

## APPENDIX B: EVIDENCE ON SELECTED TREATMENTS FOR BREAST CANCER

### Extended Radical Mastectomy

Extended radical mastectomy is the most extensive surgery used in the primary treatment of cancer of the breast. The rationale behind this technique is to eliminate the cancer and stop its spreading by removing all of the lymphatic drainage pathways in the breast region. Halsted noted the existence of malignant metastasis to the chest wall and breast bone via the chain of internal mammary nodes under the sternum, but soon abandoned the resection of the supraclavicular nodes because the “procedure did not improve upon long-term survival rates” (29).

Sampson Handley of the Middlesex Hospital in London further researched Halsted’s comments on the role of the internal mammary nodes and began to report the resection of this chain of nodes (32). Finding that the internal mammary nodes were not uncommonly involved in the spread of cancer, Handley devised an operation to remove them as well as the axillary nodes. The procedure did not improve mortality rates and was soon discontinued.

After World War II, the extended radical mastectomy was again pursued. Dr. Jerome Urban of Memorial Hospital in New York (51) and Drs. Andreassen, Dahl-Iverson, and Sorenson of Copenhagen (3) began to perform and report upon results obtained by the extended radical. Andreassen and his associates ran four series of trials. In the first series, involving 98 patients, the supraclavicular as well as axillary nodes were removed. None of the 98 patients manifested clinically palpable supraclavicular nodes, but microscopic metastasis was present in these glands in 17 patients (33 percent). All 17 patients were clinical stage II cases. In the second series of the study, involving 53 patients, the internal mammary nodes were removed along with the axillary glands. Of 53 patients, 24 percent of those with metastasis in the axillary nodes were found to have microscopic metastasis in the internal mammary glands. In the third and fourth series (1951 and 1952), the axillary glands, supraclavicular and internal mammary nodes were removed. The third series of 76 patients showed the internal mammary nodes to be involved twice as often as in the second series, but this difference was due in part to an alteration in operative techniques. In all the series, there were no cases of supraclavicular node involvement without axillary node involvement. After retrospective analysis, Dahl-Iverson abandoned the extended radical mastectomy in 1957. Its results, in his view, were not superior to those of the standard radical mastectomy (3).

Caceres and Urban (10,50,52) also noted the high incidence of cancer metastasis to the internal mammary nodes. In a large retrospective nonrandomized study, Caceres compared results from the radical mastectomy v. the supradical mastectomy. The latter consists of a radical mastectomy combined with en bloc extrapleural resection of the internal mammary chain together with the overlying chest wall; the supraclavicular nodes, however, are not excised. The results of this study are shown in table B-1. The difference in survival rates between the two groups was not considered statistically significant.

In 1952, Urban and Baker (53) published the results of including the en bloc resection of the internal mammary lymph nodes, while performing the standard radical mastectomy on women manifesting invasive breast carcinomas located in the central and medial quadrants of the breast. They followed the long-term progress of these women, reporting that “as compared with results following radical mastectomy the patients had fewer local recurrences, longer survivals and approximately the same morbidity and mortality.”

Urban’s data are used as a guideline at Memorial Hospital in New York for the treatment of patients with circumareolar and inner quadrant lesions. The extended radical is recommended for these patients, providing their ages are not too advanced and there are no other medical contraindications. Adjuvant prophylactic radiation therapy is prescribed when there is extensive nodal involvement. Patients manifesting noninvasive lesions, histologically low-grade invasive carcinoma, lesions less than 1 cm in diameter with a negative internal mammary node biopsy are subject to radical or modified radical mastectomies and subsequent radiotherapy when indicated.

The extended radical mastectomy is considered by some surgeons to be a massive and disabling operation. According to Dr. Oliver Cope, it has now been largely abandoned by most surgeons because of the morbidity associated with it and because its results seem no better than those obtained by the standard Halsted procedure.

