



# Additional value of electrical impedance scanning: experience of 240 histologically-proven breast lesions

A. Malich<sup>a,\*</sup>, T. Böhm<sup>b</sup>, M. Facius<sup>a</sup>, M. Freessmeyer<sup>a</sup>, M. Fleck<sup>a</sup>,  
R. Anderson<sup>c</sup>, W.A. Kaiser<sup>a</sup>

<sup>a</sup>*Institute of Diagnostic and Interventional Radiology, Friedrich-Schiller University Jena, Bachstr. 18, D-07740 Jena, Germany*

<sup>b</sup>*Institute of Diagnostic Radiology, University Zuerich, Raemistr. 100, CH-8032 Zuerich, Switzerland*

<sup>c</sup>*Siemens-Elma AB, Special Systems — Women's Health, Röntgenvägen 2, SE-171 95 Solna, Sweden*

Received 24 October 2000; received in revised form 25 June 2001; accepted 9 August 2001

## Abstract

The aim of this study was to quantify the clinical value of using electrical impedance scanning (EIS) as an adjunct to other diagnostic techniques in order to identify cancerous tissue based upon its inherent altered local dielectric properties. 210 consecutive women with 240 sonographically and/or mammographically suspicious findings were examined using EIS. All lesions were histologically-proven. 86/103 malignant and 91/137 benign lesions were correctly identified using EIS (87.8% sensitivity, 66.4% specificity). NPV and PPV of 84.3% and 65.2% were observed, respectively. Excluding cases as defined by *a priori* criteria, i.e. lesions located deeper than 35 mm, lesions larger than 35 mm, and retroareolar lesions, a sensitivity of 85.5% was observed, and for invasive cancers, 91.7%. The detection rate for ductal carcinoma *in situ* (DCIS) was poor (57.1%,  $n=14$ ). By adding EIS to mammography and ultrasound, the sensitivity rose from 86.4 to 95.1%, whereas the accuracy decreased from 82.3 to 75.7%. EIS appears to be of interest as an adjunct to breast diagnostic techniques, performing with a reasonable sensitivity. Further investigations on histomorphological characteristics and the reasons for false-negative findings are essential to gain further knowledge about the bioelectricity of breast lesions, and prove the value of this new technology. © 2001 Elsevier Science Ltd. All rights reserved.

**Keywords:** Breast cancer; Electrical bio-impedance; EIS; Diagnostic adjunct; Biopsy-proven; Conductance

## 1. Introduction

Breast carcinoma is the most common malignant tumour in women in the Western world. Statistically, almost every eighth woman is affected by carcinoma of the breast during her lifetime, and the incidence is currently rising [1,2]. Early detection and treatment of breast tumours are critical for a favourable prognosis. However, classical techniques offers as yet insufficient specificity. As depicted by Elmore and coworkers, the estimated cumulative risk of a false-positive result was 49.1% after 10 mammograms (9762 screening mammograms were introduced in that study) [3]. In Europe, a high rate of biopsies of benign lesions (80%) is also

documented [4]. Of 5 patients biopsied, only one tissue sample leads to a malignant histological diagnosis, and this illustrates that the established methods still do not offer an adequate specificity [4]. In addition, an estimated 10–25% of breast cancer lesions were not detectable by the aforementioned methods in a 2-year follow-up [5–7]. This lower sensitivity is often attributed to dense breast tissue that is common among younger patients, and post-menopausal women undergoing hormone replacement therapy (HRT) [7].

An active topic of scientific research since the 1920s is the principle that the electrical impedance properties of tissues can offer interesting and potentially valuable information—quantifiable as the parameters of electrical conductance (1/resistance of an alternating current) and electrical capacitance (storage of electrical potential) [8], factors influencing tissue impedance. In the normal breast, moderate variations in these values are observed, reflecting the differences among various

\* Corresponding author. Tel.: +49-3641-939-506; fax: +49-3641-939-181.

