

Adjunctive Diagnostic Value of Targeted Electrical Impedance Imaging to Conventional Methods in the Evaluation of Breast Lesions

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Szabó BK, Saracco A, Wilczek B, Boné B, Aspelin P. Adjunctive diagnostic value of targeted electrical impedance imaging to conventional methods in the evaluation of breast lesions. *Acta Radiol* 2005;46:782–790.

Purpose: To determine the diagnostic accuracy of targeted electrical impedance imaging in characterizing breast lesions, and to evaluate whether lesion size, depth and histopathology affect the diagnosis.

Material and Methods: A total of 137 women with 145 lesions (79 malignant and 66 benign) found by palpation or mammography were prospectively enrolled in this study. The patients were examined by means of clinical breast examination, mammography, ultrasonography, and electrical impedance imaging with TransScan TS2000. A level of suspicion (LOS) post-processing algorithm (v2.67) was used for TS2000 lesion assessment. Imaging findings were correlated with cytologic ($n=54$) and histologic diagnoses ($n=91$). Patients with benign lesions were followed up for a mean of 36 months.

Results: TS2000 showed a high sensitivity (86%) which did not differ significantly from that of mammography (87%) and ultrasonography (US) (75%). The specificity of TS2000 (49%) was significantly lower compared to mammography (97%, $P<0.0001$) and US (100%, $P<0.0001$). The additive use of TS2000 to mammography and US yielded no significant increase in sensitivity (97%), but the decrease in specificity was significant (46%, $P<0.0001$). Diagnostic effectiveness of TS2000 ($A_z=0.68$), as measured by the area under the ROC curve, was significantly lower than for mammography ($A_z=0.93$, $P<0.0001$) and for US ($A_z=0.91$, $P<0.0001$). When using TS2000 in addition to mammography and US ($A_z=0.86$), a significant impairment was found ($P=0.0003$).

Conclusion: The role of targeted electrical impedance imaging as an adjunct to mammography and ultrasonography in the diagnosis of breast lesions is not justified by the result of this study.

Key words: Breast neoplasms; comparative studies; diagnostic accuracy; electrical impedance imaging; mammography; ultrasound

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Accepted for publication 11 August

Various attempts have been made to improve the diagnostic efficiency of conventional breast imaging methods by introducing novel techniques. Methods based on the detection of electrophysiological properties of breast tissue are currently under development. One method is to collect and analyze differences in electrical potential at the skin level caused by neoplastic activity (4). Other approaches focus on measuring conductivity and capacitance of tissues using multiple frequencies of alternating electric current (2,3,9). The principle behind multi-frequency impedance imaging is not a new discovery. In 1926, FRICKE & MORSE found that

capacitance of tumors differed significantly from that of normal or benign breast tissues (5). Although there is a long-known underlying scientific basis, it took more than 60 years before an electrical impedance imaging system was constructed (8,15).

TransScan TS2000 (TransScan Medical, Migdal Ha'Emek, Israel was distributed by Siemens-Elcoma, Solna, Sweden until 2001) has been introduced as the first commercial product that uses impedance technology (2). Special attention has been directed to the development of this new modality because it is a generally safe, non-invasive, radiation-free, and

low-cost solution. TS2000 produces a real-time skin-level impedance map of the area under examination and displays the data on gray-scale images. Highly conductive areas and inhomogeneities in impedance maps are found to be strongly associated with breast malignancies. Several clinical trials have been conducted to test this modality, and these have suggested that TS2000 has adjunctive value to conventional imaging methods, especially in mammographically suspicious lesions (6,10–12). However, other studies have not confirmed these findings (13,19).

The aims of our study were to determine the diagnostic accuracy of the *LOS* (level of suspicion) analysis algorithm of targeted mode TS2000 in characterizing breast lesions compared to mammography and ultrasound, and to evaluate whether lesion size, depth and histopathology affect the diagnosis established by impedance imaging.

Material and Methods

Patients

All patients gave informed consent to participation and the local ethics committee approved the study.

A total of 137 women (median age 56 years; range 33–92 years) with 145 lesions were prospectively enrolled in the study. Eligible patients were required to have had a breast abnormality found either by clinical breast examination (CBE) or mammography. Primary exclusion criteria were an implanted cardiac pacemaker, pregnancy, previous chemotherapy, radiation therapy, or breast surgery on the side to be examined. The following procedures were included in the diagnostic work-up: CBE, mammography, ultrasonography (US), and electrical impedance imaging. The imaging findings were correlated with the results of fine needle aspiration cytology (FNAC, $n=54$), core needle biopsy ($n=5$), or histopathologic analysis of the surgically excised specimen ($n=86$). Patients with benign lesions were followed up for a mean period of 36 months. All patients in whom malignant breast disease developed during the follow-up period were excluded from the analysis. Of the 64 patients with 66 benign lesions, there were 28 (44%) who had a breast complaint but were diagnosed as benign during the follow-up; 36 (56%) remained asymptomatic. The World Health Organization (WHO) classification was used for typing histologic tumor samples. Histologic grade of invasive carcinomas was assessed using the Elston-Ellis grading system. Lesion size was determined either by the histopathologic or ultrasound examination. Depth

was measured from the skin level to the upper border of the lesions by ultrasound.

