

Simplified Treatment of Cancer of the Breast: *

Early Results of a Clinical Study

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I. Introduction

THERE is mounting evidence that conventional radical operations combined with radiation increase the morbidity of patients with breast cancer without increasing their survival rate above that of simpler treatments. Paterson and Russell's⁷ double blind study in Manchester showed that radiation after radical mastectomy had no effect on survival or local recurrence rates of patients whose axillary nodes were involved, and it seemed actually to diminish the survival rate of patients whose nodes were not involved. Smith and Meyer,⁹ and Williams, Murley and Curwen¹⁰ have shown that the survival rate of patients treated by simple mastectomy is similar to that following radical operations or may be slightly higher. The blind study of Kaae and Johansen⁸ shows no difference in the three- and five-year survival rates of patients treated by ultraradical mastectomy with internal mammary and supraclavicular node dissection, and patients treated by simple mastectomy and radiation. Finally, Mustakallio⁶ has shown that in 127 patients local excision of small cancers followed by radiation therapy resulted in an 84 per cent rate of survival at five years and 72 per cent at ten years.

The results of the following study suggest that in favorable stages of breast cancer the early (3 to 6 years) results of treat-

ment are just as good following simple operations with radiation used in only one-fourth of the cases as they are following more radical operations with radiation used in one-half of the cases. In clinical stage I cases, it is even possible that there is a slightly higher survival rate in patients treated by simple operations, usually without radiation, as compared with radical ones, with or without radiation. If such a difference actually exists, it is further evidence that in certain types of systemically metastasizing cancer we must pay less attention to the possible involvement of lymph nodes by tumor and more to the possible immunologic role of the lymphocytes in the nodes as a defense against the cancer cells that are circulating in the blood.

II. Materials and Methods

A. Plan of Study

In January, 1955, I decided to use simple mastectomy, usually without radiation therapy, as the standard treatment of most patients with cancers that had no clinical evidence of cancer beyond the breast. At the same time my colleagues in the Cleveland Clinic, who together did approximately the same number of breast operations as I did, continued in most cases to do the conventional radical operations and often added postoperative radiation. The stages of the disease, the size of the tumors, and the ages of the patients were similar in the simple mastectomy and the radical

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mastectomy series. Despite this, as will be seen later, factors of selection still were present and occasionally made it difficult to compare results.

B. Selection of Cases

The series of cases here reported includes all patients with previously untreated cancer of the breast seen in all departments of the Cleveland Clinic in the five-year period, 1953 to 1957 inclusive. All presently living patients have had the diagnosis histologically confirmed. Among these there were several patients who had intraductal cancer without invasion. Because this special type of cancer usually is included in reports of survival, we have included them in our over all survival figures. All types except invasive cancer have been eliminated from the tables in which the results of simple and radical operations are compared. Also eliminated from these tables but included in the over all figures are senile patients to whom no surgical treatment was given.

C. Plan of Clinical Staging

In the 1955, 1956, and 1957 series, the patients were staged before operation by the surgeon in charge and at least one other. The clinical stage assigned before operation was not changed regardless of the operative findings or the pathologist's report. The 1953 and 1954 cases were staged retrospectively on the basis of the physical examination recorded in the chart and without reference to the pathology report.

D. Definitions

Clinical Stage 1. Disease apparently limited to the breast—no apparent involvement of axillary nodes. Tumor not fixed to chest wall; no satellite skin nodules. No striking edema.

Clinical Stage 2. Same as clinical Stage 1 except axillary nodes appear to be involved. Nodes not fixed.

Clinical Stage 3. Axillary nodes are fixed, or supraclavicular nodes are involved; tumor is fixed to chest wall or has satellite metastases to skin of chest wall, or there is striking inflammatory type edema.

Clinical Stage 4. Distant metastasis demonstrable.

E. Method of Staging

In this study patients were considered to be in Stage 1 unless there were enlarged firm nodes dissimilar to the nodes on the unaffected side. As a result only two per cent of the clinical Stage 2 cases subjected to radical mastectomy were found by the pathologist to have no involvement of the axillary nodes.

Usually there was agreement among the various examiners as to the staging of Group 1. Since several examiners including the surgeon in charge examined the majority of these patients before the decision as to treatment was made, and since the staging was not changed regardless of the operative findings, the cases in Stage 1 were uniformly and objectively selected. In 32 per cent of the clinical Stage 1 cases in which no nodes were palpable and radical mastectomy was done, the nodes were found by the pathologist to be involved. In 22 per cent of the clinical Stage 1 cases treated by simple mastectomy without radiation, involvement of nodes later became apparent.

Although it was easy to agree on Stage 1, clear agreement as to the stage could not always be obtained between advanced Stages 2 and 3. Here it was difficult to decide whether tumors or their regional nodes were or were not "fixed" and even whether the supraclavicular nodes were or were not involved. But since there are approximately the same proportions of Stage 3 cases in the series of each surgeon, and since the survival rates of the Stage 3 cases in each of the surgeon's series are the same, the staging probably was similar.

