

Physicians React to MD Anderson Study on Partial Breast Radiation

On Wednesday, December 7, researchers from the MD Anderson Cancer Center presented an abstract, *Partial breast brachytherapy is associated with inferior effectiveness and increased toxicity compared with whole breast radiation in older patients*, at the 2011 San Antonio Breast Cancer Symposium. The study was based on Medicare billing claims for more than 130,000 patients over the age of 66 who were diagnosed with early stage breast cancer between 2000 and 2007 and received a lumpectomy and radiation.

Researchers observed a small but statistically significant increase of 1.8 percent in the rate of mastectomies among women who received accelerated partial breast irradiation (APBI) compared to those treated with whole breast irradiation (WBI). In addition, researchers claim brachytherapy was associated with higher rates of infection and increased toxicity.

Since the release of the abstract, members of the medical community—including professional organizations like the American Society of Breast Surgeons (ASBS), American Brachytherapy Society (ABS) and the American Society for Radiation Oncology (ASTRO)—have spoken out against the conclusions.

According to many physicians, the study design suffers from several shortcomings, making it insufficient for drawing clinical conclusions or influencing current treatment recommendations. In addition, physicians say news reports about the data are misleading and have led to unnecessary anxiety and confusion among women.

Flawed Study, Misleading Reports

In particular, many physicians object to mastectomy being considered a validated surrogate for local failure, contending that there are many indications for mastectomy unrelated to APBI, such as a new primary cancer or elsewhere failure, and that claims data do not provide sufficient clinical information to draw such conclusions.

"It is questionable that mastectomy rates correlate exactly with recurrence rates. Women undergo mastectomies for a variety of reasons, including subsequent genetic susceptibility testing, personal choice, contralateral breast cancers, and fear as a result of misunderstood studies such as this one. Since mastectomy with reconstruction is easier after PBI than after WBI, this introduces bias into the analysis," says radiation oncologist Robert Kuske, MD, of Arizona Breast Cancer Specialists, Scottsdale, Ariz.

"The mastectomy rate was only 1.8% different in absolute terms, reaching statistical significance because of the large numbers of patients included. This difference is probably not clinically important or relevant," Dr. Kuske adds. "The news media reports of this paper have been misleading and harmful to our patients. Spotlighting a 'two-fold increased risk of mastectomy and complications with PBI'—instead of presenting the absolute differences—seems irresponsible to me."

"This abstract and presentation were drawn from the Medicare claims-SEER database, which is a large database

with cancer-patient data linked to Medicare claims data,” says surgical oncologist Peter Beitsch, MD, FACS, director of the Dallas Breast Center in Dallas, Texas. “The database has information about cancer type and treatments, but it has no specific data on margin status, prognostic factors such as estrogen receptor/progesterone receptor (ER/PR) and HER2/Neu receptor—or even local, regional or distant recurrence.”

“The study states that infections were higher for APBI but there was no statement regarding severity,” adds Dr. Beitsch. “Fat necrosis and breast pain were also significantly higher in the APBI group, although there is absolutely no uniform definition of what fat necrosis is nor a statement about the severity of the fat necrosis or breast pain. Lastly, the researchers state there was a 9.6 percent hospitalization rate for APBI patients vs. 5.7 percent for WBI patients, which is puzzling since no diagnosis was given for hospitalization nor was there information on the time period over which patients were hospitalized.”

Radiation oncologist Constantine Mantz, MD, of 21st Century Oncology in Fort Myers, Fla., says a study based on claims data is “entirely inadequate for making useful clinical decisions.”

“We should recognize the inherent limitations of data quality and clinical quality control of any study based on claims data,” says Dr. Mantz. “As a result, NCCN and other consensus guidelines do not recognize such studies in any of their assessments of clinical practice but rather make sound conclusions based on the results of controlled clinical trials. So, we view a study such as this as hypothesis generating at best.”