E-mail address: ansgar.malich@med.uni-jena.de (A. Malich).

types of breast tissue [8]. In contrast to these observations in normal tissue, malignant tumours show substantially increased capacitance and conductance values resulting in a decreased impedance [9–11]. *In vitro* studies have shown 20–40-fold higher values for both parameters in malignant compared with normal tissue [9]. These differences are attributed to changes of cellular water content, amount of extracellular fluid, membrane properties, packing density, destruction of tight junctions and cell membranes and a changed orientation of malignant cells [12,13]. Of key importance is the fact that most benign lesions exhibit the electrical properties of normal tissue, and not of malignancies, thereby leading to the potential to differentiate benign versus malignant lesions [10,14]. A technique for measurement of passive skin-surface electropotentials has been investigated [13]. However, electrical impedance scanning (EIS) differs significantly from this approach in that EIS measures active, applied alternating currents as opposed to inherent, biological electricity (DC versus AC).

Early EIS results were published in 1990 by Piperno and colleagues [15]. During the last decade, the technical equipment and application mode has undergone significant refinement. The current EIS system, TransScan TS2000 (TransScan Medical, Ltd., Israel, distributed by Siemens-Elema, Stockholm, Sweden) is a real-time, non-invasive method by which the increased conductance and capacitance of a malignant tumour is measured on the skin surface of the breast. To date, only limited clinical experience and initial results of electrical impedance scanning in the detection of malignancies have been published [16,17]. In 1999, TS2000 was approved for use by the American Food and Drug Administration (FDA) as an adjunct to Mammography for the evaluation of equivocal breast lesions.

Due to the fact that final arbitration of whether a lesion is malignant or benign can never be based upon imaging but must rather be histologically based, all included cases were histologically-proven.

Therefore, the aim of any additional imaging technique should be to determine the complementary value—in this case, the value of EIS in addition to mammography and ultrasound examinations for breast lesion diagnosis. In so doing, this study aimed to answer whether EIS adds to the sensitivity of cancer detection by indicating cases for histological confirmation which would not have been indicated by clinical examination, mammographic and ultrasound imaging.

## 2. Patients and methods

From April 1999 to June 2000, 210 consecutive eligible patients (mean age 57 years, standard deviation (S.D.) 13 years) presenting 240 suspicious lesions were included in this study performed at our institution.

Patients were previously selected by clinical examination and imaging. A screening programme was not available during the period this study was conducted. Due to the known limitations of EIS, it is, at present, necessary to know the location of the lesion which should be examined using EIS [16,18]. Consequently, only symptomatic patients having an abnormal finding in mammography and/or ultrasound, who were not pregnant, and did not have a pacemaker were included. It was not possible to include patients without clinical or imaging abnormalities. Clinical abnormality (e.g. by palpation) without any corresponding imaging abnormality did not occur in our patient population. However, if such a case had been encountered, the patient would have undergone a MRM: MR-mammography examination. If the clinical findings had been clearly localisable, an EIS examination would then have been performed. Consequently, the absence of imaging abnormalities in clinically suspicious localisable areas was not an exclusion criteria. Each patient received information about this technique; all voluntarily accepted the examination.

Results of the diagnostic modalities were not considered individually but, rather, collectively. These determinations were made based on a synopsis of all of the results of the established techniques. Hence the clinical, mammographical and sonographic examinations were performed and the collective results classified by an experienced radiologist (including a double reading of mammography) according to the LOS (level of suspicion) categorisation method: category 1: no lesion, no finding in clinical examination; category 2: benign lesion; category 3: lesion most probably benign; category 4: lesion probably malignant; category 5: lesion very suspicious for malignancy.

Cases scored as category 1 had to be excluded from the study due to the fact that there was no modality available to prove EIS outcome. In addition, it is documented that EIS is an additional technique for the clarification of known lesions and should therefore be utilised only for the investigation of lesions first identified by one of the listed established techniques.

Lesions of LOS 2–5 for which pathology results were available were included in the study. Patients with lesions of category 2 were recommended to undergo a clinical, as well as an imaging follow-up (1 year), unless the patient requested immediate clarification (biopsy/cytology) followed by re-evaluation. For lesions of category 3, a clinical, as well as an imaging short-term follow-up (1/2 year) was indicated, and immediate histologically-based clarification was performed only upon patient request. Lesions of categories 4 and 5 immediately underwent a histological clarification. The EIS examination was performed with full knowledge of the results of mammography and ultrasound, prior to biopsy/surgery. The procedure was performed as follows:

A low-level, biocompatible electrical current was applied via a metal cylinder (base electrode) held in the recumbent patient's hand. This current flowed through the patient's body.