The separation of Stage 4 cases presented no difficulty.

III. Type of Treatment

A. Simple Mastectomy Series

1. *Clinical Stage 1 (Simple Mastectomy Series)*. In the simple mastectomy series most of the patients with Stage 1 cancer (apparently limited to the breast) were treated by simple mastectomy. In selected Stage 1 cases with very small and peripheral lesions nothing but a wide quadrant excision or a hemimastectomy was done (13%). Occasionally a few of the low axillary nodes were removed with the axillary tail of the breast, but no formal axillary dissections were done. The flaps were made short and thick, and all wounds were closed primarily without grafting. Cobalt-60 teletherapy* was given after operation in only 25 per cent of the Stage 1 cases.

Since most of the patients with breast cancer came from Cleveland or nearby areas, it was possible to re-examine most of them at intervals of from three to six months. In those patients in whom involvement of axillary nodes later became apparent the axillary nodes were removed without sacrifice of muscles. In a few of these patients, when the involvement was extensive, radiation therapy was added.

Prophylactic endocrine therapy or oophorectomy was not used in any Stages 1 or 2 cases. It is important to note that the treatment in this series is not comparable with that of McWhirter's,⁵ for radiation therapy was not given prophylactically in most of the Stage 1 cases.

2. *Clinical Stage 2 (Simple Mastectomy Series)*. When operable axillary involvement was diagnosed preoperatively, treatment was by simple mastectomy followed by cobalt-60 teletherapy.

3. *Clinical Stage 3*. In the locally advanced group that is conventionally considered inoperable, treatment was usually by cobalt-60 teletherapy. Occasionally simple mastectomy and radiation were used with or without endocrine, endocrine-ablational, or chemotherapy. When operation was not done, the diagnosis often was confirmed by needle biopsy.

4. *Clinical Stage 4*. When distant metastasis was evident, treatment was by combinations of endocrine-ablational, radiation, and chemotherapy. The diagnosis again was often confirmed by needle biopsy.

B. Radical Mastectomy Series

1. *Clinical Stage 1 (Radical Mastectomy Series)*. In the 1953 and 1954 series, three-fourths of the radical mastectomies for Stage 1 cancer were of conventional type with thin skin flaps and sometimes with grafting. The other operations were modified radicals with preservation of the muscles. Two hundred and fifty kv. radiation therapy was given after operation in one-half of the cases, some surgeons selecting patients for radiation and others radiating routinely.

In the Clinical Stage 1 cases of the 1955, 1956, and 1957 series, nearly three-quarters of the radical mastectomies were of the modified type with preservation of muscles. Radiation therapy was given in less than one-half of the cases.

2. *Clinical Stage 2 (Radical Mastectomy Series)*. In the clinical Stage 2 cases of the 1953 and 1954 radical mastectomy series, almost all the operations were of the conventional type and nearly one-half of the patients were radiated after operation.

In the clinical Stage 2 cases of the 1955 through 1957 series, less than one-half of the radical operations were conventional and less than one-half of the patients were radiated after operation.

* Radioactive material obtained on authorization of the United States Atomic Energy Commission.

TABLE 1A. *Clinical Staging*

Clinical Stage	No. Cases	1953 and 1954	No. Cases	1955-1957	No. Cases	1957 Only
1	69	65.1%	103	56.3%	44	58.6%
2	22	20.8%	35	19.1%	12	16.0%
3	8	7.5%	31	16.9%	14	18.7%
4	7	6.6%	14	7.7%	5	6.7%
Totals	106	100%	183	100%	75	100%

IV. Follow Up

In the years 1953 and 1954, before the change in treatment was begun, four per cent of the patients could not be traced for three years. In the group from 1955 through 1957, all patients operated on in 1957 have been followed for three years, all in 1956 for four years, and all in 1955 for five years. Most of the patients have been re-examined periodically at the Cleveland Clinic. They were not considered to have reappearance of cancer unless there was objective evidence of disease. All patients who died are assumed to have died of cancer. There were no deaths attributable either to operation or to radiation therapy.

V. Results

A. Comparison of Crude Survival Rates in Various Periods: a) 1953 Through 1954, b) 1955 Through 1957, and c) 1957 Alone

The crude survival rate is the survival rate of all previously untreated patients in all stages of the disease, regardless of whether they were treated or not and regardless of how they were treated. Crude survival rates reflect not only differences in survival that may occur as a result of differences in treatment, but also differences in the stages of the disease in which the patients were first seen. Unless the stages of the disease are the same from year to year, the crude survival rates do not accurately reflect the success or failure of treatment.