Mammography

Mammography was performed with dedicated equipment (Mammomat 3000; Siemens, Solna, Sweden/Senographe DMR; G.E. Medical Systems, Milwaukee, Wisc., USA). The Kodak Min-R2 film-screen cassette system was used with Kodak Min-RE films (Eastman Kodak, Rochester, N.Y., USA). Films were processed in a Kodak X-omat 300 daylight machine using extended cycle processing. Each breast was examined in three standard views (cranio-caudal, mediolateral oblique, and lateromedial), and additional views (spot and/or direct magnification) were taken when it was necessary for better visualization. Mammographic findings were categorized on the basis of a 5-point rating scale describing the degree of suspicion for malignant disease. These five groups were defined according to the ACR/BI-RADS (Breast Imaging Reporting and Data System of the American College of Radiology) assessment scoring system (1).

Mammograms were read and evaluated in consensus by three experienced radiologists. Observers were blinded to other imaging methods, but were aware of the result of CBE.

Ultrasonography

The US examinations were performed with an Acuson Aspen ultrasound system (Acuson Inc., Mountain View, Calif., USA) using the L7 (5–10 MHz) and L10 (6–11 MHz) linear transducers. Gray-scale US evaluation of the indicated breast and axilla was performed. Spiculated lesions, angular margins, marked hypoechogenicity and back shadowing were considered as signs of malignancy. Features associated with benign lesions were the following: intense hyperechogenicity, echogenic pseudocapsule, and ellipsoid shape (18). Lesions identified by US were scored on a level of suspicion scale from 1 to 5.

US was performed with the knowledge of the clinical and mammographic findings and analyzed in consensus by three radiologists.

Electrical impedance imaging

Electrical impedance measurements were carried out using the TS2000 imaging device. The main components of the TS2000 system are as follows: a PC workstation with a connected laser printer and data transfer devices, reference electrode, and scanning probes. The sensing area of the probes

contains a matrix of electrodes (large probe, 16×16 ; small probe, 8×8). The reference electrode is the source of biocompatible alternating electric current (0.1–2.5 V, 5 mA). Patients hold this electrode in the hand contralateral to the side being examined while lying in the supine position. A thin layer of conducting gel is applied as the contact medium between the skin and the sensors of the probe. TS2000 produces real time conductivity and capacitance gray-scale images using 7 different frequencies for measurements: 1, 2, 10, 20, 30, 40, and 50 kHz.

TS2000 examinations were performed with the full knowledge of the patient's history and the findings of CBE, mammography, and US. All breast lesions were scanned using the targeted mode. The region of the nipple on the indicated side was required to be recorded first. Then each palpable and/or mammographically detected lesion was recorded at its known location. External objects like air bubbles in the conductive gel, scars, moles, pimples, scratches, and other skin lesions may alter the conductivity and capacitance maps. These artifacts were identified and excluded from the analysis.

For lesion assessment, a post-processing algorithm (LOS algorithm, software version 2.67) was used which operates by displaying the result on a 5-level scoring scale (1=normal, 2=benign, 3=probably benign, 4=suspicious of malignancy, 5=highly suspicious of malignancy). The LOS algorithm uses conductivity and capacitance data measured in the sector of concern, as well as in the nipple area. The algorithm is also influenced by patient age, as the system uses different algorithms for different age groups. TS2000 finding was considered as malignant if a red frame appeared around the recorded sector (LOS 4 or 5). This LOS algorithm was compared to the assessment method used in the previous versions of TransScan (spot method), where the presence of a bright (white) spot on the recorded conductivity image was interpreted as a suspicious finding.

Statistical methods

Sensitivity, specificity, percent correct diagnostic accuracy, positive (PPV) and negative (NPV) predictive values were calculated using standard formulae. The results of the combined methods were defined as the highest score obtained with either method. Empiric receiver operating characteristic (ROC) curves were drawn, and the diagnostic accuracy of each imaging method was determined by calculating the area under the ROC curve (A_z). The method of HANLEY &

MCNEIL was used to test paired data for significant difference (7).

The comparison of two percentages was performed using McNemar, Pearson's χ^2 , or Fisher's exact test when appropriate. Spearman's correlation test was performed for comparison of ordinal variables. The Mann-Whitney U test was used to evaluate the differences between two groups of non-parametric quantitative variables. Statistical calculations were carried out using SPSS 10.0 for Windows (SPSS Inc., Chicago, Ill., USA).

