Preoperative MRI in Breast Cancer Grows Contentious

By Karyn Hede

Since its introduction in breast imaging, the use of magnetic resonance imaging (MRI) technology has become a source of contentiousness between its ardent supporters and its fierce critics. No sooner had consensus been reached that MRI screening for breast cancer should be restricted to high-risk women than a new controversy flared over its preoperative use in early-stage breast cancer patients.

Fueling the debate is a recent flurry of reports suggesting that MRI use increases mastectomy rates, prolongs the time from diagnosis to treatment, and may increase the rate of overdiagnosis (detection of clinically insignificant cancers). Staunch advocates of preoperative MRIs, however, argue that in their hands it reduces reexcision surgeries and therefore reduces costs.

Most recently, in a review of more than two dozen recent studies, Nehmat Houssami, Ph.D., of Sydney Medical School, University of Sydney, Australia, and Daniel Hayes, M.D., of the University of Michigan Comprehensive Cancer Center, Ann Arbor, conclude that little evidence exists to support the routine use of MRI in the care of newly diagnosed breast cancer patients.

When the investigators pooled data from 12 primary studies on changes in surgical management based on MRI detection, they found that 11.3% of patients had more extensive surgery than initially planned and that 8.1% of women originally thought eligible for breast-conserving surgery converted to mastectomy because of MRI findings of additional suspicious lesions. The review, published in CA: A Cancer Journal for Clinicians, argues that MRI could have a potentially harmful effect.

“What really breaks my heart is seeing an increased rate of mastectomies after 40 years of battling over doing breast conservation,” said Hayes. “I lived through the mastectomy versus breast conservation wars . . . but because of randomized trials, and surgeons willing to challenge their [own] dogma, and because we chose appropriate endpoints, we convinced ourselves that breast conservation was every bit as good as a mastectomy. And now we are reversing those great successes.”

Identical Outcomes

The authors say that preoperative MRI has been based on an assumption that MRI’s proven sensitivity at detecting suspicious lesions would improve surgical planning and reduce the need for reexcision surgery, as well as potentially reduce recurrence in the treated breast. However, studies challenge that assumption, they say. Lawrence J. Solin, M.D., and his colleagues at the University of Pennsylvania’s Abramson Cancer Center reported in the Journal of Clinical Oncology in 2008 nearly identical 8-year outcomes for patients regardless of whether they had a preoperative MRI. Solin’s group found that 96% of the 541 women who had breast-conserving surgery without an MRI were free of local recurrence at 8 years, versus 97% of the 215 women who had MRI. The difference was not statistically significant.

Similarly, a recent review of 577 breast cancer cases referred to the multidisciplinary breast clinic at the Fox Chase Cancer Center, between July 2004 and December 2006, concluded that patients who had a preoperative MRI were 1.8 times more likely to opt for a mastectomy than those with similar diagnosis who did not have the MRI. Senior author Richard J. Bleicher, M.D., said that the evidence shows MRI use does change the surgical planning but that the data to show those changes improve patient outcomes just are not there.

He pointed out that the recurrence rate for early-stage breast cancer treated with local excision and radiation is already below 10%. Moreover, it’s been known for decades that unrecognized multifocal breast cancer exists and that’s why patients receive radiotherapy after surgery, he added.

“It appears that MRI detects foci of cancer that are clinically insignificant,” said Bleicher, whose study appeared online in the Journal of the American College Surgeons in June. “But the problem is that once you have that data, you can’t tell what is and what isn’t significant; you have to treat all of it.”

Bleicher’s coauthor, Monica Morrow, M.D., has been a vocal opponent of routine preoperative use of MRI. She said that if someone could produce a randomized study showing that MRI reduces the rate of...
local recurrence, that would be a worthwhile endpoint. But unless that happens, clinicians should “curb [their] enthusiasm” for MRI, she wrote in an editorial accompanying the Solin study.

Those in Favor
The Solin article prompted criticism from investigators at University Medical Center Utrecht, in The Netherlands, who are studying the use of MRI in patients with nonpalpable breast cancer (the Mammography of Nonpalpable Breast Tumors [MONET] trial). They pointed out in a letter to the editor of the Journal of Clinical Oncology that selection bias in deciding who receives MRI could limit interpretation of the Solin study and potentially underestimate the benefit of breast MRI. The MONET trial aims to assess whether preoperative breast MRI influences the number of reexcisions and the number of conversions from breast conservation to mastectomy.

A similar trial based in the UK, the COMICE trial, reported in abstract form at the 2008 San Antonio Breast Cancer meeting, demonstrated that reexcision rates were virtually identical in women who received MRI (18.8%) or not (19.3%).

