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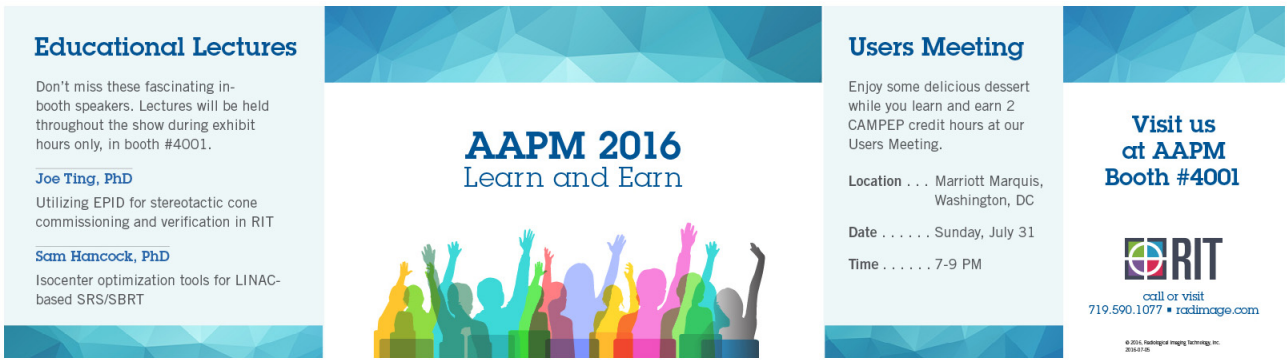

POINT/COUNTERPOINT

Suggestions for topics suitable for these Point/Counterpoint debates should be addressed to Colin G. Orton, Professor Emeritus, Wayne State University, Detroit: ortonc@comcast.net. Persons participating in Point/Counterpoint discussions are selected for their knowledge and communicative skill. Their positions for or against a proposition may or may not reflect their personal opinions or the positions of their employers.

Ultrasonography is soon likely to become a viable alternative to x-ray mammography for breast cancer screening

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OVERVIEW

With heightened concerns about radiation exposures and the cost of medicine, this is an opportune time to be seeking less expensive, nonionizing procedures for mammographic screening. Recent developments and impressive results with automated 3-D whole-breast ultrasound in combination with x-ray mammography, using lesser trained personnel and thus more efficient use of physician time, have given hope that it may be possible in the future to use ultrasound as a standalone mammographic screening modality. This is the premise debated in this month's Point/Counterpoint.

Arguing for the Proposition is Carri K. Glide-Hurst, Ph.D. Dr. Glide-Hurst obtained her Ph.D. in Medical Physics from Wayne State University in 2007, focusing her efforts on breast ultrasound tomography and utilizing acoustic parameters for breast density evaluation at the Karmanos Cancer Institute. She then spent two years in postdoctoral training in the Department of Radiation Oncology at William Beaumont Hospital, with an emphasis on motion management techniques in lung cancer, and is now Senior Associate Physicist at Henry Ford Health Systems in Detroit. Her current interests include a hybrid of teaching, clinical duties, and translational research.

Arguing against the Proposition is Andrew D. A. Maidment, Ph.D. Dr. Maidment is Associate Professor of Radiology and Chief of the Physics Section at the University of Pennsylvania in Philadelphia. He received his Ph.D. in Medical Biophysics from the University of Toronto in 1993 for developing a scanned-slot digital mammography system. From 1993 to 2002, he was Director of Radiological Physics and Assistant Professor of Radiology at Thomas Jefferson University. Dr. Maidment has more than 200 peer-reviewed journal articles, book chapters, proceedings papers, and abstracts. He is active in the ACR and AAPM, including chairing the AAPM Mammography Subcommittee. His research interests include digital mammography, 3-D x-ray imaging of the breast, contrast-enhanced breast imaging, and digital radiography detector physics.

FOR THE PROPOSITION: Carri K. Glide-Hurst, Ph.D.