Results

Cytologic and histopathologic examinations revealed 79 (55%) malignant and 66 (45%) benign lesions. Of the 79 histopathologically verified malignant lesions, there were 6 (8%) in situ and 73 (92%) invasive cancers. Seventeen (24%) grade I, 37 (53%) grade II, and 16 (23%) grade III invasive carcinomas were identified. Grading information was not available in three cases. The summary of cytologic and histologic diagnoses is given in Table 1.

There were 100 (69%) palpable and 45 (31%) non-palpable lesions. The mean lesion size was $22.4 \text{ mm} \pm 14$ (SD); range 5–74 mm (size information was available for 111 lesions). There were 22 (20%) lesions smaller than or equal to 10 mm, 42 (38%) lesions in the range 11–20 mm, and 47 (42%) lesions larger than 20 mm. The mean depth was $9.3 \text{ mm} \pm 4$ (SD) and ranged from 1 to 20 mm.

Diagnostic accuracy

The summary of diagnostic indices for each imaging method is given in Table 2. TS2000 showed a high

Table 1. The breakdown of cytologic ($n=54$, 37%) and histologic ($n=91$, 63%) diagnoses of 145 breast abnormalities in 137 patients examined by TransScan TS2000 electrical impedance scanner

Malignant lesions ($n=79$)	
Invasive ductal cancer	57
Invasive lobular cancer	8
Ductal carcinoma in situ	6
Invasive tubular cancer	5
Invasive mucinous cancer	3
Benign lesions ($n=66$)	
Negative FNAC, without histologic diagnosis	48
Simple cyst	4
Benign core biopsy	3
Fibroadenoma	3
Abscess	2
Sclerosing adenosis	2
Atypical hyperplasia	1
Chronic mastitis	1
Fibrocystic disease	1
Fibrosis	1

Table 2. Diagnostic accuracy of mammography (MG), ultrasonography (US), TransScan 2000* (TS) and the combination of methods in 145 palpable or mammographically suspicious breast abnormalities (79 malignant and 66 benign)

	MG	US	TS	MG+US	US+TS	US+MG+TS
Sensitivity (%)	87 (69/79)	75 (57/79)	86 (68/79)	92 (73/79)	92 (73/79)	97 (77/79)
Specificity (%)	97 (64/66)	100 (66/66)	49 (32/66)	97 (64/66)	49 (32/66)	46 (30/66)
Diagnostic accuracy (%)	92 (133/145)	86 (125/145)	69 (100/145)	95 (137/145)	72 (105/145)	74 (107/145)
PPV (%)	97 (69/71)	100 (59/59)	67 (68/102)	97 (73/75)	68 (73/107)	68 (77/113)
NPV (%)	87 (64/74)	77 (66/86)	74 (32/43)	91 (64/70)	84 (32/38)	94 (30/32)

*In targeted examination mode, using the LOS analysis algorithm.

sensitivity, which did not differ significantly from that of mammography ($P=1$) and US ($P=0.064$). The specificity of TS2000 was significantly lower compared to mammography ($P<0.0001$). The additive use of TS2000 to mammography and US yielded no significant increase in sensitivity ($P=0.125$), but the decrease in specificity was significant ($P<0.0001$). The percent correct diagnostic accuracy of TS2000 was also significantly lower than that of mammography ($P<0.0001$) and US ($P<0.0001$), and adding TS2000 to the basic imaging methods resulted in a significantly lower accuracy ($P<0.0001$).

Excluding mammographically normal or benign (BI-RADS I and II) cases ($n=37$) resulted in lower values of specificity: 94% (30/32) for mammography, 38% (12/32) for TS2000, 94% (30/32) for the combination of mammography and US, and 31% (10/32) for the combination of all methods. Diagnostic accuracies calculated by ROC analysis were as follows: $A_z=0.93$ (95% CI: 0.89, 0.98) for mammography, $A_z=0.91$ (95% CI: 0.86, 0.96) for US, $A_z=0.68$ (95% CI: 0.59, 0.77) for TS2000, $A_z=0.95$ (95% CI: 0.91, 0.99) for the combination of mammography and US, and $A_z=0.86$ (95% CI: 0.80, 0.92) for the combination of mammography, US and TS2000. Diagnostic performance of TS2000 was significantly lower than that of mammography ($P<0.0001$) and US ($P<0.0001$), and using TS2000 as an adjunct to mammography and US the diagnostic accuracy of the combination significantly decreased ($P=0.0003$).

Figure 1 shows the ROC curves of the single methods of mammography, US, and TS2000. Figure 2 illustrates a small malignant breast tumor as shown by mammography, US, and TS2000. A false-positive finding by TS2000 is demonstrated in Fig. 3.

False-negative results of TS2000

Of the 57 invasive ductal cancers, 6 (11%) were classified as benign by TS2000. There was 1 (13%) false-negative finding of the 8 invasive lobular cancers, and also 1 (20%) lesion of the 5 invasive tubular cancers coded as benign. Two (67%) of the 3

invasive mucinous cancers were false-negatives. One (17%) of the 6 ductal carcinomas in situ (DCIS) was classified as benign.

