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## Review of recent literature pertaining to the factors influencing the five year survival rates of breast cancer

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A REVIEW OF RECENT LITERATURE PERTAINING TO THE FACTORS INFLUENCING  
THE FIVE YEAR SURVIVAL RATES OF BREAST CANCER.

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A REVIEW OF RECENT LITERATURE PERTAINING TO THE FACTORS  
INFLUENCING THE FIVE YEAR SURVIVAL RATES OF BREAST CANCER.

During the past year, carcinoma of the breast accounted for the death of over 15,000 women in the United States.<sup>(1)</sup> It represents 10 per cent to 12 per cent of all malignant tumors. It accounts for more articles in the literature than all other cancer combined.<sup>(2)</sup> Even though gastro-intestinal cancers are three times as frequent, there are five times as many operations for breast cancer as for tumors of the entire gastro-intestinal tract.

In 1878, Billroth's statistics showed 5.6 per cent cures of mammary cancer. In 1894, Halstead published his operation for radical mastectomy and in 1898 reported a series of three and five year cures ranging from 18 per cent to 26 per cent. The discovery of x-ray by Roentgen in 1895 and its therapeutic application in 1896 have tended to better the original Halstead survival rates which were attained by utilizing only the Halstead radical surgical procedure. Since the time of Billroth and Halstead there has been a constant flow of medical literature proclaiming the merits of salves, potions, ointments, pastes, hormones and a myriad of other substances and procedures in treatment of breast cancer. However to the present time, only x-ray associated with adequate surgical procedures has proven to be anything more than a passing fancy.

It is not within the scope of this paper to discuss the relative merits of the various methods of treatment of breast

cancer nor is it the purpose of this paper to review diagnosis, etiology or management of breast cancer. Rather, it is the aim of this thesis to relate, in a statistical manner, the factors influencing the five year survival rate for cancer of the breast, as reported in the literature after 1940, and what the cure rate has proven to be, utilizing surgical-radiological combination therapy.

Age Incidence

Age Group	5 Year Cures		Recurrent Cases	
	No. Cases	Per Cent	No. Cases	Per Cent
Below 25	10	0.7	3	0.3
26-30	26	1.7	34	3.3
31-35	77	5.2	65	6.2
36-40	152	10.2	80	7.8
41-45	253	17.0	158	15.0
46-50	280	18.9	166	15.9
51-60	397	26.7	293	28.0
61-70	237	16.0	178	17.0
Over 71	54	3.6	68	6.5
	1486	100.0	1045	100.0

Table 1

Age incidence of 1486 five year cures and 1045 recurrent cases.

In 1942, MacDonald<sup>(3)</sup> reported a review of 2,636 abstract clinical records of carcinoma of the breast from the Cancer Archives of the American College of Surgeons, including 1,511 five year cures and 1,125 cases in whom recurrences or metastasis developed within the five year period. This report

presented several interesting features, one being the age incidence of breast carcinoma. In this series of 1,486 reported five year cures, only 8.6 per cent or 113 cases were below the age of 35 years whereas only 19.6 per cent or 291 cases were over the age of 60 years. 73.4 per cent of this large series of patients were between the ages of 36 and 60 years. The recurrent group demonstrates approximately the same relative incidence with 9.8 per cent below the age of 35 years and 23.5 per cent over 60 years of age as shown in Table 1, Figure 1.

