

BREAST CANCER - IMPACT OF MARGINS IN CHEMOTHERAPY

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Breast cancer remains a widely important disease in America. Two hundred thousand women each year are diagnosed with this malignancy. Physicians and researchers continue to evaluate data to determine best treatment options. Fully informed women and their families can evaluate data when selecting therapy. While it seems in the past physicians often chose therapy for women, now-a-days the options are being presented with women deciding which avenue to take. Of course medical guidance is crucial and many women have second options to best inform them about treatment.

Randomized studies have seriously shown that women undergoing lumpectomy and radiation have an equivalent likelihood of being cancer-free compared to those women undergoing mastectomy or removal of the breast. This is important data because many women were led previously to mastectomy thinking it would be a better treatment option. Now-a-days, for most women, removal of the breast is not necessary.

Randomized studies from NSABP and elsewhere have shown the equivalence of lumpectomy radiation and as well the importance of radiation. Some had thought that lumpectomy alone - by removing the cancer - would be adequate. This is not true. The addition of radiation is felt to be crucial and in fact interestingly enough many women having mastectomy are advised to undergo radiation to reduce recurrence rates and to increase cancer-free survival rates. A recent analysis by Park, et al, published in the Journal of Clinical Oncology this year has analyzed certain pathologic and treatment facts on the likelihood of women being cancer-free years after treatment. It has been long known that if the breast cancer can be totally removed by the lumpectomy or even repeat incision the likelihood of success is greater. Additionally, chemotherapy has been used in select patients to enhance survival rates.

Now an analysis was undertaken to study the impact of both pathology and chemotherapy on women with breast cancer. Researchers from Harvard evaluated 2,140 patients with stage I or II invasive breast cancer, treated between 1968 and 1987. Of these patients 533 had pathologic slides available for review and received at least 6000 rad to the tumor bed and were followed for at least eight years. Rad is a measurement of radiation dose. Patients were followed eight to fifteen years with a median of 10.6 years. Most patients received 4500 rad to the entire breast and a boost to the tumor bed or place of lumpectomy. The margins of the cancer were than analyzed by the pathologist to determine whether cancer extended to the margin, or the place where the surgeon cut and what type of cancer was at that margin. If the margin of cancer was less than or equal to 1mm it was called close. If the margin away from the place where the lumpectomy was performed was more than 1mm it was called negative. Positive margins were classified whether they were uninvolved or positive and touching the margin of resection. Furthermore those that were positive were called whether they were focally positive or extensively positive. This would reflect the degree of risk for the patient. The group then classified the results based on whether the cancer came back anywhere in the treated breast, distantly in lymph nodes or with an opposite breast cancer.

Patients were also categorized whether they had died without evidence of recurrence or were alive with no cancer.

Local recurrences were broken down more - that is whether they were within the tumor bed treatment area, whether they were adjacent to the tumor bed treatment area or elsewhere in the breast but outside of the immediate area.

At eight years, 11% of the 533 patients had recurred in the treated breast and 28% had cancer recurrent distantly, regionally or as an opposite breast cancer as a first site of failure. The

percentage of women who died from other diseases was 5% and 56% were cancer-free. For women with negative or close margins, the eight-year rate of being free of local disease was 93%. However, if there was extensively positive margins only 73% of women were free of cancer in the local area. Women with focally positive margins had a local recurrence rate of 14%, halfway between those who had negative margins and those with extensive positive margins. Furthermore it was noted that in women who had extensively positive margins there was a higher rate of distant, regional and opposite breast cancer. It was also noted that those with extensively positive margins were more likely to have local recurrences that were true recurrences.

Also evaluated was the extent of the margin necessary. Cancer-free margins from 0.1 to more than 5mm were evaluated and seemed to show no difference. This is important as many women ask the question as to what is the distance necessary between the cancer and the resection margin to feel comfortable with surgery. There is a type of non-invasive breast cancer called ductal carcinoma in-situ. In the past ductal carcinoma in-situ was thought to be an important criteria for evaluating women with invasive breast cancer undergoing lumpectomy and radiation. In women who had both invasive and ductal carcinoma in-situ at the margin the local recurrence rate was 24%. It was about 16% if there was only one of the two types of breast cancer at the margin. However if there was only focally positive margins including both invasive and in-situ cancer the local recurrence rate was 29%. Where it was 6% if there was only ductal carcinoma in-situ and 14% if there was invasive cancer focally at the margin. Chemotherapy did have some impact on local recurrence although it was not overall strong.

Of women with focally positive margins - of the 45 who received chemotherapy there was a 7% local recurrence rate compared to 18% for the 77 women who received no chemotherapy. Yet in the other groups with extensively positive margins local recurrence rate was 26% and 29% whether systemic treatment was used or not used respectively. Furthermore women with close or negative margins had a 5% or 8% of local failure depending on the presence or absence of chemotherapy use. Overall the importance of chemotherapy remains systemically. It has little bearing on the local disease where surgery and radiation play such a critical role.

The authors' suggested that "patients with focally positive margins who are treated with systemic therapy may be good candidates for breast conservation." Overall those with close or negative margins did well in terms of local recurrence. There is no particular amount of margin that was required to minimize local recurrence once the tumors seemed to be totally removed. Other institutions using 2mm cut-off found that close margins had 14% recurrence rate in the breast while negative margins had half that rate. This has been duplicated at several major centers across the country. The point may well be taken that negative margins are better than positive margins. This information is routinely relayed to women with breast cancer. The option of repeat excision is suggested to women. Some women eagerly take up the possibility while others refuse to go through additional surgery.

Data from other studies such as The National Surgical Adjuvant Breast Project, which randomized women to radiation or radiation plus chemotherapy, found markedly lower rates of local recurrence in those women receiving chemotherapy plus radiation for invasive breast cancer. Those lymph node negative women undergoing lumpectomy followed by radiation had a 13.4% local recurrence rate compared to 2.6% when treated with chemotherapy and radiation. There is also data suggesting that Tamoxifen with lumpectomy radiation can reduce the recurrence rate. A study from Sweden found that the local recurrence rate in women's breast cancer undergoing lumpectomy radiation when Tamoxifen was given cut in half- from 7% down to 3%. Obviously additional studies are necessary to collaborate this. In the meanwhile women here are encouraged to undergo complete excision of the tumor and appropriate radiation and systemic treatment as indicated by a pathologic criteria.

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