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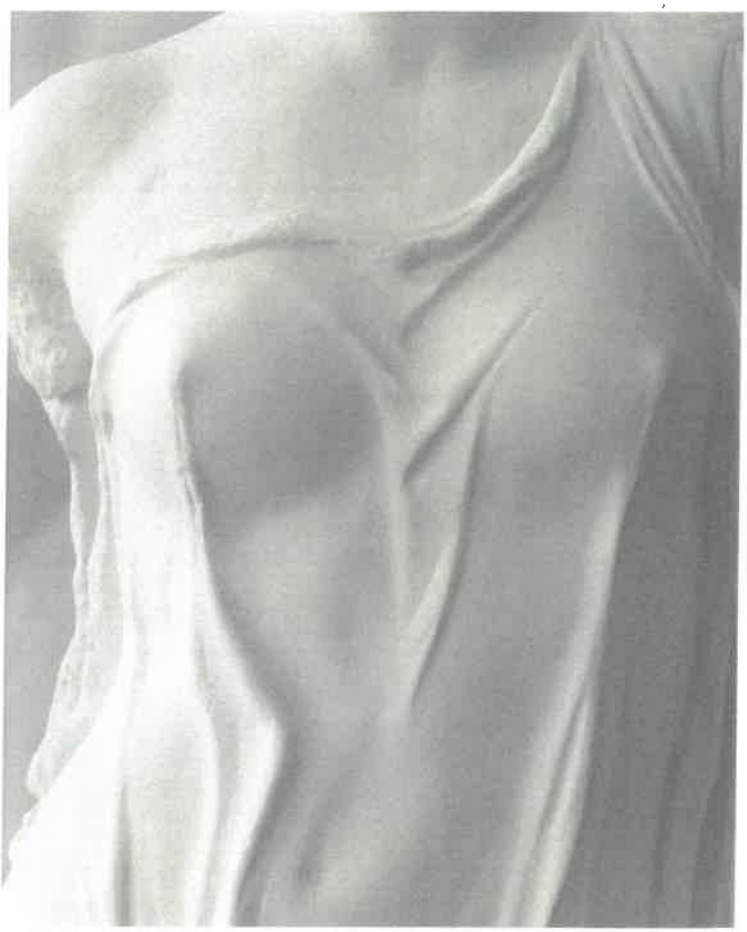

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Diagnostic Accuracy of Breast Medical Tactile Examiners (MTEs): A Prospective Pilot Study

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Keywords

Breast cancer · Clinical breast examination · Early cancer detection · Screening · Medical tactile examiners

Abstract

Background: The usefulness of clinical breast examination (CBE) in general and in breast cancer screening programs has been a matter of debate. This study investigated whether adding vision-impaired medical tactile examiners (MTEs) improves the predictiveness of CBE for suspicious lesions and analyzed the feasibility and acceptability of this approach. ***Methods:*** The prospective study included 104 patients. Physicians and MTEs performed CBEs, and mammography and ultrasound results were used as the gold standard. Sensitivity and specificity were calculated and logistic regression models were used to compare the predictive value of CBE by physicians alone, MTEs alone, and physicians and MTEs combined. ***Results:*** For CBEs by physicians alone, MTEs alone, and both combined, sensitivity was 71, 82, and 89% and specificity was 55, 45, and 35%, respectively. Using adjusted logistic regression models, the validated areas under the curve were 0.685, 0.692, and 0.710 (median bootstrapped p value (DeLong) = 0.381). ***Conclusion:*** The predictive value for a suspicious breast lesion in CBEs performed by MTEs in patients without prior surgery was similar to that of physician-conducted CBEs. Including MTEs in the CBE procedure in breast units thus appears feasible and could be a way of utilizing their skills.

Introduction

Breast cancer is the most common cancer in women in the USA [1] and in Germany [2]. There has been substantial improvement in the prognosis and treatment of breast cancer [3–6]. Numerous studies have focused on ways of reducing the morbidity and mortality of breast cancer by improving early cancer detection. Breast cancer screening and early cancer detection programs include breast self-examination [7–9], clinical breast examination (CBE) [10–19], mammography [14–16, 19–24], ultrasonography [14, 23–26], and magnetic resonance imaging [23, 27]. Although there has been constant progress in the un-

