Novel Breast Biopsy Option Appears Promising

The combination procedure is time consuming but may save patients from unnecessary surgery.

BY PATRICE WENDLING

CHICAGO — A novel procedure that combines mammographically guided hook-wire localization followed by ultrasound-guided sampling provides a minimally invasive alternative to stereotactic biopsy of breast calcifications.

The combination procedure was used in 57 groups of microcalcifications in 48 women, aged 41-79 years, who failed or were unable to have a stereotactic biopsy. The procedures were performed between January 2001 and September 2008 at Metro Health Medical Center, an inner-city county hospital in Cleveland.

In all, 52 of the 57 groups of microcalcifications were successfully sampled, resulting in a 9% failure rate, Dr. Jill J. Schieda and her colleagues reported at the annual meeting of the Radiological Society of North America. The procedure was considered a success if the targeted calcifications were identified on specimen radiography and in the specimen by pathology. There were no postprocedural adverse events.

Two of the five failures were due to the inability to place the hook wire sufficiently close to the targeted calcifications, and one was due to excessive patient motion. In one patient, the calcification was too close to the skin, and in another patient the procedure was technically successful but no microcalcifications were seen on radiography. Three of these five patients successfully underwent the procedure within 2-6 months of the first failed attempt.

"Although the combination procedure is time consuming, the patient may be saved from unnecessary surgery, which is definitely an advantage," said Dr. Schieda, a radiology resident at the hospital.

Approximately 3% of stereotactic biopsies are unsuccessful, typically because the calcification is not visible on mammography; excessive patient motion or the inability of the patient to get on the stereotactic table may also be problems.

In such cases, the options are limited to open surgical biopsy or imaging follow-up, she said.

During the combined procedure, mammographic guidance is used to place the hook wire just anterior to the calcifications of interest, preferably using a craniocaudal approach. One wire is usually used, but multiple wires can be deployed if additional groups of calcifications are being biopsied or if placement of the primary wire is unsatisfactory because of patient motion, Dr. Schieda said in an interview.

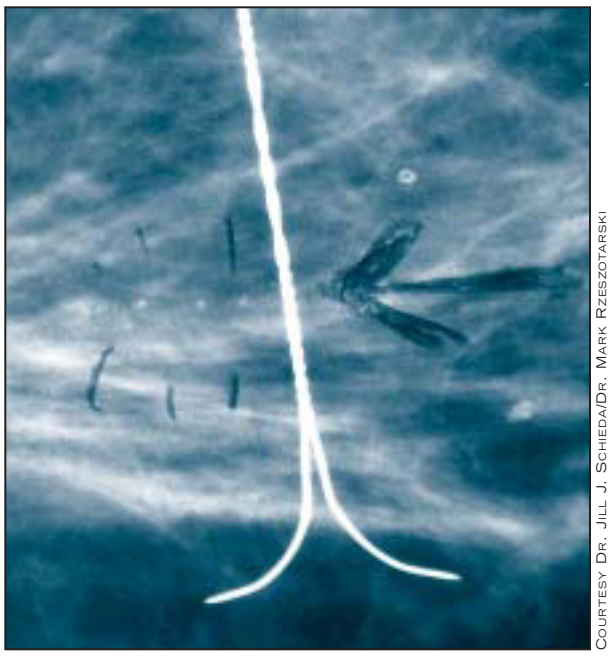
The depth of the wire is adjusted, and the relationship between sonographically visible markers on the wire and the calcifications is documented with a mammogram. If the wire is placed properly, the calcification should be located at the junction of the first set of markers, which look like beads on the wire, she said.

With ultrasound guidance, a large-core vacuum-assisted device is placed just deep to the wire, adjacent to the known location of the calcifications. Sampling is done with the open cutting aperture rotated toward the calcifications, with care taken not to engage the wire within the cutting aperture.

Dr. Schieda acknowledged that the procedure requires significant patient cooperation and performer experience. The same breast-imaging radiologist performed all the procedures in this investigation; although the procedure is novel, the radiologist's 30 years of professional experience may have shortened the learning curve.

Limitations of the study include the small population, lack of a gold standard for comparison, and lower-than-usual resolution of the hospital's stereotactic unit, which may have influenced the need for the alternative procedure.

The investigators reported no conflicts of interest or funding sources for the study. ■



COURTESY DR. JILL J. SCHIEDA/DR. MARK RZESZOTARSKI

In this medial-lateral view of the breast, the calcifications, indicated by dashes, are posterior to the wire and near the junction of the first set of tight and loose beads. The arrow is anterior to the wire and is directed toward the calcifications.