The scan probe held by the examiner was applied to the breast at the region of interest. Good contact was facilitated with the use of an ultrasound gel.



The array of sensors (8×8 matrix) on the scan probe measured the electrical current.



The computer calculated, from these data, tissue-related conductance and capacitance.



The display of both the conductance and the capacitance 'maps' of the breast were separately presented in a 256-gray scale on the monitor. An increased conductance only or conductance and capacitance value was visible as a 'bright white spot'. The reading frequency was 200 Hz.



Recordings were taken at the region of interest, the impedance 'maps' being registered on up to a five-sector screen (see Fig. 1) for conductive and capacitance.



The skin surface at the scanned location was carefully inspected, as artifacts caused by skin lesions, scars, moles, contact artifacts, bone or air bubbles can represent high conductance or capacitance and therefore also create spots [19].



The impedance images were interpreted in accordance with established criteria [16,19] and as described below. One examination was performed in approximately 5 min.

Each resulting bright spot (focal brightness in one of the sectors clearly more luminous than its surroundings) was interpreted. A spot was identified as a positive finding, i.e. indicative of malignancy, unless a skin artifact was identified at that location. In Fig. 1, a typical EIS finding is shown.

The nipple always shows as a bright signal and should be bilaterally comparable (size, intensity) within the same healthy patient. However, any inconsistency between the nipple signal of left and right breast was not registered as a positive finding due to the fact that the observed nipple signals, even in healthy patients, can differ in their appearance (due perhaps to skin alterations, prominence, size differences, etc.). Only if there were a separable focal spot in the nipple area (indicative of retroareolar malignancy), was the spot classified as a positive finding in EIS.

The clinical values as characterised by the resulting sensitivity, specificity, false-positive rate, false-negative (FN) rate, positive predictive value (PPV), negative predictive value (NPV) and accuracy were evaluated with respect to the suspicious lesion. In addition, size, location, depth and distance from the skin level were measured, for lesions that were visible in ultrasound.

Finally, and as mentioned above, all lesions were cytologically/histologically proved.

Selection of the technique was based upon the lesion and patient: ultrasound-guided puncture of liquid tissue (cysts) with cytology, ultrasound-guided core needle-biopsy (each with at least three cylinders of tissue), minimally-invasive breast biopsy (each with at least 12 cylinders of tissue), local surgical excision of the lesion, quadrant resection or mastectomy. For all proven malignancies, the elected treatment method was either

