Density Education National Survivors' Effort (D.E.N.S.E.)

Response to ACR Comments on Florida Senate Bill 96

Before addressing directly the comments of the American College of Radiology (ACR), we would like to make one point very clear. We are asking only for the unrestricted right for women to participate in their own healthcare through having knowledge of their personal physical condition, that is, their breast tissue density. The heart of SB 96 is the very simple mandate that women be provided with density information by the radiologist in the patient report. We feel strongly that the withholding of health information from the patient when there may be alternative choices that could be affected by that knowledge, amounts to a de facto failure of the principle of informed consent. A hallmark of American medicine, the doctrine of informed consent, establishes that there can be no consent for care, that is given or denied, when the patient is not provided with information that is germane to the medical decision.

The material that follows will address, in the order presented, the comments of the ACR. We have taken the liberty to cite peer-reviewed medical literature out of a concern that the issues raised should be examined by analysis of the evidence, rather than opinion. This approach is not meant to impugn the comments of the ACR; rather it is to provide clarity to the issues. Our responses are also generally longer than the original comment, which is the result of our desire to make certain that those involved with legislation will be fully informed.

- **General Comment** In its preamble, the ACR asserts that breast density and what to do with information about density is “a very complex medical issue that is not amenable to . . . governmental policy.” We disagree. Inaction and the neglect by the medical community of the impact of tissue density on both the risk of cancer and the risk that density will materially affect the sensitivity of the mammogram, has made governmental policy necessary. A parallel may be found in a requirement added to the Mammography Quality Standards Act (MQSA) in 1999 that added the requirement that the patient be directly supplied with a report of the results of her mammogram within 30 days of her exam. This provision was added to the regulations because referring physicians were not notifying patients of mammography results.

High tissue density affects a very significant portion of the mammography population. It is estimated that over 50% of women age 40-50, and more than one-third of women have breast tissue that is more than 50% dense. It has also been estimated that 36% of cancers are missed by mammography, and that half of these misses are attributable to high tissue density that has masked the ability of the interpreting physician to see the cancer on screening. Women with dense breast tissue are at risk for having their
Cancers detected when they are larger, present fewer treatment options, have poorer prognosis, and are far more costly to the healthcare system, as well as to the individual, than is the case for women with low density tissue.

- **Point #1 (significant observer variability):** We agree that there is “significant observer variability” in breast density assessment. There have been several studies in which, however subjective the density assessments, there was a significant increase in cancer detection in patients with dense breast tissue when adjuvant imaging was used to augment mammographically, and that the cancers discovered thereby were small and very treatable. There is also evidence that training and experience are important in reducing density assessment variability between physicians, indicating that the observer variability could be significantly reduced. In addition, density assessment need not be subjective, as there are two FDA cleared, volumetric density assessment tools that are commercially available in the US (Quantra™, Hologic, Bedford, MA, and Volpara™, Matakina International, Ltd, Wellington, NZ). Each of these devices is easily implemented, and automatically evaluates the raw full field digital mammography (FFDM) image with sophisticated computer algorithms to provide objective density findings.

- **Point #2 (low PPV of ultrasound-inspired biopsies):** Low positive predictive value (PPV) has been cited by the ACR as a reason for its opposition to this legislation. While ACRIN 6666 did find a decrease in PPV from 22.6% for women who proceeded to biopsy from a suspicious mammography finding to 8.6% for the based on screening ultrasound alone, it is very important to also realize that the addition of ultrasound for patients with negative mammograms also increased the cancer yield by 55%, from 7.6 to 11.8 per 1000.

Berg et al. suggested that automated whole breast ultrasound (AWBU) might facilitate an ultrasound program, although this comment cautioned that such devices might be too expensive. Subsequent to the publication of ACRIN 6666, a large prospective multi-center study was published describing the use of automated whole breast ultrasound in patients with dense breast tissue. The AWBU study, including over 4400 patients and 6400 exams, included patients with familial risk factors as well as patients with BI-RADS™ density grades of 3 or 4 (density over 50%). The cancer detection rate doubled from 3.6/1000 for mammography alone to 7.2/1000 with the addition of AWBU for mammographically negative but tissue dense women. Biopsy PPV rates compared favorably between cancers detected with mammography (39.0%) and those detected only with AWBU (38.4%). Importantly over 65% of the cancers detected only by AWBU were Stage 0 or 1.
• **Point #3 (scant data available for normal risk patients):** We do not understand the reference to the ACRIN 6666 being conducted only on high-risk patients. One of the issues surrounding breast density is whether ultrasound can detect cancers that are mammographically occult. If a woman already has a cancer, neither she nor the cancer care whether she is at high risk, or not. She just cares whether the radiologist is able to see that cancer on the mammogram. If there are 3,000 normal-risk women with 10 mammographically visible cancers and 6-10 mammographically occult cancers, or there are 3,000 high risk women with 20 mammographically visible cancers and 12-20 mammographically occult cancers, the mammogram is still missing 30% to 50% of the cancers. The only relevance to the risk factors in the study group is whether it is economically justifiable to look for those mammographically occult cancers in the “normal” dense breasted population, not whether the chance of missing a cancer that does exist might occur.

