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METASTATIC PATTERNS AND FUNCTIONAL DISABILITY
IN DISSEMINATED BREAST CARCINOMA

by

Stephen Adam Gudas

B.S., University of Pennsylvania, 1971

Thesis

submitted in partial fulfillment of the requirements for the

Degree of Master of Science in the Department of
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This thesis by Stephen Adam Gudas is accepted in its present form as satisfying the thesis requirement for the degree of Master of Science.

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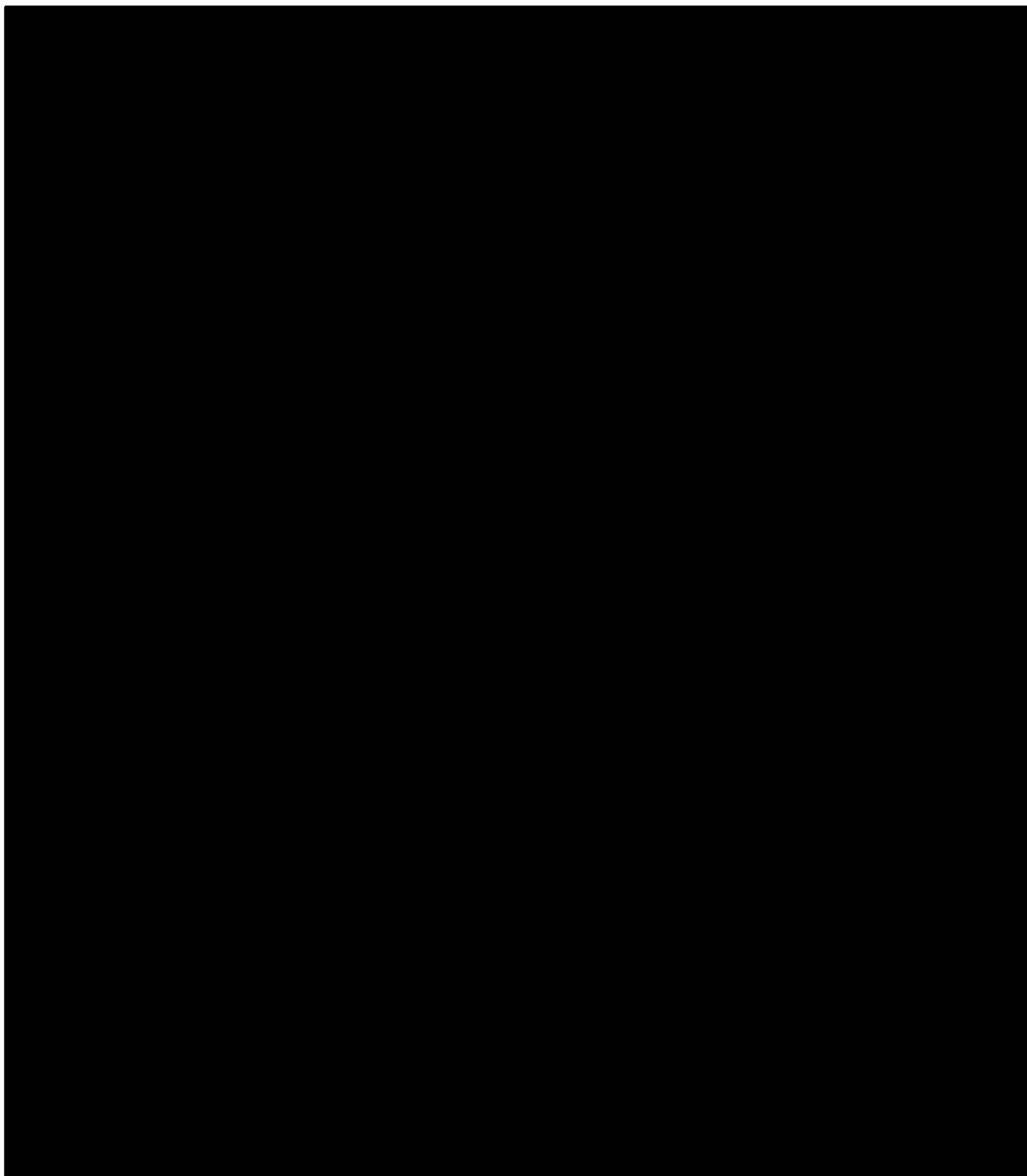
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Chairman, MCV Graduate Council, Dean, School of Basic Sciences

CURRICULUM VITAE



To

Jim and Nancy

With love

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TABLE OF CONTENTS

	Page
CURRICULUM VITAE.....	iii
DEDICATION.....	iv
ACKNOWLEDGMENTS.....	v
LIST OF TABLES.....	xiii
LIST OF FIGURES.....	xv
Chapter	
1. INTRODUCTION.....	1
DEFINITION OF THE PROBLEM.....	2
STATEMENT OF HYPOTHESES.....	6
SIGNIFICANCE: SCOPE AND LIMITATIONS.....	8
DEFINITION OF TERMS.....	11
ORGANIZATION OF THE REMAINING CHAPTERS.....	13
2. REVIEW OF LITERATURE.....	15
THE NEED FOR CLASSIFICATION OF DISTANT METASTASES..	15
INTRODUCTION TO PATHOLOGICAL CONSIDERATIONS.....	19
Patterns of Dissemination.....	24
Role of the Vertebral Venous System in Metastatic Breast Cancer.....	28
Summary.....	29
PULMONARY METASTASES.....	30
Pathology.....	30
Signs and Symptoms, Detection.....	33
Treatment.....	35
Lymphangitic Pulmonary Metastases.....	37

Chapter

Page

Summary.....	40
PLEURAL EFFUSIONS.....	40
Pathology.....	40
Symptoms.....	41
Treatment.....	41
Summary.....	42
BONE METASTASES.....	42
Extent of the Problem.....	42
Pathology.....	44
Symptoms and Detection.....	46
Complications and Treatment.....	47
Summary.....	52
LIVER METASTASES.....	52
Incidence and Pathology.....	52
Diagnosis and Symptoms.....	53
BRAIN METASTASES.....	54
Introduction and Pathology.....	54
Pathogenesis.....	55
Symptoms and Detection.....	56
Treatment.....	57
Summary.....	58
EPIDURAL SPINAL CORD COMPRESSION.....	59
Symptoms and Detection.....	59
Treatment.....	60
Summary.....	61

Chapter

Page

DISTANT LYMPHATICS.....	61
Symptoms and Detection.....	62
OTHER METASTATIC SITES AND SYSTEMIC EFFECTS.....	64
Hypercalcemia.....	64
Symptoms and Detection.....	65
Treatment.....	65
Other Sites.....	66
COMPLICATIONS DUE TO TREATMENT.....	66
Hormonal Therapy.....	67
Chemotherapy.....	68
THE ROLE OF PHYSICAL THERAPY IN THE METASTATIC CANCER PATIENT.....	72
SUMMARY.....	75
3. PROCEDURES.....	77
CONSTRUCTION AND PHYSICIAN APPROVAL FOR OPERATIONAL MODEL A.....	77
CONSTRUCTION AND THERAPIST APPROVAL OPERATIONAL MODEL B.....	79
SCORING OF THE MODELS.....	80
METHODS OF PATIENT SELECTION.....	81
PROCEDURES IN PATIENT EVALUATION AND DATA COLLECTION.....	83
Preliminary Assessment.....	83
Patient Evaluation - Model B.....	85
Patient Evaluation - Model A.....	87
METHODS OF DATA ANALYSIS.....	91
SUMMARY.....	93

