

Developments in the treatment of cancer of the breast

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In the spring of 1976, there was a development that may change the attitude of both surgeons and radiotherapists towards the primary treatment of breast cancer. This was the authorization by the National Cancer Institute of a randomized study comparing the results of treating small, Clinical Stage I breast cancers by three different methods: (1) modified radical mastectomy, (2) segmental (partial) mastectomy with axillary dissection plus radiation, and (3) segmental mastectomy with axillary dissection but without radiation.

If there had been any evidence that the survival rate following segmental resection and axillary dissection could be expected to be lower than that following modified radical mastectomy, the National Cancer Institute could not have authorized Dr. Bernard Fisher and his National Surgical Adjuvant Breast Project to conduct this trial. In fact, in the consent form that every patient must sign it is stated, "To date there is no conclusive information relative to the effectiveness of the treatments under study." Already the details of the trial have been reported in a women's magazine (*Rosamond Champion*, *McCall's*, June 1976) with the result that women will soon be alerted to the fact that seg-

mental mastectomy with or without radiation is an accepted method of treating some patients with breast cancer.

A dozen randomized or scientifically controlled studies, both in this country and abroad, have shown that in terms of survival there is no significant difference between the various combinations of simple and radical mastectomy with or without radiation. Thus there is real hope that, by giving to women the incentive of having adequate treatment without serious deformity, they can be persuaded to examine themselves every month, to have mammograms at ages 40, 45, and 50 and every 2 or 3 years thereafter and thus to have their cancers diagnosed at a time when many more of them can be cured.

A second development is the report of Bonadonna et al¹ of the striking improvement in survival and of the equally striking reduction in recurrences, both systemic and regional, in patients with axillary node involvement treated by chemotherapy. Their report confirmed the previously reported randomized trial of Fisher and the NSABP, but the treatment was more rigorous, involving radical mastectomy followed by the use of three chemotherapeutic agents (cyclophosphamide, methotrexate, and fluorouracil) for a period of a year. At 27 months only 5.7% of the 207 women given chemotherapy had experienced failures of treatment compared to 24% of the 179 controls who were treated by radical mastectomy alone. At 33 months the results (pending publication) were not as striking but were still impressive, 12% relapses as compared to 30%. Five patients in the treated group died as compared to 13 of the controls. As

time goes on, the results seem to be much less impressive in the postmenopausal patients, raising the question as to whether a large part of the benefits are not from suppression of estrogen and could not be obtained more easily by oophorectomy or by irradiation of the ovaries plus suppression of estrogen from the adrenals or by the use of the new anti-estrogen, Tamoxifen.

In the past there has been speculation, based on laboratory experiments, that removal of regional nodes might diminish systemic immunity to cancer and might thereby increase the rate of growth of metastasis. Although our experience at the Cleveland Clinic has been relatively small and not randomized, it suggested that this might be the case.² Moreover, Stjernswärd³ has reported that in all of the six studies that were randomized between surgery alone and surgery plus radiation, there have been small but definite reductions in survival when prophylactic radiation was added. On the other hand, randomized surgical trials have failed to show any lessening of survival in Clinical Stage I patients whose uninvolved nodes were removed. Since it now seems of value to employ chemotherapy (or castration) and "medical adrenalectomy" or anti-estrogens when nodes are involved, it is important to determine whether the nodes *are* involved. For this reason, in all central and outer quadrant cancers, at least a low axillary dissection should be done and the dissection should be completed if the nodes are involved.

As a result of these developments, it seems clear that (1) there is no longer any indication for performing the standard Halsted-type radical

mastectomy, (2) modified radical mastectomy or simple mastectomy with low axillary dissection is the best treatment for most breast cancers, (3) partial mastectomy with axillary dissection and with or without radiation is an acceptable treatment for some women with cancers of appropriate size, stage, and location, (4) after modified radical mastectomy, contour can be restored by an implant; often the nipple can be saved by transplanting or grafting.

The importance of these conclusions does not lie so much in the fact that the treatment will diminish the discomfort and disfigurement that has for so long been associated with radical mastectomy. Their chief importance lies in the hope that (1) simplification of surgical treatment will provide an incentive for earlier diagnosis and that this will result in a higher proportion of patients cured, (2) since chemotherapy in patients with involved nodes defers the appearance of recurrence, it is not beyond the scope of present hopes to believe that chemotherapy or treatment with anti-estrogens given early and intensively, may result in a significant increase in the proportion of patients cured. Time alone will tell.