False-positive results of TS2000

Three (75%) of the 4 simple cysts, 1/2 (50%) abscess, 1/2 (50%) sclerosing adenosis, and 1/1 fibrosis were indicated as malignant by TS2000. Twenty (39%) of the 51 otherwise non-defined benign or normal findings (48 negative FNAC and 3 negative core biopsy) were false-positive on TS2000.

Comparison of the LOS algorithm and the spot method

The spot method (white spots on the conductivity images were considered as positive findings) had a sensitivity of 77% (61/79), specificity of 79% (52/66), diagnostic accuracy of 78% (113/145), PPV was 77% (61/79) and the NPV was 79% (52/66). The spot method showed a significantly higher specificity ($P=0.0003$) and diagnostic accuracy ($P<0.0001$) compared to the diagnostic performance of the LOS algorithm, but there was no significant difference in sensitivity ($P=0.092$).

Effect of lesion characteristics

To measure the effect of lesion size and depth on diagnostic performance, the groups of correctly and incorrectly diagnosed cases were compared. There was no significant difference in size and depth when looking at the percent correct diagnostic accuracy ($P=0.59$ and $P=0.15$, respectively), sensitivity ($P=0.87$ and $P=0.68$, respectively), and specificity ($P=0.82$ and $P=0.57$, respectively).

Sensitivity, specificity, and diagnostic accuracy were 93% (14/15), 29% (2/7), and 73% (16/22) for lesions ≤ 10 mm, and 86% (24/28), 50% (7/14), and 74% (31/42) for lesions 11–20 mm, and 85% (29/34), 39% (5/13), and 72% (34/47) for lesions > 20 mm, respectively. There was no significant difference in diagnostic indices between these size groups (for difference in sensitivity: $P=0.46$, between lesions