Chapter	Page
4. RESULTS OF THE STUDY.....	94
MODEL A AND MODEL B TOTAL SCORES.....	94
MODEL A AND MODEL B SCORES AND CORRELATION COEFFICIENTS FOR SELECTED GROUPS.....	96
Age Factor.....	96
Correlation of Model A and Model B.....	96
Comparison of Age Group Means.....	98
Length of Disease Factor.....	99
Disease Free Interval Factor.....	101
Duration of Metastatic Disease.....	104
Clinic Factor.....	106
SCORE ANALYSES AND CORRELATION COEFFICIENTS FOR SIX MAJOR SITES OF METASTASES.....	108
Lung Metastases.....	109
Pleural Effusions.....	111
Bone Metastases.....	111
Liver Metastases.....	113
Brain Metastases.....	116
Metastases to Distant Lymphatics, Skin and Soft Tissue.....	118
FREQUENCY DISTRIBUTION OF PATIENTS OVER SIX CATEGORIES OF FUNCTIONAL ABILITY.....	122
RELATED DESCRIPTIVE SAMPLE CHARACTERISTICS.....	124
Bone Metastases Patterns.....	126
General Patient Information.....	128
FREQUENCY OF SPECIFIC DISABILITIES.....	133
SUMMARY.....	135

Chapter	Page
5. CONCLUSIONS AND RECOMMENDATIONS.....	137
CONCLUSIONS AND INTERPRETATIONS.....	137
Full Sample Correlation.....	137
Division by Age, Length of Disease, Disease Free Interval, Tumor Clinic.....	138
Age.....	138
Length of Disease.....	139
Disease Free Interval, Duration of Metastatic Disease.....	140
Tumor Clinic.....	142
Major Sites of Metastases.....	143
Lung Metastases.....	143
Pleural Effusions.....	144
Bone Metastases.....	145
Liver Metastases.....	147
Brain Metastases.....	148
Distant Lymphatic, Skin and Soft Tissue Metastases.....	150
Functional Classification - Performance Status...	151
Rehabilitative Goals.....	153
Frequency of Specific Disabilities.....	155
RECOMMENDATIONS.....	157
Clinical Versus Autopsy Studies.....	157
Identification of Factors Affecting Mean Model Scores.....	158
Treatment and Diagnostic Evaluation Procedures...	159
Recommendations for Physical Therapists.....	160

Chapter	Page
THESES SUMMARY.....	163
BIBLIOGRAPHY.....	167
APPENDICES	
A. MODEL A - EXTENT OF METASTASES OPERATIONAL MODEL DISSEMINATED BREAST CARCINOMA.....	179
B. MODEL B - LEVEL OF FUNCTIONAL DISABILITY OPERATIONAL MODEL.....	199
C. PRELIMINARY PATIENT INFORMATION PREPARATORY TO DATA COLLECTION.....	207
D. PERFORMANCE STATUS - FUNCTIONAL CLASSIFICATION.....	209
E. REHABILITATION GOALS AND THEIR CRITERIA.....	211

LIST OF TABLES

Table		Page
1.	Breast Cancer Metastases - Effects of Three Major Sites on Seven Minor Sites of Involvement....	26
2.	Common Chemotherapeutic Agents Used in Advanced Breast Cancer; Acute and Delayed Side Effects and Complications.....	70
3.	Scores on Operational Models A and B.....	95
4.	Analysis of Scores on Operational Models A and B - Division by Age.....	97
5.	Analysis of Scores on Operational Models A and B - Division by Disease Period Since Diagnosis.....	100
6.	Analysis of Scores on Operational Models A and B - Division by Disease Free Interval.....	103
7.	Analysis of Scores on Operation Models A and B - Division by Duration of Metastatic Disease.....	105
8.	Analysis of Scores on Operational Models A and B - Division by Clinic Attended.....	107
9.	Model Scores and Total Sites of Metastases for Patients With Lung Metastases - Group LM.....	110
10.	Model Scores and Total Sites of Metastases for Patients With Pleural Effusions - Group PD.....	112
11.	Model Scores and Total Sites of Metastases for Patients With Bone Metastases - Group BONE.....	114
12.	Model Scores and Total Sites of Metastases for Patients With Liver Metastases - Group LIV.....	115
13.	Model Scores and Total Sites of Metastases for Patients With Brain Metastases - Group BR.....	117
14.	Model Scores and Total Sites of Metastases for Patients With Distant Lymphatic and/or Skin and Soft Tissue Involvement - Group LYM.....	120
15.	Frequency Distribution Over Six Categories of Performance Status - Functional Classification.....	125

Table		Page
16.	Frequency of Metastases to Specific Bony Sites.....	127
17.	General Patient Information Part I.....	129
18.	General Patient Information Part II.....	132
19.	Frequency Distribution of Disabilities in Model B Groups.....	134

LIST OF FIGURES

Figure		Page
1.	Representative Transition from Normal Tissue to Carcinomatous Change.....	20
2.	Percentage of Patients Having Metastases to the Six Major Sites.....	121
3.	Average Model Scores for the Six Major Sites of Metastatic Tumor Involvement.....	123

Chapter I

INTRODUCTION

Interest and need of the professional physical therapist in the field of cancer has been expanding at a tremendous rate. The reasons for this interest are many: greater public awareness of the causes, effects, disabilities, and treatment of cancer; increased scientific knowledge concerning the pathogenesis and natural history of various neoplastic processes; increased concern of national cancer organizations regarding disability due to cancer; better survival rates and longer durations of the disease are producing unique and challenging disabilities for the physical therapist. Also, since the overall incidence of cancer is increasing, now ranking second only to heart disease as a cause of death in the United States, more people will develop cancer, and greater numbers of patients that the physical therapist will be called upon to treat will have cancer or cancer-related disability. The extent of the problem and the need for the physical therapist to have sophisticated approaches at his disposal and resource in meeting the needs of cancer patients are obvious.

There is a particular need for improvement in the type and kind of care given to the metastatic cancer patient. For this patient, the metastatic process spreads the disease beyond the limits of the area from which it has arisen. The problem presents a myriad of complex variables that need to be understood in order for the physical therapist to design appropriate physical therapy

procedures and programs. All too often the physical therapy programs that have been written by physical therapists or other medical professionals concentrate only on the acute and short term disabilities, such as loss of range of motion and swelling of the ipsilateral arm following radical mastectomy (Beeby and Broey, 1970; Dietz, 1969; Healey, 1971). Also, many of these disabilities are a result of the treatment for the cancer, and not really due to the disease process itself. The question concerning description of specific disabilities encountered in the metastatic breast cancer patient has not really been studied in depth. The present research stems out of a sincere desire to improve the conditions under which physical therapy evaluation and treatment of the metastatic breast cancer patient is approached.