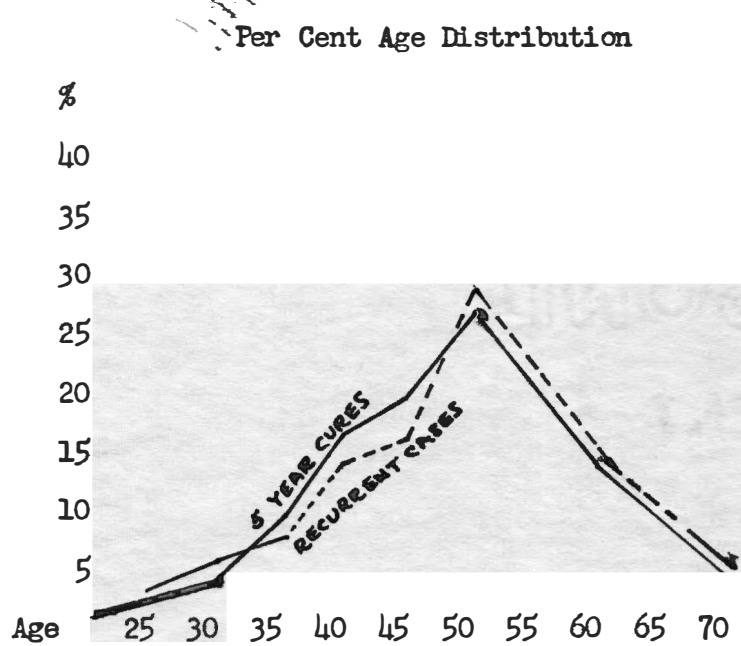


Figure 1

Per cent age distribution of 1486 five year cures and 1045 recurrent cases.

Robnett, et all<sup>(4)</sup> reported a series of 203 cases of carcinoma of the breast in which only 10.4 per cent or 21 patients were below the age of 40 years but 31.6 per cent or 54

cases were 60 years of age or older. A comparable tabulation is seen in Table 2, Figure 2.

Age Incidence of Breast Cancer

Age Group	No. Cases	Per Cent of Total
20-29	1	0.5
30-39	20	9.8
40-49	58	28.5
50-59	60	29.6
60-69	45	22.2
70-80	19	9.4
	203	100.0

Table 2

Age incidence in 203 cases of breast carcinoma.

Per Cent Age Distribution of Breast Cancer

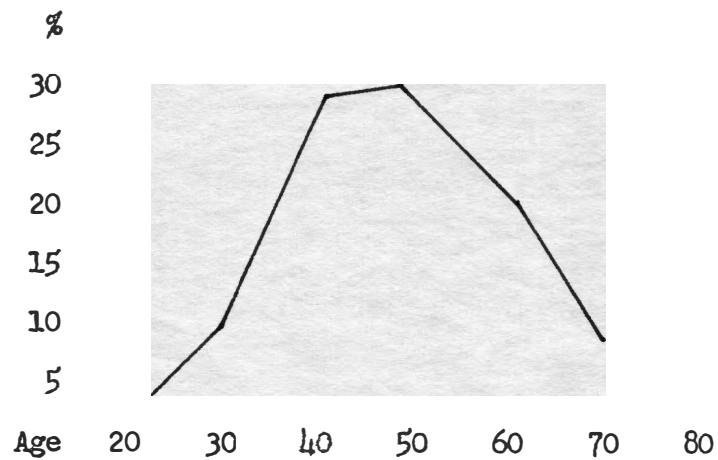


Figure 2

Per cent age distribution of 203 cases of cancer of the breast.

These two separate series present several similar facts. First, breast carcinoma is very infrequent in women below the age of 25 years. Also, though there is a slight variation between the two series, cancer of the breast is not a common pathological process beginning after the age of 60 years. Lastly, the peak incidence of breast carcinoma is in the age group between 40 and 60 years. This age group corresponds to about 38 per cent of the total United States female population<sup>(1)</sup>, Table 3.

Age Group	Female Population	
	No. in Millions	Per Cent of Total
20-29	11.5	27
30-39	9.8	22
40-44	4.4	10
45-54	7.5	18
55-64	5.1	13
65-74	3.2	8
Over 75	1.1	2

Table 3

Age distribution of the female population of the United States.

This indicates that the 38 per cent of the female population, between the ages of 40 and 60 years, have almost 60 per cent of the breast cancers, whereas 62 per cent of the total female population acquire only 40 per cent of the total number of malignant breast tumors.

It is appropriate to interject at this point the outcome of untreated breast tumors. Of a total of 100 cases, Daland<sup>(5)</sup> found the average duration of life from the time of initial symptoms to be 40.5 months and the mean duration of the disease process (50 per cent dead and 50 per cent alive) to be thirty months. This is confirmed by the work of Wade<sup>(6)</sup>, whose figures for the mean duration of life from the time of first symptom is 32.6 months. It is not surprising then to note that although at the end of one year of the disease, 79 per cent of the patients can be expected to be alive, but that by the third year of untreated breast cancer, the patients expected to be alive has dropped to 40 per cent. By the fifth year the