Evolution of APBI Technology

Even if physicians accept the data as presented, APBI technology has seen tremendous improvements since the time of the study, says radiation oncologist Rakesh Patel, MD, of Western Radiation Oncology, Pleasanton, Calif. While the study examines an older form of APBI that utilizes a balloon catheter with a single channel, newer multi-channel devices with tighter dose constraints have led to better outcomes, including fewer side effects and toxicity.

“There has been significant evolution and advancement in the catheters as well as our treatment planning systems, and the side effects and toxicity seen with these advances are far better than the results of the study,” Dr. Patel says.

“This study was done between 2000 and 2007 – before any of the newer multi-channel brachytherapy devices were widely available,” says Catheryn Yashar, MD, a radiation oncologist at the UC San Diego Moores Cancer Center in La Jolla, Calif. “What we can take away from this data is the importance of having a catheter that does a better job of shaping the dose to the patient’s anatomy, which is precisely what multi-channel catheters do.”

Negative Impact on Patients

Perhaps most troubling to physicians has been how the study and its coverage in the media has led to unnecessary anxiety and confusion among women. Within days of the first news reports on the study, Deanna Attai, MD, a breast surgeon with the Center for Breast Care, Inc. in Burbank, Calif., received calls

from two patients who previously received breast brachytherapy. Both were concerned they might need additional treatment and while they expressed confidence in Dr. Attai, their radiation oncologist and the rest of the team, both women wanted additional reassurance.

"It is unfortunate that this poorly designed study with no real valid clinical data was allowed to be presented at such a prestigious meeting, and that it received immense national media attention before the scientific community was allowed to interpret the study and respond," says Dr. Attai. "I am hopeful that this will not happen in the future, as many women (and many physicians) were caused unnecessary anxiety regarding their breast cancer treatment options."

APBI is a Safe and Effective Form of Treatment

Contrary to the study's conclusions, physicians point out that there have been multiple randomized prospective clinical trials—the scientific gold standard—that demonstrate equivalence of APBI in comparison to WBI, both for local control and complications/cosmesis.

"First and unequivocally, APBI is a safe and effective form of treating the breast after appropriately performed lumpectomy in patients over age 45-50 with early stage invasive (typically <3cm primaries and lymph node negative) and non-invasive breast cancer," says Dr. Beitsch. "Numerous retrospective studies and two prospective randomized studies have shown no

difference in survival, local-regional recurrence rates or complications between APBI and WBI. The American Society of Breast Surgeons MammoSite Registry has published more than 16 papers showing the safety and efficacy of APBI comparable to WBI."

"This [study] may be highlighting the well-known fact that patients have better outcomes when cared for by an experienced specialist," adds breast surgical oncologist Pat Whitworth, MD, FACS, of the Nashville Breast Center, Nashville, Tenn. "In particular, patients having APBI should consider care directed by members of the American Society of Breast Surgeons. Well-documented outcomes in the ASBS registry are excellent, unsurpassed in any WBI report, and far superior to those reported by MD Anderson."

In addition, another major randomized trial comparing APBI and WBI—the National Cancer Institute's NSABP B-39/RTOG 0413 trial, with 4,300 women participating—is in its final year. Dr. Kuske, a co-principal investigator for the trial, says NSABP B-39 will shed much more light on the issue than MD Anderson's Medicare-claims based retrospective study.

Dr. Beitsch concludes: "MD Anderson's retrospective study of an inherently inaccurate database with questionable outcomes and non-validated 'surrogate endpoints' should be looked at with appropriate skepticism in the face of 20 years of retrospective studies and two prospective randomized trials to the contrary."



Cianna Medical, Inc., 6 Journey, Suite 125, Aliso Viejo, California 92656
866.920.9444 • 949.360.0059 • Fax 949.297.4527
www.ciannamedical.com

©2011 Cianna Medical, Inc. All rights reserved. These products covered by U.S. Patents 7,662,082, 7,497,820, 7,497,819, 7,862,498, 7,862,496, 7,736,292, 7,601,113. Other patents pending. SAVI, SAVI Sisters and Cianna Medical are registered trademarks of Cianna Medical, Inc.