In order to accomplish this, a consideration of the disease process and its relationship to functional disability is necessary. The exact nature of this relationship is the target of study of this research project.

DEFINITION OF THE PROBLEM

The significance of breast carcinoma in the human female lies in the fact that it is the commonest cancer in women. In fact, more women die of breast cancer than any other form of cancer. Presumably, there are 70,000 new cases and 40,000 deaths from breast cancer each year in the United States (Kaufman, 1973). Seventy-two new cases per 100,000 females are diagnosed annually, and the mortality rate is 27 per 100,000. The often quoted figure is that one

in 18 women will develop breast cancer at some time in her life (Savlov, 1973). Since the disease is so common, research regarding its natural history and behavior constitutes a sound and worthwhile undertaking.

A need for the study of this type was felt chiefly due to the fact that physicians are more commonly referring metastatic patients for physical therapy treatment in order to improve the level of functional activity in these patients, who are weakened by the effects of the cancerous process which has produced widespread, disseminated disease. Metastases are usually present in more than one organ or system, and the symptoms that are produced may be either of a general or a specific nature. The disabilities that are encountered in these patients have never really been fully documented; all too often the therapist, on account of lack of access to well-defined evaluation parameters, begins treatment on a patient who has not been properly evaluated for specific disability. If the correlation between extent of disability and amount of disease can be made, better evaluation procedures can be employed and therefore more beneficial programs be devised for these patients. In effect, for the proper care of the metastatic cancer patient to be realized, the treatment must become specific, and move away from the general realm in which it is now firmly entrenched.

General treatment regimes are commonly employed for advanced cancer patients - modified whole body conditioning, functional strengthening, and assisted ambulation activities. Specific approaches are lacking because the symptoms and disabilities of metastatic cancer are not properly catalogued, and they are often

different for different types of cancer. Other medical care and treatment for metastatic breast cancer depends on the localization of the metastases, the patient's age and general condition, patterns of hormone secretion, surgery, and the tolerance of the different patients for the various chemotherapeutic agents that are available (Viadana et al., 1971). If physical therapy is to play an integral role in the care of the metastatic cancer patient, more elaborate and detailed evaluation procedures as well as a firm foundation or rationale for treatment approaches are needed.

The need can be further demonstrated if one examines the recent literature which has attempted to deal with the quality of survival in breast cancer. Craig, Comstock, and Geiser (1973) studied 134 breast cancer patients and 260 controls. They claimed that the hindrance to many efforts was the lack of clarity and uniformity in defining and assessing quality of survival. In this particular study, physical functioning was measured by extent of disability and assessment of current health status, both being graded on a scale of zero to five. The goal of the study was to estimate the degree of disability and malfunctioning attributable to the cancer and its treatment, over and above that resulting from the age and socioeconomic condition of the subjects. They summarized that the only important effects of breast cancer seemed to be a slight increase in overall physical disability by adding a small but measurable number of persons with surgery related disability. However, the disabilities were never categorized or described sufficiently to draw any conclusions as to the actual functional disability of these patients. In addition, the group was largely

composed of breast cancer patients who were in the early stages of the disease, and many of them did not exhibit distant metastases. An additional drawback was the fact that the assessment of current health status was made by the patient herself, thus adding to the subjectivity of this parameter.

Another article stated that of a number of women under age 65 at the time of mastectomy, fully 84 percent had resumed their preoperative responsibilities; this study did not document specific disabilities or dysfunctions, and did not state the percentage of patients that had distant metastases (Schottenfield and Robbins, 1970). These two endeavors to outline the quality of survival in terms of physical dysfunction demonstrate all too clearly the need for more specific documentation.

Although theoretically any type of human cancer can metastasize, effect serious symptomatology, and therefore lead to varying degrees of physical dysfunction, breast carcinoma in its many pathological forms was chosen as the target for this study for many reasons:

1. Breast cancer is the most common form of cancer in the human female, and is responsible for the greatest number of new cases and deaths annually.

2. With increased and improved methods of surgery, chemotherapy, and radiotherapy, more patients will be living longer with recurrent or metastatic disease and morbidity. This will mean an increased number of patients with probable increased dependency and disability, necessitating the procurement of physical therapy services to assist in bringing the patient to the highest level of

functioning possible in the light of the progressive disease.

3. Since in its later stages breast cancer spreads by both the lymphatic and hematogenous routes, its behavior might well represent characteristic metastatic symptomatology, that is, symptoms that will be more or less specific for designated organs or systems. Also since both routes are portals of invasion, metastases can be expected to be more widespread than if only one form of dissemination were common. The particular metastatic trends of this disease will be outlined in the collection of data, and these related to disability.

4. Since an increased number of patients with disseminated breast carcinoma will come to the physical therapist for treatment, there is a great need to specifically document the patterns and types of disabilities that will be encountered. This can only be done by a clinician who is skilled and perceptive in evaluating the problems that the metastatic cancer patient will present. To do this a thorough knowledge of the extent and symptomatology of the metastatic deposits from the disease is necessary.

STATEMENT OF HYPOTHESES

This study will attempt to gather data that will either support or refute the following hypotheses:

1. H_{01} . There will be no or a negative statistical correlation between the extent of disease, as measured by the extent of metastases in the breast cancer patient described on an operational model (Model A) and the level of disability and physical dysfunction manifested clinically and measured by performance on a test con-

structured to assess the functional impairment of the patient in levels of motility and functional activities. (Model B).

2. H_{a1} . There will be a positive statistical correlation between the extent of disease as measured on Model A and the level of disability and physical dysfunction manifested clinically as measured by Model B.

3. H_{o2} . For all persons in the sample demonstrating a specified site of metastasis, i.e. lung, there will be no or a negative correlation between the extent of disease, as measured by the extent of metastatic disease operational model (Model A) and the level of disability and physical dysfunction as measured on Model B. There will be several correlation coefficients representing groups having a certain type of metastasis.

4. H_{a2} . For all persons in the sample demonstrating a specified site of metastasis, there will be a positive statistical correlation between the scores obtained for that group on Model A with Model B.

5. H_{o3} . Those patients over age 60 and those patients living the longest (greater than 3.3 years) with disseminated disease will not exhibit any greater amounts of disability, as reflected by higher scores obtained on Model B - level of disability and physical dysfunction.

6. H_{a3} . Those patients over age 60 and the patients living the longest with disseminated disease as defined above will exhibit the greatest amounts of disability, reflected by higher scores attained on Model B - level of disability and physical dysfunction.

7. The number of patients with various types of metastases will be distributed evenly over a six category functional classification that describes the performance status regarding functional disability of women with metastatic breast cancer.