In the 1955 through 1957 series, there was a striking increase in incidence of inoperable Stages 3 and 4 cancers as compared with the 1953 and 1954 series. In

TABLE 1B. *Proportion of Cases in Which Each Type of Treatment was Employed (Clinical Staging)*

Treatment	1953 and 1954 % in Which Employed	1955, 1956 and 1957 % in Which Employed	1957 Only % in Which Employed
Radical mastectomy in Stage 1 and 2	87%	45%*	34%**
Simple mastectomy in Stage 1 and 2	13%	54%	64%
Radiation postoperative in Stage 1 and 2	45%	41%	39%
Proportion of radical operations that were modified by not re- moving muscles	24%	65%	85%

* 1 patient had no treatment.
** 2 patients had radiation only.

TABLE 1C. *Crude Survival*

Crude Survival (All Cases, All Stages)	1953 and 1954	1955, 1956 and 1957	1957 Only
Survival 3 years all cases, all stages	60% to 64% (4 untraced)	58%	65%
Survival, 5 years	56% to 60%	Insufficient time	Insufficient time
Survival, 5 years operable patients Stage 1 and 2 only	65% to 70%	Insufficient time	Insufficient time

TABLE 2. *Survival in Clinical Stage 1*

Treatment	1953 and 1954 (69 Cases)	1955, 1956, and 1957 (103 Cases)	1957 only (44 Cases)
Proportion treated by simple mastectomy	16%	54%	69%
Proportion of radical operations modified by not removing muscles	24%	55%	89%
Radiation after operation	45%	34%	36%
Survival, absolute 3 years	71% to 77% (4 untraced)	76%	77%

1955, I wrote an article on the overtreatment of cancer that was published in the lay press. This and the introduction of the first cobalt-60 teletherapy unit in the Cleveland area resulted in a striking increase in the proportion of patients with advanced breast cancer who came to the Cleveland Clinic. In 1953 and 1954, only 14 per cent of all cases were staged as inoperable Stages 3 and 4, whereas in 1955, 1956, and 1957, 25 per cent were inoperable. Despite this increase of 11 per cent in the inoperable patients (over 80% of whom were dead at 3 years) and despite a striking simplification of the treatments given in the latter years, the crude three-year survival rate in the 1955 through 1957 series was 58 per cent as compared with 60 to 64 per cent in the 1953 and 1954 series. In 1957, when the treatment was still further simplified, the survival rate was higher than in either of the preceding periods (65%). The stages of the disease, the treatments given in each of the three periods, and the three-year survival rates are recorded in Tables 1A, 1B, and 1C.*

Although the fall in the three-year survival rates between the 1953 through 1954 and the 1955 through 1957 periods are explained on the basis of the increase in advanced cancers seen in the latter period, the high survival rate in 1957 cannot be explained on this basis. In 1957, there was a higher incidence of Stages 3 and 4 cancer than in either of the preceding periods, yet the survival rate was the highest of any period. In 1957 also, there was the highest incidence of simple operations and the lowest incidence of radiation therapy. Although the number of cases involved is few, it is clear that simplification of treatment did not result in any decrease in the 3-year crude survival rate.

B. Comparison of Absolute Survival Rates by Stage in the Various Periods 1953 Through 1954, 1955 Through 1957, and 1957

1. Survival Rates, Stage 1. If the staging of cancer is carried out in the same way in two or more groups of patients, the survival rates within each stage should reflect

* If we assume that the increase in survival rate from zero per cent in Stages 3 and 4 in 1953 and 1954, to 20 per cent in 1955 through 1957 was the result of better endocrine treatment, then 3 additional patients (20% of the 15 from Stages 3 and 4 in 1953 and 1954) might have survived if modern therapy had been available in 1953 and 1954. On the other hand, there were 11 per cent more patients in Stages 3 and 4 in the 1955

through 1957 series, and 80 per cent of these died of their disease. If the incidence of Stages 3 and 4 had been the same in 1953 and 1954 as in 1955 through 1957, and if the survival rate of the Stages 3 and 4 patients had been the same in both periods, it can be calculated that the crude survival rate in the 1953 and 1954 series would have been 3 per cent lower than it is, that is, the same as that in the 1955 through 1957 series.

TABLE 3. *Survival in Clinical Stage 2. Comparison of 3-year Absolute Survival Rates in Period 1953 and 1954, Period 1955 Through 1957, and Period 1957 Correlated with Type of Treatment Given in Each Period (Stage 2 Cases Only).*

Treatment	1953 and 1954 (22 Cases)	1955, 1956 and 1957 (35 Cases)	1957 Only (12 Cases)
Proportion treated by radical mastectomy	95%	63%	50%
Proportion treated by simple mastectomy	5%	37%	50%
Survival, absolute 3 years	68% to 73% (1 untraced)	63%	83%

the success of the type of treatment that predominated in each group. For this reason, in Table 2 are listed the different types of treatments used for patients with Stage 1 cancer in the various time periods along with the survival rates that were observed in each period. It is clear that progressive simplifications of treatment did not result in any decrease in the rate of survival, in fact the highest survival rate was in the year in which the simplest treatments were given.