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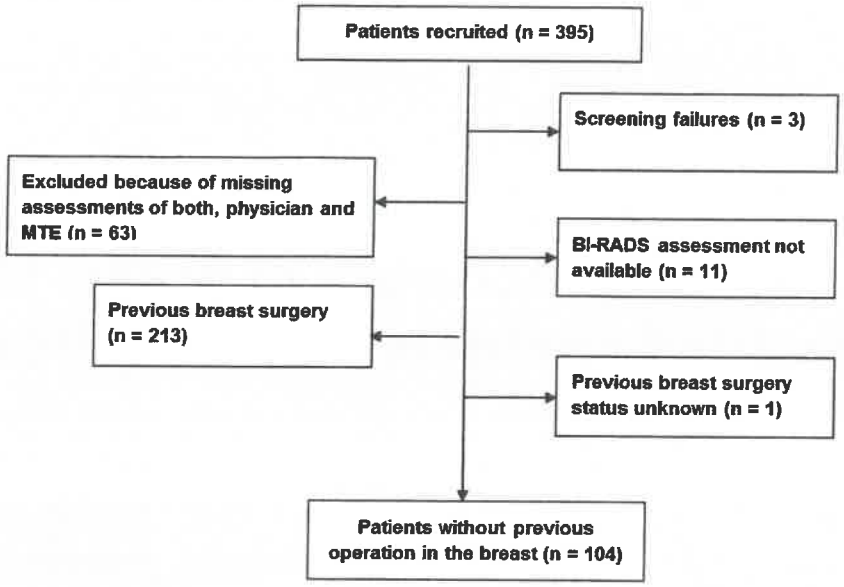

Fig. 1. Patient selection.

derstanding of risk factors and genetic dispositions for breast cancer [28–36], the majority of breast cancer cases still occur without known predictors. This study is concerned with the introduction of vision-impaired medical tactile examiners (MTEs) for performing CBE in a diagnostic breast unit in order to assess the feasibility, acceptance, and diagnostic value of this approach.

In general, acceptance of and participation in screening and early detection programs vary according to age, awareness of breast cancer risk, and other population characteristics such as income and social status [37–40]. Fear of the examination and the relationship with the physician may also play a major role [41–44]. Improving personal interactions with the patient might therefore improve the acceptability of the diagnostic process.

In addition, the quality of the CBE depends on several factors, and it may be hypothesized that MTEs could increase the diagnostic value of CBEs. It has been shown that the detection rates of CBE for breast lesions depend on body position and the duration of the examination. Up to 96% of the malignancies are detected with the patient in a prone position and with an examination duration of at least 6–10 min [45]. People with impaired vision often have an above-average tactile acuity [46, 47]. These special abilities may mean that these persons are particularly suited to carrying out CBEs. Including a dedicated MTE in CBE procedures could also create a further job opportunity for this group of persons.

Although it has not been shown that CBE has beneficial effects in reducing breast cancer mortality in a screening setting and this is a matter of debate [19, 48–50], CBE is an integral part of everyday routine in clinical practice in diagnostic breast units. The aim of this study was therefore to analyze the predictive value of CBEs carried out by physicians, MTEs, and a combination of the two.

Table 1. Patient characteristics

Total, n (%)	104
Age, mean (SD), years	48.6 (14)
BMI, mean (SD), kg/m^2	24.9 (5.3)
Menopausal status, n (%)	
Pre- and perimenopausal	61 (63.5)
Postmenopausal	35 (36.5)
Reason for referral, n (%)	
Participation in early cancer detection program	47 (46.1)
Suspicious finding	55 (53.9)

SD, standard deviation; BMI, body mass index.

Patients and Methods

Patients

This study was conducted as a single-center prospective study in the diagnostic breast unit of the University Breast Cancer Center for Franconia at Erlangen University Hospital/Comprehensive Cancer Center Erlangen – EMN. Patients are referred to the breast unit by family physicians, or themselves attend for screening or diagnostic clarification. Patients were recruited from November 2013 to February 2015. The inclusion criteria were an indication for mammography and ultrasound of the breast for diagnostic or screening purposes and age ≥ 18 years. A total of 395 women were included.

The analysis was concerned with the diagnostic value of CBE in the patient population of women with no previous breast cancer or breast surgery, in accordance with the quality assurance standards established by discovering hands® (discovering hands Ser-

Table 2. Comparison of assessments by the physicians and the medical tactile examiners (MTEs)

	Assessment by MTEs, n (%)		
	total	not suspicious	suspicious
Assessment by physicians, n (%)			
Not suspicious	43 (41)	23 (72)	20 (28)
Suspicious	61 (59)	9 (28)	52 (72)
Total	104 (100)	32 (100)	72 (100)

vice GmbH, Mühlheim an der Ruhr, Germany) [51]. Patients were excluded in the following hierarchical order: screening failure (n = 3), CBE assessment available only from a physician or MTE (n = 63), Breast Imaging Reporting and Data System (BIRADS) results not available (n = 11), and patients with previous breast surgery or breast surgery status unknown (n = 214), resulting in 104 patients for the final study population (fig. 1).