SIGNIFICANCE: SCOPE AND LIMITATIONS

The author desired in this study to document clinical dysfunction and disabilities in the metastatic breast cancer patient which were a result of the disease and its ensuing dissemination. These disabilities were expected to be a function of the number, site, size, and gross histological, radiological, and pathological characteristics of the cancer metastases in question. Since clinicians are constantly re-evaluating methods of description and classification of human diseases, and seeking alternate, more sophisticated or more practical ways of outlining these characteristics, a documentation of this type will be significant in helping cancer clinicians to achieve this endeavor.

In addition, the documentation will assist persons in quickly estimating the level and degree of involvement with metastases in patients with disseminated breast cancer. A part of this research will include the construction of a validated descriptive model for use in interpreting the extent of metastatic disease in the patient. Included in this descriptive model would also be clinical signs due to chemotherapeutic, radiological, or surgical treatment of the disseminated disease.

The lack of adequate and detailed documentation in metastatic disease has been mentioned and will be further developed and

supported in the review of literature. The dilemma that the physical therapist faces in choosing practical, rational and feasible methods and treatment approaches is largely a result of the lack of specification in both the extent of disabilities and metastases in the patient. Thus this research will hopefully be significant in alleviating this problem of treatment selection in metastatic breast carcinoma.

The further significance of this project lies in the fact that the data will assist in outlining some of the factors that might intervene and modify the correlation between the extent of disease present clinically and the amount and kind of disability shown by the patient. If this is demonstrated, it is further hoped that the specific factors and parameters that might possibly be responsible for the disabilities could be delineated.

Finally, the approach that is developed might conceivably be used for other types of cancer; with adjustments and appropriate deletions of the models, it might be applied to other types of metastatic cancer, thus enabling clinicians to document more specifically the metastatic process in disseminated cancer patients. In addition to cancer, the approach might also be applied to other chronic disabling diseases, so that the professional physical therapist can have access to a rationale for relating disease entities to resultant disabilities.

The results of this study are limited in that the sample is drawn from a population of breast cancer patients treated at Medical College of Virginia Hospitals, thus the results are biased

by any characteristics and factors that might be particular to MCV patients. This perhaps is the greatest limitation - that the results are applicable only to this sample, and caution should be used in extending any conclusions or interpretations to populations outside of this institution.

Another limitation is the vast number of intervening variables that could possibly modify the correlation between the models. Factors such as patient motivation, life style, extraneous pressure, peer or group pressure, and multiple psychological considerations perhaps all play a part in a patient's performance status regarding functional ability in activities of daily living. The present research is not designed to assess the significance of these non-medical parameters or their role in functional disability in metastatic cancer patients. The basic format of this study, which is reported as a correlational study, is not designed to imply a cause and effect sequence, but rather to describe the strength of the relationship between the metastases and functional disability.

Lastly, a number of non neoplastic medical conditions may coexist with the breast cancer metastases. Some of these disease processes or syndromes are common to populations of advanced age, such as obesity, various arthritic conditions, arteriosclerotic heart disease, and others. These might have a significant bearing upon the level of functional disability that many of these patients will demonstrate. The extent of metastases operational model will identify clearly those factors which are applicable to metastatic disease due to a primary breast cancer. A sincere effort to differentiate these factors from those due to other medical conditions

will be operative at all times during data collection, and the assumption is made that the disabilities that are encountered are related to the metastases that are present unless otherwise documented.

DEFINITION OF TERMS

1. Breast carcinoma: the result of abnormal proliferation and dissemination of epithelial cells within the breast tissue. Seventy-five percent of breast carcinomas are infiltrating ductal carcinomas, arising from the epithelial lining of a mammary duct.

2. Distant metastases: hematogenous or lymphatic spread of the cancer beyond the confines of the breast, ipsilateral axillary or internal mammary lymphatics. The following terms are not equivalent to the term distant metastases: spread, extension, involvement or metastases to ipsilateral submammary musculature (pectoralis major and minor), ipsilateral breast, homolateral axillary or internal mammary nodes, or skin recurrence within the suture line.

3. Complications due to treatment: any adverse side effects, symptoms, or other complicating sequelae that are directly or indirectly a result of the surgical, radiological, or chemotherapeutic or hormonal treatment of metastatic breast cancer.

4. Functional activities: for this study, those events directly or indirectly related to eating, personal hygiene, locomotion, and daily routine chores carried out by the patient.

5. Metastases: a growth of a cancer that is separate and distinct from its primary source. A metastasis can originate from

any part of the primary tumor (one step) or from an already existing metastasis ("cascade"), and disseminate via the lymphatic or hematogenous route.

6. Operational Model A: Extent of Disease: a validated scaled model devised to describe and give patients a score based on the characteristics of metastatic disease in patients with disseminated breast cancer.

7. Operational Model B Level of Functional Disability: a validated and scaled model constructed and designed for the purpose of assigning patients in the study a mathematical score based on performance status in functional activities. The score is a measure of the disability the patient exhibits in the performance of these functional activities.

8. Physical therapy evaluation procedures: for this study, those procedures used to assess type, level, extent and effects of disability or dysfunction manifested in functional activities.

9. Selective affinity hypothesis: one of two current major theories of the mechanism of metastatic growth of tumors in the body, contending that the development of metastases is a direct function of the site of lodgement; local characteristics of the organ in question will govern whether a metastasis grows in that location or not. Also called the soil hypothesis.

10. Mechanical hypothesis: the other major theory of the metastatic mechanism of tumor growth and dissemination, contending that the location of metastatic growths is a direct function of the number of cells passing into the general or regional circulation. Also called the circulating emboli hypothesis.

11. Palliation: the mitigation and alleviation of disease and its effects by various treatment regimes although a cure is not possible. The goal is to make the patient more comfortable and ease symptoms; physical therapy may be used as a palliative procedure.

ORGANIZATION OF THE REMAINING CHAPTERS

Because the field of cancer metastases, in particular breast cancer metastases, is one that is remarkably vast, the literature review of this study has attempted to demonstrate a more concise unification of many scientific observations that have been made and reported throughout biological and medical journals and scattered over the past decades. The chapter attempts to combine the various writings into a more complete whole. In the process the structural framework for the construction of the operational model which forms the base for the data collection of this thesis, was realized. This task was made easier by excellent bibliography and cross references that were found for each topic. Concentration in the second chapter is on the major sites of metastatic spread, although proper attention is given to the less common although equally interesting minor sites of spread.

Chapter three contains the methods of data collection and data analysis; here also the text describes the construction of the operational models for data collection. The models themselves are properly placed in the appendices because of their undue length. The procedure for model approval is outlined, as well as precise plans for the interpretation of data that was obtained. The exact

procedures used in data collection are described in full, completing this chapter.

In chapter four, tables describe the results of this study, and chapter five completes and reviews the study. Some implications for future research are given, in particular the projected use of the model to other forms of cancer.

In summary, before we can decide with certainty what kind and level of physical therapy treatment is necessary, the dysfunctions of the patient should be accurately, thoroughly, and completely understood. This also applies to dysfunctions that are a result of metastatic, disseminated cancer - the disease process chosen for the topic of this study.

This research project hopefully will facilitate evaluation and treatment of the metastatic breast cancer patient in light of this understanding.