We further find it interesting, but also somewhat puzzling, that the ACR is questioning a study that was designed under the aegis of the American College of Radiology Imaging Network (ACRIN). The basic goal of ACRIN 6666 was to “assess the efficacy of screening breast sonography” and specifically “to determine whether whole-breast bilateral screening sonography can identify cancers occult on mammography and whether such results are generalizable across multiple centers.”

Earlier studies by Kolb, et al., and Kaplan, had established that supplemental ultrasound added little additional value for women with lower tissue density, and the limitation of ACRIN 6666 to high risk women (87% of participants had tissue density in excess of 40% by visual assessment, accounting for 75% of the cancers detected by ultrasound alone) allowed the study to reach statistical significance much earlier than if a “normal” population had been enrolled.

The validity of the ACRIN 6666, and a confirmation of its importance, is perhaps best illustrated by one of the ACRIN FAQs that can be downloaded from the ACR website:

19. Why are these results from the first year being reported now if [ACRIN 6666] isn’t complete?

*Because there is a potential benefit from early detection of small, node-negative breast cancers seen only on ultrasound, we are announcing these results at this time so that women can consider these results when deciding whether or not to have ultrasound screening in addition to mammography.*
• **Point #4 (MRI superior to ultrasound):** Is the ACR suggesting that MRI be offered to all dense breasted patients?

We agree that high-risk women, as defined by the American Cancer Society (ACS) consensus recommendations, should receive breast MRI adjunct to a mammogram, beginning at age 30. The ACS clearly recognized that the high false positive rate of breast MRI was justified by the relative risk of the patient population covered by the recommendation. Of great importance, the ACS recommendations recognized that not all women are equally well served by mammography alone.

The ACS 20-25% lifetime risk threshold accounts for approximately 5% of the screening population. Women who meet the high-density criteria account for approximately 40% of the screening population. There are those women who are both dense and who meet the ACS threshold should certainly receive breast MRI.

Breast MRI is a resource intense technology that requires injection of a heavy metal (gadolinium) contrast agent that has been shown to create serious complications in a very small, but significant portion of the population. Perhaps more important, patient compliance with breast MRI recommendations is low. ACRIN 6666 sought to follow a portion of its enrollees with breast MRI and found that more than 40% refused the test out of a variety of concerns.

• **Point #5 (relationship between density and breast cancer risk):** The ACR’s assertion that there is still debate within the scientific community as to the relationship between breast density and breast cancer risk is puzzling for, with the exception of one opinion article, this is an area of universal agreement. Pisano, et al, state clearly in the DMIST study that “greater breast density reduces the sensitivity of mammography and increases the risk of breast cancer.” The justification for funding DMIST and the ACRIN 6666 study was the masking risk (reduces sensitivity) and causal risk (cancer risk) of breast cancer.

Further, this point is confusing, as it appears to address only one facet of density risk, the independent additional risk of cancer that is related to density. There is no dispute at all, however, about the affect of tissue density on mammography sensitivity, or the ability of the radiologist to find cancers in women with dense breast tissue. Improving sensitivity was a prime objective of FFDM but, while FFDM has higher sensitivity than film screen mammography, women with dense tissue are still at considerable risk of having their cancers missed. The DMIST study, in a 2008 update, found that sensitivity in pre- or perimenopausal women age 40-50 with high tissue
Density was only 59%. While this FFDM sensitivity was a considerable improvement over film screen mammography for the same cohort (27%), it leaves a great deal of room for improvement that can only be provided through adjuvant imaging.

On the issue of density’s role in risk for breast cancer (causal risk), we are not prepared to concede that there is any meaningful debate. Researchers as early as Wolfe in 1976 have postulated a connection between tissue density and the risk of breast cancer and a solid and continuing line of research by several institutions and investigators continues to find correlation between tissue density and risk for breast cancer. 

• Point #6 (who should perform a screening ultrasound exam): Regardless of the increased manpower needs that screening ultrasound may present, the issue of manpower is an economic issue that is irrelevant to whether women should be provided with information regarding their breast density. It should not be left to the radiologist to judge what she or he thinks a patient can or cannot afford and offer her care based on that assumption. An informed patient can make her own decision and decide whether she wishes to accept the directives of a third party insurer or, if that insurer will not pay for a service, whether she will pay for that service herself.

In a combined recommendation regarding breast imaging, published in early 2010, the ACR-SBI acknowledged the important findings with respect to supplementary breast ultrasound. However, The ACR-SBI also referred to the practical issues of lack of radiologists and the high false positive rate that had been found in ACRIn 6666. In answer to those issues the committee took the position that: “. . . many facilities have chosen not to offer ultrasound screening [and] [t]he ACR and SBI consider such a choice to be acceptable within the standard of care.”

