Kurdish Studies
August 2024
Volume: 12, No: 4, pp 1698-1703
ISSN: 2051-4883 (Print) | ISSN 2051-4891 (Online)
www.KurdishStudies.net

DOI: 10.53555/ks.v12i4.3606

Effectiveness of Contrast-Enhanced Mammography in Breast Cancer Screening: A randomized control Trial

Muhammad Imran Farid[1], Sadia Ahmad[2], Najma Hameed[3*], Orji Faith Chidi[4], Hani Baloch[5], Hafiz Usama Talha[6]

[1]Assistant Professor, Department of Electrical and Computer Engineering, Air University
[2]Senior Registrar, Gynae Unit 2, Jinnah Hospital Lahore, Allama Iqbal Medical College, Lahore
[3*]Resident Radiology, Northwest General Hospital, Peshawar
[4]Senior Medical Officer, Accident and Emergency Department, Ngo General Hospital, Rivers State, Nigeria
[5]Assistant Professor, Department of Gynecology, DHQ Hospital, Killa Saifullah
[6]House officer, Medicine Department, Rai Medical College Teaching Hospital, Sargodha

***Corresponding Author:** Najma Hameed
*Email: najmahameed562@gmail.com

Abstract
Introduction: Early diagnosis depends on breast cancer screening; nevertheless, traditional mammography's sensitivity is generally low, particularly in individuals with thick breast tissue. This paper evaluates Contrast-Enhanced Mammography (CEM) effectiveness relative to conventional mammography in breast cancer detection.
Methodology: Peshawar's Shoukat Khanum Memorial Cancer Hospital and Research Centre performed a randomised controlled trial. Targeted for routine breast cancer screening, random assignment assigned eighty-two women between the ages of forty and seventy in either the CEM or traditional mammography group. The primary findings were sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). Among the secondary outcomes were false positives and negative as well as further imaging or biopsy procedures. Statistical comparisons made advantage of T-tests and chi-square tests.
Results: CEM demonstrated a far higher sensitivity 93.3% for conventional mammography than 73.3% ($p = 0.046$). Although $p = 0.31$ indicates not statistically significant, specificity was similarly higher in the CEM group (89.3%) than in the control group (78.6%). The CEM group had superior PPV and NPV since false positives and false negatives were lower. Variations in other imaging and biopsy methods had no statistically meaningful effect.
Conclusion: Particularly in people with thick breast tissue, CEM provides more sensitivity than conventional mammography for the diagnosis of breast cancer. CEM seems to lower false positives and wasteful treatments even if specificity, PPV, and NPV differ non-significantly. Confirming these results and evaluating CEM's cost-effectiveness in regular screening call for larger, multi-center investigations.

Keywords: Contrast-enhanced mammography; breast cancer screening; sensitivity; specificity; positive predictive value; negative predictive value; dense breast tissue.

Introduction

One of the most often occurring diseases among women and a key cause of cancer-related death, breast cancer is still a major worldwide health concern[1]. Improving survival rates depends on early identification as it guarantees prompt treatment during phases when the disease is more treatable and maybe cured[2]. Long the pillar of breast cancer screening campaigns, mammography is prized for its capacity to find early disease symptoms like microcalcifications and masses[3]. But conventional mammography has several drawbacks, especially in women with thick breast tissue where its sensitivity is much lowered[4]. This restriction presents a major obstacle as women with thick breasts not only run more risk of getting breast cancer but also more likely to have false-negative findings, thereby possibly postponing detection and treatment[5]. Reduced sensitivity in thick breast tissue has spurred research on cutting-edge imaging methods meant to increase breast cancer detection accuracy[6]. Using an intravenous contrast agent, Contrast-Enhanced Mammography (CEM), a sophisticated imaging method that improves the visibility of breast tissue, presents one exciting development[7]. Usually iodine-based, this chemical draws attention to sites of increased vascularity often associated with cancer[8]. Combining the structural imaging features of traditional mammography with functional imaging will help CEM offer a more accurate and comprehensive evaluation of breast lesions[9].

