

Thermography Is Not a Feasible Method for Breast Cancer Screening

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ABSTRACT

Breast cancer is a common malignancy causing high mortality in women especially in developed countries. Due to the contribution of mammographic screening and improvements in therapy, the mortality rate from breast cancer has decreased considerably. An imaging-based early detection of breast cancer improves the treatment outcome. Mammography is generally established not only as diagnostic but also as screening tool, while breast ultrasound plays a major role in the diagnostic setting in distinguishing solid lesions from cysts and in guiding tissue sampling. Several indications are established for contrast-enhanced magnetic resonance imaging. Thermography was not validated as a screening tool and the only study performed long ago for evaluating this technology in the screening setting demonstrated very poor results. The conclusion that thermography might be feasible for screening cannot be derived from studies with small sample size, unclear selection of patients, and in which mammography and thermography were not blindly compared as screening modalities. Thermography can not be used to aspirate, biopsy or localize lesions preoperatively since no method so far was described to accurately transpose the thermographic location of the lesion to the mammogram or ultrasound and to surgical specimen. Thermography cannot be proclaimed as a screening method, without any evidence whatsoever.

Introduction

Breast cancer is a common malignancy causing high mortality especially in developed countries. Due to the contribution of mammographic screening and improvements in therapy, between 1990 and 2007 the mortality rate from breast cancer in the United States has decreased by 31%^{1,2} and a similar trend was observed in Sweden where long-term (29-year) effects of mammographic screening could be evaluated³. In Croatia, breast cancer causes the death of more than 900 women annually and its incidence is steadily increasing over the years; since 2006, women from 50 to 69 are invited biannually in the context of a national program for mammographic screening⁴.

An imaging-based early detection of breast cancer improves the treatment outcome. In fact, breast conserving surgery is currently established as a standard of care of

small breast cancers, combined with sentinel node biopsy and followed by radiation therapy, systemic chemotherapy, and/or hormonal/targeted therapy⁵. Radiologic-pathologic correlation is crucial for the proper management of patients⁶.

Imaging Methods Used for the Diagnosis of the Diseases of the Breast

While mammography is generally established not only as diagnostic but also as screening tool, breast ultrasound plays a major role in the diagnostic setting in distinguishing solid lesions from cysts and especially in guiding tissue sampling using fine needle aspiration cytology and, increasingly in the last decades, core needle

biopsy⁷. Mammography has well-known limitations in sensitivity in young women and dense breasts and breast ultrasound has advantages in these conditions as shown not only in the diagnostic⁸ but also in the screening setting^{9,10}. Digital mammography¹¹, thomosynthesis^{12,13}, and contrast-enhanced mammography¹⁴ are recent advances.

Contrast-enhanced magnetic resonance imaging (MRI) has entered this field in the last two decades. The diagnosis is based on morphology and the functional parameters reflecting pathologic neovascularization by various patterns of lesion enhancement, which can be analyzed by generating dynamic (kinetic) curves for targeted region-of-interests¹⁵. Several indications are established for breast MRI, the most important among them being screening of high-risk women, search for carcinoma unknown primary, prediction and evaluation of the effect of neoadjuvant chemotherapy, suspected local recurrence^{16–18}. A debate is still open on the use of breast MRI in the preoperative setting^{19–21}.

Imaging features of benign and malignant breast lesions often overlap and imaging-guided needle biopsies are needed to define the diagnosis. Whenever possible, ultrasound-guidance is used while mammographic stereotactic and MRI guidance are used for findings such as microcalcifications/architectural distortions and contrast-enhancing lesions not detectable at mammography or ultrasound, respectively. In the case of malignancy, pathologic diagnosis of cancer subtype, grade, estrogen and progesterone receptor status, and human epidermal growth factor receptor 2 (HER2) expression, which are important and robust prognostic biomarkers²², are obtained by means of core-biopsy or vacuum-assisted biopsy and confirmed/completed at final pathology of surgical specimen.

Breast Thermography

Breast thermography, also known as infrared imaging of the breast is a noninvasive method that measures temperatures and temperature differences across the skin surface using infrared cameras. Results are displayed as maps of different colors. The rationale is that breast cancers have higher temperatures compared to normal breast tissue due to neoangiogenesis and increased metabolic activity. It was firstly performed in 1956, and studied forty years ago. In 1977 Feig et al. reported results of a very large study comparing mammographic and thermographic breast cancer screening in 16,000 women: sensitivity of thermography was 39%, specificity 82%. Authors concluded that thermography was not a viable screening tool²³.