Chapter 2

REVIEW OF LITERATURE

THE NEED FOR CLASSIFICATION OF DISTANT METASTASES

Attempts to classify breast carcinoma for both academic and prognostic interest have been common in the literature. One system which was used quite extensively employed four groups designated by roman numerals (Sicher and Waterhouse, 1973). This system grouped patients according to the stage of the disease which progressed from the lesion being confined to the breast to the patient having widespread, disseminated disease. Haagensen (1971) has employed a four stage system based on factors such as number and location of involved lymph nodes, size of primary tumor, degree of skin involvement, and other local characteristics.

During this century, clinicians discovered that although detailed localization of the primary tumor within the breast appeared to have little influence on prognosis, a supplementary classification of node involvement proved to be a valuable adjunct to assessment of likely survival. Thus the TNM system of classification was conceived. In this system the letter T represents characteristics of the primary tumor, the letter N the state of the regional lymphatics, and the letter M the presence or absence of distant metastases outside the defined zone of regional lymphatic drainage. Separate descriptions were set up by the International Union Against Cancer (UICC) and the American Joint Committee for Cancer Staging (AJCC) for the clinical classification

of breast cancer. In these systems a tremendous amount of detail and attention is paid to local characteristics of the lesion, such as the primary tumor, ipsilateral axillary node status, and skin condition overlying the tumor.

However, in all discussions pertaining to classification, the M division is only graded M_1 or M_0 , that is, if disseminated disease is present or not. There are no provisions in the classification system for the number, site, type, and growth of the distant metastases. In addition, no definitions as to exactly what constitutes a distant metastasis were offered.

Philips (1973) reported the results of a prospective five year clinical trial of the TNM system of classification as proposed by the UICC. Fifty-nine out of a total of 1,517 cases had distant metastases when first examined. This demonstrated a clear need for further breakdown of the M category. It is illogical to assume that primary tumor and nodal involvement exert the main influences on likely survival when it is distant metastases or their complications that most often kill the patient. Distant metastases can conceivably be present but dormant in a considerable segment of the population coming for initial treatment for their breast tumor (Sicher and Waterhouse, 1973).

Recently, a group of investigators have attempted to classify patients with disseminated breast carcinoma. Cutler, Sidney, Asire, and Taylor (1969) contended that the time interval between initial diagnosis of the primary disease and the number and types of organ sites involved influenced the survival time. The authors indicated that the more obvious advantages of a classification

which included such parameters would facilitate evaluation of therapeutic results and also help physicians select the treatment for individual patients (Cutler et al., 1969).

Slack, Blumenson, and Bross (1969) formulated a mathematical model which might characterize the course of breast carcinoma. One of the purposes of the model was to develop a formal method of testing a two disease hypothesis - Type A being the more malignant, faster growing tumors and type B less malignant or slower growing tumors. Included were parameters measuring or estimating the tumor doubling time, nodal involvement, delay time, and chance of distant metastases. Effects of treatment were considered important in significantly influencing the clinical picture of the patient.

As in other similar studies, there was reason to question the accuracy of the number of positive nodes detected. Also, the model by Slack and his colleagues professed the growth rate of the primary tumor and the metastatic lesions to be the same, but the selective affinity hypothesis of metastatic cancer - where the site of metastasis is the stronger determinant of growth of the tumor - may not fully support this. The conclusion was that the data did support a two disease hypothesis, but more significantly, proper attention was beginning to be paid toward the distant metastatic aspect of breast carcinoma and its impact on the natural history of the disease.

Reventos (1969) wrote concerning the current status of clinical classification of breast cancer. He suggested that distant metastatic involvement be assessed and incorporated into the schema by the addition of a checklist for sites of distant spread;

this could be used as an addendum to the already established TNM system. Although his concepts needed further development and delineation, the importance of distant metastases and their means of detection was given further support.

Cutler (1970) outlined some parameters of prognostic factors in breast cancer. He stressed abstracting pertinent information from the medical record of the patient, including distant metastases status. No attempt was made to further divide the distant metastatic factor, despite the admitted fact that less than half of breast cancers diagnosed were confined to the breast. Cutler (1970) did find that relationships between the clinical characteristics of each group, the percentage having pathologically involved nodes, and prognosis suggested that this information may be useful in deciding on individual treatment plans. His mathematical three digit model, where tumor size, fixation and edema, and axillary node status were graded respectively, neglected distant metastases entirely. The author did reiterate the need for a more complex and comprehensive checklist for distant metastases in each patient (Cutler, 1970; Cutler and Myers, 1967).

As early as 1967, the latter authors studied a series of 2,034 cases in an empirical statistical approach to classification. Staging recommendations based on American and international committees were compared. They found that the same evaluation and treatment plan was not appropriate for all patients falling into the same prognostic class, due precisely to variations in clinical characteristics. Because schemes did not provide homogenous groups, a fairly detailed and inclusive checklist of relevant characteris-

tics, including distant metastatic sites, was provided to help physicians in assessment of the disease. Galasko (1974) stated that "although TNM classification is well described in the literature and in the majority of textbooks, very few mention modern methods of determining distant metastases, even though ultimately the prognosis depends on the degree of dissemination".

The extrapolation of the preceding paragraphs is that physical therapists as well as physicians need a specific classification of disseminated breast carcinoma for evaluation and treatment procedures to be correct and appropriate. However, admittedly clinicians could anticipate much disagreement if distant metastases were incorporated into the existing classification systems; since many different sites can be effected in a variety of ways, the added permutations and combinations could be truly complicating.

Because not only the presence or absence of distant spread, but also the location, number, symptomatology, and characteristic nature of the metastases effect prognosis and morbidity, the need for further classification of disseminated breast carcinoma has been demonstrated.

