

New technologies in |
breast | cancer diagnosis
Information update



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Abbreviations

FDA	Food and Drug Administration (USA)
FDG	[¹⁸ F]2-Deoxy-2-fluoro-D-glucose (fluorine-18 fluorodeoxyglucose)
MGy	milligray. A measure of radiation
USA	United States of America



Glossary

Capacitance	The property of being able to store an electric charge
Conductivity	The capacity for conveying energy, such as electricity
Supine position	Lying with the face upward

Electrical impedance scanning

Description and indications

Electrical impedance scanning is a non-invasive, radiation-free technique that maps the local electrical impedance properties of breast tissue to differentiate between normal and malignant tissue. Impedance is a measure of how a material affects the flow of electricity as a result of its conductivity and capacitance. Malignant lesions have lower impedance values than normal tissue or benign lesions.

A low voltage (between 1 and 2.5 volts) is applied to the patient via an electrode the patient holds in her hand while lying in the supine position. The electrical current is then measured on the surface of the breast via a hand-held transducer. Ultrasound gel is used as the contact medium between the skin and the transducer. The transducer is connected to a computer which displays real-time images of the area under examination. Malignant lesions, which have an increased conductivity only or increased conductivity and capacitance (decreased impedance), appear as bright white spots on a grey background on the monitor. The examination takes between five and 10 minutes.

The indication for electrical impedance scanning is as an adjunct to mammography in patients who have equivocal mammographic findings. However, electrical impedance scanning is not indicated in women with mammographic or non-mammographic indications for biopsy. It has been suggested that the use of electrical impedance scanning in conjunction with mammography for the evaluation of suspicious lesions can reduce the number of unnecessary biopsies.



Electrical impedance scanning is not intended to replace conventional methods of detecting or diagnosing breast cancer, such as mammography, clinical breast examination, ultrasound, or biopsy evaluation, but is intended to be used as an adjunct to them.

Different resolution modes are used for different types of examinations. The standard-resolution mode is used for routine overview examination, while the high-resolution mode is used for the local examination of a suspicious lesion.

Sensitivities of 93.1% and specificities of 65.5% have been reported for targeted high-resolution examinations. For standard resolution examinations sensitivities of 75.9% and specificities of 72.4% have been reported.¹

The manufacturers of the device claim that small lesions, as small as 1mm in diameter, are more readily visualised by electrical impedance scanning than large palpable lesions. The manufacturers also claim that breast density does not appear to affect electrical impedance scanning. Furthermore, the manufacturers indicate that despite an estimated recording depth of 30mm, all lesions can be scanned as flexible patient positioning allows the transducer to be placed in close proximity to all lesions.

Use of the technique in breast cancer diagnosis

In Australia

- There are no tissue electrical impedance imaging systems in Australia.

Internationally

- Tissue electrical impedance imaging systems are available in a limited number of hospitals in the US, Israel, France and Italy.

Evaluation and future research

- An electrical impedance scanning system known as TS2000 received FDA approval in the USA in 1999 for use as a follow-up step to mammography for patients whose mammograms are ambiguous.
- As a condition of TS2000 FDA approval the manufacturers were required to conduct a post-market study on the effects of hormonal changes during the menstrual cycle on the device's ability to detect and distinguish among breast abnormalities. Findings of these studies are yet to be published.



References

1. Malich A, Fritsch T, Anderson R, Boehm T *et al.* Electrical impedance scanning for classifying suspicious breast lesions: first results. *Eur Radiol* 2000;10:1555-61.

Further reading

Assenheimer M, Laver-Moskovitz O, Malonek D, Manor D *et al.* The T-SCAN technology: electrical impedance as a diagnostic tool for breast cancer detection. *Physiol Meas* 2001;22:1-8.

Cherepenin V, Karpov A, Korjenevsky A, Kornienko V *et al.* A 3D electrical impedance tomography (EIT) system for breast cancer detection. *Physiol Meas* 2001;22:9-18.

Cuzick J, Holland R, Barth V, Davies R *et al.* Electropotential measurements as a new diagnostic modality for breast cancer. *Lancet* 1998;352:359-63.

Malich A, Fritsch T, Mauch C, Boehm T *et al.* Electrical impedance scanning: a new technique in the diagnosis of lymph nodes in which malignancy is suspected on ultrasound. *Br J Radiol* 2001;74:42-7.