2. *Survival Rates, Stage 2.* The number of Stage 2 cases in each period is too small to be of any statistical significance (Table 3) and is of interest mainly to show that the staging between Stages 1 and 2 was similar in all periods. Thus, in the 1953 and 1954 series, 24 per cent of the Stages 1 and 2 cases were classified as 2's; from 1955 through 1957, 25 per cent were classified as 2's; and in the 1957 cases, 21 per cent were so classified. If there is any superiority of results in one period over another in Stage 2 it seems to lie in the years in which the greatest proportion of cases was treated with radical mastectomies.

Of the 45 inoperable (Stages 3, 4) patients in the 1955 through 1957 group, 82 per cent were dead in three years and only seven per cent were classified as well. All of the Stages 3 and 4 patients in the 1953 and 1954 group were dead in three years, but in this period fewer patients were treated by endocrine ablation.

3. *Survival Rate in Stages 1 and 2 Combined.* To make certain that the staging between Stages 1 and 2 has been similar in each year and has not given an apparent advantage to one method of treatment over another, the survival rates of all patients in Stages 1 and 2 combined have been calculated (Table 4). Despite the striking simplification of treatment, there is no significant difference in the survival rates, and the highest rate is in the period in which the highest proportion of simple operations was done.

C. Local Recurrences

In the 1953 and 1954 series, the patients were not as closely followed as they have been subsequently, and there are no adequate data either on the incidence of local recurrence or on the date of the first indication of recurrent disease. It is, therefore, impossible to compare recurrence rates between the earlier and the later series. In most of these cases all we know is the dates of the patients' deaths.

The local recurrence rate can be calculated in the 1955 through 1957 series, and in Stages 1 and 2 was 7.4 per cent of all cases, radical and simple (8 and 7%, respectively). Half of the recurrences were in patients who had received prophylactic radiation. In the 1957 series, there were only two local recurrences in 56 cases. These figures are based on a three-year follow up and include all recurrent cancer on

the chest wall or axilla up to the time of the patient's death, but do not include involvement of axillary nodes that developed following simple mastectomy and were eradicated by delayed axillary dissection. It is interesting that the incidence of local recurrence was lowest in the year in which the number of simple operations was highest.

There were no local recurrences in the ten patients in whom the tumor was excised locally and the breast not removed. Half of these patients were radiated prophylactically.

D. Comparison of Results—Radical Compared with Simple Mastectomy

1. The Danger of Comparing Results in Selected Cases. The world literature on the survival of patients with cancer is filled with claims of better results from changed methods of treatment, but few of these reports stand up under critical analysis. The trouble is that when better results are reported it is usually because of selections of more favorable cases for treatment. An example is the fact that, in the 1953 and 1954 series, the five-year survival rate of patients treated by simple mastectomy was only 50 per cent, while in 1957 it was 79 per cent. In 1953 and 1954, only 13 per cent of the operable patients had simple mastectomies and in 1957, 65 per cent had simple operations. The difference in the re-

sults was due to the type of case selected for simple mastectomy. Little confidence can be placed in the reports of the superiority of one type of operation as compared with another unless the selection of cases for each type of operation is part of a planned study and is determined by sheer chance.

Although I recognize the inaccuracies that may be involved in any study that is not conducted by the "blind" method, I have tried to evaluate our results in each stage according to the type of treatment that was given. As a check on the accuracy of the staging there are the crude survival rates in Table 2 that cannot be changed no matter how the cases are staged. As a further check, there are also the survival rates obtained by various surgeons, each of whose material is similar in staging to that of the others and will be presented.

2. Selection of Cases for Study and Definition of Treatments. In order to eliminate one of the factors of selection, senile or debilitated patients who had no surgical treatment and 7 patients with intraductal cancer were eliminated. All other patients in Stages 1 and 2 received surgical treatment, and all had invasive cancers. From this point on it is not crude survival rates but survival in the above defined group that is being reported.

Radical mastectomy is here understood to include modified radical procedures in

TABLE 4. Absolute Survival Rates of all Patients in Clinical Stages 1 and 2 Correlated with Proportion of Patients Treated by Simple Operations in Each Period

Treatment	1953 and 1954 (91 Cases)	1955, 1956 and 1957 (126 Cases)	1957 Only (56 Cases)
Proportion of patients treated by simple mastectomy in each period	12%	54%	73%
Absolute 3-year survival rates of all stages 1 and 2 patients whether treated by simple or radical means	70% to 75% (5 untraced)	72%	79%

TABLE 5. *Comparison of 3-year Survival After Simple and Radical Operations in Clinical Stage 1 in Period 1955 Through 1957 (Intraduct Cancer Excluded)*

Survival	Radical Operation (40 Cases)	Simple Operation (56 Cases)
3-year	75%	80%
3-year (free of disease)	63%	71%

Note: Cobalt-60 teletherapy was given to 45 per cent of the patients treated by radical operations and to only 25 per cent of those treated by simple ones.

which muscles were not sacrificed, but complete axillary dissections were done. Simple mastectomies include local excisions of small peripheral lesions and the occasional removal of a few low axillary nodes along with the axillary tail of the breast. When radiation was employed, it was given by cobalt-60 teletherapy to axilla, supraclavicular and internal mammary areas.

