

Book report

Mammography and beyond: developing technologies for the early detection of breast cancer

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Introduction

Publication of this report from the Committee on Technologies for the Early Detection of Breast Cancer, chaired by JC Lashof and I Craig Henderson (vice chair), is timely and important. The Institute of Medicine Committee assembled a 16-member interdisciplinary group, and the contributions included in the book reflect this wide-angle approach to the problem. Each specialist may find less than he or she would like, but I found many interesting details that are useful for gaining a general understanding of the technological future of breast cancer screening. Imaging technology is examined within the context of the complex natural history of breast cancer; advances in current understanding of genetic and biological issues, and in therapeutic approaches are less briefly, but exhaustively, presented.

Emerging technologies

Following a short presentation of the history of mammography, the theory of efficacy evaluation through randomized clinical trials (all referenced) and the more recent evaluations of screening programmes that are ongoing in several countries are critically re-examined. The second chapter discusses new developments in breast imaging and in related technologies; a table presents the current status of imaging technologies for a large number of devices, few of which are currently of interest with regard to early detection. Most of the technologies discussed pertain to clinical diagnosis, and are unlikely to surpass mammography in the field of early detection in the near future.

A chapter entitled *Technologies in development: genetic and tumor markers* reports on the progress that has been made in this important field, but it states that "... the ability to predict who will develop breast cancer is modest at best." We are still in the realm of basic research, and application of these technologies in screening is far from reaching routine daily practice. However, the authors emphasize the opportunity to improve predictive oncology in the early stages of breast cancer. Furthermore, with private companies developing genetic tests, and the fact that "The tests are not subject to FDA [Food and Drug Administration] regulation and thus clinical validity and utility did not have to be documented before entry into the market", there is a need for a new policy and for genetic counselling for women who request testing.

The following chapter on the development and regulation of new technologies (which is referred to only within the context of the USA) is original to the best of my knowledge, at least for a European audience. The narrative of the initiatives and collaborations that have been active between government agencies, private industries and associations, and the examples of funding mechanisms for medical technology development confirm the massive investment into breast cancer care in recent years. The US FDA regulation process for the approval of technologies is well described in relation to the approval of imaging and laboratory devices. Core to this book is an understanding of how the approval process of screening devices by a regulatory agency, and clinical outcome evaluations should be related.

Efficiency evaluation of novel technologies

The last chapters deal with evaluation of efficiency and policy issues. In this context the cost coverage of technologies by insurance agencies (e.g. Medicare and Medicaid in the USA) is discussed, as are the implications for dissemination of their use to large populations. Technology assessment is not subject to approval by the FDA, and the report here poses two questions. First, can the technology positively impact on patient outcomes? Second, how does the technology compare with other technologies that are on the market?

The role of evidence-based research is growing to address these questions, and both randomized clinical trials and nonexperimental studies are briefly presented. The role of meta-analysis and overview of the existing research is also considered. The conclusion supports the concept of large surveillance studies to evaluate the effectiveness of technologies in clinical practice. The Breast Cancer Surveillance Consortium, established by the US National Cancer Institute in 1994, is an original and important initiative that was initiated to evaluate population-based screening mammography in the USA. It covers a large population, and it is expected to contribute to research and technology assessments.

Finally, the use and availability of screening mammography is presented, with specific reference to the US health system. Guidelines, information and promotion, access to the service, and training and reimbursement are briefly discussed.

The Executive Summary

Without questioning the efficacy of mammography, the Executive Summary looks at how the development of this technology may inform the development and assessment of emerging imaging technologies. What can we learn from the history of the evaluation of mammography in order to assess the efficacy of other screening technologies? Also, how should we adapt our assessment of new approaches in the light of future technological advances?

In recent years imaging technologies for early detection of breast cancer have improved relative to traditional imaging, but such development has mainly had consequences for facilitating storage, transmission and comparison in order to improve diagnostic accuracy. However, the question remains as to what extent these new technologies (sometimes with substantial incremental costs) will impact on our ability to detect cancers early in terms of better outcomes. The change could be a positive one, in terms of better outcomes, but it could also be negative (higher costs, over-diagnosis and over-treatment). The most difficult question remains; how can we assess the incremental benefit and the possible adverse effects of early diagnosis?

Biomolecular technologies, such as markers of susceptibility, present similar problems with evaluation to those of imaging technologies; success should be measured in terms of better prevention strategies, and not just greater knowledge. The dominant framework for regulation and evaluation of medical technologies has historically been based on therapeutics: detection technologies are not assessed in the same way, and as such their evaluation is not regulated at all.

The long and controversial history of mammography should not be considered as a paradigm for future technology evaluation. The history and controversies that have arisen in medical and lay journals should inform future guidelines for early detection assessment. It is quite remarkable that screening by Pap smear for cervical cancer, which was criticized because it was introduced as a screening modality in the absence of any demonstration of efficacy, is now more readily accepted than mammography, which has been subjected to the most rigorous experimental evaluation. Conclusions from empirical studies have been shown to be prone to subjective interpretations and prejudices.

The report recommends that, for new screening technologies, "approval by the FDA and coverage decisions ... should depend on evidence of improved clinical outcome" at an early stage in the evaluation process. Attempts to detect early evidence of improved outcome surrogates for decreased disease-specific mortality may be appropriate, although rigorous research into these surrogates is required.

Acceptance of these recommendations will radically change the evaluation of screening modalities and diagnostic devices. It has recently been suggested that guidelines developed for early detection devices may also be used to assess biomarkers [1]. In the book preliminary (unpublished) work from Gatsonis is reported, and he suggests phases of the process of evaluation that are comparable to those used for drugs. More work and debate is needed on these topics, and the process of evaluating new screening technologies should represent an occasion for implementation of guidelines in the field of early detection assessment.

Conclusion

As Lashof points out, many issues, especially knowledge of the natural biological history of the disease, need a large and interdisciplinary research effort, and much remains to be done to improve our early-stage detection technologies. The contributions that this book makes to development of better and more comprehensive processes for the evaluation of early detection devices, and to establishing rules for the approval of early detection technologies by governmental agencies are certainly

worthy of consideration by scientists who are interested in breast cancer research.

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Reference

1. Pepe MS, Etzioni R, Feng Z, Potter JD, Thompson ML, Thornquist M, Winget M, Yasui Y: **Phases of biomarker development for early detection of cancer.** *J Natl Cancer Inst* 2001, **93**:1054-1060.