Melloul M, Paz A, Ohana G, Laver O *et al.* Double-phase ^{99m}Tc-sestamibi scintimammography and trans-scan in diagnosing breast cancer. *J Nucl Med* 1999;40:376-80.

Morucci JP, Rigaud B. Bioelectrical impedance techniques in medicine. Part III: Impedance imaging. Third section: medical applications. *Crit Rev Biomed Eng* 1996;24:655-77.



Useful website links

Information about TransScan's TS2000 Impedance Imaging System is available at <http://www.transscan.co.il>

Information about the FDA approval of TS2000 is available at <http://www.fda.gov/bbs/topics/ANSWERS/ANS00950.html>



Breast thermography

Description and indications

Breast thermography, also known as thermal breast imaging, is a technique that produces 'heat pictures' of the breast. Thermography is described as a test of physiology, which detects differences in the temperature of the skin of the breast. The rationale behind thermography is that the skin overlying a malignant lesion may be warmer than the skin over other areas of the breast, perhaps because of higher metabolic activity or increased vascularity of the malignant lesion compared to normal breast tissue.

There are two types of thermographic equipment available for use in clinical practice: liquid crystal (contact) thermography and telethermography.

- Liquid crystal (contact) thermography involves placing a heat-sensitive plastic film on the skin of the breast. The mix of crystals used in the film determines the film's ability to distinguish between different temperatures
- Telethermography, also known as digital infrared thermal imaging (DITI), uses an infrared camera as a detector. The image obtained by the detector is displayed digitally on a computer screen. This type of thermography offers images in real time and does not involve contact between the camera and the skin.



Over the last 35 years thermography has been proposed as a breast screening tool and also as a risk indicator of breast cancer. In the 1970's there was great interest in thermography as it offered a radiation-free alternative to mammography, which at that time involved significantly higher exposure to ionising radiation than present day techniques (40-90mGy compared to 2mGy today). Early evaluation of thermography produced promising results with true positive rates between 75% and 85%.¹ The false positive rate, however, was high and ranged from 15% to 40% depending on the population examined and the criteria of the interpreter.¹ In addition, the promising findings of some early studies could not be replicated in studies that included smaller cancers.

In support of the use of thermography as a risk indicator of breast cancer, Guthrie and Gros reported in 1980 that of the 740 patients who met their criteria for isolated suspicious thermograms, 40% had developed breast cancer within 10 years.² However, their findings have not been corroborated by other studies. For example, findings from the Breast Cancer Detection Demonstration Project, which was conducted in Cincinnati, USA between 1973 and 1979, indicated that of the 1,260 patients with more than one positive thermogram from 1973 to 1976, 1.9% subsequently developed breast cancer from 1977 to 1983.³ Moskowitz indicated that this finding was not significantly different from the 1.3% of patients who developed breast cancer and never had a positive thermogram.³

It has been reported that thermography has made significant progress in recent years as a result of military research in night vision.⁴ However, this "new thermography" is yet to be evaluated.

Use of the technique in breast cancer diagnosis

In Australia

- There has been renewed interest in breast thermography in recent years. The potential role of thermography in the early detection of breast cancer has been promoted in the advertising material of some breast clinics and some reports have appeared in the State/Territory media. However, BreastScreen Australia released a statement in 1999 indicating that the use of thermography is not recommended for the early detection of breast cancer.⁵ The Breast Imaging Reference Group of the Royal Australian and New Zealand College of Radiologists also adopted a policy position in 2000 that thermography was not a suitable imaging modality for symptomatic women or breast cancer screening because of the technique's poor accuracy in cancer detection.⁶

Medicare Benefits Schedule (MBS) rebate: MBS funding for breast thermography is not available.

Internationally

- Breast thermography is used at a small number of medical centres in the USA, Canada and Europe.
- Thermography does not have FDA approval for breast examination in the USA. However, in the USA, clinicians who advocate the use of the technique for breast examination are able to offer breast thermograms to their clients.



Future research

Further research in the development of more sensitive sensors and clinical studies are required to determine whether thermography has a role in breast cancer diagnosis.