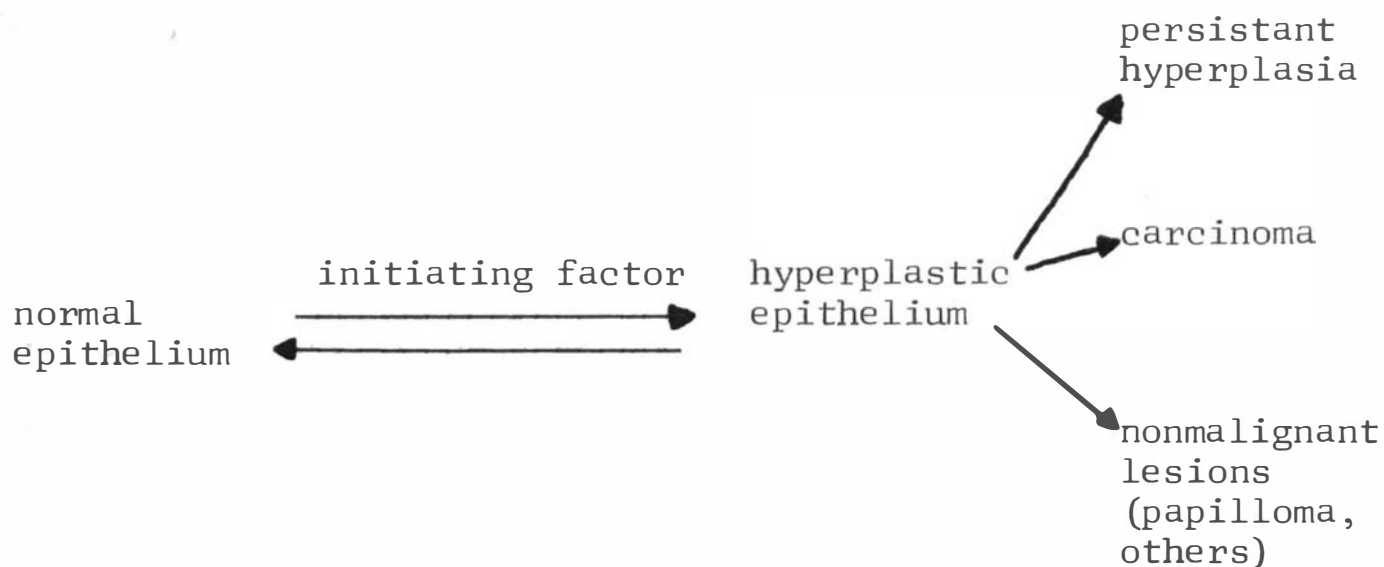
INTRODUCTION TO PATHOLOGICAL CONSIDERATIONS

The pathology of early and late carcinoma of the breast is a function of the number of types of neoplastic disorders that can affect the breast. Excluding the rare sarcomas, Haagensen (1971) offered at least eight distinct forms. These are distinguishable mainly and principally according to anatomical location within the mammary tissue, cell size and type, and patterns of growth. The

so called infiltrating ductal carcinoma comprises 75 percent of all breast cancer, so it will be described in more detail.

The earliest morphologically recognizable step in the transition from normal to neoplastic histology is the multiplication of the epithelial duct lining cells in numbers greater than are required for normal homeostasis. In ductal carcinoma, once the actual transformation has taken place, the process was irreversible and progressed inexorably and often rapidly to involve areas of the epithelium and to invade adjacent breast tissue; the origin was considered to be multifocal by many authors. Gallagher and Martin (1970) proposed the model described in Figure 1, explaining breast carcinoma in terms of a transition from normal epithelial lining to an invasive carcinoma.

Figure 1



Representative Transition from Normal Tissue to Carcinomatous Change

Ductal carcinoma of the infiltrating type may actually arise outside of a duct, and so distend a lobule that the carcinoma appears to be a true ductal carcinoma. Other carcinomas commonly arise from epithelial cells of the lobules themselves, the larger ducts, and from intralobular tissue (Wellings and Jensen, 1973). A variety of histological appearances can present. The reader is referred to Haagensen's treatise for a detailed discussion of the microscopic pathology of breast carcinoma.

Breast cancer commonly spreads by both the lymphatic and hematogenous routes. As a rule, but by no means under all circumstances, hematogenous dissemination follows lymphatic spread by some months or years. However, blood borne metastases without lymphatic spread can occur, and may be present when the patient comes for primary treatment of her breast tumor. Current thinking stresses the relationship between the two routes.

Metastases were most common in the lungs, liver, bones, brain, and kidneys - organs which have extensive parenchyma, and were highly vascular were more prone to develop metastatic growths (Coman, DeLong, and Cutcheon, 1951). A preliminary step to metastasis was invasion of the primary tumor, governed by the rate of growth, motility of the cancer cells, and loss of cohesiveness of the malignant cells. Elaboration of lytic substances, such as enzymes and proteins, also probably played a part in the ability of the tumor to invade contiguous structures (Terry, 1974).

Coman et al., (1951) studied the mechanical hypothesis using the Brown Peace Rabbit tumor, and observed that embolitic tumor cells were more likely to establish themselves and form new

tumors if they lodged in the capillaries than if they arrested in the arterioles. This study had some implications for breast carcinoma - perhaps the sites of spread were determined by how many emboli reached the capillary bed; the soil hypothesis could support this, as the skeletal, nervous, and pulmonary systems were all richly endowed with an extensive capillary network (Coman et al., 1951). Still unresolved, both theories have their proponents - it is likely that tumor emboli are commonly destroyed by immune mechanisms in organs where metastases are rare, such as muscle, fibrous, and cartilaginous tissue.

Medical professionals today recognize that disseminated breast cancer has an extremely wide variability in its natural behavior; every case is truly individualistic. There is no precise way of determining changes in the neoplastic cell population quantitatively at frequent intervals, so relating tumor characteristics to the clinical presentation is difficult and at best only approximate. In addition, the description of an individual breast carcinoma according to any of the accepted parameters is not final, because progression of the disease allows a change in the tumor cell population towards new clinical states over time (Brennan, 1967). Thus, clinicians are encouraged to view breast carcinoma metastases as fluid, dynamic transitional states, upon which a multitude of factors can act.

The history of breast cancer could be easily divided into two phases: the invisible or preclinical period of growth, and a visible or clinical phase (MacDonald, 1966). He proposed that fully three-fourths of the life cycle of a mammary carcinoma

passed before clinical diagnosis was possible. The biological balance between the host and neoplasm could become established long before the clinician could exert any influence on the process. Implications for metastases and their clinical presentation were equally clear: the metastatic growths were established and developed a significant biological balance with their host so that when they became clinically detectable, the relationship had probably reached an irreversible course (MacDonald, 1966).

If distant spread were the result of dissemination of tumor cells remaining in the treated area, one would think that local recurrences and manifestations might become evident long before the distant metastases had declared their presence clinically, but according to one study, this was not the case (Bruce, Carter, and Fraser, 1970). Concerning distant spread to bone without local recurrence, it was very conceivable that when a physician performed a radical mastectomy and three years later the bone metastases appeared, the neoplastic entity was present in the bone or serum during that time and somehow later reactivated to produce clinically evident metastases (Bruce et al., 1970). This gathered further significance considering the fact that in 25 percent of early patients coming for primary treatment, there were already bone metastases present that did not show up radiographically.

The fact that lymphatic metastases could appear in distant rather than proximal lymph nodes was a fact frequently ignored by surgeons for a long time (Fisher, 1969). This author also indicated that there was a closer relationship between hematogenous and lymphatic spread of tumor cells than was currently believed. For

example, tumor cells that were primarily growing in lymph nodes could extend to the vascular system and disseminate, and theoretically blood borne metastases could find a way into the thoracic or other large lymph duct and disseminate lymphatically. The latter was probably much less likely, considering the reverse pressure gradient that exists from lymph to blood portals, and the fact that tumor cells were not likely to travel against the natural flow of lymph which is toward the large lymph ducts.

That tissues which were damaged physically or chemically might provide fertile soil for the development of metastases was a definite possibility; this might be one of the factors which controlled the trapping of the circulating tumor cells and influenced their subsequent growth. For example; the vertebrae, pelvis, and upper femur which are constantly subjected to the physical strains of bearing the weight of the body in locomotion, were by far the most common sites of bony metastases. Likewise, the lungs which were possibly repeatedly traumatized by tobacco smoke and/or other irritants, were a common site of distant spread.