### Modified Radical Mastectomy

Until very recently, radical mastectomy was considered the treatment of choice for patients with breast cancer. Over the last several years, however, the trend has shifted and the modified radical is now the favored procedure. In 1971, a poll of New Jersey

**Table B-1.—Survival Rates by Type of Operation: Radical v. Extended Radical Mastectomy: 5. and 10-Year Survival**

Type of operation	5-year survival			1 0-year survival		
	Patients	Survivors	Percentage of patients surviving	Patients	Survivors	Percentage of patients surviving
<i>Without axillary metastasis</i>						
Radical mastectomy. . . . .	43	32	74.4%	43	28	65.17.
Extended radical mastectomy.	184	153	83.1	52	35	67.3
<i>With axillary metastasis</i>						
Radical mastectomy. . . . .	70	33	47.1	70	22	31.4
Extended radical mastectomy.	241	106	44	77	19	24.7
<i>Total</i>						
Radical mastectomy. . . . .	113	65	57.6	113	50	44.2
Extended radical mastectomy.	425	259	60.9	129	54	41.8

SOURCE, E Caceres, "Incidence in the Internal Mammary Chain in Operable Cancer of the Breast," *Surg Gynecol Obstet* 108(6) 715, 1959

surgeons showed that 83 percent preferred the radical mastectomy and only 15 percent performed modified radicals. In 1977, a similar survey showed only 37 percent of surgeons performing the radical procedure and 60 percent favoring the modified operation. It is estimated that today the figure for the radical procedure has dropped to 15 percent (14).

A 1974 survey of breast surgeons in Pennsylvania showed less than half the procedures were radical. A similar 1978 survey would probably show less than 25 percent were radical (17). Tables B-2 and B-3 report types of surgery from the American College of Surgeons' review of breast cancer treatment (2).

The modified radical mastectomy removes all of the breast tissue, its overlying skin, and the contents of the axilla nodes. In a procedure designed by Patey in the 1930's to reduce cosmetic deformity, the pectoralis minor muscle is removed, but the pectoralis major is left intact. Auchinchloss devised a variation of the surgery that preserves both muscles (17). The modified radical is less debilitating than the radical because there is less chance of impaired arm movement and postoperative edema of the arm.

At the Long Island Jewish/Hillside Medical Center in New York City, most of the staff and attending surgeons have begun to perform the modified radical nearly twice as frequently as the traditional Halsted procedure. One surgeon affiliated with the Community Health Program at the Medical Center states (49):

I believe breast cancer to be multi-focal and feel it absolutely essential to view the axillary nodes before I begin the operation [ think best for the patient, In general, I prefer the modified radical mastectomy, to the radical procedure, but will do a radical if called for by medical or anatomical considerations.

**Table B-2.— Distribution of 15,132 Cases of Breast Cancer Diagnosed in 1972, by Type of Surgery**

Type of surgery	Percentage of cases
None . . . . .	5.4%
Wedge excision (lumpectomy, tylectomy). . . . .	3.4
Total (simple) mastectomy . . . . .	11.5
Total mastectomy with axillary dissection . . . . .	6.4
Modified radical mastectomy . . . . .	26.2
Radical (Halsted) mastectomy . . . . .	45.3
Radical mastectomy with internal mammary node biopsy . . . . .	1.5
Super (extended) radical mastectomy . . . . .	0.3
<b>Total. . . . .</b>	<b>100%</b>

SOURCE: American College of Surgeons, Commission on Cancer, "Final Report. Long-Term Patient Care Evaluation Study for Carcinoma of the Female Breast" (mimeo) (Chicago ACS, Feb. 21, 1979)

According to Dr. Leslie Wise (55):

The two arguments usually given against modified radical mastectomy are that it does not provide adequate access to resection of the axillary lymph nodes and that the pectoral lymphatics are not removed. If the arm is lifted so that the forearm lies in front of and parallel to the chest, then the pectoralis major is relaxed and can be retracted to expose the pectoralis minor, which may be divided; under these conditions the upper reaches of the axilla come in full view. There is supportive evidence that removal of the pectoralis major and the interpectoral nodes is unlikely to be of value unless the internal mammary nodes are also removed.