The average age of the patients treated by radical mastectomies was 55 and of those treated by simple operations, 57. The average size of the primary tumors was 2.7 cm. for the radical operations and 2.5 cm. for the simple ones.

3. Comparison of Survival Rates of Patients Treated by Radical as Compared with those Treated by Simple Operations in Each Operable Stage.

a. Stage 1. In the 1955 through 1957 series, there were 40 Stage 1 patients treated by radical mastectomy. The three-year survival rate was 75 per cent. At the same time 60 patients were treated by simple mastectomy. The three-year survival rate was 80 per cent (Table 5). Since the crude survival rate at three years may not be a good measure of the effectiveness of treatment, the survival rate free of disease was also calculated. In the radical series 63 per cent were well. In the simple series, 71 per cent were well (Table 5).

To compare the later results of radical and simple mastectomy, the five-year survival rate of patients treated in 1955 and

the four-year survival of those treated in 1956 were calculated and pooled, the follow up in these cases averaging four and one-half years. Fifty-nine per cent of the radical group survived as compared with 68 per cent of the simple (a slight gain in the advantage of the simples over that seen at 3 years—Table 6). At the average follow up of four and one-half years the advantage of the simples over the radicals is even more apparent if it is calculated on the basis of living without evidence of disease, for 52 per cent of the radicals were living and well as compared with 66 per cent of the simples (Table 6, Fig. 1).

Of the Stage 1 patients subjected to radical mastectomy, 45 per cent received cobalt-60 teletherapy as compared with 25 per cent of the simples.

b. Stage 2. In clinical Stage 2 there were 16 patients treated by radical mastectomy with a three-year survival rate of 44 per cent. Only seven patients were treated by simple mastectomy with two survivors. When the axilla was grossly involved, the surgeons placed more confidence in axillary dissection than in radiation. This preponderance of radicals in Stage 2 invalidates any comparison of the survival rates of simple and radical operations in all Stages 1 and 2 cases combined, but has no effect on the survival rates of the above reported pa-

TABLE 6. *Comparison of 4½-year Survival After Simple as Compared with Radical Operations in Clinical Stage 1—1955 and 1956 (Intraduct Cancer Excluded)*

Survival	Radical Operation (27 Cases)	Simple Operation (29 Cases)
5-year (all 1955 cases)	59%	69%
4-year (all 1956 cases; average is 4½ yr. survival)		
Same as above except all patients are free of disease	52%	66%

SURVIVAL CURVES... SIMPLE VS. RADICAL
0-5 years

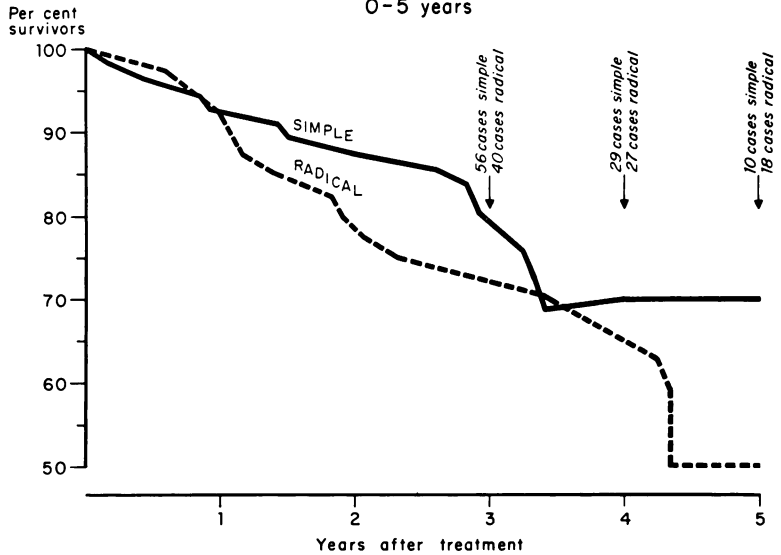


FIGURE 1.

tients who were preoperatively classified in Stage 1.

E. Survival Rates Obtained by Other Surgeons

Changes from year to year in the crude survival rates may reflect chiefly the yearly changes in the incidence of the various stages. Differences in survival rates after different methods of treatment may reflect chiefly the differences in the type of case selected for each type of treatment. But within each stage of the disease, the results obtained by two or more surgeons should reflect the success of the treatments that each employs.

1. Comparison of Results of Various Surgeons in Clinical Stage 1 Cases, 1955 through 1957.

Surgeon 1—Operated on 49 patients in Stage 1.

Seventy-eight per cent of his operations were simple mastectomies and 22 per cent were radicals. Only 18 per cent were radiated after operation. Eighty per cent survived three years. Sixty-nine per cent were free of disease (Table 7).

Surgeon 2—Operated on 23 patients in Stage 1.

Twenty-two per cent of his operations were simple and 78 per cent were radical. Forty-three per cent were radiated after operation. Seventy-four per cent lived three years. Fifty-seven per cent were free of disease.