Natural Course of the Disease

Months From First Symptom	Per Cent Survival
1	79
2	60
3	40
4	30
5	18
6	10
7	5
10	5
1	0

Table 4

Duration of life in a series of 100 cases of untreated carcinoma of the breast.



survival rate can be anticipated to have reached 18 per cent and continue downward to 5 per cent in the tenth year. This can be seen in Table 4. With a five year survival rate of 18 per cent untreated, it seems self-evident that prompt and adequate measures must be instituted to treat breast cancer patients and that adequate treatment can materially increase the expected five year survival rate. However, McKinnon<sup>(7)</sup> in his series, isn't satisfied that this difference in survival rates actually exists. As an added stigma to the medical professions efforts to control breast malignancies, the incidence of reportable deaths<sup>(1)</sup>, attributed to cancer of the female breast has increased almost five fold since 1920, Table 5.

Census Report	
1900	3,500
1920	6,485 (15.3%/100,000 female population)
1940	15,308 (23.3%/100,000 female population)

Table 5

Deaths attributable to breast cancer as census reportable.

The tremendous increase in breast cancer deaths since 1920 is not entirely an absolute rise however, but a relative increase. It can be explained, at least partially, upon the basis of the increased proficiency of the medical profession in diagnosis, the increase in the female population reaching the cancer age, and perhaps an actual absolute increase in the frequency of breast cancer.

Another factor studied that greatly influences the five year survival rate is the known duration of the tumor at the time treatment is instituted. The relationship is inversely proportional with a precipitous fall in five year survivals as the duration of untreated disease process is allowed to continue.<sup>(8)</sup> Graphically, Figure 3 will illustrate this point. This graph

Duration Related to Survival

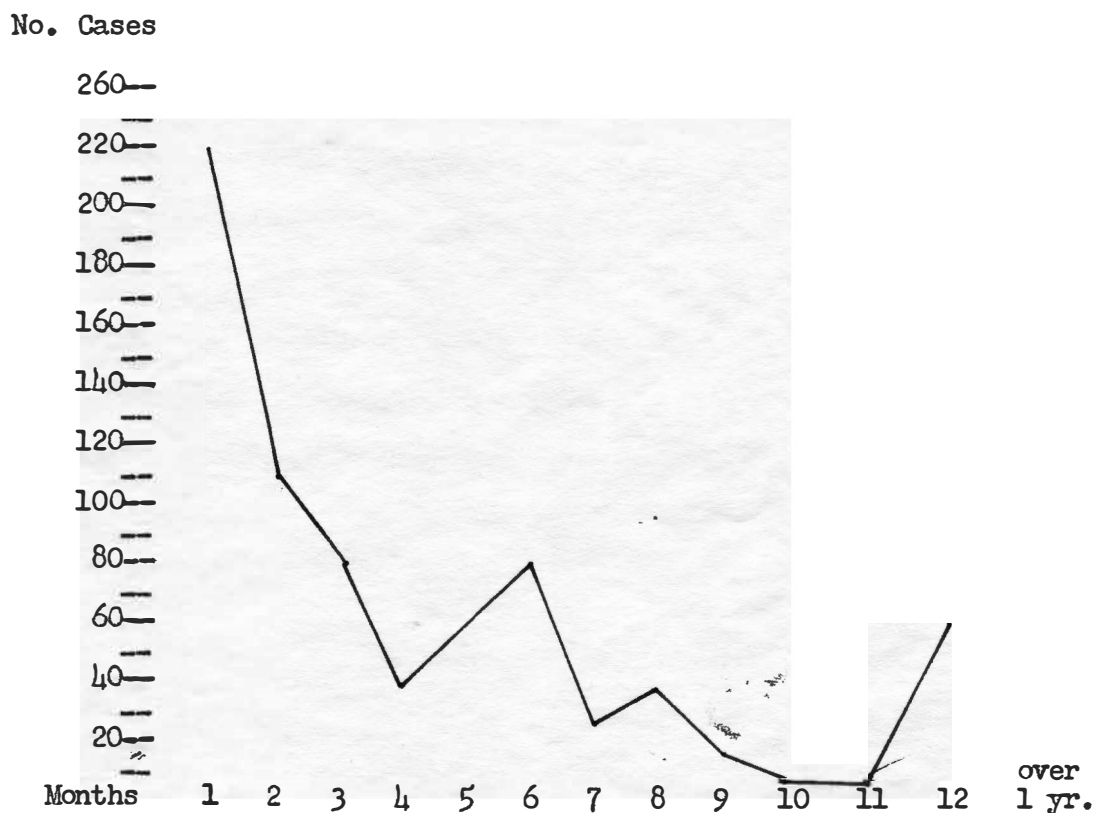


Figure 3

Known duration of tumor with five year cure distribution in 1,048 cases.