We believe that this position implies that women be notified of density by the radiologist in order to both consult with the physicians involved in her care. This Information Is necessary if each woman Is to make an informed decision to change providers if she believes it is in her interest to receive an adjuvant screening procedure, and if her radiology provider is unwilling or unprepared to offer adjuvant screening. As previously indicated, AWUB may provide an effective alternative to conventional manual supplementary breast ultrasound.

• Point #7 (confusion associated with the notification process): The first thing to note about this comment is that early in 2009 the Radiological Society of Connecticut changed its earlier opposition to the Connecticut density legislation to one of support for the bill. In its notification of the committee the RSC cited specifically the ACRIn 6666 results and added: “RSC
believes that women should know about all of the options that are available in the way of safe and effective breast examinations.\textsuperscript{xix}

It does not seem reasonable that enforced ignorance is the appropriate response to confusion. It is the medical community’s duty to articulate complex issues to patients in a manner that is understandable so the patient can make an informed consent to the course of diagnosis or treatment that they receive.

It is irresponsible to dismiss the benefits of sharing this life-saving information because of perceived confusion on the part of the patient and health provider. Radiologists and other breast imaging personnel have a duty to be active participants in communicating and educating the patient and health care provider about the implications of breast density for the early detection of breast cancer.

As an example, Jefferson Radiology, the largest private imaging company in Connecticut, held an educational forum inviting referring health care providers to discuss the issue of dense breast tissue, patient notification, Connecticut’s legislation, and adjuvant screening procedures available to the patient. Dr. Ethan Foxman, Radiologist and CEO of Jefferson Radiology, invited Dr. Nancy Cappello, President and Founder of Are You Dense, Inc. to participate in this forum. He writes, "on behalf of more than 600 members of our medical community, I want to express our gratitude for tremendous accomplishments that you and your organization have achieved in advancing the early detection of breast cancer. Your efforts have changed the landscape of care in Connecticut and I believe they will shape the understanding of breast cancer detection on a national level."

Concern for creating undue anxiety and “confusion” has been raised in several of the comments. While we appreciate this concern, we implore legislators to recognize that nothing about a recall for a diagnostic study, or a biopsy that is negative, compares with the anxiety and confusion of relying on mammography for years only to find that you have an advanced breast cancer that was not detectable by screening mammography because it was obscured by dense breast tissue.

- **Point #8 (false security):** We do not understand the statement regarding the false sense of security and women with fatty breasts. Mammography performs better on women with fatty breasts and the greater sense of security they have in a normal mammography report is justified. We must point out that, all other factors being constant, women with low breast density are at lower risk of breast cancer, both in terms of density as a risk for the disease, and for the risk of delayed diagnosis attendant with low mammographic sensitivity. On the other hand, under the current system, women with dense tissue do have a false sense of security. MQSA requires that
the patient receive a report in *lay language*. The lay understanding of the following sentence, which is verbiage recommended by the ACR, is clearly misleading to a patient whose mammogram is compromised due to low sensitivity:

> We are pleased to inform you that the results of your recent mammography... examination are normal/benign (not cancer). "xxx"

- **Point #9 (BI-RADS recommendations):** We understand that BI-RADS™ recommends that mammography reports to referring physicians include a description of breast density. Our concern, however, is that there is no similar recommendation that ensures that density information is passed on to the patient. The failure to communicate directly with the patient creates the often-inaccurate assumption that the patient need not be concerned with her mammogram.

However, as indicated in the first of the ACR’s comments, there is little noted confidence in the ability of radiologists to make visual assessments. Note also that, in the comment on the Connecticut experience it appears that referring physicians in Connecticut were unaware of the implications of breast tissue density, raising serious questions about whether these physicians are advising their patients regarding density and risk. Perhaps more important, however, is the fact that the utilization of BI-RADS is not mandated by the ACR and, in fact, the ACR has promulgated an entirely separate ACR Practice Guideline for the Performance of Screening and Diagnostic Mammography.  "xxx"

Please do not take our response to the ACR comments as being critical of that organization or its many members. We understand fully the challenges to incorporating adjuvant studies into screening women for breast cancer. It must be recognized, however, that the overwhelming weight of medical evidence, a small portion of which has been referenced here, has found clinical benefit for women with dense breast tissue through the adjuvant use of other imaging modalities along with screening mammography. The objections, lack of staff, lower PPV, etc., however, are all economic issues, and as such, all have solutions. We do not seek to mandate any particular adjuvant technology, rather we need, and we believe that women deserve, the knowledge that will enable each of them to become active participants in their own healthcare.

**References**


xvi Access the website using the following URL, scroll down to Research, then click on ACRIN Ultrasound Frequently Asked Questions. *Accessed January 15, 2011.*

http://www.acr.org/SecondaryMainMenuCategories/quality_safety/BreastImgResources.aspx


xxx Access via the following URL. http://www.acr.org/accreditation/mammography/mammo_sample_letters.aspx