Before discussing symptoms and clinical manifestations of metastatic disease in breast carcinoma, a brief exposition of the importance of location of the metastases is necessary.

Patterns of Dissemination

Viola (1971) offered some diagnostic clues to different types of metastases, and outlined some of the sites that could give rise to treatable complications. Among common sites were brain, lung and bone metastases, and obstruction of abdominal or media-

stinal lymph nodes. Freid and Goldberg (1943) emphasized skin, skeletal, pulmonary, pleural, cerebral, hepatic, and intraabdominal metastases as being significant sites. Skeletal involvement occurred in well over one-half, liver involvement in at least one-half, and pulmonary spread in approximately one-third or more of patients (Freid and Goldberg, 1943).

Recently a group of researchers carried out an autopsy study of routes of dissemination of cancer of the breast (Viadana, Bross, and Pickren, 1973). Their notable summary reported 647 primary breast carcinoma cases, and explained the one step process of the dissemination of cancer, whereby all cancer cells were derived directly from the primary tumor and spread to metastatic sites throughout the body, compared to the much more plausible multistep or "Cascade" process where secondary metastases themselves give rise to other metastases. Pathologically, it is not possible to determine with certainty whether a growth in question is indeed from the primary tumor or a secondary metastases.

They reported that at autopsy, 66 percent of patients had lung involvement, 61 percent liver involvement, and 70 percent had osseous metastases. These three major areas were considered to be potential sources of further metastatic dissemination because they were the most common sites and locations of distant metastases in breast cancer (Viadana et al., 1973). The researchers found a low frequency of metastases in various minor sites when the three major sites (lung, bone and liver) were not affected or seeded. Conversely, if one or more of the three major sites were involved in the metastatic process, a higher incidence of metastases to various

minor sites was observed. A partial list of effects of the three major sites is shown in Table 1. As an illustrative example, the first line signifies that 66 percent of tumors metastatic to the pituitary also metastasized to bone; and 15 percent also metastasized to the lung.

Table 1
Breast Cancer Metastases - Effects of
Three Major Sites on Seven Minor
Sites of Involvement

SITE	GREATEST EFFECT	SECOND GREATEST EFFECT
Pituitary	66% to bone	15% to lung
CNS	61% to lung	21% to liver x bone
Stomach	erratic pattern	
Pancreas	48% to liver	29% to lung
Kidney	41% to lung	25% to liver
Uterus	77% to bone	13% to lungs x bone
Thyroid	52% to lung	22% to bone

It appeared that the lungs might tend to release metastases into the circulation and thereby establish metastases in the CNS, pancreas, pituitary and thyroid (multistep, hematogenous). Any single effect could simply have been a measure of the strength of the association between the two organs, and not necessarily an actual dissemination of metastases from one of the three major sites to one of the minor ones (Viadna et al., 1973).

One study classified metastatic cancer patients with breast primaries into the following five groups: bone, chest, and soft tissue, brain, and visceral (McCorkle, 1973). Other sources have

grouped all chest and mediastinal spread under the heading thoracic.

Shields and Withan (1933) outlined the distribution of metastases from breast carcinoma, stating that few malignant tumors metastasize as widely. The study was based on 162 autopsies, and reported the following sites of metastases in order of decreasing frequency: distant lymph nodes, lungs, liver, bone, skin, pleura, and adrenals.

The authors agreed that in hematogenous dissemination metastases were usually present in the lungs and disseminated from that organ - they explained bone metastases without demonstrable lung involvement as minute viable tumor emboli being able to bypass the pulmonary circulation (Shields and Withan, 1933).

Cutler, Asire, and Taylor (1969) indicated that much more complete information was needed concerning the history and clinical course of metastatic breast cancer. Their model, which provided one of the groundworks for the model used in the present study, outlined four sites of metastases as associated with a high mortality: liver, brain, peritoneum, and spinal cord. Two major points evolved from this study: (1) If the high mortality sites were excluded, specific sites of metastases were not correlated with variation in survival time, but that the number of sites involved was significant, and (2) the longer the free interval, that is, the longer the interval between primary treatment and the diagnosis of recurrence of distant metastases, the longer was the survival time after that diagnosis (Cutler et al., 1969). Both the more common sites of metastases (bone and lung) and those that typically carry a high mortality are among those included in the

descriptive model.

Therefore, certain metastatic sites, among them the more common areas of spread (lung, bone) although significant, might imply longer survival times than those of other metastatic sites (brain, liver). This fact might be helpful in assessing morbidity and in choosing treatment approaches in patients with disseminated disease. Likewise, patients with long free intervals could be expected to have fairly long survival times.

Role of the Vertebral Venous System in Metastatic Breast Cancer

Before describing the various sites of metastases from breast cancer, a very important related phenomenon deserves special attention; the vertebral venous system and its relation to tumor spread. Many authors have outlined the characteristics of this type of spread (Batson, 1942; Haagensen, 1971; Henriques, 1962).

At one time, it was thought that all hematogenous dissemination of breast cancer occurred and originated from pre-existing metastases in the lung. Tumor emboli were thought to lodge in the first vascular bed that they encountered (Henriques, 1962). However, careful autopsy studies revealed that many breast cancer patients harbored distant metastases, particularly in bone, without demonstrating pulmonary spread.

Anatomically, it is possible for the tumor cells to reach distant sites without passing through the lung. The vertebral veins form intricate plexuses inside and outside the vertebral canal; these basal vertebral veins form wide channels within the vertebral bodies, emptying into the vertebral plexuses, which in

turn communicate at each costal segment with the intercostal veins. The intercostal veins drain portions of the breast, as well as the thoracic area of each segment. Further investigation (Batson, 1942; Henriques, 1962) showed that the system also connected with the pelvic girdle, upper ends of the femur and humerus, shoulder girdle, and skull. These areas are the commonest sites of metastases of bony involvement from metastatic breast carcinoma.

Henriques (1962) also contended that the vertebral system lay outside the body cavity per se and therefore was not subjected to the same pressure changes. There was radiological evidence that demonstrated reflux shunting of blood could occur into the vertebral veins at all levels of the spine during such activities as coughing, straining, performing a valsalva maneuver, or lifting.

Additional factors which supported the vertebral venous system were the fact that it was found to be for the most part without valves and had a low venous pressure, thus retrograde flow was common. Even without physiological need, there was much more blood present in the vertebral vessels than was practically or metabolically needed (Haagensen, 1971). This alternate merited further discussion above because (1) bone metastases are the most common distant metastases in breast carcinoma, and (2) bone metastases carry a significant morbidity and potential disability.

Summary

The preceding section has presented material and concepts concerning the general pathology of breast carcinoma with particular reference on disseminated disease. The text alluded to the

anatomical differentiation between distant and regional spread offered in chapter one, and the two main routes of dissemination were compared. Consensus of the literature was that significant interplay between lymphatic and hematogenous dissemination occurred; support for both the soil and the mechanical theory of metastatic growth, and the rationale for separation of major and minor sites of metastases were outlined. The vertebral venous system and its alleged role in the distant spread of breast cancer was explained in the light of increased bony metastases to areas supplied by this system.

