annual International Conference of the IEEE Engineering in Medicine and Biology Society, Orlando, FL, August 16-20, 2016
29. Kakileti ST, Venkataramani K: Automated blood vessel extraction in two-dimensional breast thermography. Presented at the IEEE International Conference on Image Processing, Phoenix, AZ, September 25-28, 2016
30. Kakileti ST, Madhu HJ, Manjunath G, et al: Personalized risk prediction for breast cancer pre-screening using artificial intelligence and thermal radiomics. Artif Intell Med 105:101854, 2020
31. Yankaskas BC, Schell MJ, Bird RE, et al: Reassessment of breast cancers missed during routine screening mammography: A community-based study. AJR Am J Roentgenol 177:535-541, 2001
32. Food and Drug Administration: Guidance for industry and Food And Drug Administration staff: Computer-assisted detection devices applied to radiology images and radiology device data - premarket notification [510(k)] submissions. https://www.fda.gov/media/77635/download
33. Sankaranarayanan R, Ramadas K, Thara S, et al: Clinical breast examination: Preliminary results from a cluster randomized controlled trial in India. J Natl Cancer Inst 103:1476-1480, 2011

