ACR, SBI Statement on JAMA/Kerlikowske et al Breast Cancer Screening Study

Kerlikowske et al, recently published in the *Journal of the American Medical Association*, used obsolete clinical endpoints to assess effectiveness of modern mammography screening, is fundamentally flawed regarding participant selection in the two study groups (annually vs biennially), and does not include critical information that, should a biennial screening approach be adopted, thousands of women each year would die from breast cancer who otherwise would not.

An analysis published in the *American Journal of Roentgenology* has already showed that under a biennial screening model, such as that discussed in this study, approximately 6,500 additional women each year in the U.S. would die from breast cancer. It is also likely that thousands more would endure more extensive and expensive treatments than if their cancers were found early by a mammogram.

The most clinically meaningful indicators of whether mammography screening is successful are cancer detection rate, tumor size, nodal status, and cancer stage, because these demonstrate whether screening is identifying small, clinically occult (nonpalpable) early stage breast cancer (that is, the kind of true-positive outcomes that are likely to make a difference). Placing the cut point between early and late cancer between stages IIa and IIb is something that may have been pertinent in the pre-mammography era (1970 and before), but today early stage cancer as identified at mammography screening is stage Ib or earlier. Study results likely would have been much different if this correct/modern endpoint was used.

In addition to incorporating outdated mammography (film/screen vs. digital), the groups of women were not randomly assigned to be screened every year or every two years. They are not identical groups. Identical groups are the only way to accurately look at the question of time between screens. Instead the authors, retrospectively, compared women who were screened every year to those who were screened every two years. It is unclear why some women were screened less frequently. There may very well have been major differences between the two groups in terms of breast cancer risk. This is well known selection bias. The authors acknowledge this problem in the first full paragraph on page E8, but explain that they had insufficient power to adjust for it. This renders the study virtually unusable regarding the question of whether to screen women every two years vs. annually.

Also, study authors would pose that a false-positive outcome is as bad as a true identification of cancer is good, when in fact the relevance of a false alarm pales in comparison to that of a potential life saved. Medical science cannot distinguish which cancers will never threaten the woman and which will become lethal. So the best medicine remains to find and treat the cancers found so they do not kill more women.

Importantly, the computer models cited by the study authors show that the most lives are saved by annual mammography beginning at the age of 40. In fact, every major American medical organization with expertise in breast cancer care, including the
American Congress of Obstetricians and Gynecologists (ACOG), American Cancer Society, American College of Radiology, and Society of Breast Imaging recommend that women start getting annual mammograms at age 40. This remains the position of the ACR and SBI.