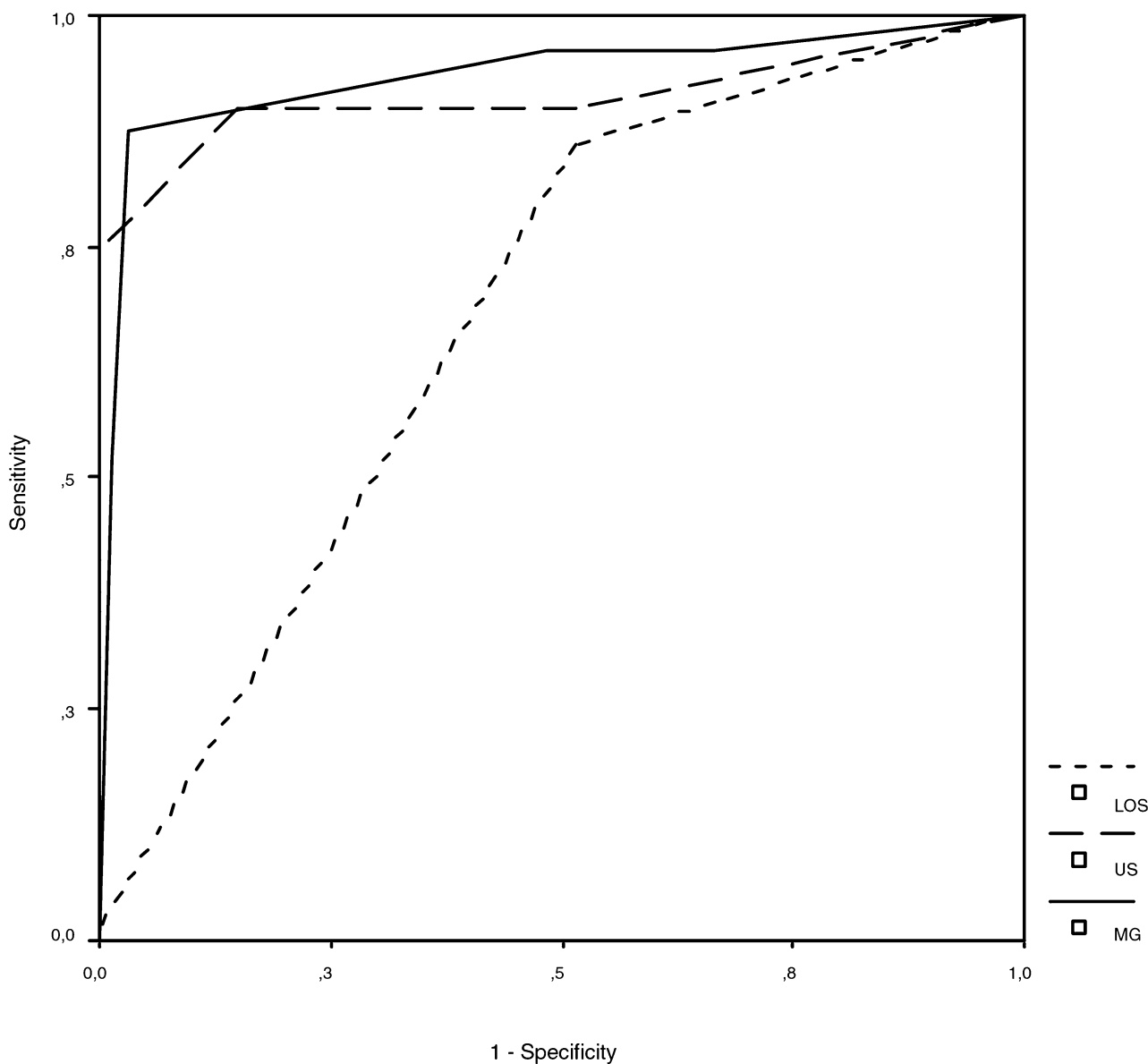


Fig. 1. Receiver operating characteristic (ROC) curves of mammography (MG), ultrasonography (US), and TransScan TS2000 electrical impedance scanner (LOS) in 145 palpable or mammographically suspicious breast abnormalities (79 malignant and 66 benign).

≤ 10 mm and 11–20 mm, and $P=0.39$, between lesions ≤ 10 mm and >20 mm).

There was no significant difference in sensitivity between in situ and invasive lesions ($P=1$). No significant correlation was noted between histologic grade and TS2000 findings ($P=0.89$).

Discussion

The results of our study show that targeted TS2000 examination could not provide significant adjunctive diagnostic aid to mammography and US. TS2000 showed a considerably high sensitivity, but at a cost of reduced specificity (approximately half

of the benign lesions were false-positives). Furthermore, this high sensitivity does not differ significantly from that of mammography, US, and even from the classical (spot versus no spot) TS2000 assessment method. On the other hand, examining the specificity and diagnostic accuracy, significant impairment was found as compared to mammography and US. Since the percent correct diagnostic accuracy is highly dependent on the prevalence, the diagnostic performance as shown by area under the ROC curve was also evaluated. ROC analysis revealed highly significant differences in diagnostic effectiveness between TS2000 and the conventional breast imaging modalities.