Clinical Data

The CBEs were documented on prespecified forms by physicians and MTEs. The MTEs used special laptops for persons with impaired vision. The patients received a questionnaire inquiring into breast cancer awareness, breast cancer risk perception, lifestyle (primary prevention), participation in screening, awareness of the examination methods, and the perception of persons with impaired vision in society. Patient characteristics, breast imaging data, patient questionnaires, and CBE assessment results were documented using a modified electronic case report form (eCRF), based on the standard documentation for certified breast cancer centers in Germany [52].

Study Procedure

The MTEs were trained with a 9-month curriculum and underwent a standardized exam [51]. The training program included practical training in breast examination, knowledge of the anatomy and diseases of the breast, basic diagnostic and therapeutic methods, basic medical knowledge, patient-centered social behavior, and medical documentation.

First, the patient was examined by the physician, followed by examination by the MTE who was blinded to the results of the physician's assessment. The CBE assessments by the physicians and MTEs were categorized as either 'without suspicious findings', or 'suspicious finding', or 'not assessable'. The individual assessments by the physicians and MTEs were analyzed, as well as the combination of both assessments. The rules used to classify the combination of the 2 assessments are shown in online supplementary table 1 (for all online supplementary material, see *www.karger.com/doi/10.1159/000495883*). After the CBEs, imaging with ultrasound and mammography was performed in all patients. Suspicious findings (BIRADS 4 or 5) were further diagnosed with a core biopsy.

Clinical Breast Examinations

The CBE was performed by 13 doctors and 4 MTEs. All doctors had >2 years of experience in CBE, and 7 of 13 doctors were medical specialists in gynecology and obstetrics. During the CBE, the patient was in a standing upright position. There were no specifications regarding arm position and no time limitation for the CBE in the protocol. The exact examination time was not documented.

Statistical Analysis

Age and body mass index (BMI) were calculated as means with standard deviation. Menopausal status, reason for referral, number of pregnancies and childbirths, specific findings in the breast, and the size of tumors were given as frequencies with the respective percentage distribution.

The study analyzed the diagnostic value of CBEs performed by a physician, an MTE, and the 2 assessments combined (online supplemental table 1). Sensitivities and specificities are provided for each setting. Prediction performance was assessed using 4 logistic regression models with the variable 'suspicious finding on mammography or ultrasound' (yes/no) as the dependent variable. In each logistic regression model, the clinical predictors, BMI (continuous in kg/m^2) and age (continuous in years), were included as covariates.

The first model did not include any other predictors. For the remaining 3 models, 1 additional predictor was added: assessment by physicians (categorical: suspicious vs. not suspicious), assessment by MTEs (categorical: suspicious vs. not suspicious), and the combination of physician and MTE (categorical: suspicious vs. not suspicious).

For validation, 100 bootstrap samples (random samples with replacement, n = 95) of the dataset were drawn. With each bootstrap sample, all 4 models were trained, and class probabilities were predicted for observations that were not in the bootstrap samples. Prediction performance was estimated by calculating the area under the receiving operating characteristic (ROC) curve (AUC) for the predicted values with 95% confidence intervals (CIs). DeLong tests [53] were performed to check for significant differences between the AUCs of the 4 models. Benjamini-Hochberg corrected p values of <0.05 were regarded as statistically significant. The mean odds ratios for the resulting 100 models were calculated, and 95% bootstrap CIs were given for AUCs and odds ratios.

All statistical analyses were performed using the statistical programming language R (version 3.4.3; R Development Core Team, Vienna, Austria, 2017).

Results

Patient Characteristics

The study population consisted of 104 patients with no previous breast surgery who were referred to the diagnostic breast unit. Their reasons for presenting were participation in the early detection program (n = 47; 46.1%) or referral to the diagnostic breast unit with a recently diagnosed suspicious finding (n = 55; 53.9%). The patients' mean age was 48.6 years (±14.0), and their average BMI was 24.9 kg/m^2 (±5.3). Patient characteristics are shown in table 1.