Other surgeons—Operated on 24 patients in Stage 1.

Fifty-four per cent of their operations were simples and 46 per cent radicals. Sixty-two per cent were radiated after operation. Seventy-nine per cent survived three years. Sixty-six per cent were free of disease.

Although the number of cases is small for statistical significance, it is interesting that again the patients who had the least

TABLE 7. Comparison of Results Obtained by Various Surgeons Correlated with the Type of Treatment Each Gave—Clinical Stage 1 Cancer 1955 Through 1957

	Surgeon 1 (49 Cases)	Surgeon 2 (23 Cases)	Other Surgeons (24 Cases)
Proportion of radical operations	22%	78%	46%
Radiation	18%	43%	62%
3-year absolute survival	80%	74%	79%
3-year survival (free of disease)	69%	57%	66%

treatment whether by surgery or by radiation, had the highest rate of survival (Table 7).

2. Comparison of Results of Various Surgeons in Clinical Stage 2 Cases.

Clinical Stage 2 is such a small group that its survival rates are of little statistical significance. All they prove is that there apparently was no difference in the staging of the cases by the different surgeons.

Surgeon 1 did 38 per cent radicals with 62 per cent survivors. Surgeon 2 did 100 per cent radicals with 64 per cent survivors, and other surgeons did 63 per cent radicals with 63 per cent survivors.

F. Study of Patients Thought to Have No Axillary Involvement but Proved to Have Metastasis in Nodes

The most interesting feature of this study is the analysis of the clinical Stage 1 patients who were thought to have no involved nodes, but later proved to have involvement of axillary nodes. These cases can be divided in two groups: 1) those who had radical mastectomies, and the pathologist reported involved nodes; and 2) those who had simple mastectomies, and involvement of the nodes appeared later.

The patients in Group 1 were treated by immediate radical mastectomy. Four of the 13 patients were found to have only one node involved, and seven had three or less.

In Group 2 the time of reappearance of cancer in the axilla varied from one to 36 months after simple mastectomy, averaging 14. In all but two of ten patients in whom nodes later appeared, the nodes were removed by axillary dissection. In the other two patients, the involvement appeared early and was so diffuse that it seemed better to treat it by radiation. Despite an average delay of 14 months between mastectomy and axillary dissection or radiation, five of the ten patients in Group 2 had only one node involved; seven of the ten had three or less. It is interesting that the proportion

of cases with minimum involvement of axillary nodes was higher in the patients in whom there was an average delay of 14 months than in those who received prompt prophylactic treatment. Each of three patients in whom the delay was 18 months, 34 months, and 36 months, respectively, was found to have only one node involved. This suggests that in many cases of cancer of the breast there is little or no tendency for the tumor to metastasize from node to node for a long time after the primary tumor is removed.

The survival rate of the patients with delayed treatment of the axilla was similar to that of the patients treated by radical mastectomy. At three years, four of the 13 patients treated by radical mastectomy were well, four were living with disease and five were dead, whereas five of the ten in the delayed group were living and well, two were living with disease, and three were dead. The staging seems to be similar, because in the 1953 and 1954 series there were 12 patients staged as "1" who had involved nodes, and 71 per cent of these lived three years—compared with 62 per cent of the radicals and 70 per cent of the simples in the 1955 through 1957 series (Table 8). Despite the similarity of the three-year survival rate in both periods, the three-year survival rate free of disease in the 1955 through 1957 series in both the simple and the radical group was lower than in the 1953 through 1954 series.

Another interesting problem brought up by the study of the patients subjected to delayed axillary dissection is the effect of prophylactic radiation in preventing the appearance of axillary metastases. Sixteen Stage 1 patients were treated prophylactically by cobalt-60 teletherapy after simple mastectomy. In none of these has axillary metastasis appeared. Since 32 per cent of the Stage 1 patients treated by radical mastectomy were found to have nodes involved, five of the 16 patients treated by

simple mastectomy and cobalt-60 would be expected to have developed palpable involvement of axillary nodes if the radiation did not suppress the growth of the cancer.

Since 16 of the 60 Stage 1 patients treated by simple mastectomy were given prophylactic cobalt-60 teletherapy to the axilla, and since such therapy usually prevents the appearance of cancer in the axillary nodes,⁵ the incidence of cancer developing in axillary nodes after simple mastectomy should be calculated on the basis of the patients who had simple mastectomy without radiation. There were 44 such patients, and 10 of them later developed metastases in axillary nodes, an incidence of 22 per cent as compared with the 32 per cent incidence of pathologically positive nodes in the clinical Stage 1 patients treated by radical mastectomy. The three- to six-year period of observation may be too short to observe reappearance of cancer in all involved nodes. Nevertheless, the lower than expected incidence of cancer appearing in axillary nodes after simple mastectomy suggests that occasionally after the primary tumor is removed, cancer fails to grow progressively in minimally involved nodes (Table 8).