represents a series of 1,048 five year cures whose history was reliable enough to determine, with moderate accuracy, the onset

of the disease. Of this total, approximately 220 cases had a duration of less than one month. Whereas less than 10 cases had a known duration of 10 to 11 months prior to treatment<sup>(3)</sup>. However, approximately 200 patients undergoing treatment after more than a year of elapsed time from the onset of the first symptom survived five years. These figures suggest that the early treatment is paramount if five year survival rates are to be increased. The high incidence of five year cures with very late treatment (long duration) can be explained on a basis of slow distal spread in certain cases of the disease. Although the late treatment cases number almost as many as the very early, the late comprise only a small percentage of the total. Taylor<sup>(9)</sup>, utilizing the Portmann<sup>(10)</sup> classification for the stage of the disease, published a report of 143 cases in which he separated the five year survivals into groups treated within 6 months of the onset of the first symptom and those treated more than 12 months after the onset of symptoms, Table 6. The overall survival in

Duration and Survival

Portmann Group	Less Than 6 Months (92)		More Than 12 Months (51)	
	% Total	% 5 Yr. Cures	% Total	% 5 Yr. Cures
I	36.9	88.2	13.7	100.0
II	36.9	61.7	35.3	72.2
III	26.2	16.6	47.1	16.6
IV	0.0	0.0	3.9	0.0

Table 6

Five year survivals related to duration of the disease process. (Note: The Portmann classification ranges from Group I with the tumor completely confined to the breast and without skin involvement to Group IV which have distant metastasis.)

those cases treated within 6 months is almost 13 per cent greater than those treated after twelve months. This difference is markedly smaller than in the series of Cohn<sup>(8)</sup>, but can be explained on the rapid fall in five year cures per one month increase in duration of the tumor between the first and the tenth months.

Another facet of breast cancer survival is closely associated with the actual macroscopic size of the tumor mass at the time treatment is begun. This differs from the association of duration and survival in that no two tumors proceed at the same rate of growth and differs from survival related to histologic type of tumor tissue in that individual variation is so marked.<sup>(11)</sup> Handley<sup>(12)</sup>, published a series of 106 cases in which he related the size of the malignancy to the actual five year survival rate. He based his series on the maximum diameter of the lesions as reported by the pathologist as the index of macroscopic size. He divided the group into two divisions; those with tumor masses 2.0 centimeters in diameter or below and those of 4.0 centimeters diameter or larger in size. In this series he found that the overall survival rate of those patients with lesions of 4.0 centimeters or greater in maximum diameter is 46.3 per cent less than the survival rate of patients whose lesions had a maximum diameter of no more than 2.0 centimeters, Table 7. The mean five year survival in this series of patients with lesions less than 2.0 centimeters in diameter is over 80 per cent while the mean for those with lesions over 4.0 centimeters in diameter is less than 40 per cent. It will be noted that in this series of cases, over 60 per cent of the lesions in the over 4.0 centimeter group were

well advanced cases, the majority of them falling into the Portmann Group III classification. (Group III tumors in this classification involve the overlying skin, are infiltrative and are fixed to the chest wall and have marked axillary node involvement without signs of distant metastasis.)

Size Related To Survival

Portmann Group	<u>46 Cases</u>		<u>60 Cases</u>	
	0-2.0 cm. in Max. Diameter % Total	% 5 Yr. Cure	Over 4.0 cm. in Max. Diameter % Total	% 5 Yr. Cure
I	45.7	95.2	16.7	90.0
II	39.1	83.3	21.7	46.1
III	15.2	42.8	58.3	21.8
IV	0.0	0.0	3.3	0.0
	100.0	82.6	100.0	38.3

Table 7

Tumor size related to five year survival in 106 patients.