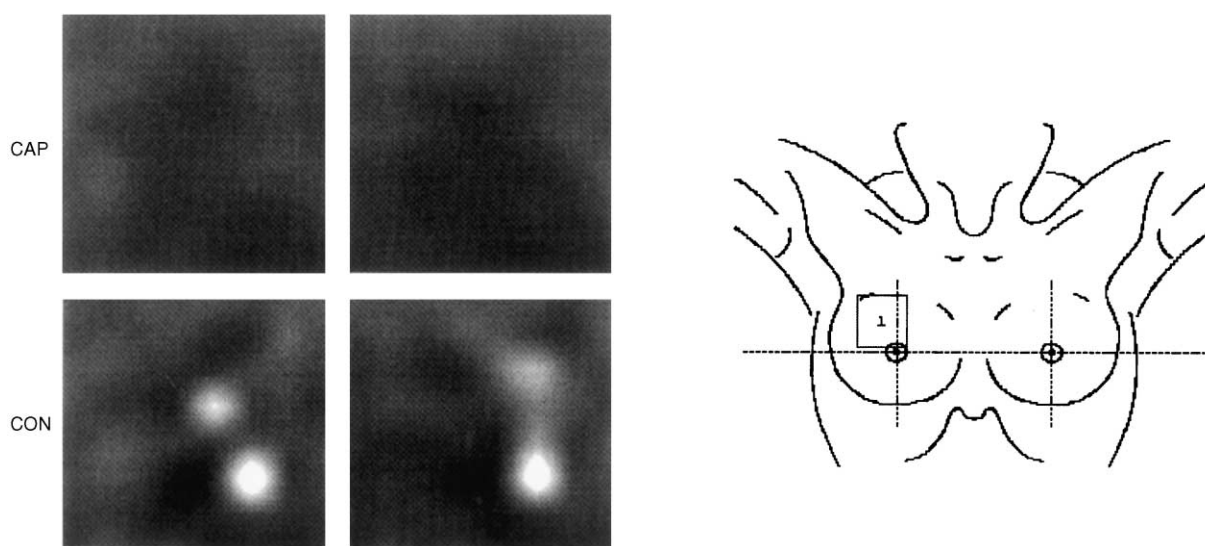


Fig. 1. A typical two-sector positive electric impedance scanning (EIS) result: focal brightness of conductance (CON) at the location marked on the sketch; surrounding area displayed is relatively homogeneously gray. As in ultrasound, EIS is an interactive imaging, consequently spots induced by artifacts are best detectable and interpretable during examination. A retrospective differentiation of an artifact- or cancer-induced focal increase in conductance values is, consequently, difficult to perform. CAP, capacitance.

Table 1  
LOS categorisation after mammographical and sonographical examination

	Cat. 1	Cat. 2	Cat. 3	Cat. 4	Cat. 5	Total
Number of lesions	0	37	79	66	58	240
%	0	15.4	32.9	27.5	24.2	100

LOS, level of suspicion; Cat, category. % = percent of lesions, each category

local surgical excision of the lesion, quadrant resection, or mastectomy, followed by other appropriate therapeutic measures.

In Table 1, the lesions visualised by mammography and ultrasound are listed. Scoring that was analogous to the LOS categorisation was used with knowledge of ultrasound and mammography as well as clinical examination.

In order to determine the additional benefit of EIS as an adjunct to the other modalities, it was necessary to define which cases were scored as malignant or benign using imaging as well as clinical examination. If clinical examination, mammographical and ultrasound revealed a level of suspicion 4 or 5, this was scored as suggesting malignancy (as mentioned above). In contrast to that, lesions scored as LOS 2 and 3 were considered likely to be benign based upon clinical, mammographical and ultrasound examinations. A focal spot finding in EIS was scored as positive and consequently suggestive of malignancy (after exclusion of artifacts), the absence of

Table 2  
Histopathological findings

Histopathological finding	Number of lesions	Percentage
Invasive ductal carcinoma	57	55.3
Invasive lobular carcinoma	21	20.4
Invasive tubular carcinoma	5	4.9
Squamous cell carcinoma	1	1.0
Mucinoid adenocarcinoma	1	1.0
DCIS	14	13.6
Medullary carcinoma	1	1.0
Lymphoma	1	1.0
Neuroendocrine carcinoma	1	1.0
Metastasis of an ovarian carcinoma	1	1.0
Total of malignancies	103	100
Hyperplasia/metaplasia	32	23.4
Fibroadenoma	29	21.2
Cystic tissue	16	11.7
Fibrotic tissue	23	16.8
Adenosis/adenoma	19	13.9
Papilloma	8	5.8
Other histologies (necrosis, lipoma, etc.)	10	7.3
Total of benign lesions	137	100
Total of all lesions	240	–

DCIS, ductal carcinoma *in situ*.

Table 3  
EIS results for DCIS and invasive cancers

	DCIS	Invasive malignancies
Total no. of cases	14	89
TP	8	78
FN	6	11
Detection rate	57.1	87.6

EIS, electrical impedance scanning; CIS, carcinoma *in situ*; TP, true positive; FN, false-negative.

a focal spot, as negative (suggesting the lesion was benign). The results of the examinations were compared with the histological findings in order to determine the sensitivity, specificity and accuracy.

### 3. Results

The following suspicious findings by histopathology were observed (Table 2).

As depicted in Table 2, 14 of the examined lesions were proven by histopathology to be ductal carcinoma *in situ* (DCIS). With respect to this histopathological finding, 8/14 DCIS cases were correctly detected by EIS, whereas 6/14 were false-negatives. Consequently, the system reached a sensitivity of 57.1% in the detection of DCIS.

Taking into account only the invasive malignancies, EIS detected 78/89 lesions correctly as positive, yielding a sensitivity of 87.6% in the detection of invasive cancers. These data are presented in Table 3.

#### 3.1. Performance parameters, EIS

86 of the 103 histologically-proven malignant lesions were correctly detected using EIS (sensitivity 83.5%). 91 of the 137 benign lesions correctly showed no spot using EIS (specificity 66.4%), leading to a NPV and PPV of 84.3 and 65.2%, respectively. Accuracy was observed as 75%.