In view of these confusing considerations all that can be said is that up to three years' delay in the axillary dissection has not seemed to increase the number of nodes involved and has not resulted in more systemic metastasis than is observed after the conventional prophylactic axillary dissection.

G. Morbidity

The chief morbidity of radical operations for cancer of the breast is edema of the arm and limitation of the motion of the shoulder. After the conventional radical operations in this series, 22 per cent of the women had some edema of the arm, rarely severe or crippling. When intense radiation was added to the conventional radical mas-

tectomy, the incidence of edema increased to 36 per cent and some patients were handicapped by the edema and limitation of motion of the shoulder. Modified radical

TABLE 8. (1955 Through 1957). Patients Classified as Clinical Stage 1 Who Later Showed Evidence of Metastasis in Axillary Nodes

Classified as Clinical Stage 1 Treated by Radical Mastectomy—Nodes Involved		
No. of Nodes		Result*
1		Well
2		Dead
12		Dead
6		Living with dis.
1		Living with dis.
5		Well
16		Living with dis.
16		Living with dis.
2		Well
3		Dead
1		Dead
10		Living with dis.
1		Well
4 of 13 had only 1 node each		4 well 4 dead 5 living with dis.
Classified as Clinical Stage 1 Treated by Simple Mastectomy—Nodes Later Enlarged and Axillary Dissection Done		
No. of Nodes	Months Between Operations	Result**
3	7	Well
1	18	Dead
(no. of cobalt)	6	Living with dis.
3	12	Living with dis.
1	34	Well
1	12	Dead
12	12	Dead
(no. of cobalt)	1	Well
1	6	Well
1	36	Well
5 of 10 had only 1 node	average, 14	5 well 3 dead 2 living with dis.

* 32 per cent of all radicals were Clin. 1, Path. 2.

** Sixteen patients of the 60 with simple operations had prophylactic cobalt-60 treatment and none developed nodes. Twenty-two per cent of the nonirradiated patients developed metastasis in nodes by 3 years; none later.

TABLE 9. *Incidence of Edema of Arm After Various Treatments*

Treatment	No. Cases	% Edema
Conventional radical mastectomy with radiation	36	36
Conventional radical mastectomy alone	87	22
Modified radical mastectomy with radiation	19	21
Modified radical mastectomy alone	56	7
Simple mastectomy (28 with radiation)	73	0

mastectomy resulted in edema in only seven per cent of the patients, but in those in whom radiation was added to modified radical mastectomy, the incidence of edema was 21 per cent (Table 9). Simple mastectomy with or without radiation was not followed by edema.

Radiation occasionally caused pulmonary fibrosis with annoying cough and persistent discomfort in the radiated area. Since the morbidity following radical operations is increased by radiation and since according to Paterson and Russell,⁷ survival rate in Stage 1 is decreased, it seems clear that radiation should not be used routinely after radical operations for Stage 1 cancer.

H. Conventional Versus Modified Radical Mastectomy

It is not possible to make a fair comparison of the survival rates of conventional radical and modified radical mastectomies in this series (77 and 79% 3-year survival, respectively), because too many factors of selection entered into the picture. Nevertheless, the patients operated on in the year in which the highest proportion of modified radicals was done had the highest survival rate and so did the patients of the surgeon who did the highest proportion of modified radicals. Since deformity, interference with motion of the shoulder, and

edema of the arm are less when muscles are preserved, the modified radical seems preferable to the conventional operation unless someone can prove that it is less curative. A blind experiment is urgently needed to settle this point.

If Haagenson's thesis is correct, that a patient with involvement of the nodes at the apex of the axilla is not curable by radical mastectomy, it is futile to carry the dissection to the apex. Dissection of the low and mid axilla up to the axillary vein with preservation of muscles should be as curative as the standard radical operation and has the advantage of not causing significant edema of the arm unless radiation is added (Table 9).

VI. Discussion

It is not clear why simple operations without radiation appear to control breast cancer as well as radical ones with radiation. There is evidence in the literature that the incidence of metastasis of tumors in mice is increased by either radical operations or by radiation,^{4, 8} but the mechanism of this spread has not been explained. Probably it is biologic rather than mechanical. Perhaps the lymphocytes in the nodes that axillary dissections and radiation destroy are an important part of the hosts' resistance to systemic spread of cancer.

If there is an antigenic difference between certain tumors and their hosts, the tumor cells circulating in the blood can be viewed as tiny homografts looking for a place to grow. In the homograft-rejection reaction the homograft is destroyed by the sensitized lymphocytes circulating throughout the body from the regional nodes in which the sensitization occurs. In certain stages of the development of homograft immunity it is lymphocytes only from the regional nodes draining the graft that can transfer immunity to another animal.^{1, 2} Lymphocytes from contralateral nodes and from the spleen are not apt to carry im-

munity. This regional reaction of lymph nodes to antigen is apparent when a localized tonsilitis causes enlargement of only the cervical nodes and not generalized adenopathy or enlargement of the spleen. It is possible, therefore, that in certain types of localized cancer the regional lymph nodes are an integral part of the body's defense against systemic metastasis. In this connection Black² has observed a positive correlation between sinus histiocytosis of the nodes draining cancers of the breast and the survival of the patient.