The pathological histology of breast cancer has also been studied as a factor influencing the five year survival rate. Hoopes<sup>(13)</sup> has presented a small series, 203 patients, in which he had determined the histologic type of the tumor with the best pathologic means available, at the time of treatment. Five years later he instituted a close follow-up to determine which of the patients were still alive. He found that of the five classified tumor types and the one tumor he was unable to classify, there existed only a 7 per cent variation among the entire surviving group, Table 8. This series strongly suggests that survival is much more dependent upon the extent of the lesion at the time of

treatment and may be modified only to a lesser degree by the pathological type of lesion present.

Five Year Evaluation By Pathological Type

Type	Number	% of Total	Net Followed 5 Yrs.	% Dead	% Alive
Scirrhus	63	31.0	48	51.7	48.3
Simplex	67	33.0	54	50.0	50.0
Medullary	39	19.2	39	51.3	48.7
Adeno-	32	15.8	32	44.0	56.0
Coil-Gland	1	0.5			
Inclass.	1	0.5			

Table 8

Five year survival rate related to the pathological histology of the individual tumor patient.

Development of breast tumor in young, lactating women markedly affects the survival in a small group of patients. Cancer in this group of patients may be acute inflammatory carcinoma which constitutes about 1 per cent of mammary carcinoma. Although the group is small, five year survivals are almost non-existent. Over one-half of these cases develop widespread skin metastasis when seen and over 75 per cent have widespread lymphatic involvement.

Probably the most important factor relating to the five year survival rate of breast cancer is the stage of the disease process at the time therapy is started. There are various methods of stage classification and none are universally accepted. Histologic grading has proven grossly inaccurate. Clinical signs

as a criteria for determining the extent of the neoplasm is strewn with pitfalls. It seems therefore, that any method, to be satisfactory, must be based upon the best features of both histological and clinical findings. Portmann's classification engenders both of these important features. Utilizing his scheme of classification, Robnett<sup>(4)</sup> published a series of 200 cases in which five year cures were determined in relation to the stage at the time of treatment. (Details of Portmann classification have been given in a preceding paragraph.) In this series, the first three groups were considered operable. The series is further divided in groups arranged according to the type of treatment given. (The discussion of treatment related to survival rate will be found in a following paragraph but will be mentioned here for the sake of completeness.) In this series there are 59 cases in Group I, 71 cases in Group II and 70 cases in Group III. The best survival rate is in Group I who were treated by radical mastectomy only. The lowest survival rate is in Group III who were treated by radical surgery followed by radiation. The difference in the two group's survival rates is over 80 per cent, Table 9, A, B and C. But the difference in Group's I and III even with the same type of treatment, is consistently over 70 per cent, and treatment variation will be found in all series. It seems therefore, that the desirability of instituting therapy at the earliest possible moment cannot be over-emphasized. The extent of the disease process can be limited only by adequate therapy.

Five Year Results in Operable Cases Related  
to Stage of Disease at Time of Operation.

Group I	<u>All Cases</u>			<u>Operation Only</u>			<u>Op. + Post-Op X-Ray</u>		
	Total No.	% Total	% Net	Total No.	% Total	% Net	Total No.	% Total	% Net
Cases Treated	59	100.0		52	100.0		7	100.0	
Operative Deaths	2	3.4		2	3.8		0	0.0	
Lost	5	8.5		4	7.8		1	14.3	
Dead, Unrel. Causes	4	6.8		3	5.8		1	14.3	
Net, Followed 5 Years	48	81.3	100.0	43	82.6	100.0	5	71.4	100.0
Dead of Disease	4	6.8	8.3	3	5.8	6.9	1	14.3	20.0
Alive	44	74.5	91.7	40	76.8	93.1	4	57.0	80.0

Table 9-A

Five year results in 59 cases classed as Group I (Portmann)



Group II	All Cases			Operation Only			Op.+Post-Op X-Ray		
	Total No.	% Total	% Net	Total No.	% Total	% Net	Total No.	% Total	% Net
Cases Treated	71	100.0		56	100.0		15	100.0	
Operative Deaths	1	1.4		1	1.8		0	0.0	
Lost	9	12.7		7	12.9		2	13.3	
Dead, Unrel. Causes	5	7.0		5	8.9		0	0.0	
Net, Followed 5 Years	56	78.9	100.0	43	76.8	100.0	13	86.7	100.0
Dead of Disease	22	30.9	39.3	20	35.7	46.5	2	13.3	15.4
Alive	34	48.0	60.7	23	41.1	53.5	11	73.4	84.6