Although there have been few clinical trials testing the efficacy of the modified radical mastectomy, a series run by Handley gave results which seem to be comparable to those published for radical mastectomy.

Table B-3.—Distribution of 24,136 Cases of Breast Cancer, by Stage of Cancer\* and Type of Surgery, 1950-72

Type of surgery	In situ (N= 462)	Localized (N= 11,845)	Regional (N= 10,040)	Distant (N= 1,626)
None . . . . .	2.2%	1.60/0	3.5%	42.90/.
Wedge excision . . . . .	12.6	3.3	1.3	8.5
Total (simple) mastectomy.....	32.5	14.1	5.8	19.9
Total mastectomy with low axillary dissection.	9.1	5.8	5.5	4.4
Modified radical mastectomy, . . . . .	20.1	24.3	26.1	9.9
Radical (Halsted) mastectomy . . . . .	23.2	49.3	54.5	12.4
Radical mastectomy with Internal mammary n o d e b i o p s y	0.4	1.4	2.0	1.6
Super (extended) radical mastectomy. . . . .	0.0	0.2	0.2	0.4
Total . . . . .	100/0	100%	1000/0	100%

\*163 cases stage not known

SOURCE American College of Surgeons Commission on Cancer Final Report Long Term Patient Care Evaluation Study for Carcinoma of the Female Breast\* (mimeo)(Chicago HI ACS Feb 21 1979)

## Simple or Total Mastectomy

The simple or total mastectomy is considered one of the "lesser" surgical procedures used to treat breast cancer. The simple mastectomy was the first operation used in clinical trials to test the efficacy of the radical mastectomy against a less extensive surgical technique. It was also the procedure used in trials featuring comparisons between radical surgery and combination forms of treatment—usually total mastectomy plus radiation.

During a simple mastectomy, only the breast tissue and overlying skin are removed. The chest remains intact as does the axilla. The surgery is often accompanied by adjuvant radiotherapy. Unlike a radical mastectomy, a simple mastectomy leaves no cosmetic deformity of the chest wall.

In 1948, Dr. Robert McWhirter of Scotland began performing simple mastectomies followed by radiation therapy at Edinburgh's Royal Infirmary (45). McWhirter's results after 5- and 10-year studies were no worse and no better than results following radical mastectomy (44). A similar study was carried out in Finland by Professor Mustakallio (45). About 30 years ago, Mustakallio began removing only the breast and irradiating suspicious lymph nodes in order to destroy any remaining cancer. In some cases when the lesion was tiny, he removed only the tumor itself. His reports also showed results comparable to those obtained by radical mastectomy (45).

Two fairly recent prospective clinical trials utilizing simple mastectomy are also available for study. Brinkley and Haybittle (5) compared the results of simple mastectomy plus radiation and radical mastectomy with radiotherapy for clinical stage II (axillary node involvement) cases of breast cancer. The patients were randomly allocated to a particular treatment group; 113 received simple mastectomies

and 91 had radicals. In many cases, the simple mastectomy involved removal of accessible axillary nodes, but there was no formal en bloc dissection of the axilla. Results suggest that patients with simple mastectomies did slightly better than patients with radicals in a 6-year recurrence-free followup. In 1971, the two groups were again reviewed. At this point, all patients had been followed for at least 5 years and some for 12 years. There was no significant difference in survival rates between the groups (radical, 49.2 percent; simple, 46.4 percent). An increased incidence of edema of the arm was noted in the radical mastectomy patients (5,6,55).

From 1951 to 1957, a prospective clinical trial was carried out in Copenhagen by Kaae and Johansen (37). The results of extended radical mastectomy (removal of the breast, chest muscles, axillary, supraclavicular, and internal mammary nodes) without postoperative radiation were compared with simple mastectomy with postoperative radiation. A group of 335 patients were randomly selected for extended radical mastectomy and 331 patients for simple mastectomy plus radiation therapy. For a variety of reasons, not all of the patients were included in the results. The 5-year study includes only 206 patients from the extended radical group and 209 from the simple mastectomy. The overall survival and recurrence rates at 5- and 10-year intervals were similar with both treatments.