Recent studies have examined a newer infrared technology, the so-called digital infrared thermal imaging (DITI). Arora et al. imaged with DITI 92 women with 94 suspicious lesions detected by mammography or ultrasound: sensitivity was 94% but specificity 28%²⁴. Wishart et al. examined with DITI (combined with a new software) 100 women with suspicious lesions undergoing

core needle biopsy and found for DITI a sensitivity of 78% and a specificity of 89%²⁵. Kontos et al. studied with DITI 63 symptomatic women who underwent surgical excision or core biopsy. Thermography had a sensitivity of 25% and a positive predictive value of 24%. Authors conclude that thermography is not indicated for the primary evaluation of symptomatic patients, nor should it be used for breast cancer screening²⁶. All these recent studies compared the performance of DITI to mammography in a population of symptomatic patients with suspicious or highly suspicious lesions. None of these studies tested thermography in a screening setting.

The Society of breast imaging (SBI), the leading U.S. scientific and professional society in the field, has issued in 2011 a position statement regarding breast thermography²⁷: SBI does not support the use of thermography or infrared imaging as either a screening tool in the detection of breast cancer or as an adjunctive diagnostic tool. According to this view, there are no studies supporting the use of thermography alone or as an adjunct to mammography that show clear benefits of the technique and it is unclear how the abnormal areas detected by thermography were aspirated or biopsied; moreover, no method was described to accurately transpose the thermographic location of the lesion to the mammogram and then to the actual location in the breast²⁷.

The Food and Drug Administration (FDA), which is the official agency of the U.S. Department of Health and Human Services, has issued a strong statement in June 2011²⁸ expressing concern regarding facilities, mobile units, and websites promoting the use of thermography as a stand-alone tool for screening and diagnosing breast cancer, claiming that it is substitute for mammography or superior to mammography, that thermography can detect precancerous abnormalities and diagnose breast cancer long before mammography and that compressing breast during mammography will cause spread of cancer. FDA is concerned that women will believe these misleading claims about thermography and not receive needed mammograms. FDA has alerted public, including women and health care providers, that thermography is not a replacement for screening mammography and should not be used by itself to diagnose breast cancer. FDA is not aware of any valid scientific data to show that thermography devices, when used on their own, are an effective screening tool for any medical condition, including early detection of breast cancer or other breast diseases. Public health agencies and national medical and professional societies agree with FDA that mammography is still the most effective method of detecting breast cancer in its earliest, most treatable stages. These organizations include the American Cancer Society, the American College of Radiology, the Centers for Disease Control and Prevention, the National Cancer Institute, and the SBI²⁸.

The Croatian Society of Radiology and Croatian Society of Senology have issued similar public statements in February 2013^{29,30}, as a reflection of public promotion in Croatia of thermography as a stand-alone tool for screen-

ing and diagnosing breast cancer and precancerous abnormalities.

Reply to the Paper Claiming that Breast Thermography Might Be a Feasible Method for Screening of Breast Cancer

In this context, in the current issue of *Collegium Antropologicum* a paper is published by Kolarić et al., entitled »Thermography – A feasible method for screening of breast cancer?«³¹. Authors claim that thermography had sensitivity of 100% and specificity of 79% and that sensitivity of thermography is superior to mammography. Authors conclude that their »results indicate that it would be prudent to use thermography as a primary screening method in detection of breast carcinoma«. This conclusion is not only contradictory to the aforementioned position statements but is also not supported by the data presented by the authors.

The analysis of the paper by Kolarić et al. is difficult because crucial information is often missing, incomplete, or contradictory. The main heavy problems and limitations of this study can be summarized as follows.

First, a too small group of patients was studied, consisting of only 26 women. With such a sample size, any statistical evaluation cannot allow for reliable conclusions. According to the authors, of 27 ductal carcinoma in situ (DCIS) (N=12) or invasive cancers (N=15, as declared in Table 2, but they are only 13 in Table 1), mammography detected 85% (we assume 23/27) and thermography 100% (27/27). However, had the authors really calculated 95% interval confidence (as they declare in the text), they would have found 71%–98% for mammography and 87%–100% for thermography, with 11% of overlapping. With only 4 (or also 5) different results, also the nonparametric McNemar test cannot provide any significant p value. Thus, no superior sensitivity of thermography versus mammography, no potential use of thermography for an earlier detection of breast cancer can be claimed on the basis of these results. By the way, why are no results provided for the breast ultrasound?

Second, selection of the patients is unclear. We only know that this is a (really consecutive?) series of 26 women scheduled for breast surgery. Were they symptomatic or asymptomatic? Do they come from screening or diagnostic mammography or ultrasound? Which was the size of the index lesions? In fact, it is clear that if also only part of them were not asymptomatic, independently from the small sample size, no inference about screening could be derived. Of note, the author present a series of 26 women scheduled for surgery but 6 of them (23%) had no cancers, thus 5 of 20 women with malignant disease had synchronous bilateral cancers (25%), a too high rate which generates some doubt about a possible selection bias and nonconsecutiveness of the series.