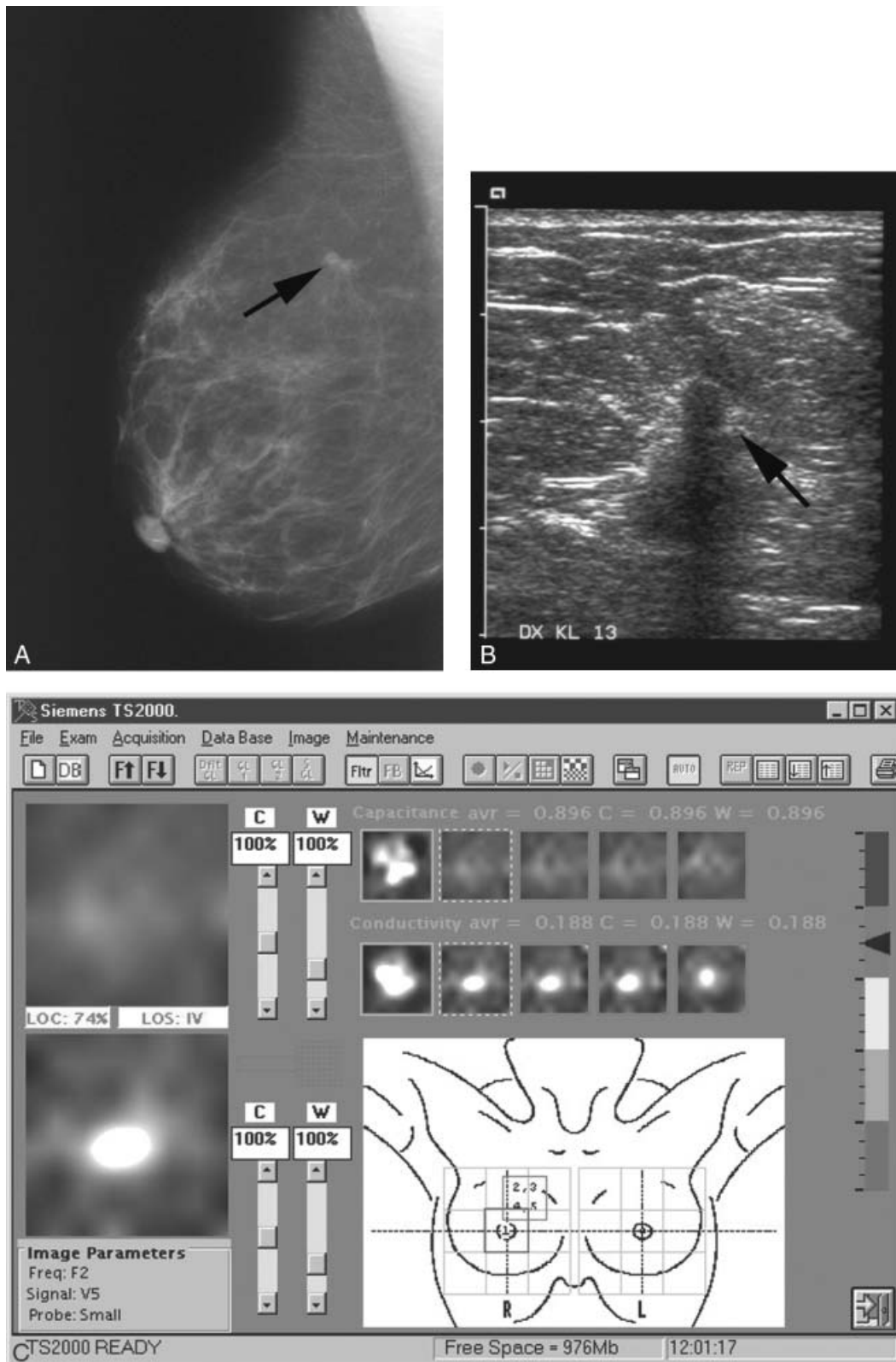


Fig. 2. Histopathologically proved 10-mm-large invasive ductal carcinoma in a 57-year-old woman's right breast. A. Mammography revealed a suspicious lesion (arrow). B. Ultrasonography showed a small hypoechoic lesion with back shadowing. C. Targeted electrical impedance imaging showed a bright spot on conductivity images which was classified as suspicious for malignancy (LOS 4). Note that the first sector is the nipple.