The histology of the false-negative lesions are depicted in Table 4, and false-positive lesions in Table 5.

Table 4  
Histology of false-negative cases

Histology	FN/total number	Percentage distribution
DCIS	6/14	42.9%
ILC	4/21	19.0% (two retroareolar, one > 35 mm)
IDC	6/57	10.5% (one retroareolar)
Metastasis of ovarian cancer	1/1	100% (retroareolar)

FN, false-negative; DCIS, ductal carcinoma *in situ*; ILC, invasive lobular carcinoma; IDC, invasive ductal carcinoma.

Table 5  
Histology of false-positive lesions

Histology	FP/total number	Percentage distribution
Papilloma	4/8	50.0
Metaplasia/hyperplasia	15/32	46.9
Adenosis	7/19	36.8
Fibrotic findings	7/23	30.4
Fibroadenoma	7/29	24.1
Cystic tissues	3/16	18.8
Other tissue types	3/10	30.0

FP, false-positive.

### 3.2. Performance parameters, mammography and ultrasound

89 of the 103 histologically-proven lesions (sensitivity 86.4%) were correctly categorised as LOS 4 or 5 by mammography and ultrasound. 107 of 137 cases revealed correctly assessed benign findings (specificity 78.1%).

With the additional use of EIS, 98 of the 103 histologically-proven malignant lesions were identified as suspicious by at least one of the three modalities (sensitivity 95.1%), whereas for 77 of the 137 benign lesions all three modalities showed a concordance of not suspicious findings (specificity 56.2%). Accuracy of mammography and ultrasound alone were observed to be 82.3%, whereas this value decreased to 75.7% with the addition of EIS. However, using EIS as an adjunct to these two technologies, 9 additional cancer cases could be identified, whereas five cancer lesions remained not suspicious in all techniques (LOS 3 after clinical examination, mammography and ultrasound and negative in EIS). EIS introduced 30 false-positive findings in cases regarded by mammography and ultrasound to be probably benign.

A summary of these values is given in Table 6.

### 3.3. Consideration of *a priori* criteria

An 'optimal sensitivity' was calculated, excluding from the data-set those cases meeting the well-defined *a priori* criteria, i.e. lesions where the technology experiences limitations [18,19]:

Table 6  
Effects of EIS as an additional examination

	Mammography/ ultrasound (%)	Adjunctive EIS (%)	All methods (%)
Sensitivity	86.4	83.5	95.1
Specificity	78.1	66.4	56.2
Accuracy	82.3	75.0	75.7

EIS, electrical impedance scanning.

- retroareolar location, not larger than the nipple itself and at depth <2 cm ( $n=8$ , 6 malignant)
- >35 mm size ( $n=13$ , 11 malignant)
- depth from the surface >35 mm ( $n=9$ , 6 malignant) one lesion retroareolar and too large, one lesion too large and too deep.

Consequently, this modified data set included 212 of the 240 lesions. In this 'optimized' patient-group, EIS-examination revealed a true-positive finding in 72/82/83 cases (sensitivity 87.8%). 86/130 lesions were correctly detected as negative (specificity 66.2%). These exclusion criteria can be determined *a priori*, and may prospectively serve as exclusion criteria for the EIS examination, although the resulting 'optimized' values are not significantly different from those reported for the entire data-set. However, respecting the *a priori* limitations, an analysis of only the invasive cancers shows a sensitivity of 91.7% (66/73 invasive cancers).

## 4. Discussion

The classification of nine additional malignant lesions using EIS, leading to an overall sensitivity of 95.1% when implementing mammography, ultrasound and EIS (versus 86.4% with mammography and ultrasound alone) is promising. A reasonable tumour detection rate of EIS used as an additional technology to mammography and ultrasound can be reached, such that the technology is worth consideration. The sensitivity could be increased only slightly when *a priori* criteria were applied, i.e. retrospective exclusion of cases where EIS technology is unlikely to be effective. The highest sensitivity was among the invasive cancers.

Fields and colleagues found slightly higher values of sensitivity than this study: 86% sensitivity, 51% specificity, 87% negative predictive value [20]. Nissan and coworkers described also a sensitivity of 86% for EIS, but slightly different study protocol conditions were used (EIS findings scored in a range of 1–5, rather than positive/negative) [21].