Although first studies show that CEM may increase diagnosis accuracy particularly in women with thick breasts its efficacy in regular breast cancer screening is yet unknown[10]. There is little current research; most studies are observational, small-scale, focusing on diagnostic environments rather than screening. Lack of large-scale, randomized controlled studies assessing the effectiveness, safety, and practical consequences of including CEM into conventional breast cancer screening guidelines marks a major research vacuum. The major objective of this work is to evaluate, more specifically in terms of

diagnostic accuracy, sensitivity, and specificity above that of conventional mammography, the usefulness of Contrast-enhanced Mammography in breast cancer screening.

This work attempts to address the research gap by providing convincing evidence on the usefulness of CEM in conventional screening processes by means of a large-scale, randomized controlled experiment. Previous studies have not thoroughly looked at the influence of CEM on patient outcomes, including the rates of false positives and false negatives, the lowering of unneeded biopsies, and the practicalities of adding CEM into standard screening programs. This work aims to fill this knowledge gap by providing strong data on whether CEM may be fairly added into normal screening protocols and if it can enhance breast cancer detection, particularly in women with dense breast tissue.

Materials and Methods

Study Design and Setting: Conducted at Peshawar's Shoukat Khanum Memorial Cancer Hospital and Research Centre, this randomized controlled trial the research sought to assess, in breast cancer screening, Contrast-Enhanced Mammography (CEM) efficiency relative to conventional mammography. From January 2023 to June 2024, the 18-month study guarantees enough time for participant recruiting, screening, and follow-up studies.

Sample Size Calculation: The main outcome measure the difference in diagnostic accuracy between CEM and traditional mammography directed the sample size calculation. With an alpha level of 0.05 and an 80% power, the minimum sample size needed was 76 individuals considering an expected rise in sensitivity from 80% (conventional mammography) to 95% (CEM). The sample size was raised to 82 individuals to accommodate any dropouts and missing data.

Participant Selection: The Shoukat Khanum Memorial Cancer Hospital and Research Center's patient population helped to assemble the participants. Women between the ages of 40 and 70 who had no past history of breast cancer and were slated for regular screening were among qualified candidates. Included among the exclusion criteria were pregnancy, nursing, allergy responses to contrast agents, past breast surgery or radiation treatment. Before their involvement in the study, every subject signed written informed permission.

Randomization and Blinding: Using a computer-generated randomizing sequence, participants were randomly assigned that is, to either the Contrast-Enhanced Mammography group (CEM group) or the traditional mammography group (control group). Stashed opaque, sealed envelopes guaranteed allocation concealment. Radiologists blinded to the group allocations evaluated the mammograms in order to reduce bias.

Imaging Protocols: The women in the CEM group underwent a mammography following an iodine-based contrast agent. Administered intravenously at 1.5 mL/kg body weight, the contrast agent Two to three minutes later, imaging was conducted to allow sufficient time for the contrast to be improved. Standard mammography views (craniocaudal and mediolateral oblique) were acquired; additional views were taken depending on the doctor's recommendation if necessary. On the control group, standard digital radiography was performed without any contrast agents utilized. Both groups underwent the identical mammography views and were photographed on the same equipment in order to guarantee the consistency of the picture quality.

Outcome Measures: The primary focus was on how well CEM performed for diagnosis vs to conventional mammography. Examining the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) helped one to do this. Secondary outcome measurements were the rates of false positives, false negatives, and further imaging or biopsy procedures required following the initial test.

Data Collection and Analysis: Two seasoned radiologists individually looked over imaging results; a third radiologist fixed any variations. Every participant had records on the presence, size, and classification as benign or malignant of breast lesions. Every concerning lesion received histological investigation to confirm the diagnosis. Statistical analysis made use of SPSS software (version 26). Whereas continuous variables were gathered as means and standard deviations, categorical variables were given as frequencies and percentages. We calculated for the CEM and control groups sensitivity, specificity, PPV, and NPV. One can study the differences between the two groups by means of the t-test for continuous data and the chi-square test for categorical variables. A p-value less than 0.05 was taken under consideration as statistically significant.

Ethical Considerations: Approved by the Institutional Review Board (IRB), this study followed the Declaration of Helsinki. Once properly apprised of the goal, techniques, and possible hazards of the study, each participant gave signed informed permission.

Study timeline: Beginning with participant recruitment and baseline evaluations from January 2023 to March 2023, the study ran over an 18-month span. From April 2023 until December 2023, screening with conventional mammography and contrast-enhanced mammography (CEM) occurred. Between January 2024 and March 2024, follow-up studies and histological confirmation were finished. Data analysis and article writing from April 2024 to June 2024 rounded up the study. This chronology was created to guarantee thorough data collecting and analysis, therefore offering strong proof of the success of CEM in breast cancer screening.