Table 9-B

Five year results in 71 cases classed as Group II (Portmann)

Group III	All Cases			Operation Only			Op.+Post-Op X-Ray		
	Total No.	% Total	% Net	Total No.	% Total	% Net	Total No.	% Total	% Net
Cases Treated	70	100.0		41	100.0		29	100.0	
Operative Deaths	1	1.5		1	2.4		0	0.0	
Lost	7	10.0		5	12.2		2	6.9	
Dead, Unrel. Causes	6	8.5		4	9.8		2	6.9	
Net, Followed 5 Years	56	80.0	100.0	31	75.6	100.0	25	86.2	100.0
Dead of Disease	47	67.1	83.9	25	60.9	80.6	22	79.9	88.0
Alive	9	12.9	16.1	6	14.7	19.4	3	10.3	12.0

Table 9-C

Five year results in 70 cases classed as Group III (Portmann)

Accepted treatment for breast carcinoma in the United States at the present time seems to be a combination of surgery with radiation. Both simple and radical mastectomies are done with radicals the more frequent and both pre and post-operative radiation is utilized. The most frequent treatment for proven cases of breast malignancy is radical surgery followed by extensive x-ray radiation. McWhirter<sup>(14)</sup> has recently published an article however, in which he strongly advocates excising the breast with a simple procedure and following the surgery with extensive x-ray therapy. His entire series comprises some 2,500 cases. He states that in operable cases, in a period from 1930 to 1934, utilizing radical surgery only, he elicited a five year survival rate of 35 per cent. From 1935 to 1940, adding post-operative radiation to the radical surgery, the five year survival rate was increased to 44 per cent. In the period of 1941 to 1945, using the simple operating procedure coupled with extensive post-operative radiation, he has estimated the five year survival rate to have increased still further, to 56 per cent. He also states that utilizing the simple surgical procedure plus radiation, he has an estimated five year survival rate of 14 per cent in inoperable cases which with radical procedures plus radiation had produced only 2.5 per cent five year cures. McWhirter also states that in this series, 80 per cent of the patients had lymph node involvement at the time of operation. Finney<sup>(15)</sup> reports for a fifteen year period ending in 1945, a series of 298 private patients who were treated with radical

surgery alone except for 68 patients who received x-ray therapy post-operatively and all were closed without skin grafts. The five year survival rate was 49 per cent. 6 per cent of the routine cases developed local recurrences. The Lahey Clinic<sup>(16)</sup> reported that prior to 1936, utilizing radical surgery alone, they elicited a five year survival rate of 38.6 per cent. Since 1936, radical surgery was followed by extensive x-ray radiation in 228 cases and their group survival rate was 52 per cent. The cases with axillary lymph node involvement at the time of operation had a five year survival rate of 37 per cent whereas those patients without axillary lymph node involvement had a five year survival rate of 75 per cent. Of the total group, 62 per cent had axillary lymph node involvement at the time therapy was instituted. Adair<sup>(17)</sup> reports 277 cases in which treatment consisted of radical mastectomy followed by radiation. In this series the five year survival rate for the group was 53 per cent. Those cases with axillary node involvement at the time of surgery had a five year survival rate of 41.8 per cent while those cases who did not have axillary nodes had a five year survival rate of 76.8 per cent. Presbyterian Hospital, New York, New York<sup>(18)</sup>, reported 640 radical mastectomies performed by staff members in twenty years. The group survival rate was found to be 36.1 per cent and the local recurrence rate was 22.8 per cent. The Mayo Clinic<sup>(19)</sup> reported a series of 6558 patients with breast carcinoma. Their method of treatment was radical mastectomy followed by x-ray radiation. They experienced 47 hospital deaths or a mortality rate of 0.7 per cent. Their five year survival rate was 48.1