References

1. Dodd GD. Present status of thermography, ultrasound and mammography in breast cancer detection . *Cancer* 1977;39:2796-805.
2. Gautherie M, Gros CM. Breast thermography and cancer risk prediction. *Cancer* 1980;45:51-6.
3. Moskowitz M. Thermography as a risk indicator of breast cancer. Results of a study and a review of the recent literature. *J Reprod Med* 1985;30:451-9.
4. Foster KR. Thermographic detection of breast cancer. *IEEE Eng Med Biol Mag* 1998;17:10-4.
5. BreastScreen Australia. *Statement on the use of thermography to detect breast cancer*. (Developed in Consultation with the National Advisory Committee to BreastScreen Australia). November 1999.
6. The Royal Australian and New Zealand College of Radiologists. *Breast Imaging Reference Group News March 2000*.
<http://www.medeserv.com.au/racr/open/breastimagingref.htm>
The Royal Australian and New Zealand College of Radiologists, (last updated 2000).

Further reading

Head JF, Wang F, Elliott RL. Breast thermography is a noninvasive prognostic procedure that predicts tumor growth rate in breast cancer patients. *Ann N Y Acad Sci* 1993;698:153-8.

Jones BF. A reappraisal of the use of infrared thermal image analysis in medicine. *IEEE Trans Med Imaging* 1998;17:1019-27.

Sterns EE, Zee B, SenGupta S, Saunders FW. Thermography. Its relation to pathologic characteristics, vascularity, proliferation rate, and survival of patients with invasive ductal carcinoma of the breast. *Cancer* 1996;77:1324-8.

Useful website links

Information about DITI is available at
<http://www.meditherm.com/default.htm>



Positron emission tomography (PET)

Description and indications

Positron emission tomography (PET) is a nuclear medicine imaging procedure. PET uses functional and metabolic properties of tumours, such as their increased metabolic rate and vascularity, to determine a diagnosis. The tracer most commonly used in PET is [¹⁸F]2-Deoxy-2-fluoro-D-glucose (FDG). This tracer assesses the metabolism of glucose, that is how much and how fast glucose is used by tissues, the tracer is injected intravenously into the patient one hour before the procedure. Patients lie supine for the procedure.

PET has been in use internationally for approximately 20 years, mainly as a research tool. PET scanners were first developed to study the brain and were found to be useful. The major clinical applications of PET are in the areas of cardiology, neurology and oncology. In oncology, which accounts for over 80% of clinical PET examinations, PET is used for the staging of malignant tumours, detection of tumour recurrences and monitoring response to treatment. Lung and brain tumours are the tumours most commonly studied using PET. In recent years, interest has developed in using PET in breast cancer. Dedicated positron emission mammography systems are currently being developed and evaluated. The positron emission mammographic detectors are attached to X-ray mammographic systems and the breast is compressed for the procedure.



Several uses of PET in breast have been proposed including its use as a screening tool in particular for high risk women, for the detection of primary breast tumours, for the preoperative staging of breast cancer, for the detection of regional and distant metastasis, and for axillary node staging. PET has the ability to reveal increased glucose metabolism in malignant tumours, affected lymph nodes and in distant metastasis in a single examination.¹

Regarding the use of PET as a screening tool, it has been reported that the technique is not yet mature enough and that even after further development it is unlikely that PET will replace mammography due to its use of radioactive tracers, its cost, and the fact that it is time-consuming and requires an injection.²

Reports of the sensitivity of PET to detect a primary breast cancer range between 64% and 100%^{1,3,4} with specificity between 33% and 100%.^{1,3,4} The diagnostic accuracy of PET appears to be dependent on tumour size, with the test having poorer detection rates for small breast cancers³ and better detection rates for multifocal lesions.¹ PET has been shown to have a high positive predictive value.³

Several authors advocate that the main use of PET in breast may be for the determination of lymph node status and the staging of tumours. PET appears to accurately predict axillary status in patients with breast cancer⁵ and to detect disease in the mediastinum and internal mammary node chains⁶ and distant metastases.¹ However, these findings should be confirmed in larger studies before changes to clinical practice are recommended.

Use of the technique in breast cancer diagnosis

In Australia

- There are less than 10 PET systems in use in Australia. Breast PET examinations are conducted at some of the centres with a PET system.

No MBS funding is available for breast PET examinations.

Internationally

- There are over 200 PET systems in use internationally. The majority of these are in the USA and Europe.