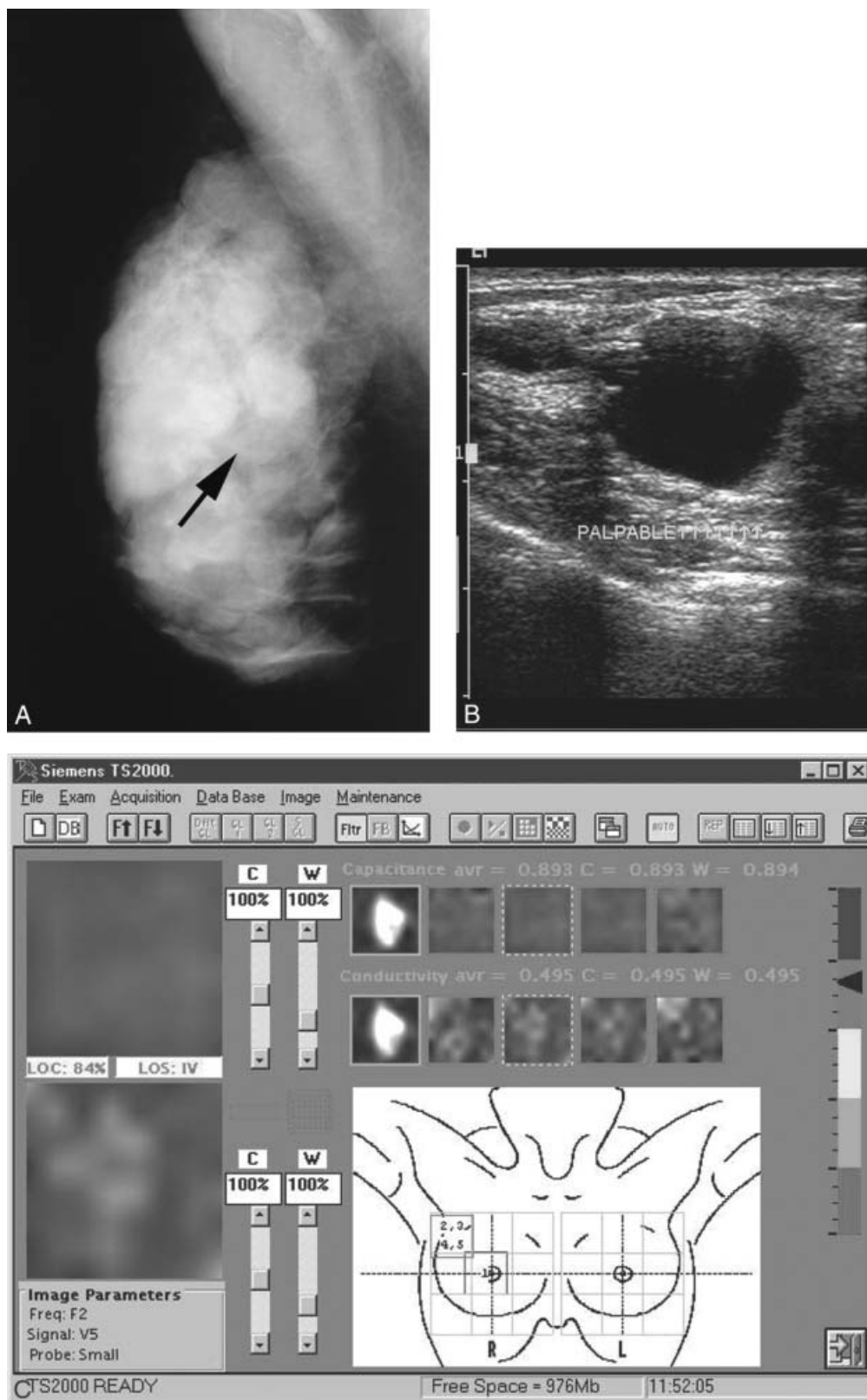


Fig. 3. A 46-year-old woman referred to mammography due to a suspicious palpable lump in her right breast. A. Mammography showed several circumscribed lesions (*arrow*) which were classified as probably benign. B. Ultrasonography showed an anechoic lesion with pronounced acoustic enhancement at the location of the palpable lump, and described as a simple cyst. C. This image represents a false-positive case. TransScan showed marked inhomogeneity in conductivity maps; the finding was classified as suspicious for malignancy by the LOS algorithm.

There is controversy in the scientific literature about the diagnostic value of targeted electrical impedance scanning. A wide variety of diagnostic indices has been reported in different studies, the sensitivity ranging from 62% to 93% and specificity from 50% to 82% (6,10–13, 19). However, most of the studies emphasized the high sensitivity of TS2000 and suggested that it could be used as a complementary tool to mammography and US in diagnosing breast cancer (10–12). Moreover, one study claimed that the area under the ROC curve was significantly higher for TS2000 than other imaging methods (6). In contrast to these reports, there are two studies that found mediocre diagnostic effectiveness of impedance imaging (13,19). Our study supports the high rate of false-positive findings of TS2000 continuing to be an issue, and this limitation prevents wide clinical use of the technology. Although the high sensitivity of TS2000 could be confirmed, no additive value for conventional imaging was proved.

According to the established criteria described in preliminary studies on electrical impedance imaging (6,12), each spot representing high conductivity or capacitance, which is not caused by an artifact, should be interpreted as suspicious for malignancy. The LOS post-processing algorithm provided by the new versions of TS2000 was developed to replace the old assessment approach. In our study, this spot method showed significantly higher diagnostic accuracy and specificity than the LOS software. Our findings indicate that this advanced setup does not represent real diagnostic improvement, and the apparently high sensitivity of the LOS method could only be achieved at the cost of decreased specificity.

When evaluating a diagnostic test, the method of selecting patients might be a cause that accounts for differences in results among studies. In this study, besides mammographically equivocal or highly suspicious findings (BI-RADS III-V), mammographically normal or benign (BI RADS I and II) cases were also included, but only those which turned out to be suspicious at physical examination. One can explain our results by the relatively high proportion of benign or negative mammograms compared to other studies. In order to clarify how selection criteria affect diagnostic accuracy in this case, the relevant diagnostic indices were also calculated for the subgroup of mammographically suspicious lesions (BI-RADS III-V). The results show that specificities decreased for all methods, consequently TS2000 performs better in terms of specificity among mammographically negative or benign cases,

and patient selection is unlikely to be the source of the poor diagnostic accuracy.

However, although the small number of in situ lesions included in this study probably prevents a thorough comparison with invasive disease, we found that TS2000 had similar sensitivity in invasive and in situ cancers. This finding is in agreement with one study (12), although another group reported on significantly lower detection rates for DCIS than invasive lesions (10). The literature is consistent in reporting the highest sensitivity for ductal invasive cancers, but there is a little evidence of the special types of breast cancer. In our study, it was surprising that only 1 of the 3 mucinous cancers was identified as malignant by TS2000, achieving the lowest sensitivity of 33%. Larger sample size and further investigations of mucinous cancer are needed if any conclusions are to be drawn for this histologic group.

With regard to specificity, no correlation was found with histologic type or any other factors. The proportions of false-positive findings among different histologic types of benign lesions are found to be similar in our study. Where the principles of electrical impedance imaging are concerned, we can assume that proliferative benign disease is responsible for most of the false-positive results, although ours and previous investigations could not explore such an association. Another explanation that has been suggested is that hormonal status of the patients may influence the electrical properties of breast tissues. Recent studies have shown that false-positive findings are common in young premenopausal women (12,14), and estrogen activity in breast tissue affects the electrical impedance pattern (16). Since the LOS software algorithm uses not only measured conductivity/capacitance data, but also patient age, and selects the appropriate calculation method according to different age groups, the effect of patient's age and hormonal status was not investigated in this study.