Third, while the proclaimed aim of the study by Kolarić et al. was »to evaluate thermography as possible method for early detection of breast carcinoma, and to

compare its sensitivity and specificity to that of mammography«, this was not performed at all since mammography and thermography were not compared as screening modalities, nor were they compared in a fashion blinded to the results of mammography and ultrasound, preventing from any possibility to analyze results from thermography alone, but only from thermography as an adjunct to mammography and/or ultrasound.

Fourth, no explanation was given on how lesions only detected at thermography were aspirated and localized for surgical excision. No method so far was described to accurately transpose the thermographic location of the lesion to the mammogram or ultrasound and to surgical specimen. Authors do not mention any method of preoperative image-guided tumor localization and it is impossible to understand how the changes observed on thermography could be correlated to the lesions found in the resection specimens. Authors claim that only thermography was able to diagnose several DCIS. And if DCIS was observed only on thermography, how can the invisible DCIS be removed when thermography cannot localize it within the breast since it is well known that thermographic location of the lesion cannot be accurately transposed to the surgical specimen? The current practice is to perform preoperative localization under imaging guidance of palpable lesions, including DCIS in patients undergoing conservative surgery. How did the authors perform this, or have they subjected patients with DCIS to mastectomy? If yes, is this justifiable?

Fifth, there is a complete lack of information about type of surgery performed (conservative surgery versus mastectomy). Sixth, as mentioned above, 6 of 26 patients (23%) had nonmalignant findings histopathology. We should think that this was done due to the presence of a non better specified atypia/proliferation at cytology, but this really seems a too high rate of surgical biopsy of non-malignant findings. Seventh, an unusual categorization of histopathological results was used, without providing information about subtype and grade of cancer, evaluation of intraductal component associated with invasive cancers, receptor status, HER2neu expression, and so on. By the way, this paper being a small radiology-cytopathology-pathology-surgery correlation study, we should note that neither surgeons nor pathologists are among the co-authors.

Eight, it is quite unexpected that a number of DCIS (we do not know their grade) were only detectable on thermography. In fact, being DCIS noninvasive lesions with relatively low neoangiogenesis³², how can we explain that a method based on differences in (skin) temperature is so sensitive for non-invasive lesions? A potential higher sensitivity should be somehow thought for invasive highly neoangiogenetic cancers, not for DCIS. However, the authors do not discuss this issue.

Conclusion

Breast cancer screening is very important for women and for the public all over the world. Mammography was

studied and validated as a screening modality in hundreds of thousands of patients in organized screening programs performed for decades in the developed countries with the best health care systems and meticulous quality control evaluation. We are aware of the scientific discussion about the relative contribution of mammographic screening to the decrease of breast cancer mortality as well as about limitations of screening mammography and the debatable rate of »overdiagnosis« and negative effects of mammographic screening^{33–37}. However, unlike mammography, thermography was never used nor validated as a screening tool and the only study

performed long time ago demonstrated very poor results²³.

To summarize, the study by Kolarić et al. does not add any valid information to support the use of the thermography as a primary screening of breast cancer. Unfortunately statements like those contained in this study are misleading for the public, and may raise false hopes and confuse many women who are exposed to the aggressive advertising of unproven »advantages« of thermography. Thermography cannot be proclaimed as a screening method, without any evidence whatsoever.

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TERMOGRAFIJA NIJE PRIKLADNA METODA ZA PROBIR KARCINOMA DOJKE

S A Ž E T A K

Karcinom dojke je česta bolest koje uzrokuje visoku smrtnost žena, osobito u razvijenim zemljama. Mamografski probir (skrining) i poboljšanja u liječenju doprinijeli su značajnom smanjenju smrtnosti. Otkrivanje karcinoma dojke u ranom stadiju temeljeno na slikovnim metodama poboljšava ishod liječenja. Mamografija je općenito etablirana ne samo kao dijagnostička metoda nego kao i metoda probira. Ultrazvuk ima veliki dijagnostički značaj u razlikovanju solidnih lezija dojke i cista, a osobito pri nadzoru punkcija i biopsija. Magnetska rezonancija dojki uz intravensku primjenu kontrasta ima nekoliko utvrđenih indikacija. Termografija nije validirana kao metoda probira; jedino davno provedeno istraživanje u kojem je ova tehnologija istraživana u probiru pokazalo je vrlo loše rezultate. Zaključak da bi termografija mogla biti prikladna za probir ne može se izvesti na temelju studija provedenih na malom uzorku, s nejasnom selekcijom bolesnica, u kojima mamografija i termografija nisu uspoređene kao metode probira. Termografija ne omogućuje aspiraciju, biopsiju niti preoperacijsku lokalizaciju lezija jer do sada nije opisan način kako bi se termografska lokacija lezija točno prenijela na mamogram, ultrazvuk ili kirurški uzorak. Termografija se ne može proglašavati metodom probira (skrininga) bez ikakvih valjanih dokaza.