Dr. George Crile, Jr., of the Cleveland Clinic, an early advocate of simple mastectomy (1957), has studied comparative, but not randomized, groups of simple mastectomies and radicals (15). His results showed that in clinical stage I cases, simple mastectomy, and, if necessary, later therapeutic axillary dissection, was as good as initial treatment with the radical mastectomy. The 5-year survival rates for radical mastectomy with or without radiotherapy

were 71 percent; for simple mastectomy without radiotherapy, 82 percent; and for simple mastectomy with radiotherapy, 73 percent.

Although a number of clinical trials have suggested that the combination of simple mastectomy and post-operative radiation therapy is as effective as radical mastectomy in most cases, critics of the simple procedure cite the Haagensen and Miller study (27) as evidence against it. All patients included in that trial had cancers defined as Columbia clinical classification stage A lesions. The 10-year survival rate for the radical mastectomy group was **70.2** percent, while that for simple mastectomy patients was 39 percent. Dr. Leslie Wise points out that one element often disregarded in the presentation of this study is the fact that the radical mastectomy group came from Haagensen's series at New York's Columbia-Presbyterian Hospital, whereas the simple mastectomy patients were treated in Detroit by Kennedy at a much earlier period when cancers were much larger (55). The two groups were completely unmatched.

### Local Excision, Lumpectomy, Tylectomy

A local excision or lumpectomy involves the removal of the cancerous tumor and a margin of healthy tissue surrounding it (36). As early as 1943, F. E. Adair experimented with local excision, reporting on **63** cases of operable breast cancer treated in this way. In seven patients, only the lumpectomy was performed; of this group, six patients survived 5 years. Preoperative radiotherapy followed by excision of the tumor was used in **27** cases. These patients had a 70-percent 5-year survival rate. There was no mention of clinical staging of the disease in this study (55).

A further inquiry into the efficacy of local excision was made in Helsinki by Professor Mustakallio. In 1954, he published the results of a study involving 127 patients with clinical stage I cancer who were treated by lumpectomy and postoperative radiation to the remaining breast (45). The results compared favorably with those treated by radical mastectomy: 84 percent survived 5 years, and 72 percent survived 10 years. These results were backed up by F. Baclesse in Paris, who, like Mustakallio, began to treat women refusing mastectomy by local excision and irradiation. Baclesse began his study of 100 patients in 1940 and reported on the work in 1960 showing comparable results to the Helsinki study (13). By 1958, J. G. DeWinter, of Brighton, England, had also reported on a smaller series of patients treated by lumpectomy. In a 1961 publication, DeWinter stated that local excision and radiotherapy in an unselected

group offered, "a reasonable alternative to the standard operation," that is, radical mastectomy (55).

In 1963, Sir Arthur Porritt presented the results of a series of 265 patients with operable breast cancer who were randomly selected to undergo radical mastectomy with radiation therapy (156 cases) or local excision plus irradiation (107 cases). The **5- and 10-**year survival rates were respectively: radical mastectomy, 50 and 34 percent; local excision, 65 and 45 percent. According to Dr. Leslie Wise, these data suggest that the lesser operation is at least as effective as the radical procedure (55).

Dr. George Crile, Jr., reported several series of trials with local excision. In one series reported in 1965, 20 patients who received local excisions achieved a 65-percent survival rate that was comparable to that obtained by more extensive procedures. In that series, 12 patients had stage I tumors and 8 had stage II cancers. Crile reported on an additional 24 patients treated by local excision in 1967. In that group, the 5-year survival rate was 67 percent. Crile and Hoerr published the results of local excision on 55 patients in 1977. The patients, 40 of whom had clinical stage I cancers and 15 of whom had stage II lesions, were treated from 1955 to 1964. Thirty-one of the patients with stage I cancers were treated by local excision alone; 6 patients had axillary dissections as well as lumpectomy (local excision); and 3 had postoperative C. teletherapy. Of the stage II cases, 4 patients had axillary dissections and 11 had postsurgical C. teletherapy. The 5-year survival rate for the entire group was 67 percent. There was an 11-percent incidence of local recurrence.