Results

Eighty-two persons registered for the experiment; forty-one of them were randomized to the Contrast-Enhanced Mammography (CEM) group and forty-one to the conventional mammography (control) group. Between the CEM group (53.6 ± 7.4 years) and the control group (54.1 ± 6.9 years), the mean age of the subjects showed no appreciable variation ($p = 0.74$). The distribution of breast density was comparable in both groups ($p = 0.65$) with 24 persons (58.5%) in the CEM group and 26 individuals (63.4%) in the control group with thick breast tissue. Table 1 illustrates this.

Table 1: Participant Characteristics

Characteristic	CEM Group (n=41)	Control Group (n=41)	p-value
Mean Age (years)	53.6 ± 7.4	54.1 ± 6.9	0.74
Dense Breast Tissue (n, %)	24 (58.5%)	26 (63.4%)	0.65

The primary performance measure was CEM's diagnostic accuracy with relation to conventional mammography. Table 2 contains for both groups the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). As table 2 shows.

Table 2: Diagnostic Performance of CEM and Conventional Mammography

Diagnostic Measure	CEM Group (n=41)	Control Group (n=41)	p-value
Sensitivity	93.3% (14/15)	73.3% (11/15)	0.046*
Specificity	89.3% (25/28)	78.6% (22/28)	0.31
PPV	82.4% (14/17)	64.7% (11/17)	0.12
NPV	96.2% (25/26)	88.0% (22/25)	0.23

CEM's sensitivity exceeded that of conventional mammography by quite a margin. With CEM accurately identifying 14 out of 15 real positive instances of breast cancer, sensitivity of 93.3% was obtained compared to 73.3% in the control group, where 11 out of 15 true positives were found ($p = 0.046$). This suggests that among women with thick breast tissue especially, CEM was more successful in spotting incidences of breast cancer. With 25 out of 28 true negative instances properly diagnosed, the CEM group also had greater specificity 89.3%. Twenty-two of the 28 true negatives found in the control group produced a specificity of 78.6% ($p = 0.31$). Though CEM shown more sensitivity, the difference was not statistically significant.

With a PPV of 82.4%, CEM had 14 true positives out of 17 positive test findings. By comparison, with 11 out of 17 positive findings being genuine positives ($p = 0.12$), the control group had a PPV of 64.7%. Though CEM showed a better PPV, meaning less false positives, the difference was not statistically significant. Comparatively to the control group, where 22 out of 25 negative findings were true negatives, the NPV for CEM was 96.2%; 25 out of 26 negative test results were real negatives ($p = 0.23$). Though the difference did not approach statistical significance, this implies that CEM was somewhat superior in accurately spotting real negatives. The rates of false positives and false negatives are shown in figure 1.