However, Alan Hollingsworth, M.D., a breast surgeon at Mercy Health Center in Oklahoma City, Okla., and a critic of the COMICE trial, is quick to point out that women in that trial were already planning on having breast conservation; therefore, the trial could not address how many patients who had been planning on having a mastectomy converted to breast conservation after having a clean MRI scan.
In Hollingsworth’s experience, MRI use decreased the number of mastectomies at his institution. He and his colleagues reported in a 2008 American Journal of Surgery article that breast conservation rates increased from 48% to 60% upon the introduction of MRI. The study looked at 603 consecutive newly diagnosed breast cancer patients from March 2003 to December 2006, all of whom received MRI. Also, Hollingsworth and his colleagues report an 8.8% reexcision rate, in contrast to reexcision rates of, for example, 38% in a recent examination of mastectomy rates published in October in the Journal of the American Medical Association.

Hollingsworth concedes that if overall survival is the only acceptable endpoint, will be difficult to prove that MRI use saves more lives, but decreasing the reexcision rate and thus saving women additional surgeries and reducing cost should be a worthwhile endpoint, he said.

Clinicians across the country are incorporating MRI into treatment decision making, despite cries to the contrary, said Melvin J. Silverstein, M.D., medical director of the Norris Comprehensive Cancer Center’s breast center at the University of Southern California, Los Angeles.

“You can’t turn back the clock and say, ‘You can’t use this anymore,’ because there are machines all over the country, and anecdotally everybody has got some cases where [MRI use] has made a profound and very positive difference,” said Silverstein.

Silverstein recently led a diverse, interdisciplinary group of breast cancer physicians who met in June 2009 to discuss their experiences with image-detected breast cancer and draft a consensus report on the use of various imaging methods. That report, published in October in the Journal of the American College of Surgeons, took a positive view of the role of MRI in treatment decision making. At the same time, the authors acknowledge that no evidence yet exists from randomized trials that MRI will reduce the risk of local recurrence or improve survival.

“I use MRI with every single patient with breast cancer,” Silverstein said. “I want to look at every single bit of information that’s available, discuss it with the patient, and then figure out the best thing for that patient. That’s the way I work.”

Silverstein also pointed to an emerging treatment that he said would incorporate MRIs. Single-dose intraoperative radiotherapy is being compared to conventional postoperative radiotherapy in the TARGIT trial, an international randomized controlled clinical trial for women with early-stage invasive breast cancer who are scheduled for breast-conserving surgery. The study is enrolling 2,400 women older than 40 years who have been diagnosed with a single invasive breast cancer of 3 cm. or less. Intraoperative radiotherapy differs from partial breast irradiation in that it consists of one 30-minute dose during surgery, as opposed to a 5-day dose. The Norris Cancer Center is one of the trial sites.

“One-shot radiation therapy is coming to this country, and it’s going to be a big thing,” said Silverstein. “We are starting a trial with it, and one of the things we require is an MRI to make sure there isn’t a second lesion somewhere else that would make this trial fail.”

Comparing Effectiveness

More data on preoperative MRIs could come from comparative effectiveness research, an evaluation of the effect of different diagnostic and treatment options that looks at “real world” data, not just clinical trials in controlled, randomized settings. One of the first such studies funded through the federal government’s economic stimulus act will compare the effectiveness of mammography, MRI, ultrasound, PET–CT (positron emission tomography–computed tomography), and tumor biomarkers for establishing extent of disease among newly diagnosed stage I–III breast cancer patients. The $4 million study, known as ADVICE, will be led by principal investigator Larry Kessler, Sc.D., professor of public health at the University of Washington, Seattle, and former U.S. Food and Drug Administration staffer. Plans call for it to establish a network of health care delivery systems to include the University of Washington, Group Health, the Veterans Administration, several private health insurance companies, the Health Care Authority of the State of Washington, Medicaid, and the Seattle Cancer Care Alliance. The funding will not include traditional measures of sensitivity and specificity. Instead, the investigators will test the hypothesis that the likelihood of receiving surgery, chemotherapy, or radiation therapy will not differ among patients who have MRI, PET–CT, both, or neither technology within 6 months of a diagnosis of breast cancer.

“What we are trying to do is look at the variability across the community and exploit the variability over time, place, and provider to see if treatment and possibly morbidity and local recurrence are different because of the use and existence of these technologies,” Kessler said.

He acknowledges that looking at endpoints such as mortality or recurrence will be impossible in the short, 2-year span of the grant, but once the infrastructure is in place, the group plans to collect prospective data to look at the use of imaging technologies in staging breast cancers and at outcomes. Gathering those data will take many years. In the interim, oncologists such as Silverstein say they will continue to use MRI despite the absence of clinical trials showing its effectiveness.

“If you want to base it on science, [Monica Morrow] is probably closer to correct than the rest of us,” said Silverstein. “We like MRI. We think it’s valuable to us, but if you get me into the corner and say, ‘Prove it to me,’ I can’t prove it to you.”