In 1971, Vera Peters of Toronto reported another similar trial. Treated by local excision and irradiation, her patients showed 5- and 10-year survival rates of 76 and 45 percent (55). These results were similar to those of her radical mastectomy series. Taylor and his associates from Great Britain also reported on a group of 77 patients manifesting stage I and II cancers. Seventy-seven patients were treated by local excision and radiotherapy. The 5- and 10-year survival rates were 71 and 50 percent. The incidence of local recurrence or the appearance of a new cancer which was treated by simple mastectomy was 18 percent (55).

Drs. Leslie Wise, Aubrey York Mason, and Lauren V. Ackerman conducted a comparative retrospective survey of 96 patients treated by local excision followed by radiotherapy on a 1,500 Curie telecesium unit and 207 patients treated by radical mastectomy with or without radiation therapy, depending on the histologic status of the axillary nodes (54). That study was carried out between 1950 and 1964 at St. Helier's Hospital in London. Only patients with stage

I and stage II breast cancer, designated according to the Manchester Plan, a clinical method of rating the progression of the disease, were included in the study. All of the patients were women. The age range of patients was 25 to 90 years, and the age distribution between the two groups was statistically similar. There was no statistically significant difference in the distribution of the local excision and radical mastectomy cases as to the size of the tumor. The 5- and 10-year survival rates by stage were, respectively: stage I, local excision-96 percent and 68 percent; stage I, radical mastectomy-81 percent and 69 percent; stage II, local excision —74 and 53 percent; stage II, radical mastectomy —70 and 59 percent.

The Wise, Mason, and Ackerman study was the first published attempt to critically compare the results from a group of local excisions of mammary carcinoma with radical mastectomies. According to Dr. Wise, the mode of treatment apparently did not significantly alter the overall prognosis. There was no significant difference between the survival rates of the two groups, a finding **which suggests that local excision with moderate irradiation** may be a suitable alternative to radical surgery for early, operable breast cancers. Dr. Wise plans to run a 15-year followup on the patients involved in the trial.

The results of a prospective, randomized trial for stage I and II breast cancers were reported in 1972 by Atkins, Hayward, Klugman, and Wayte. A total of 370 patients, all aged 50 years and over, participated in the trial, which was carried out between 1961 and 1971. One group of 188 patients was treated by radical mastectomy, and another group of 182 patients received lumpectomy and postoperative radiation. There was no significant difference in overall sur-

vival rates between the two groups at any time up to 10 years after surgical intervention.

The arguments against local excision are varied. Some say that lumpectomy is an inadequate cancer operation, partly because the tumor and its draining lymph nodes are not removed en bloc. Proponents of the procedure argue that if this criterion is applied, then radical mastectomy is not adequate either, because only the axillary nodes are resected. Two other drainage pathways are left intact: the supraclavicular and internal mammary nodes.

Another argument used against local excision is that some breast cancers are multicentric and therefore local recurrence rates will be much higher with lumpectomies than mastectomies. Dr. Guy Robbins, of the Memorial Sloan-Kettering Hospital in New York, stresses this point as one that completely invalidates the use of such limited surgery (47). Advocates of local excision counter by pointing out that there are no facts that support the assertion.

A third argument against lumpectomy is that any breast in which a cancer has developed is likely to be the location of a second tumor; thus, local excision would leave the patient with the possibility of a second breast malignancy. Supporters of lumpectomy argue in response to this that a breast cancer patient has a 7-percent chance of developing a contralateral cancer in her lifetime. Supposedly, this applies to the remaining breast, but if that breast is irradiated, the chance of a second cancer may be less. If concern over the 7-percent possibility of recurrence was so great, **then according to the argument every breast cancer patient should have a prophylactic total mastectomy** on the opposite side (54).