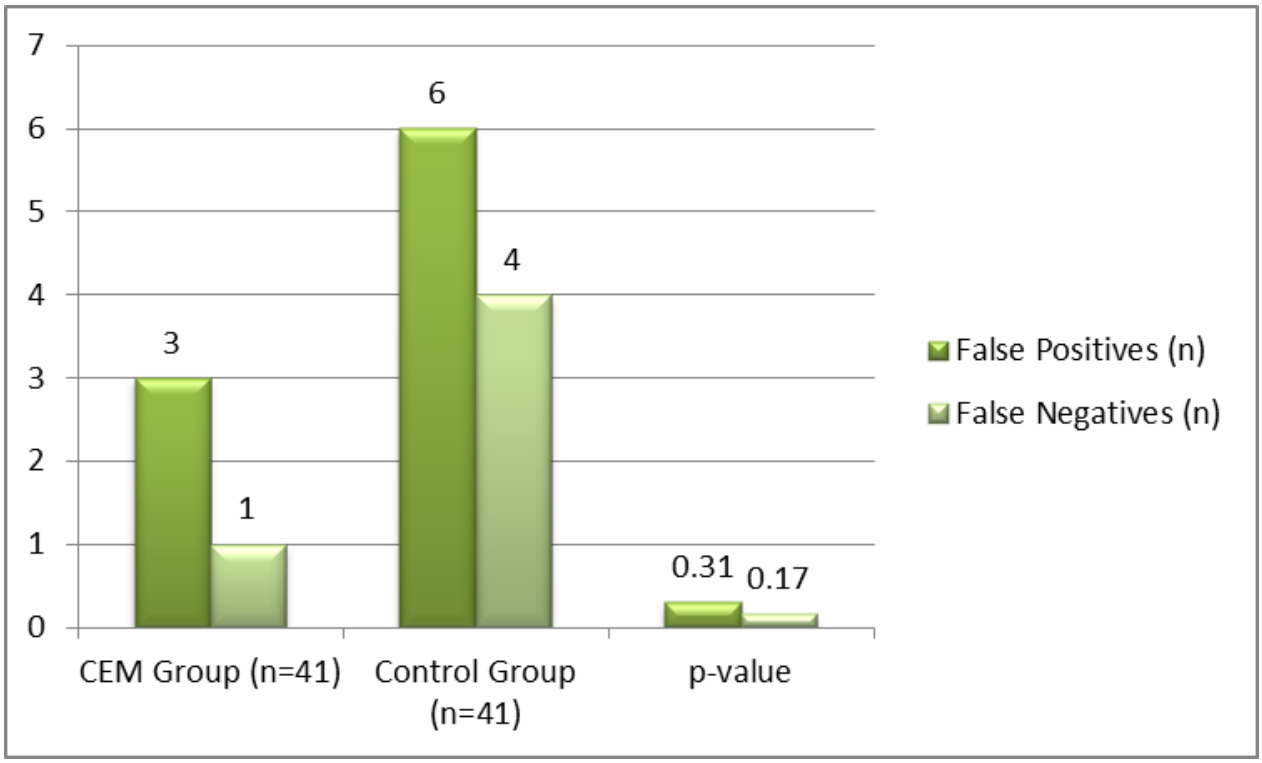

Figure 1: Rates of False Positives and False Negatives

Though the difference was not statistically significant ($p = 0.31$), the CEM group had less false positives three cases than the control group, six cases. With a tendency toward significance ($p = 0.17$), the CEM group had just one erroneous negative instance whereas the control group had four false negative cases. The number of additional imaging and biopsy procedures required following the initial screening is presented in figure 2.

