E15. Mammographic screening in Europe – Where are we with mammography?

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Introduction

Breast cancer incidence is still rising and we have not seen the end of it. Early detection as a result of opportunistic and/or service screening programmes became, internationally, one of the back bones in the fight against breast cancer. The combination of increasing incidence and ongoing improvement of mortality rates will show, within 10 years from now, almost a doubling of the prevalent cases. ¹ This will have a significant impact on healthcare in general and especially on diagnostic imaging. In the Netherlands, breast cancer screening is, compared to other screening programmes, the most cost effective programme organised by the Government. So if significant diagnostic improvements could be made, there is theoretically financial space.

At this point in diagnostic imaging, we are in a state of transition. Multiple screening modalities are being introduced like MRI and ultrasound and even the old 'work horse' mammography is being digitised. This might be a reason to have a critical look at this specific screening test and its competitors in the context of mass screening programmes.

Breast imaging

Breast imaging is no longer a single modality specialty. Still, mammography continues to lead as the most accurate, accessible and cost-effective screening modality (MRI and ultrasound are quickly becoming elevated to the same standard of care) for women at high risk. Breast MR imaging does not replace conventional imaging. So, in general, one can say that mammography in every thinkable protocol or diagnostic work-up will keep its position.

The recent quest for additional imaging tools in breast imaging has been driven mainly because of:

- 1. The poor performance of mammography in dense breasts within the target population (in the Netherlands the age cohort is 50–74, in a number of other countries screening starts at 40 or 45, without a sharp end point). ³
- 2. The need for a screening tool in the younger population because of the rising incidence and the recognition of high to very high risk subpopulations.

Ad 1: The basic limitation of mammography is the low contrast of roentgen between cancer and water containing tissue like glandular and fibrotic tissue. This also accounts for roentgen based techniques like tomosynthesis and breast CT. ^{4,5}

In the Dutch target population an overall sensitivity of mammographic screening between 60 and 70% is observed. At the extremes, in the young high risk group the sensitivity is below 50%, and in the elder women with complete fatty involution, the sensitivity approaches 98%. ^{6,7}

A significant problem is also the higher risk in denser breasts. Women in the highest quartile of mammographic density have a risk of breast cancer that is approximately four to six times as high as that among women of similar age who are in the lowest quartile. ^{8,9} Only two other factors increase the risk of breast cancer more than mammographic density: age and mutations in the breast cancer-susceptibility genes BRCA1 and BRCA2.

Ad 2: Breast cancer in the younger age groups tends to be more aggressive then in the older age groups. Therefore, a screening interval of 2 years might be insufficient. On the other side, the radiation burden should, when screening starts at younger age, not be underestimated. ^{10,11} So here the knife cuts in both negative ways for mammography. Younger women in general have more dense breasts and are more vulnerable to radiation. This is the reason why MRI attracted so much attention in this field despite a relative large number of false positives. ⁶

Ad 3: Digital mammography. The main concern about digital mammography since it was introduced in 2000 was not if it proved to be of more value than analogue mammography, but if it was good enough to replace it. This because of the obvious advantages of digital radiology in general, and the expected end of the life cycle of film technology. Complete digital and paperless screening systems are feasible, like in the Netherlands where it will be implemented in 2008. Better contrast resolution seems to result in a better cancer detection in dense breasts. ¹² This is relevant to the younger cohorts and might influence, in a number of countries, the policy towards younger age groups.

Recently, the predicted coming of high resolution digital detectors combined with a higher refresh rate pushed mammography vendors to grab back at the old tomo-technique described by Ziedses des Plantes in 1932. It has theoretically the obvious advantage of eliminating overlying structures. The impact on screening is at this moment uncertain.

MRI. MRI of the breast will mainly find invasive tumours larger than 0.5 cm. It has proven potential to be useful in screening of the high risk group, ^{6,13} and in estimating the size of specific tumours like invasive lobular carcinoma. ⁵ Until now there have only been a few communications showing that MRI is also capable of detecting with a high sensitivity Ductal Carcinoma in Situ (DCIS). ¹⁴

Ultrasound. Hand held ultrasound never proved to be a useful screening tool. The reason for this is a relatively low sensitivity and specificity. This has repeatedly been proven and even in selected cases like in the ACRIN 6666 trial, the preliminary results show that breast ultrasound significantly increases detection of cancers in high-risk women but takes a big toll on the rate of benign biopsies. ¹⁵ Ultrasound has a strong negative predictive value (up to 99%) for a number of 'lesions' resulting in false positive referrals. ¹⁶ The most recent figures of the national screening monitor in the Netherlands (NETB annual report 2006) show that 60% of the women do not undergo biopsy. These women are released after further work up with extra exposures and ultrasound.