Evaluation and current research

- A national review of PET conducted by the Department of Health and Aged Care (Diagnostics and Technology Branch) in 2000, which included an assessment of PET by a supporting committee of the Medicare Services Advisory Committee (MSAC), did not include the use of PET in breast. Further to the indications included in the review, the report recommended that MSAC have an ongoing involvement in evaluating the role of PET in six additional indications. Breast cancer is not included in this list of additional indications.⁷
- Most PET research aims to identify new clinical applications for PET and to develop new tracers. In regards to PET in breast, several research projects are being funded by the National Cancer Institute (NCI) in the USA. For example, a project at the University of California and another being conducted by a commercial firm in Massachusetts aim to develop PET systems for specific use in breast and the axilla. A project being conducted at



the University of West Virginia aims to develop and evaluate a positron emission mammography-guided breast biopsy system.

References

1. Schirrmeister H, Kuhn T, Guhlmann A, Santjohanser C *et al.* Fluorine-18 2-deoxy-2-fluoro-D-glucose PET in the preoperative staging of breast cancer: comparison with the standard staging procedures. *Eur J Nucl Med* 2001;28:351-8.
2. Warren R. Screening women at high risk of breast cancer on the basis of evidence. *Eur J Radiol* 2001;39:50-9.
3. Avril N, Rose CA, Schelling M, Dose J *et al.* Breast imaging with positron emission tomography and fluorine-18 fluorodeoxyglucose: use and limitations. *J Clin Oncol* 2000;18:3495-502.
4. Smith IC, Gilbert FJ. Role of positron emission tomography in the management of breast cancer. *The Breast* 1999;8:303-10.
5. Greco M, Crippa F, Agresti R, Seregini E *et al.* Axillary lymph node staging in breast cancer by 2-fluoro-2-deoxy-D- glucose-positron emission tomography: clinical evaluation and alternative management. *J Natl Cancer Inst* 2001;93:630-5.
6. Eubank WB, Mankoff DA, Takasugi J, Vesselle H *et al.* 18fluorodeoxyglucose positron emission tomography to detect mediastinal or internal mammary metastases in breast cancer. *J Clin Oncol* 2001;19:3516-23.
7. Department of Health and Aged Care. *PET Report of the review of positron emission tomography*. Canberra: Commonwealth of Australia, 2001.

Further reading

DeGrado TR, Baldwin SW, Wang S, Orr MD *et al.* Synthesis and evaluation of ¹⁸F-labeled choline analogs as oncologic PET tracers. *Journal of Nuclear Medicine* 2001;42:1805-14.

Kamm BL. Breast procedures and imaging techniques. *Radiol Technol* 1999;71:58-72.

Miles KA. An approach to demonstrating cost-effectiveness of diagnostic imaging modalities in Australia illustrated by positron emission tomography. *Australas Radiol* 2001;45:9-18.

Murthy K, Aznar M, Bergman AM, Thompson CJ *et al.* Positron emission mammographic instrument: initial results. *Radiology* 2000;215:280-5.

Orel SG, Troupin RH. Nonmammographic imaging of the breast: current issues and future prospects. *Semin Roentgenol* 1993;28:231-41.

Pisano ED, Parham CA. Digital mammography, sestamibi breast scintigraphy, and positron emission tomography breast imaging. *Radiol Clin North Am* 2000;38:861-9, x.

Raylman RR, Majewski S, Weisenberger AG, Popov V *et al.* Positron emission mammography-guided breast biopsy. *J Nucl Med* 2001;42:960-6.

Raylman RR, Majewski S, Wojcik R, Weisenberger AG *et al.* The potential role of positron emission mammography for detection of breast cancer. A phantom study. *Med Phys* 2000;27:1943-54.

Schuhmacher J, Kaul S, Klivenyi G, Junkermann H *et al.* Immunoscintigraphy with positron emission tomography: gallium-68 chelate imaging of breast cancer pretargeted with bispecific anti-MUC1/anti-Ga chelate antibodies. *Cancer Res* 2001;61:3712-7



Warren R. Screening women at high risk of breast cancer on the basis of evidence. *Eur J Radiol* 2001;39:50-9.

Yutani K, Shiba E, Kusuoka H, Tatsumi M *et al.* Comparison of FDG-PET with MIBI-SPECT in the detection of breast cancer and axillary lymph node metastasis. *J Comput Assist Tomogr* 2000;24:274-80.

Useful website links

The Department of Health and Aged Care report of the review of PET and the MSAC assessment report of PET are available on <http://www.health.gov.au/haf/pet/petfinal.htm>

The Journal of Nuclear Medicine often includes articles about PET. Abstracts are available on <http://jnm.snmjournals.org/>

