

EVALUATING THE USE OF RADIATION THERAPY AFTER MASTECTOMY

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Recently, there have been several studies evaluating the use of radiation therapy after mastectomy for women with breast cancer to try to determine the best treatment results.

Randomized studies from Canada and from Scandinavia have shown the benefit of radiation in addition to mastectomy for women. Breast cancer poses significant risks. This data is important because many women were previously felt to have adequate therapy with mastectomy for local treatment plus or minus chemotherapy depending upon the tumor extent. Radiation was seldom discussed after mastectomy. Yet, we now know that treatment after mastectomy should be discussed on a routine basis. Treatment options will seem more complex but a greater likelihood of cancer-free survival exists for those with breast cancer.

Many women in the past even say they chose mastectomy in an attempt to avoid radiation. Now it is known that this is an unreasonable trade-off. Radiation may well be used in women with invasive breast cancer whether or not the breast is maintained with lumpectomy or lost during mastectomy. Thus the thinking and strategy of women and their physicians must include this factor.

A recently reported meta-analysis by Whelan and published in the prestigious Journal of Clinical Oncology evaluated the best treatment option for those undergoing mastectomy.

Data has been presented both in medical journals as well as in important medical meetings that have shown for women with positive lymph node breast cancer, even after mastectomy, radiation can further improve survival compared to those women receiving no similar radiation. These studies were randomly allocating treatment - radiation or not - to enhance the significance of observed results.

Also, studies have shown that even women with no lymph node involvement after mastectomy should receive radiation in the setting of certain sized invasive breast cancer.

A prior Canadian study found benefit to the use of radiation after mastectomy and in fact was published in the New England Journal of Medicine. To further elaborate the results, additional studies were analyzed.

To answer this critical issue, randomized published studies using radiation after mastectomy were collected and evaluated. The data from multiple studies were pooled to make this evaluation. Studies were included if they were published in a peer-reviewed journal, if all patients had mastectomy, if all patients had the same systemic treatment and if radiation was randomly allocated - half yes, half no. Radiation was to be delivered to the regional lymph nodes as well as chest wall area and there was to be a median follow-up of at least five years.

Eighteen randomized studies met the criteria described. Fifteen were published as separate studies while 3 were parts of prior metastatic analysis compilation. These studies included 6,367 women between the years of 1973 and 1984. Nine other studies had fewer than two hundred patients while two studies had more than 1,000 patients. The follow-up ranged from 7 1/2 to 14 years median.

Women generally included were those who were pre as well as post-menopausal. Two studies had only pre-menopausal and one had only post-menopausal women.

Most studies involved those who were node positive while several studies had lymph node

negative cancer or tumors greater than 5cm (centimeter) or involvement of the skin or muscle. One study had lymph node negative breast cancers with tumors measuring 2cm to 5cm in size.

In these studies reported over the last 27 years, most women had radical mastectomies. Women having lumpectomies and radiation were not included in this analysis. Other studies have evaluated the role of radiation after lumpectomy (removal of the lump of cancer) and found marked benefit to this approach. Lumpectomy and radiation also has the added benefit of maintaining the breast, a physical, cosmetic and psychologic plus.

Nine studies included the use of CMF chemotherapy, which consists of Cyclophosphamide, Methotrexate and Fluorouracil. Other studies included Adriamycin or a combination chemotherapy. Two studies included only one agent. In three studies chemotherapy and also hormonal therapy were instituted.

The radiation included that delivered to the chest wall, supraclavicular or lymph node areas above the clavicle, axilla areas and internal mammary nodes. Internal mammary nodes are located just behind the breast bone or sternum.

In three studies the internal mammary nodes were not radiated. Radiation was generally delivered using megavoltage linear accelerators. The most common dosage was 50 gray or 5000 cGy (centigray) delivered in 25 fractions over five weeks. Toxicity was reported in some of the patients and was generally minor. It included skin irritation, suppression of the blood counts and effect on the underlying lungs.

When chemotherapy and radiation were given concurrently there appeared to be a greater toxicity. No damage to the brachial plexus was reported. The brachial plexus are the major nerves running from the spine to the arm. Arm swelling occurred in 10% to 54% of irradiated patients (median 12%). No increased incidence of second cancers were found in women receiving radiation.

The major point was outcome. Did radiation save life? Was one more likely to be cancer-free if radiation was given?

The authors reported, "radiation was shown to reduce the risk of any recurrence." Early studies showed that radiation decreased local and regional recurrence rates. The benefit to survival had not been previously described until recent years. In prior years, radiation was known to damage the heart. New radiation techniques implemented avoid the heart therefore minimizing the chance of this adverse reaction.

As the authors reported, "results of the meta-analysis are consistent with three recently published trials, i.e., locoregional therapy not only reduced local failure, but improved disease-free and overall survival. Why are the results of our meta-analysis different from those of previously randomized trials and meta-analyses? First this meta-analysis focused only on patients who were treated with systemic therapy."

Furthermore, it was noted that, "systemic therapy, particularly chemotherapy, though effective in preventing distant metastases, is likely to be less effective in preventing locoregional recurrence in which the tumor burden is high. In patients who have distant failures reduced with chemotherapy, the effect of radiation therapy on preventing locoregional recurrence and resulting secondary systemic recurrence may be more evident."

The authors also noted that radiation should be given within six months after the initiation of chemotherapy or it is less effective. Concluding, "The results of this meta-analysis support an evolution in oncologists thinking concerning the biology of breast cancer. One half century ago, the prevailing theory was that breast cancer was spread by stepwise local extension, which resulted in more extensive surgery. By the 1970's and 80's this view had been replaced by that of

breast cancer as a systemic disease. The recent thinking is that both hypotheses are valid. Our results support the notion that, in the presence of adjuvant systemic therapy, local regional control is important and that reduction in locoregional recurrence may prevent secondary systemic spread from regional sites and thus prolong survival. Since the inception of these trials, many changes have occurred in the management in breast cancer, and it remains unclear how locoregional radiation should be incorporated into current practice."

Thus, women undergoing mastectomy for breast cancer should be seen by radiation oncologists for consultation as well as surgeons and medical oncologists to discuss treatment options and the best strategy even after mastectomy is performed. Of course, since randomized studies have already shown that for most breast cancers that the avoidance of mastectomy can be given with chemotherapy used in certain situations and radiation in most cases to optimize disease-free survival. Not every woman, unfortunately, can choose to conserve or maintain the breast. In certain situations especially when the cancer is diffuse, spread throughout the breast, mastectomy is necessary to deliver the best treatment.

Each case is individualized and best evaluated by a fully informed woman with the best medical guidance she can find.