Sensitivity and Specificity

Assessment by the physicians delivered suspicious findings in 61 cases. The MTEs rated 72 examinations as suspicious. Table 2 provides a comparison of the 2 assess-

Table 3. Clinical breast examination (CBE) assessments relative to BIRADS findings on ultrasound and mammography

	BIRADS 4 or 5		
	total	no	yes
CBE by physicians, n (%)			
Not suspicious	43 (41)	27 (55)	16 (29)
Suspicious	61 (59)	22 (45)	39 (71)
Total	104 (100)	49 (100)	55 (100)
CBE by MTEs, n (%)			
Not suspicious	32 (31)	22 (45)	10 (18)
Suspicious	72 (69)	27 (55)	45 (82)
Total	104 (100)	49 (100)	55 (100)
CBE, combined assessment (physician + MTE), n (%)			
Not suspicious	23 (22)	17 (35)	6 (11)
Suspicious	81 (78)	32 (65)	49 (89)
Total	104 (100)	49 (100)	55 (100)

BIRADS, Breast Imaging Reporting and Data System; MTE, medical tactile examiner.

Table 4. Logistic regressions in the predictive models

Prediction models/covariates	Odds ratio	95% CI
Clinical prediction		
Age	1.04	1.01–1.08
BMI	1.03	0.95–1.11
Prediction by physician		
Assessment by physician		
Not conspicuous	1.00 (reference)	
Conspicuous	4.44	1.10–11.23
Age	1.04	1.01–1.08
BMI	1.07	0.98–1.19
Prediction by MTE		
Assessment by MTE		
Not conspicuous	1.00 (reference)	
Conspicuous	6.18	1.49–23.06
Age	1.04	1.01–1.08
BMI	1.06	0.98–1.20
Prediction by physician in combination with MTE		
Combined assessment by physician and MTE		
Not conspicuous	1.00 (reference)	
Conspicuous	13.23	1.54–33.10
Age	1.04	1.01–1.08
BMI	1.08	0.99–1.21

BMI, body mass index; CI, confidence intervals; MTE, medical tactile examiner.

ments. The MTEs did not concur with the physicians' nonsuspicious findings in 20 out of 43 cases (47%). Similarly, the physicians did not concur with nonsuspicious findings by the MTEs in 9 out of 32 cases (28%). The combined assessment resulted in suspicious findings in 81 cases. Imaging with ultrasound and mammography as the reference method showed BIRADS 4 or 5 results in 55 cases in the 104 patients. Comparison of the results of the clinical breast examinations and imaging findings (BIRADS categories) are shown in table 3. The sensitivities of CBEs by physicians, MTEs, and both combined were 71, 82, and 89%, respectively. The corresponding specificities were 55, 45, and 35%.

The diagnostic biopsies identified malignancy in 26 out of 54 biopsies from the 104 patients. The clinical tumor sizes based on imaging (mammography and/or ultrasound) were cT1 in 10 cases (40%), cT2 in 14 cases (56%), and cT3 in 1 case (4%).

Comparison of Methods

Table 4 shows the results of the logistic regression models. In each model, the assessment by CBE was predictive of a suspicious finding in the imaging modalities. AUCs were calculated for each regression model and validated. The clinical prediction model without the breast assessment showed the lowest validated AUC of 0.612 (95% bootstrap CI 0.482–0.745). Adding the CBE by physicians resulted in a validated AUC of 0.685 (95% bootstrap CI 0.534–0.819); adding the CBE by MTEs yielded an AUC of 0.692 (95% bootstrap CI 0.563–0.811). Finally, the combined assessment showed an AUC of 0.710 (95% bootstrap CI 0.593–0.833). ROC curves are shown in figure 2. Comparison of the AUC values does not show any significant differences (mean p value (DeLong): 0.416). The ROCs for the bootstrapping are shown in online supplementary figure 1.

Patient Questionnaire

The majority of the patients (80 out of 82 women, 97.6%) perceived the CBE by the MTE as positive and would recommend it to other patients. Detailed results from the patient questionnaire on the way in which CBE by the MTEs was perceived and experienced are summarized in online supplementary table 2.

Discussion

The present study evaluated the results of including MTEs in diagnostic procedures in a diagnostic breast unit. The sensitivity and specificity levels are comparable between physicians and MTEs. The predictive values for suspicious findings on ultrasound/mammography are also comparable between physicians and MTEs, adjusted for the patients' age and BMI.