Other factors hypothesized as altering the detection of impedance signals include lesion size and depth measured from the surface. A simulation study has shown that increasing object size and depth decreases its detectability by impedance imaging (17). Another study found that TS2000 showed the highest sensitivity in detecting small lesions (11–20 mm) compared to large lesions (> 20 mm) (19). In our study, the highest detection rate was found in the group of smallest lesions (≤ 10 mm): 14 of the 15 malignant lesions in this group were classified as suspicious by TS2000, although the difference in sensitivity was not

significant. In addition, the correctly or incorrectly diagnosed lesions did not differ in lesion size or depth in this study. It should be noted that different types and histologic grades of invasive cancers did not differ in electrical properties, our results thus suggesting that electrical impedance maps do not carry prognostic information.

In conclusion, the role of targeted electrical impedance imaging as an adjunct to mammography and ultrasonography in diagnosing breast lesions is not justified by the results of this study. Targeted mode TS2000 showed high sensitivity, but limitingly low specificity compared to conventional imaging techniques. The theory behind electrical impedance imaging is promising, but TransScan TS2000 must undergo further developments before it is used in a broad clinical application.

References

- American College of Radiology. Breast imaging reporting and data system (BI-RADS), 2nd edn. Reston, Va: American College of Radiology; 1995.
- Assenheimer M, Laver-Moskovitz O, Malonek D, Manor D, Nahaliel U, Nitzan R, et al. The T-SCAN technology: electrical impedance as a diagnostic tool for breast cancer detection. *Physiol Meas* 2001;22:1–8.
- Cherepenin VA, Karpov AY, Korjnevsky AV, Kornienko VN, Kultiasov YS, Ochapkin MB, et al. Three-dimensional EIT imaging of breast tissues: system design and clinical testing. *IEEE Trans Med Imaging* 2002;21:662–7.
- Cuzick J, Holland R, Barth V, Davies R, Faupel M, Fentiman I, et al. Electropotential measurements as a new diagnostic modality for breast cancer. *Lancet* 1998;352:359–63.
- Fricke H, Morse S. The electrical capacity of tumors of the breast. *J Cancer Res* 1926;16:340–76.
- Fuchsjaeger MH, Helbich TH, Ringl H, Funovics MA, Rudas M, Riedl C, et al. Electrical impedance scanning in the differentiation of suspicious breast lesions: comparison with mammography, ultrasound and histopathology. *Rofo Fortschr Geb Rontgenstr Neuen Bildgeb Verfahr* 2002;174:1522–9.
- Hanley JA, McNeil BJ. A method of comparing the areas under receiver operating characteristic curves derived from the same cases. *Radiology* 1983;148:839–43.
- Jossinet J. A hardware design for imaging the electrical impedance of the breast. *Clin Phys Physiol Meas* 1988;9 Suppl A, 25–8.
- Kerner TE, Paulsen KD, Hartov A, Soho SK, Poplack SP. Electrical impedance spectroscopy of the breast: clinical imaging results in 26 subjects. *IEEE Trans Med Imaging* 2002;21:638–45.
- Malich A, Bohm T, Facius M, Freessmeyer M, Fleck M, Anderson R, et al. Additional value of electrical impedance scanning: experience of 240 histologically-proven breast lesions. *Eur J Cancer* 2001;37:2324–30.
- Malich A, Fritsch T, Anderson R, Boehm T, Freessmeyer MG, Fleck M, et al. Electrical impedance scanning for classifying suspicious breast lesions: first results. *Eur Radiol* 2000;10:1555–61.
- Martin G, Martin R, Brieva MJ, Santamaria L. Electrical impedance scanning in breast cancer imaging: correlation with mammographic and histologic diagnosis. *Eur Radiol* 2002;12:1471–8.
- Melloul M, Paz A, Ohana G, Laver O, Michalevich D, Koren R, et al. Double-phase ^{99m}Tc-sestamibi scintimammography and trans-scan in diagnosing breast cancer. *J Nucl Med* 1999;40:376–80.
- Perlet C, Kessler M, Lenington S, Sittek H, Reiser M. Electrical impedance measurement of the breast: effect of hormonal changes associated with the menstrual cycle. *Eur Radiol* 2000;10:1550–4.
- Piperno G, Frei EH, Moshitzky M. Breast cancer screening by impedance measurements. *Front Med Biol Eng* 1990;2:111–7.
- Piperno G, Lenington S. Breast electrical impedance and estrogen use in postmenopausal women. *Maturitas* 2002;41:17–22.
- Scholz B, Anderson R. On electrical impedance scanning – principles and simulations. *Electromed* 2000;68:35–44.
- Stavros AT, Thickman D, Rapp CL, Dennis MA, Parker SH, Sisney GA. Solid breast nodules: use of sonography to distinguish between benign and malignant lesions. *Radiology* 1995;196:123–34.
- Wersebe A, Siegmann K, Krainick U, Fersis N, Vogel U, Claussen CD, et al. Diagnostic potential of targeted electrical impedance scanning in classifying suspicious breast lesions. *Invest Radiol* 2002;37:65–72.