Zoledronic Acid Boosts Antitumor Effects of Chemotherapy

BY KERRI WACHTER

SAN ANTONIO — The addition of the bisphosphonate zoledronic acid to standard neoadjuvant chemotherapy reduces tumor size and results in more patients with a pathologic complete response than does chemotherapy alone, which suggests that the drug has direct antitumor activity, study results showed.

In a retrospective exploratory analysis involving more than 200 women, the adjusted mean residual invasive tumor sizes (RITS) in chemotherapy-alone and chemotherapy plus zoledronic acid groups were 42.4 mm and 28.2 mm, respectively—a significant difference ($P = .002$), Dr. Robert Coleman reported at the annual San Antonio Breast Cancer Symposium.

The pathologic complete response (pCR) rate (both breast and axilla) was 5.8% in the chemotherapy-alone arm and 10.9% in the combination arm ($P = .033$). In a multivariate analysis, the difference in pCR significantly favored the combination arm with an odds ratio of 3.7 ($P = .03$).

"It is the first patient-related evidence that this class of drugs may have direct antitumor activity," he said at a press conference during the meeting. "What these data suggest is that perhaps zoledronic acid is doing something more than just affecting bone." Dr. Coleman, an oncologist at the cancer research centre at Weston Park Hospital in Sheffield, England, presented the findings in a poster at the meeting.

"This is not a practice-changing study," he cautioned. "It's a hypothesis-generating study, which will lead to the design of specific neoadjuvant trials to look at this in more detail."

'It is the first patient-related evidence that this class of drugs may have direct antitumor activity.'

DR. COLEMAN

In the Neo-Adjuvant Zoledronic Acid to Reduce Recurrence (AZURE) trial, 3,360 women with stage II/III breast cancer were recruited to determine whether treatment with zoledronic acid in addition to neoadjuvant therapy improves disease-related outcomes. Women had to have a tumor size greater than 5 cm (T3) or features of locally advanced disease (T4) or biopsy-proven lymph node involvement (N1).

They also had to be scheduled for definitive surgery and/or radical radiotherapy with curative intent within 6 months of starting neoadjuvant therapy. In addition, the time between the start of neoadjuvant treatment and the start of zoledronic acid had to be no greater than 30 days.

In AZURE, eligible patients received neoadjuvant chemotherapy according to local practice and were randomized to also receive 4 mg IV zoledronic acid (every 3-4 weeks for 6 months in the neoadjuvant period) or no additional treatment.

The primary surrogate end point for response was RITS at surgery. Secondary end points included pCR, number of positive axillary nodes, and percentage of patients requiring mastectomy. In a multivariate analysis, the researchers adjusted for T stage, estrogen-receptor and progesterone-receptor status, chemotherapy type (anthracycline/taxane), treatment duration, and menopausal status, Dr. Coleman said.

A total of 205 patients received neoadjuvant chemotherapy—104 in the chemotherapy-alone group and 101 in the chemotherapy plus zoledronic acid group. The baseline characteristics and treatments were similar, and the median number of chemotherapy cycles and treatment duration were the same in both groups.

Most women in both arms were estrogen-receptor positive—64% in the chemotherapy-alone arm and 68% in the combination arm.

In terms of progesterone-receptor status, 46% of the women in the chemotherapy-alone arm were negative, 25% were positive, and 29% were of unknown status; in the zoledronic acid arm, 34% were negative, about a third were positive, and a third were of unknown status.

Almost half of the women in both arms were HER2 positive—47% in the chemotherapy-alone arm and 48% in the combination arm.

The unadjusted median RITS was 30 mm in the chemotherapy-alone group, compared with only 20.5 mm in the combination group. In a multivariate analysis (171 patients with complete data), zoledronic acid, estrogen-receptor status ($P = .034$), and treatment duration ($P = .002$) were independent significant predictors of smaller RITS with negative estrogen-receptor status and increasing treatment duration.

There was no significant difference in the median number of positive lymph nodes at surgery. The proportion of patients requiring mastectomy in the chemotherapy-alone and combination arms was 77.9% and 65.3%.

Dr. Coleman reported that he has received grant support from Novartis and he is on the speakers bureau with Novartis and Amgen Inc. Novartis makes Zometa. The study was sponsored in part by Novartis. ■