Opening statement

X-ray mammography, the current standard of care for breast cancer screening, has reduced women's overall breast cancer mortality by ~16%.[1] However, in younger women with dense breasts, mammography has significantly reduced sensitivity due to the difficulty in detecting small tumors in a

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background of dense parenchyma. Also, some women are reluctant to get mammograms due to the pain and anxiety associated with breast compression. Finally, the radiation dose associated with mammographic screening, although low, is of concern. To address these limitations, magnetic resonance imaging (MRI) has emerged as an additional breast screening modality, with improved sensitivity (98%) over mammography (48%).[2] However, the costs, limited availability, exam length, and contraindications (i.e., implanted metal clips and pacemakers) have prevented the widespread acceptance of MRI for routine breast screening. As a result, the American Cancer Society currently recommends MRI breast screening only for women with ~20%–25% increased lifetime risk of breast cancer.[3]

Such limitations in the current state of the art provide compelling evidence that a nonionizing, noninvasive, efficient, and accurate methodology with reasonable costs would be ideal for breast cancer screening. Whole-breast ultrasound fulfills all of these needs. The current role of ultrasound in breast cancer screening is mainly through adjunct imaging, primarily for the discrimination of cysts, with improved sensitivity using mammography combined with ultrasound (63%) when compared to mammography alone (48%).[2] However, a direct benefit has been observed for ultrasound screening in asymptomatic women with dense breasts—*after* negative mammographic findings—and resulted in a diagnosis of 15–34% of the total detected cancers in the studies described.[4] Further, the detection benefits of screening ultrasound have been validated in a large, multicenter trial (ACRIN 6666), which revealed slightly increased diagnostic accuracy of ultrasound screening when compared to mammography in a high-risk population with similar screening sensitivities between the two modalities. While ultrasound presents an increased risk of false-positive results (8.1%, negative biopsy or short-term follow up),[5] this is also true for MRI, where increased sensitivity leads to higher call-back rates.[3]

Previous generations of conventional B-mode ultrasound scanning were once criticized for their operator-dependence, limited penetrating ability, and small fields of view. However, advances in ultrasound transducer assembly, namely, through added elements, cylindrical geometry, and ring/linear arrays, have addressed these shortcomings and permitted larger region-of-interest scanning or, in some cases, automated whole-breast scanning.[6–8] Many of the recent ultrasound systems introduced are multimodality, yielding attenuation, sound speed, reflection, and other mutually registered images that provide more quantitative tissue characterization than previously available with reflection-based ultrasound.[6]

Ultrasound poses a practical and affordable solution for screening younger women with dense breasts, pregnant females, and those who do not meet the risk level requirements of breast MRI screening. Overall, whole-breast ultrasound is advantageous because it is volumetric, noninvasive, and nonionizing, and the current literature supports the routine implementation for breast cancer screening, particularly for women with dense breasts.

AGAINST THE PROPOSITION: Andrew D. A. Maidment, Ph.D.

Opening statement

At the current time, there are no compelling data to support the use of ultrasonography as an alternative to x-ray mammography for breast cancer screening. While studies in combined mammography and ultrasound screening suggest a possible benefit in combined screening, the data do not support independent use of ultrasound for screening due to poor specificity. In the ACRIN 6666 screening study of 2637 women, Berg *et al.*[5] have shown that mammography and ultrasound each identified cancers in 20 women, while combined screening identified cancers in 28 women. In that study, the positive predictive value (PPV) of mammography was 22.6%, while ultrasound was only 8.9%. Thus, ultrasound required nearly three times as many biopsies to achieve the same cancer yield as mammography. The results of Weinstein *et al.*[9] showed similar trends in PPV and sensitivity for ultrasound—digital mammography identified seven cancers from 20 biopsies in a group of 569 women and ultrasound identified three cancers from 20 biopsies in the same group.

The ACRIN 6666 study also illustrates another shortcoming of ultrasound. In that study, the median time to perform bilateral ultrasound was 19 min. The ultrasound examinations were all performed by skilled radiologists with extensive ultrasound experience. The total study time could easily exceed 30 min if one considers the time for comparison to prior studies, discussion of results with the patient, creation of a report, prep and clean-up time, etc. Thus, a single radiologist could not scan more than two patients per hour. Admittedly, this time is long compared to the 5–10 min reported by Kolb *et al.*[10] and Kaplan;[11] however, those two trials were simpler to perform, as the ACRIN 6666 trial required compounding and Doppler measurements to achieve the reported sensitivity and specificity.