Conclusion

The search for alternative imaging and screening modalities is because of the poor performance of mammography in dense breasts and not because the technique is at the end of its life cycle. Digital mammography will keep its place in mass screening programmes.

All the existing and upcoming alternative breast imaging techniques suffer from severe practical shortcomings for mass screening programmes.

Ultrasound is, with mammography, the most valuable tool in the work up of symptomatic patients. One of the biggest challenges of the coming years is to combine the strong points of ultrasound and mammography in a workable screening logistic. This in such a way that ultrasound reduces the false positives of mammography and repairs its weak performance in the dense breast, without causing too many false positive recalls.

Conflict of interest statement

None declared.

References

- [1] Louwman WJ, Voogd AC, van Dijck JA, et al. On the rising trends of incidence and prognosis for breast cancer patients diagnosed 1975–2004: a long-term population-based study in southeastern Netherlands. Cancer Causes Control 2007, Nov 24 [Epub ahead of print].
- [2] Rausch DR, Hendrick RE. How to optimize clinical breast MR imaging practices and techniques on your 1.5-T system. *Radiographics* 2006;26(5):1469–84.
- [3] International Cancer Screening Network. http://appliedresearch.cancer.gov/icsn/breast/policies1.html. [Last accessed 5 January 2008].
- [4] Yang WT, Carkaci S, Chen L, et al. Dedicated cone-beam breast CT: feasibility study with surgical mastectomy specimens. AJR Am J Roentgenol 2007;189(6):1312–5.
- [5] Rafferty EA. Digital mammography: novel applications. *Radiol Clin North Am* 2007;45(5):831–43, vii.
- [6] Kriege M, Brekelmans CTM, Boetes C, et al. Efficacy of MRI and mammography for breast-cancer screening in women with a familial or genetic predisposition. N Engl J Med 2004;351:427–37.
- [7] Kolb TM, Lichy J, Newhouse JH. Comparison of the performance of screening mammography, physical examination, and breast US and evaluation of factors that influence them: an analysis of 27,825 patient evaluations. *Radiology* 2002;225(1):165–75.
- [8] Kerlikowske K. The mammogram that cried Wolfe. N Engl J Med 2007;356(3):297–300.
- [9] Boyd NF, Guo H, Martin LJ, et al. Mammographic density and the risk and detection of breast cancer. N Engl J Med 2007;356:227–36.
- [10] Preston DL, Mattsson A, Holmberg E, Shore R, Hildreth NG, Boice JD Jr. Radiation effects on breast cancer risk: a pooled analysis of eight cohorts. *Radiat Res* 2002;158:220–35. Erratum in: *Radiat Res* 2002;158:666.
- [11] Berrington de Gonzalez A, Reeves G. Mammographic screening before age 50 years in the UK: comparison of the radiation risks with the mortality benefits. Br J Cancer 2005;93:590-6.
- [12] Pisano ED, Gatsonis C, Hendrick E, et al. Digital Mammographic Imaging Screening Trial (DMIST) Investigators Group. Diagnostic performance of digital versus film mammography for breastcancerscreening. N Engl J Med 2005;353:1773–83.
- [13] Liberman L. Breast cancer screening with MRI-What are the data for patients at high risk? N Engl J Med 2004;351(5): 497–500.
- [14] Kuhl CK, Schrading S, Bieling HB, et al. MRI for diagnosis of pure ductal carcinoma in situ: a prospective observational study. *Lancet* 2007;370(9586):485–92.
- [15] http://www.acrin.org/6666_protocol.html [last accessed 6 January 2008].
- [16] Zonderland HM, Coerkamp EG, Hermans J, van de Vijver MJ, van Voorthuisen AE. Diagnosis of breast cancer: contribution of US as an adjunct to mammography. *Radiology* 1999;213(2):413–22.