

Prone Breast Radiation May Spare Heart, Lungs

BY MITCHEL L. ZOLER
Philadelphia Bureau

NEW YORK — Positioning women with breast cancer facedown when they undergo radiation therapy may substantially cut the radiation dose that reaches their heart and lungs, say radiation oncologists at Memorial Sloan-Kettering Cancer Center in New York, where the technique has been used for about 10 years.

The Memorial Sloan-Kettering oncologists designed a pallet that they call the breast board to help women more comfortably lie facedown for radiotherapy. (See photo.) The board has an adjustable cutout through which the ipsilateral breast and chest wall hang down in a dependent fashion away from the thorax, while the contralateral breast is cushioned and remains on top of the board.

This setup has been used at Memorial Sloan-Kettering for breast irradiation since 1998, Dr. Beryl L. McCormick told attendees at a symposium on cardiovascular disease in cancer patients sponsored by the University of Texas M.D. Anderson Cancer Center. “We now treat as many of our breast cancer patients as possible with a prone breast board,” she said.

With a maximum follow-up of 10 years on the first pa-



The “breast board” at Memorial Sloan-Kettering Cancer Center is an immobilization device for treatment of breast cancer in the prone position.

tients treated this way, it’s too soon to assess the impact of this approach on long-term outcomes, but the technique has attracted interest from other cancer centers, said Dr. McCormick, acting chair of radiation oncology at the

cancer center in New York. The idea is to limit the radiation dose to the heart and lungs as much as possible. “The radiation dose is the same [as with standard treatment]. We just flip the patient over” from the standard supine position to prone, she said in an interview.

The danger of irradiation to the heart when breast therapy is delivered in the supine position has been documented in several studies. The heart is especially vulnerable to damage when the left breast is treated this way. For example, study results reported last year by researchers at the University of Michigan, Ann Arbor, from 795 patients with unilateral disease showed that women treated using the conventional radiation approach on their left breast were about eightfold more likely to have a later cardiac event, compared with women whose right breast was treated (Cancer 2007;109:650-7).

“Late cardiac events are real and relate to the radiation therapy technique, dose, and the volume of the heart that gets treated,” Dr. McCormick said at the meeting, also sponsored by the American College of Cardiology and the Society of Geriatric Cardiology. Adverse effects may be minimized by “avoiding treatment to as much of the heart and lung as possible.”

Tracking Chemo’s Cardiotoxicity by Serum Troponin Level Leaves Gaps

BY MITCHEL L. ZOLER
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NEW YORK — An elevated troponin level immediately after cancer chemotherapy is only partially effective for identifying patients at risk for chemotherapy-induced cardiotoxicity, according to one of the pioneers of the troponin monitoring approach.

Among a total of 500 women who underwent chemotherapy for breast cancer, 395 were initially troponin negative, but within this subgroup were 20 patients (5%) who nonetheless had a significant drop in left-ventricular function, a sign of chemotherapy-induced cardiotoxicity, said Dr. Daniela Cardinale, director of cardiology research at the University of Milan.

These patients probably had a false-negative troponin level because the marker was measured only immediately after a cycle of chemotherapy was complete, she noted. It’s now known that in some patients who develop chemotherapy-induced cardiotoxicity, a spike in serum troponin level does not appear until more than 72 hours after treatment, said Dr. Cardinale at a symposium on cardiovascular disease in cancer patients sponsored by the University of Texas M.D. Anderson Cancer Center.

“To detect all cardiac dysfunction, additional, late troponin measurement is needed,” she said. As many as 30% of patients who eventually have increased serum troponin following cancer chemotherapy don’t show the elevated level until more than 72 hours after their treatment ends, she said at the meeting, also sponsored by the American College of Cardiology and the Society of Geriatric Cardiology.

Dr. Cardinale and her associates pioneered the concept of monitoring cardiotoxicity following cancer chemotherapy by measuring serum troponin levels. They also developed the

approach of treating patients who have a troponin rise following chemotherapy with an ACE inhibitor, such as enalapril. This strategy was proved to prevent the eventual development of left-ventricular dysfunction in these patients (Circulation 2006;114:2474-81). After their paper was published, Dr. Cardinale and coworkers followed the 500 women with breast cancer, who were each treated with one of three standard chemotherapy regimens that included agents such as cyclophosphamide, doxorubicin, fluorouracil, and methotrexate.

Immediately after treatment, serum troponin levels rose significantly in 105 of the patients (21%). The average left-ventricular ejection fraction in these patients fell from 65% at baseline to 54%, with many patients having a significant drop in left-ventricular function, defined as a decline of more than 10%.

But among the 395 patients who remained troponin negative, the overall ejection fraction fell from 63% at baseline to 61%, a drop that was statistically significant. Greater scrutiny of the troponin-negative group showed that 5% actually had a substantial cut of more than 10% in their left-ventricular function.

Another limitation of monitoring is that until now the only marker of cardiac damage from chemotherapy has been troponin. A recent study by Dr. Cardinale and her associates examined the ability of serum levels of B-type natriuretic peptide (BNP) to predict cardiac dysfunction following chemotherapy. They found that elevations in serum BNP in the absence of elevated troponin levels identified an additional 5% of patients with risk for significantly reduced left-ventricular function.

“A multimodal approach [such as measuring serum level of both troponin and BNP] seems like a promising way to identify high-risk patients,” Dr. Cardinale said.

Modafinil May Cut Fatigue In Patients During Chemo

BY KERRI WACHTER
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CHICAGO — The wakefulness-promoting drug modafinil (Provigil) reduced self-reported severe fatigue, according to a study of more than 600 cancer patients undergoing chemotherapy that was presented at the annual meeting of the American Society of Clinical Oncology.

Gary R. Morrow, Ph.D., of the University of Rochester (N.Y.) and his colleagues randomized 631 patients undergoing four cycles of chemotherapy to receive either 200 mg modafinil daily or placebo. Among those with severe fatigue at baseline, patients on modafinil had significantly greater reductions in fatigue, compared with those on placebo.

Participants were asked to rate their level of fatigue at baseline (during the second cycle of chemotherapy) and during the final cycle. They rated fatigue on a 10-point scale: mild (1-4), moderate (5-6), and severe (7-10). A total of 67 patients reported mild fatigue at baseline; 106 and 458 reported moderate and severe fatigue, respectively.

Among patients with mild and moderate fatigue, modafinil also reduced fatigue, compared with placebo,

but the differences were not significant. This was not surprising, Dr. Morrow said during a press briefing. “With side effects, quite often the potency of the effect is somewhat dependent on where you began,” he said.

Modafinil—a nonamphetamine stimulant—is currently indicated for the treatment of excessive sleepiness resulting from obstructive sleep apnea, shift-work sleep disorder, and narcolepsy.

Last year, researchers also at the University of Rochester reported success with modafinil in treating “chemo brain,” a reduction in cognitive function that has been associated with chemotherapy.

There may be some overlap between chemo brain and fatigue, Dr. Morrow said in an interview. Problems with executive function are commonly described in chemo brain. Cancer-related fatigue appears to particularly affect tasks associated with executive function. Cancer patients complain of not being able to “get around” to doing things they know they should do.

Cephalon Inc. provided modafinil and placebo for the trial. Dr. Morrow reported that he has no relevant financial relationships.

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