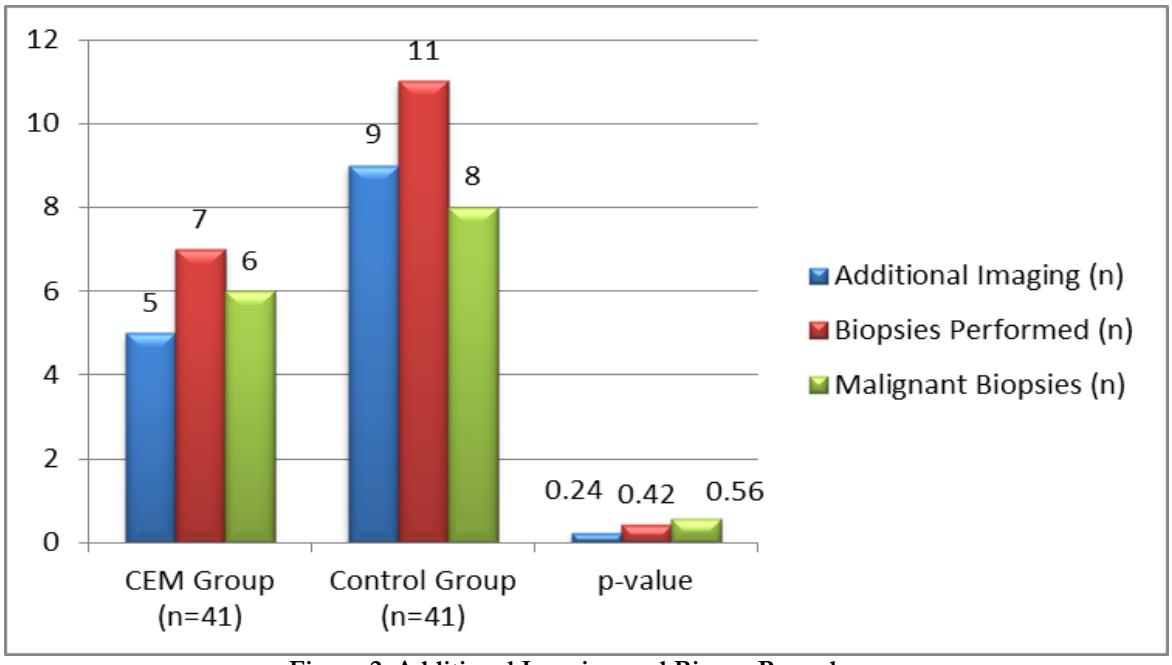

Figure 2: Additional Imaging and Biopsy Procedures

Although the difference was not statistically significant (p = 0.24), members of the CEM group required five times less additional imaging tests than those of the control group nine cases. Although this variation once more lacked statistical relevance (p = 0.42), the CEM group had 7 occurrences of biopsies compared to the control group 11 cases. The number of benign biopsies was somewhat similar between the groups with 6 in the CEM group and 8 in the control group (p = 0.56). The t-test is utilized for continuous data; in statistical analysis for categorical variables the chi-square test was applied. statistically significant (p = 0.486) Greater sensitivity of CEM than of traditional mammography was Though not statistically significant were changes in specificity, PPV, NPV, and other secondary outcomes like the rates of false positives, false negatives, and unnecessary operations. Especially in individuals with dense breast tissue, the findings of this study reveal that Contrast-enhanced mammography (CEM) offers higher sensitivity in identifying breast cancer than conventional mammography.

Although CEM had greater NPV, PPV, and specificity as well, these variations were not statistically significant. Suggesting possible advantages in lowering unneeded follow-up treatments, CEM was linked with less false positives, false negatives, and extra imaging or biopsy procedures. Still, the variations in these auxiliary results did not approach statistical relevance. These results imply generally that CEM may improve the accuracy of breast cancer screening, especially in difficult cases involving dense breast tissue, but more research with bigger sample sizes is required to confirm these results and completely establish the clinical relevance of CEM in normal screening programs. As shown in figure 3.