In the meantime, the following are the descriptions and results of the randomized or scientifically controlled studies that have been done throughout the world:

1. Forrest APM, Roberts MM, Preece P, et al: The Cardiff-St. Mary's Trial. *Br J Surg* **61**: 766-769, 1974.

Simple mastectomy and axillary biopsy—radiation if nodes were involved vs. radical mastectomy—radiation if nodes were involved.

Number of patients = 243—randomized.

Duration of follow-up = 1 to 7 years.

Conclusion = simple mastectomy with selective postoperative radiotherapy is a safe policy of treatment.

2. Kaae S, Johansen H: Simple vs. radical mastectomy for primary breast cancer, *in* Prognostic Factors in Breast Cancer; Tenovus Symposium, 1st, Cardiff, Wales, 1967, Forrest APM, Kunkler PB, eds, Baltimore, Williams & Wilkins, 1968.

Superradical mastectomy vs. simple mastectomy and radiation.

Number of patients = 425—randomized.

Duration of follow-up = 10 years.

Conclusion = no difference; 42% were free of recurrence in both groups.

3. Brinkley D, Haybittle JL: Treatment of stage-II carcinoma of the female breast. *Lancet* **2**: 1086-1087, 1971.

Simple mastectomy and radiation vs. radical mastectomy and radiation.

Number of patients = 204—randomized.

Duration of follow-up = 5 to 12 years.

Conclusion = no difference in survival. Trial concluded because of increased morbidity in radical group.

4. Burn JI: Early breast cancer; the Hammersmith trial. *Br J Surg* **61**: 762-765, 1974.

Simple mastectomy and radiation vs. radical mastectomy and radiation.

Number of patients = 195—ran-

- domized.
Duration of follow-up = 4 to 9 years.
Conclusion = no difference in survival or local recurrence.
5. Hamilton T, Langlands AO, Prescott RJ: The treatment of operable cancer of the breast; a clinical trial in the South-East Region of Scotland Trial. *Br J Surg* **61**: 758-761, 1974.
Radical mastectomy vs. simple mastectomy and radiation.
Number of patients = 394—randomized.
Duration of follow-up = 5 years.
Conclusion = “There is no significant difference in survival.”
 6. Murray JG: Cancer research campaign breast study. *Br J Surg* **61**: 772-774, 1974.
Clinical stages I and II.
Simple mastectomy alone vs. simple mastectomy and radiation.
Four months after simple mastectomy persistent nodes could be treated.
Number of patients = 2000—randomized.
Duration of follow-up = 4 years.
Conclusion = “A larger number of people die within 3 years or have distant metastases in the irradiated group than in the watch policy group.”
 7. Wise L., Mason AY, Ackerman LV: Local excision and irradiation; an alternative method for the treatment of early mammary cancer. *Ann Surg* **174**: 393-401, 1971.
Radical mastectomy with or without radiation vs. partial mastectomy with or without radiation.
Number of patients = 186—retrospective match.
Duration of follow-up = 10 years.
Conclusion = no significant difference in survival.
 8. Peters V: Cutting the gordian knot in early breast cancer. *Ann R Coll Phys Surg, Canada*, pp 186-192, 1975.
Radical mastectomy and radiation vs. local excision and radiation.
Number of patients = 434—retrospective match.
Duration of follow-up = 10 years.
Conclusion = no difference in survival.
 9. Hayward J: Conservative surgery in the treatment of early breast cancer. *Br J Surg* **61**: 770-771, 1974.
Radical mastectomy and irradiation vs. wide local excision and irradiation.
Number of patients = 370—randomized.
Duration of follow-up = 5 to 10 years.
Conclusion = “Wide excision with conservation of the breast must be considered a safe alternative to mastectomy in the treatment of patients with clinical stage I breast cancer.”
 10. Crile G Jr: Results of conservative treatment of breast cancer at 10 and 15 years. *Ann Surg* **181**: 26-30, 1975.
Partial mastectomy with or without irradiation vs. total mastectomy with or without axillary dissection and radiation.
Number of patients = 84—retrospective match.
Duration of follow-up = 10 years.
Conclusion = conservative and radical operations give the same rate of survival at 10 and at 15 years.

References

1. Bonadonna G, Brusamolino E, Valagussa P, et al: Combination chemotherapy as an adjuvant treatment in operable breast cancer. *N Engl J Med* **294**: 405-410, 1976.
2. Crile G Jr: Possible role of uninvolved regional nodes in preventing metastasis from breast cancer. *Cancer* **24**: 1283-1285, 1969.
3. Stjernswärd J: Decreased survival related to irradiation postoperatively in early operable breast cancer. *Lancet* **2**: 1285-1286, 1974.