This is the first study to compare the diagnostic accuracy of physicians, visually impaired MTEs, and a com-

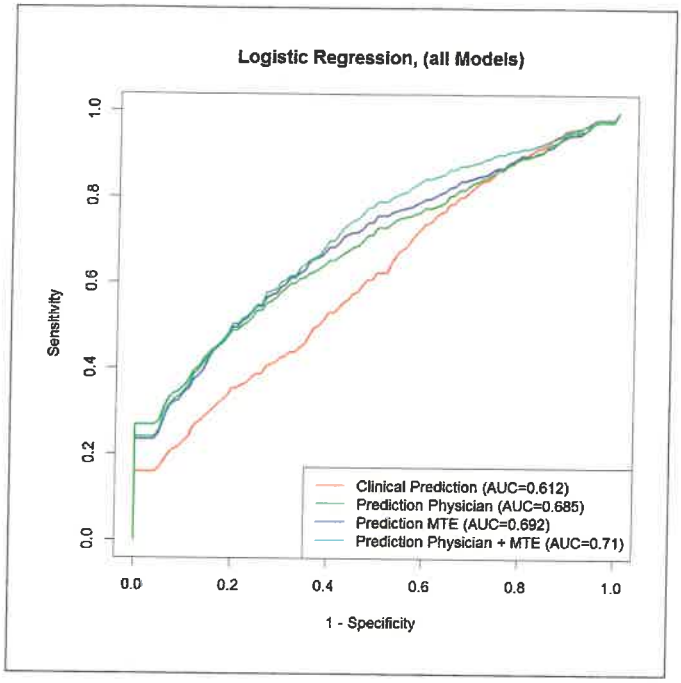

Fig. 2. Averaged receiver operating characteristic (ROC) curves of the prediction models.

bination of both. To the best of our knowledge, there have been no other prospective studies addressing this procedure. Including MTEs could lead to benefits in healthcare and breast diagnosis, while also generating occupational opportunities for visually impaired people. These initial results are only concerned with the feasibility and general diagnostic accuracy of the approach. The influence of CBE on benefits for specific subgroups or on mortality and morbidity in the screening process is not addressed. However, these issues will need to be evaluated for further development in this field.

The feasibility and clinical value of CBE depends on various factors, including the characteristics of patients and examiners. On the patients' side, breast morphology and medical history have a strong influence on diagnostic accuracy. BMI, age, previous operations, breast composition, and breast density have been described as having an influence on the predictive value of mammography, ultrasound, and CBEs [16, 31, 32, 54, 55]. An association between age, BMI, and mammographic breast density has been described in numerous studies [56–58]. This study only included patients with BMI and age-adjusted data without previous breast surgery. Further studies will need to address the question of how CBEs by physicians and MTEs might be extended to additional groups of patients, or how to identify patient populations in which these procedures are most helpful. On the examiners' side, experience and training can increase the predictive value of CBE [12, 16, 24]. It has been reported that the quality of the CBE increases along with the examiner's level of experience [59–65]. A systematic program with dedicated breast examiners could therefore be beneficial for the diagnostic process and improve quality in this setting.

A major issue in screening and early cancer detection programs is the low participation rate, which significantly reduces the effectiveness of the programs. Including MTEs might increase the acceptance of the diagnostic process by conveying positive perceptions in a clinical setting. 98% of the participants in the present study were willing to recommend the examination to other women. The MTE might spend more time with the patient, and the patients might feel well taken care of. 57% of the patients expected and appreciated special skills with regard to the sense of touch in persons with impaired vision, and 54% appreciated the fact that the examination by the MTE lasted longer.

There are 1.2 million people with impaired vision of <30% living in Germany [66], with a high unemployment rate among them [67]. From this point of view, the development of a standardized 9-month vocational training course with an emphasis on the needs and special skills of people with impaired vision holds considerable opportunities for this group.

The present study has a few limitations. It was performed as a single-center analysis at a specialized university outpatient department for breast diseases. The findings can therefore not be generalized for systematic screening and early cancer detection programs. In addition, the study population was restricted to patients without previous breast surgery. However, a large number of breast cancer survivors receive regular CBEs as part of their follow-up care. Future studies will have to address whether CBEs by physicians and MTEs can be implemented in that population as well. Finally, it should be noted that the physician had information about suspicious findings in a few cases that had led to referral to the diagnostic breast unit. The physicians' diagnostic accuracy might therefore have been overestimated.

Conclusion

CBEs by MTEs with impaired vision appear to have an accuracy level similar to that of examinations by physicians or a combination of both. The patients perceived the examination as being useful. Further studies on the implementation of this procedure are therefore warranted.

Acknowledgment

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Statement of Ethics

The Ethics Committee of the Medical Faculty of the Friedrich Alexander University of Erlangen-Nuremberg approved the study.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent was obtained from all individual participants included in the study.

Author Contributions

MPL contributed to the conception and design of the study. MPL, MRB, MW, CS, CP, CR, SMJ, FH, HL, TG, A-LB, CCH, RS-W, and MWB contributed to the acquisition of clinical data. WA, PAF, and PG performed the statistical analysis and interpretation of data. MPL, JE, PAF, and PG were involved in drafting the manuscript. All authors gave final approval of the version to be published, revised the manuscript critically, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Disclosure Statement

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