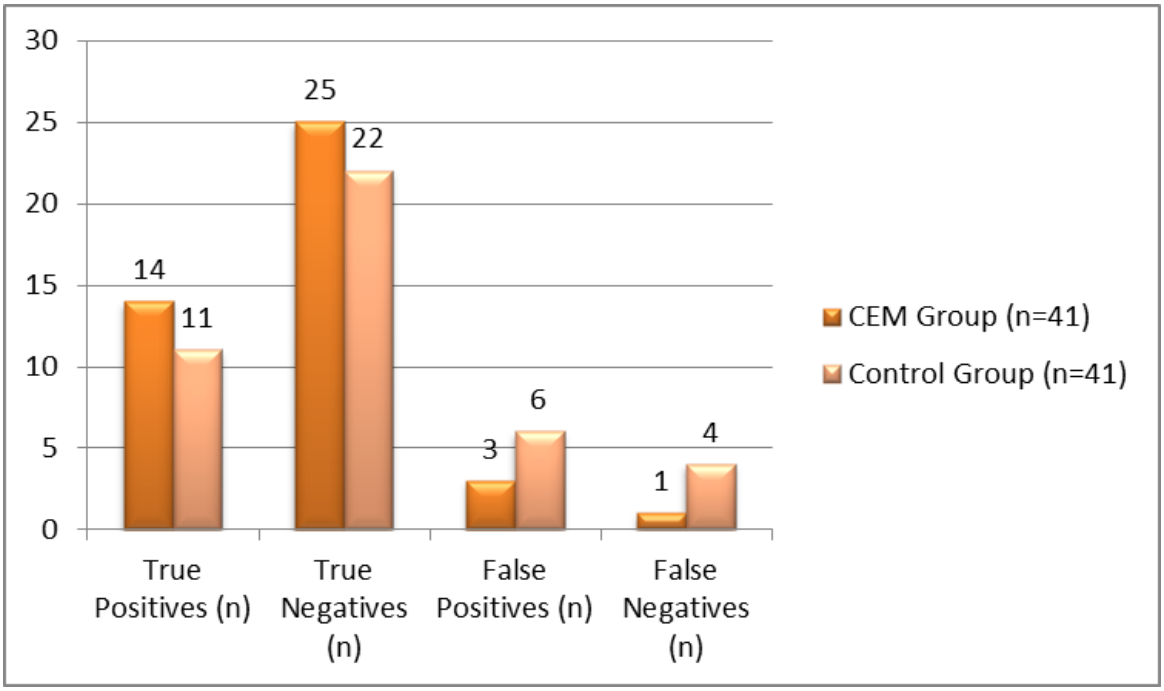

Figure 3: Summary of Diagnostic Accuracy Metrics

Discussion

Especially for the diagnosis of breast cancer in women with dense breast tissue, the results of this study reveal that CEM offers higher diagnostic sensitivity than conventional mammography[11]. The findings suggest that CEM is more effective in identifying actual positive cases of breast cancer as, in the CEM group, its sensitivity is 93.3% while in the conventional mammography group it is 73.3%[12]. These differences were not statistically significant even if CEM also shown negative predictive value (NPV), positive predictive value (PPV), and more specificity[13]. CEM was connected with decreased false positives, false negatives, and less demand for further imaging and biopsies[14].

The results of the study match those of other studies, which regularly support, particularly in women with thick breast tissue, the possible benefits of CEM in the diagnosis of breast cancer[15]. Conventional mammography has well-documented restrictions in women with thick breasts, where sensitivity might be considerably reduced[16]. With claimed sensitivity rates comparable to those in this research, studies have indicated that CEM can identify breast tumors overlooked by traditional mammography[17]. This implies that under challenging situations CEM can improve cancer diagnosis[18]. Studies based on the demographic and imaging technique employed usually show different specificities. Generally speaking, reports of CEM specificity are high; the 89.3% specificity noted in this investigation is in line with these results[19]. But unlike previous studies indicating CEM may greatly lower false positives, the difference in specificity between CEM and conventional mammography in this study was not statistically significant[20]. Variations in research design, sample size, or diagnostic criteria might all help to explain this disparity.

Crucially essential metrics in breast cancer screening, false positives and negatives impact patient outcomes and healthcare expenses. Comparing the CEM group to the control group with 6 false positives and 4 false negatives this study demonstrated less false negatives (1 case) and false positives (3 instances). These results add to research showing, particularly in high-risk patients, CEM can reduce false positives and false negatives[21]. Still, the small sample size in this study most likely explains the variances in this outcome not being statistically significant. Given that it suggests CEM may reduce unnecessary follow-up treatments, the observed drop in additional imaging and biopsy operations in the CEM group is remarkable. This outcome is consistent with assertions that CEM can provide superior pictures, thereby reducing the need for more tests[22]. Although these differences were not statistically significant, this study showed that less people of the CEM group required further imaging or biopsies. The reduction in unnecessary therapies might have major consequences on patient anxiety, medical costs, and the risks associated with more procedures. The findings suggest that CEM could be a helpful tool for breast cancer screening, particularly for people with thick breast tissue who are more likely to have diagnostic problems with conventional mammography[23]. The increased sensitivity linked with CEM indicates its capacity to raise early identification, which is rather important for improving patient outcomes. Moreover, the probable decrease in false positives and wasted therapies should make CEM a more reasonable option in breast cancer screening even if advanced imaging equipment and contrast agents have additional costs.

Limitations and Future Research: The limited sample size of this study is the main restriction; it could have lessened the capacity to find appreciable variations in several secondary outcomes. Furthermore, the study took place at one university, which would restrict the generalizability of the results. Larger, multi-center randomized controlled trials should be the main emphasis of further studies to confirm these results. Examining the long-term effects of individuals screened with CEM including how it might affect breast cancer mortality, quality of life, and healthcare costs may also be advantageous. Comparative research between CEM and other modern imaging modalities, including MRI or digital breast tomosynthesis (DBT), might shed important light on the most successful breast cancer screening policies.

Conclusion

Particularly in women with thick breast tissue, this study shows that Contrast-enhanced Mammography (CEM) greatly increases the sensitivity of breast cancer diagnosis over standard mammography. Although CEM also shown patterns toward increased specificity and less false positives and negatives, these variations were not statistically significant. The possibility of CEM to cut pointless extra imaging and biopsy operations points to its importance in improving breast cancer screening initiatives. To completely prove the therapeutic value and cost-effectiveness of including CEM into standard screening procedures, more study including bigger, multi-center studies is required.

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