Additional concerns include the cost and availability of quality ultrasound screening. In 2008, the global Medicare reimbursement for breast ultrasound (billed as CPT 76645) was $85. Given the extended amount of time for physician-operated screening ultrasound image acquisition and interpretation, this reimbursement level seems insufficient. There is the additional concern that currently, there are not enough radiologists to perform breast ultrasound screening. Assuming a radiologist could perform 4000 ultrasound studies a year (16 per day), nearly 10 000 trained radiologists would be required to screen the approximately 36 million women who get mammograms annually.

Since ultrasound can distinguish solid tumors from fluid-filled cysts, it has a clear clinical role as a diagnostic tool in breast imaging. However, ultrasound does not appear useful for routine screening because of lower sensitivity and specificity compared to mammography, the suboptimal imaging of microcalcifications with ultrasonography, and the projected costs.

Rebuttal: Carri K. Glide-Hurst, Ph.D.

My esteemed opponent poses a valid argument regarding the shortage of radiologists to perform routine ultrasound screening. While this may be true, automated whole-breast ultrasound, where the entire breast is scanned via computer-driven transducers operated by technicians, will reduce the dependence on physicians to perform ultrasound screening.[8,12] In addition, automated scanning reduces exam time, which should effectively lower overall costs, and thereby address concerns regarding current reimbursement levels. Although it should be noted that while the average global Medicare reimbursement for breast ultrasound is $85, similar reimbursement levels also exist for film-screen mammography ($83).

Ultrasound has been widely supported for breast cancer screening of high-risk populations, including those with a personal history of breast cancer. The ACRIN 6666 study revealed that for 1400 women with this risk factor, 28 were found to have cancer, with nine of these cases seen *only* on ultrasound.[5] Moreover, the benefits of ultrasound breast screening have been further illustrated through a combined analysis of over 42 000 ultrasound exams across six institutions, where 150 cancers, the majority of which were <1 cm in size, were identified in 126 women through the use of *ultrasound alone*. Clearly, screening ultrasound has the potential to detect occult cancers not visible with mammography, particularly in the early stages of disease. Furthermore, while the ACRIN 6666 study demonstrated a lower PPV for ultrasound, a more recent whole-breast ultrasound screening study of 6425 high-risk cases found insignificant differences in the PPV of biopsy between mammography and ultrasound (39.0% and 38.4%, respectively).[12]

The benefit of screening ultrasound has been shown to increase breast cancer detection yield by 4.2 cancers per 1000 high-risk women.[5] Overall, ultrasound is likely to become a viable alternative to mammography for breast cancer screening, particularly for high-risk women.

Rebuttal: Andrew D. A. Maidment, Ph.D.

In her opening statement, Dr Glide-Hurst argues correctly that improved breast imaging is needed for young women and women with dense breasts. However, the cited work only supports breast ultrasound when used in conjunction with mammography. Standalone whole-breast ultrasound screening lacks sensitivity and substantially lacks specificity.

The use of ultrasound in combination with mammography will naturally increase cancer yield, but will concomitantly increase the costs and decrease the PPV. Consider breast MRI. MRI is more sensitive than mammography, but has poorer specificity, much like ultrasound. At the current time, the increased cost and low specificity do not justify using MRI as a strict alternative to mammography. Rather, MRI is currently performed in combination with mammography in only a small subset of women at high risk of breast cancer, for whom the cost is commensurate with the benefits.

Unfortunately, there is no research to demonstrate that the combination of mammography and ultrasound is cost-effective, nor does it appear that the small increase in sensitivity achieved with the combination is worth the decrease in specificity. After the widespread implementation of the breast MRI guidelines, mastectomy rates increased significantly without obvious clinical benefit.[13,14] There is no reason to think that the situation with ultrasound will be different.

As MRI also illustrates, specific triage strategies must be developed when implementing new screening methods to identify the population(s) of women for whom the new modality is superior to mammography. These data do not currently exist for ultrasound imaging. This should be a focus for breast ultrasound researchers in the near-term.

In summary, an appropriate standalone imaging modality to replace mammography does not currently exist for any subgroup of women. Whole-breast ultrasound screening may have benefit in combination with mammography in selected populations. However, studies to identify an appropriate screening strategy for any such population are lacking.

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