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HIGHLIGHTS OF THE INSTITUTE OF MEDICINE AND THE NATIONAL RESEARCH COUNCIL'S STUDY OF NEW TECHNOLOGIES FOR BREAST CANCER

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Mammography to Molecular Biology: Opportunities and Obstacles in Developing Early Breast Cancer Detection Methods

The use of screening mammography to locate early stage breast cancer now is a key component of preventive health strategies in the United States. But can we do better? Mammography still has significant limitations, especially among women with dense breast tissue. About 15% of breast cancers are missed by mammography (false negative results), and as many as three-quarters of all breast lesions biopsied as a result of suspicious findings on screening mammograms turn out to be benign (false positive results). Screening mammography also can lead to overdiagnosis and overtreatment of some women with small lesions that might never have developed into a life-threatening disease if they had been undetected and left untreated. Because of these limitations, many additional technologies are being developed with the goal of improving on the accuracy and effectiveness of breast cancer screening. So, is mammography still the gold standard, or do opportunities exist to improve early detection by adopting newer technologies? The obstacle to answering that question is the difficulty in determining which methods are likely to result in real improvements in health and integrating those technologies into medical practice.

The Institute of Medicine (IOM) and the National Research Council recently established a committee that examined new technologies for breast cancer detection and the process by which these technologies are developed, approved by the U.S. Food and Drug Administration (FDA), covered by insurance providers, and disseminated into clinical practice. The committee included experts in oncology, radiology, genetics, public health, epidemiology, and women's health, as well as a breast cancer survivor who provided a very important voice in the deliberations. Upon completion of the yearlong study, the committee made 10 recommendations—five that aim to improve the development and adoption process for new technologies and five that aim to make the most of current technologies. The report concluded that while many technologies show promise and deserve further study, none of the newer technologies have been tested adequately as screening tools, including digital mammography and computer-assisted detection programs. Thus, conventional film-screen mammography remains the imperfect gold standard.

Technologies for early breast cancer detection could take many forms, from traditional imaging technologies that identify structural changes associated with cancer to biologic technologies that aim to identify molecular or genetic changes in cancer cells. The committee examined a wide array of imaging methods, including ultrasound, magnetic resonance imaging, optical and thermal imaging, electrical measurements, positron emission tomography, and scintimammography. Because the potential of the various methods all are at different stages of development, directly comparing them was difficult. Several have FDA approval, but most still are used primarily for research and are not covered by insurance as a result of the lack of data on clinical effectiveness. Most of the biologically based methods are at very early stages of development but may offer new opportunities in the future for detecting changes in genes or gene products, such as RNA or protein and in breast cells, breast fluids, or serum.

Indeed, the committee first recommended that a primary research focus for screening and diagnosis should target technologies for the biologic characterization of tumors and premalignant lesions, because the maximal benefits of early detection will be realized only when we are able to distinguish which lesions will become lethal. Currently, neoplastic lesions are diagnosed imprecisely using pathologic (microscopic) assessment that has been practiced for 100 years. Ultimately, the real breakthroughs in early detection are likely to come from combining imaging technologies with molecular biology. But first we need a better understanding of the biology and etiology of breast cancer. Therefore, establishing and maintaining patient specimen banks that cover the entire spectrum of cancer progression from normal tissue to invasive lesions is essential. Without validated biologic markers, it is unclear what we should be looking for or what should be done when we find it.

The committee was quite concerned about the premature adoption of detection technologies for screening purposes before they had been accessed adequately for that use. Appropriate evaluation of screening methods is essential because of the potential risks associated with screening, including false positive or false negative results, overdiagnosis, and overtreatment. The ideal end point for measuring clinical effectiveness in screening trials is reduced disease-specific mortality. However, because such screening trials are very large, lengthy, and costly, technology sponsors generally seek FDA approval through diagnostic studies, which are not sufficient for assessing screening tests. (Screening tests are performed on asymptomatic women, whereas diagnostics tests are performed to further evaluate women with suspicious lesions). Once a technology is on the market, practitioners might use it for screening and, subsequently, patients might demand coverage for the test as a screening method. This could lead to increased medical costs without actually improving women's health. At the same time, the committee acknowledged that premature assessment of a new test could lead to the rejection and loss of promising technologies that have not been developed yet to their full potential.

To address these concerns, the committee recommended a new approach for assessing screening methods, with coordinated oversight and support from all relevant participants (including the FDA, the National Cancer Institute [NCI], health insurers, and breast cancer advocacy organizations) at a very early stage in the evaluation process. Insurers would be asked to conditionally cover the test until enough data had been collected to determine whether it was effective as a screening tool. In other words, insurers would pay for tests only if they were conducted within approved large-scale screening trials to assess clinical outcomes. The cost of providing tests within clinical trials would be much less than the costs associated with broad adoption by the public, with the associated pressure to provide coverage in the absence of experimental evidence for improved clinical outcome. Participation by private insurers would be particularly important for the assessment of new technologies intended for use in younger women who are not eligible for Medicare coverage.

Many other issues were addressed in the report as well. The committee acknowledged the concerns expressed by many mammographers

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