If removing regional nodes by a radical operation or destroying their lymphocytes by radiation so weakens the immunologic defenses of the body that a circulating tumor cell implants itself and grows, then more harm than good was done by the treatment. In other cases, in which immunologic factors are not important or when the cancer has spread to regional nodes and a wider area of the body's lymphatics has been immunized, it is likely that neither radiation nor lymphadenectomies damage the host's resistance. In such cases resection of the involved nodes may prevent the ultimate spread of the cancer.

The interplay between the good and bad of various types of treatment makes it difficult to decide how to treat the individual patient. What is needed now is a series of carefully planned blind experiments in which all factors except the type of treatment are the same. The only conclusions that can be drawn from the three- to six-year follow up of this series is that no injustice will be done to patients in clinical Stage 1 who are treated by simple operations without prophylactic radiation therapy.

VII. Summary

1. In the treatment of clinical Stage 1 cancer of the breast, simple mastectomy without prophylactic radiation appeared to be at least as effective as radical mastectomy with or without radiation.

2. In those patients with clinical Stage 1 cancer who were treated by simple mastectomy without radiation and whose disease later reappeared in the axillary nodes and then was removed by axillary dissection, the patients' chances of survival did not seem to be any less than if the axillas had been treated prophylactically by radical mastectomies. In such patients the number of nodes involved was not increased by the delay.

3. In favorable clinical Stage 2 cancers modified radical mastectomy, with preservation of the muscles and without radiation therapy seemed to be as effective as any other treatment or combination of treatments. It caused less disability than the conventional radical operation and was less cumbersome than simple mastectomy and radiation.

4. The success of simple treatments is well enough established that controlled clinical studies can now be done without fear of doing an injustice to the patients receiving the simpler treatments.

5. Controlled (blind) clinical studies are urgently needed to determine what treatment of patients in each stage of breast cancer will produce the highest survival rate with the lowest morbidity.

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DISCUSSION

DR. J. E. DUNPHY: I would like to congratulate both speakers on their excellent and thoughtful presentations. Both of these papers indicate how little we know about cancer, and how difficult it is to explore this problem.

I would like particularly to speak on Dr. Crile's paper, because it would be easy for the casual listener or reader to misinterpret his thesis. I have had the privilege of reading his paper and I think it is a thoughtful contribution to our knowledge of cancer of the breast.

Briefly, if we knew enough about cancer of the breast, we know that there are patients in whom the disease is confined to the breast alone. We know this only retrospectively, to be sure. If we had a test, which established this for certain, we could do a simple mastectomy with confidence that it was the correct operation. If we knew that the tumor is confined to the breast and axilla, we could do a radical mastectomy; and if we knew the disease was disseminated, we could use some other variation, castration, irradiation, and limited mastectomy. These are three clear-cut modalities of treatment.

For the past 25 years, we have applied radical mastectomy somewhat blindly and almost religiously, hoping to catch the right group in the sac, so to speak.

What Dr. Crile is suggesting is that we try to sort out the stage one cases and do a limited operation. The difficulty in doing this, as I see it, is recognizing the cases. Dr. Crile is a very astute clinician. He examines these patients very carefully. He puts them clinically in stage one, and he has been correct about 75 per cent of the time. And thus far, with the three to five-year follow up, he has not seen any reason to feel badly about the 25 per cent in which he was wrong. And that's the present state of affairs. We cannot yet predict the future for the 25 per

cent in which the tumor was not confined to the breast.

I don't think at this moment there is any justification for a general adoption of simple mastectomy for stage one carcinoma of the breast; first because they may not be able to recognize it as well as Dr. Crile; and secondly, because there is 25 per cent error in trying to make the diagnosis.

So that my own belief is that until we have more information available, and until Dr. Crile's studies and the very important double-blind study which I think should be done—as he has suggested—is completed, that we should in stage one and stage two do either a standard radical mastectomy or a modified radical mastectomy. I personally think the modified mastectomy used by Dr. George Crile, Sr. for many years, with excellent results, and used more recently by Mr. David Patey at the Middlesex Hospital, London, is a very good compromise operation. If the patient has obvious extensive lymph node involvement some modification of these approaches should be used.

In conclusion, this is an important contribution to our understanding of cancer of the breast, but a good deal of time must elapse before we can draw final conclusions. This is a step in the right direction, but until we can predict the biology of a cancer before we operate, we will never know which one of these operations to apply. And that is the crux of the problem not only in cancer of the breast, but of all cancer therapy.

Until we have solid answers we cannot be emotionally didactic about any position we assume because we are groping in the dark most of the time.

DR. ALFRED BLALOCK: I have enjoyed these papers by Dr. McLaughlin and by Dr. Crile, and I did have the pleasure of reading this paper which Dr. Crile sent to Dr. Firor.