The false-negative rate may be due to physical limitations as discussed by Scholz and Anderson using mathematical models, to demonstrate the theoretical limitations of the technique which are mainly due to interference of the current flow in cases of deep lesions [18]. Due to the limited discrimination of the conductance values between lesions and normal tissue for lesions 3 cm or deeper, the interfering non-malignant tissue between the lesion and surface acts as a buffer in assimilating the electrical parameters of both tissues. This can explain the failure to register conductance values that were high enough to induce a focal spot.

In cases of large tumours, conductance of the measuring field is increased and, consequently, the relative

changes are smaller. Thus, it is hypothesised that larger, homogeneously-structured lesions would not induce a visible focal increase that is clearly brighter than its surroundings, and therefore in the electrical parameter maps this may lead to negative EIS results.

Cancer-induced lesions located directly behind the nipple may also be impossible to discern, or at least difficult to interpret, as the nipple-induced bright spot when it is superimposed onto another signal often does not result in a visibly increased (superimposed, cumulative) brightness. Consequently, it is likely that malignant lesions in this location, especially minor ones, would not be detected by EIS.

Cysts usually do not cause a focal increase of conductance, perhaps because the cystic membrane isolates the liquid from the surroundings (but they are sometimes visible as a slightly darker area in EIS). However, some cancer-induced tissues are also surrounded by membranes or capsules (e.g. the ovarian metastasis in this study), which may be the source of false-negative cases.

The reasons for changes in the conductance of malignant tissue are still under investigation. This property of the tissues seems to be associated mostly with changes that are typical for invasive cancers such as destroyed tight junctions and cell membranes, increased pathological perfusion, the amount of extracellular fluid, etc. [12]. This might explain why the detection rate of carcinoma *in situ* was significantly lower than that of invasive cancers, as suggested by Rigaud and coworkers [12]. However, to the best of our knowledge, there are no investigations to date specifically focusing on EIS detectability of non-invasive cancers.

However, fast-growing tumours, are in part characterised by a larger necrotic component. In these necrotic structures, the current flow should be better than in the surrounding tissue. This might explain the differences in the detectability of the cancer-induced lesions. Both phenomena are topics for future investigation.

It is documented in several studies that because of the currently high false-positive rate of the available EIS system, its usage should be limited to adjunctive examinations of lesions with known locations [17,20,21]. In addition, there is currently no minimally invasive biopsy capability available based on electrical impedance measurement. Due to these limitations, it is currently, unfortunately, neither possible nor useful to investigate whether EIS is able to identify cancers which remain completely obscure after clinical and imaging modalities. In addition, it is known that while scanning special care must be taken since air bubbles, interfering bones (rib), muscles, superficial skin lesions (moles, scars, hairs, naevi and insect bites), subcutaneous changes and poor contact of the scanner can result in bright spots mimicking the increased conductance of malignant tissue. Additionally, the rate of false-positive spots

has been shown to be directly related to the hormonal state and phase of the cycle [22]. It remains unclear why the false-positive value differed in our study between the various histological findings (between 18.8% and 50.0%). Further studies should address whether there are histopathological changes associated with papilloma and hyper/metaplasia (e.g. proliferation ratio), in contrast to cysts and fibroadenomas, that induce an increased conductance by themselves. Moreover, when used in addition to clinical examination, mammography and ultrasound, the high false-positive-rate of EIS decreases the overall accuracy from 82.3 to 75.7%.

Consequently, to summarise:

1. the EIS technique is promising because it adds to the sensitivity in detecting cancer by indicating cases for histological clarification which would not have been indicated following the clinical examination, mammographical and ultrasound imaging findings.
2. the practical value of EIS depends critically on a further reduction of false-positive results and is limited to known lesions of known location.

Our institution continues to actively pursue this new technology. Further developments in software, as well as scientific studies, should focus on reducing the false-positive findings of EIS, in general, in order to achieve a higher accuracy value.

## Acknowledgements

Special thanks are given to R. Kühne-Heid, M.D., Institute of Pathology of Friedrich-Schiller-University Jena, Germany and to A. Schneider, M.D., MPH, Clinic for Gynaecology, Friedrich-Schiller-University Jena, Germany, who both contributed to the work reported in this manuscript.