per cent in 2757 traced cases. In 1972 cases that could be traced, who had axillary lymph node involvement at the time of operation, the five year survival rate was found to be 30.5 per cent. In 1685 traced cases that did not have axillary node involvement at the time of operation, the five year survival rate was 75.8 per cent. In this series, 60 per cent of all cases treated had axillary lymph node involvement at the time the mastectomies were performed. St. Lukes Hospital, New York City<sup>(20)</sup>, reported 516 ward cases operated (radical surgery) for carcinoma of the breast. The five year survival rate was 34 per cent or 175 patients. There was 60 per cent of the entire group that had lymph node metastasis at the time of surgery and the local recurrence rate was 17.4 per cent. Ramsdell<sup>(21)</sup> published a report of 138 personally operated cases. Of this group 60 per cent had axillary lymph nodes involved at the time of operation. Of the total group, 131 patients were treated by radical mastectomy, Caüterdyne technic, followed by x-ray therapy. Seven cases had simple mastectomies followed by x-ray therapy. The group five year survival rate was 42 per cent. There were local recurrences in 16.3 per cent of the patients. In those patients with node involvement when operated, their five year survival rate was 18.1 per cent, 60.2 per cent less than the group without axillary lymph nodes involved.

In summarizing, it seems pertinent to restate that breast carcinoma is killing over 15,000 women annually in the United States. The radical surgical procedure for breast removal as introduced by Halstead in 1894 is still accepted as

the nuclear portion of adequate treatment by most authorities. The greatest incidence of malignant breast tumors occurs in the 40 to 60 year age group. This is a slightly lower age group than shown in popular opinion. It is somewhat surprising to find that in a series of 2,636 cases, only 19.6 per cent occurred in women over 60 year old. It is less surprising to learn that in the same 2,636 patients, only 7.6 per cent of them were below 35 years of age. This 40 to 60 year old group comprises only 38 per cent of the total female population but acquires over 60 per cent of the breast cancers. Untreated breast cancer has a mortality rate within the five year period, almost three times that of adequately treated breast malignancies. The rate of five year survivals drops markedly as the duration of the malignancy is allowed to progress untreated. As the tumor size increases, five year survival rate decreases. This is especially true in advanced cases although less significant in early cases. In 106 cases, using 4.0 centimeters as the size differential, there was almost 50 per cent variation in five year survival rates with the smaller lesions demonstrating the greater longevity. In 203 cases reported in reference to histologic pathology, there was less than 10 per cent variation between the highest and lowest five year survival rate, suggesting that the pathological type has surprisingly little effect on mortality within the five year period. Of the factors studied, the stage of the disease process at the time therapy is instituted exerts the greatest influence upon the five year survival rate. In a series of 59 early cases, the five year survival rate was between 80 and 93 per cent. In

71 cases of moderately early breast cancer, the five year survival rate dropped to 53 to 84 per cent. In 70 cases of moderately advanced breast carcinoma, the survival rate continued to fall reaching 12 to 19 per cent. The most optimistic results in advanced breast cancer report a five year cure rate of 14 per cent and the majority of authorities report rates below 5 per cent. McWhirter has instituted a variation in therapy which he believes will further increase the five year survival rate. He advocates using a simple surgical procedure and following it with extensive x-ray therapy. He estimates that the five year survival rate will be 56 per cent in his series of 2,500 patients. Most individuals and groups in the United States, however, are continuing to use the radical surgical procedure along with post-operative radiation. These groups and individuals are publishing reports of five year survival rates ranging from 34 to 53 per cent.

In conclusion, the following statements seem warranted;

1. The greatest incidence of breast carcinoma occurs between the ages of 40 and 60 years.
2. Reports from the principle clinics of this country would suggest that there is general agreement that the best treatment of carcinoma of the breast is radical mastectomy followed by an intensive course of x-ray therapy.
3. It would probably be agreed that the five year post-operative survival rate averages 40 to 50 per cent.

4. Adequate treatment raises the five year survival rate some 20 to 30 per cent over the rate of untreated breast cancer patients.
5. It would also probably be agreed that the five year survival rate of patients without axillary node involvement at the time of operation have approximately an added 45 per cent chance of surviving the five year period.
6. A longer period of time must elapse before the true five year survival rate can be actually evaluated in light of the simple surgery followed by x-ray as advocated by McWhirter in Scotland.
7. The most important factor influencing the five year survival rate is the stage of the tumor at the time of treatment.
8. The patients age, type of tumor, size of tumor, and known duration of tumor are of importance only in so far as they affect the stage of the disease process at the time of treatment.



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