## References

1. Von Fournier D, Anton HW, Junkermann H, et al. Brustkrebs-screening. *Radiologie* 1993, **33**, 227–235.
2. Kopans B. *Breast Imaging*, 2nd edn. Lippincott-Raven, 1998, 29–54.
3. Elmore JG, Barton MB, Moceri VM, Polk S, Arena PJ, Fletcher SW. Ten-year risk of false positive screening mammograms and clinical breast examinations. *New England J Med* 1998, **338**, 1089–1096.
4. Schaumlöffel-Schulze U, Heywang-Köbrunner SH, Alter C, Lampe D, Buchmann J. Diagnostische Vakuumbiopsie der Brust — Ergebnisse von 600 Patienten. *Fortschr Röntgenstr* 1999, **S1-170**, 72.
5. Morrow M, Schmidt R, Cregger B, Hasset C. Preoperative evaluation of abnormal mammographic findings to avoid unnecessary breast biopsies. *Arch Surg* 1994, **129**, 1091–1096.
6. Rosenberg RD, Hunt WC, Williamson MR, et al. Effects of age, breast density, ethnicity, and estrogen replacement therapy on screening mammographic sensitivity and cancer stage at diag-

- nosis: review of 183,233 screening mammograms in Albuquerque, New Mexico. *Radiology* 1998, **209**, 511–518.
7. Kerlikowske K, Grady D, Barclay J, Sickles EA, Ernster V. Effect of age, breast density, and family history on the sensitivity of first screening mammography. *JAMA* 1996, **276**, 33–38.
  8. Fricke H, Morse S. The electric capacity of tumors in the breast. *J Cancer Res* 1926, **16**, 340–376.
  9. Surowiec A, Stuchly S, Barr R, Swarup A. Dielectric properties of breast carcinoma and the surrounding tissues. *IEEE Trans Biomed Eng* 1988, **35**, 257–263.
  10. Jossinet J. The impedivity of freshly excised human breast tissue. *Physiol Meas* 1998, **19**, 61–75.
  11. Mitsuyama N, Morimoto T, Kinouchi Y, et al. In vivo measurements of electrical bio-impedance of breast tumors. *Nippon Geka Gakkai Zasshi* 1988, **89**, 251–255.
  12. Rigaud B, Morucci JP, Chauveau N. Bioelectrical impedance techniques in medicine part I: bioimpedance measurement. *Clin Rev Biomed Eng* 1996, **24**, 257–351.
  13. Cuzick J, Holland R, Barth V, et al. Electropotential measurements as a new diagnostic modality for breast cancer. *Lancet* 1998, **352**, 359–363.
  14. Jossinet J. Variability of impedivity in normal and pathological breast tissue. *Med Biol Eng Comput* 1996, **34**, 346–350.
  15. Piperno G, Frei EH, Moshitzky M. Breast cancer screening by impedance measurements. *Frontiers Med Biol Eng* 1990, **2**, 111–117.
  16. Malich A, Fritsch T, Freesmeyer MG, Fleck M, Anderson R, Kaiser WA. Electrical impedance scanning (EIS) for classifying suspicious breast lesions: first results. *Eur Radiol* 2000, **10**, 1555–1561.
  17. Malich A, Facius M, Marx C, et al. Electrical impedance scanning—clinical value in the verification of uncertain breast lesions. *2nd Int Congress MR Mammography, Eur Radiol* 2000, **36**, S1–S10.
  18. Scholz B, Anderson R. On electrical impedance scanning—principles and simulations. *Electromedica* 2000, **68**, 35–44.
  19. TransScan. *TS 2000 User Manual*. Israel, TransScan Medical Ltd.
  20. Fields SI, Rossman M, Phillips E, et al. Adjunctive improvement of mammographic accuracy using electrical impedance scanning (EIS). *Radiology* 1998, **S209**, 272–273.
  21. Nissan A, Spira RM, Freund HR, Fields S. Imaging of the breast with electrical impedance scanning as an adjunct of mammography. In Senology Congress, Cancun, Mexico, 5/2000. *Eur J Surg Oncol* 2000, **S1-28**, 282.
  22. 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**, 1550–1554.