A detailed outline of each major metastatic site, diagnosis, clinical characteristics, and treatment will comprise the remainder of chapter two. In the following order, pulmonary, pleural, bone, liver, central nervous system, spinal cord, and distant lymphatic metastases will be described.

PULMONARY METASTASES

Pathology

There are three ways for carcinomatous emboli to reach the lungs from the breast:

1. Lymphatic spread from the breast can reach the central lymphatic terminus at either side of the neck at its base, next emptying into the innominate vein, then to the vena cava and in turn to the pulmonary circulation.

2. Tumor emboli that have eroded capillaries or venuoles reached the internal mammary or axillary veins, in turn to the innominate vein, and thus to the pulmonary circulation.

3. Tumor cells can embolize in the intercostal veins, and either travel in a retrograde manner to the vertebral venous system as previously described, and eventually back to the lungs by the systemic circulation or directly empty into the azygous veins, and thus to the vena cava and the pulmonary circulation to set up metastatic growths.

Whatever route is used, the tumor emboli had several alternatives regarding their history. Some of them were choked and destroyed by the fibrosis that developed around them; some grew into the pulmonary parenchyma to become true pulmonary metastases; or others may have bypassed the pulmonary capillaries entirely and reached the systemic circulation.

An early study described the fate of carcinoma emboli that reached the lungs (Saphir, 1947). Twelve lungs were studied which had histologically disclosed tumor but no frank metastases. When tumor cells failed to penetrate the vessel wall and form metastases, they caused the formation of hyaline thrombi which grew adjacent to the tumor cells and caused the latter to atrophy (Saphir, 1947).

There are many factors which make the lung an ideal location for secondary spread of tumors (vascularity, size, rich epithelial lining). However, the ideal conditions which are required for emboli to attack the capillary wall, break through, and set up a distinct growth which eventually develops its own blood supply describe a remarkable process or setting that is not completely understood.

One research report outlined a clinical-radiological study of pulmonary metastases on a group of 299 patients with diffuse

carcinomatosis; 77 of these were breast primaries (Minor, 1950). The author described five different groups of pulmonary metastases according to radiographic appearance. They were nodular, or round discrete well circumscribed lesions within the lung parenchyma; amorphous, or infiltrative appearing as diffuse shadows and thickenings within the parenchyma; lymphangitic, confined mainly to the pulmonary lymphatics; miliary, greatly diffuse, spotty spread with much replacement of lung parenchyma; and finally massive consolidation with frequent atelectasis (Minor, 1950). He stated that overlapping of classification was the rule rather than the exception. Haagensen's description only included the basic nodular and lymphangitic types, the latter will be discussed in detail in subsequent text.

Nodular lesions in the lung may be notoriously asymptomatic for long periods, an observation noted by many authors (Bates, 1964; Clagett and Woolner, 1964; Haagensen, 1971; Heitzman, 1973; Minor, 1950). According to Clagett and Woolner, (1964) in reporting a series of 165 pulmonary metastatic cancers (21 or 12.7 percent breast primaries), nodular lesions were much more often multiple than single or solitary. Because the tumors were usually located in the lung parenchyma and the bronchi were not typically involved extensively, symptoms were few (Clagett and Woolner, 1964).

These same authors stressed that a single lung shadow particularly in the hilum or apex of the lung, was much more likely to be a primary lung tumor. Cahan and Castro (1975) shared this same view. A solitary nodular lung shadow in a person with a known primary breast carcinoma was a very ambiguous clinical presentation,

requiring prompt clarification as to its histological nature so that proper treatment could be instituted. The authors maintained that the combination of lung and breast primaries would occur more often because (1) more females are surviving their breast cancers, and (2) the rate of lung cancer in women is rising precipitously.

Some nodular lesions did produce local problems, perhaps by rapid growth and pressure or eruption into a contiguous bronchus. Obstruction of a main bronchus with resultant atelectasis occurred occasionally (Minor, 1950). He also stated that carcinoma of the breast was the commonest primary lesion to metastasize to the lung, and that breast carcinoma metastases produced the greatest degree of pleomorphism in the lungs, and furthermore was more prone to metastasize to the pleura and the mediastinum than any other type of cancer.

Signs and Symptoms, Detection

The symptomatology of breast carcinoma metastatic to the lung will depend a great deal on the type of metastases. Nodular growth may become symptomatic as mentioned above if the deposits are large and obstructing. Symptoms for the various types included cough, dyspnea or tachypnea, sputum production; anorexia, fever, and weight loss were the systemic manifestations. Infections, with purulent drainage and hemoptysis or bloody sputum could occur, but were much less common (Hauser and Steer, 1951; De Wys, 1974). Typically, respiratory embarrassment and severe pulmonary symptoms were not seen until late in the course of the disease.

For that reason, the most common method of detection of

pulmonary metastases was via X-rays or tomograms, and the majority of cases were diagnosed and discovered incidentally by routine follow-up radiographs. The miliary type of spread or massive consolidation produced pulmonary symptoms such as dyspnea and cough earlier in their course than simple nodular spread. Decreased vital capacity was a finding that depended on the amount of parenchymal tissue replaced or rendered insufficient for normal pulmonary physiology by obstruction, collapse, or destruction. Tumors could invade the pulmonary vasculature and cause hemorrhage which could be a serious complication. Finally, lung metastases might lead to pleural spread from blood borne emboli in the pulmonary arteries. Carcinoma cells could also be shed directly into the pleural cavity and effect a pleural effusion (Haagensen, 1971).

The concept of tumor doubling time (TDT) has enjoyed particular relevance in relation to pulmonary spread. In a recent series review, a group of investigators evaluated 45 patients with pulmonary metastases (Joseph, Morton, and Adkins, 1971a). TDT was easily calculated for lung metastases if they are discrete and clearly outlined on chest radiographs. Thirty-seven cases met those criteria and were classified as rapid, intermediate, or slow according to their growth rates.

Some of the factors which possibly governed the TDT were number of proliferating cells; length of cell cycle; extent of cell loss or death due to cell necrosis; embolization; destruction of cells by immune response; and the number of non-proliferating cells. The same authors (Joseph, Morton, and Adkins, 1971b) in a separate

publication, released the results of a study of 113 patients, nine of which were breast primaries. Quite often breast carcinoma metastases did not meet the criteria necessary for the precise determination of the TDT.

The investigators supported their previous research: the shorter TDT's correlated with a shorter free interval from primary lesion resection to onset of pulmonary metastases. Also, (1) conversely, longer TDT's had longer free intervals and longer survival times, and (2) the use of the TDT as a prognosticator for survival was limited as it only could be employed in breast cancer cases with a certain type of lung metastases (Joseph et al., 1971b). The conclusion was that the operability, behavior of the lesion, and chance for survival appeared to be more a function of the TDT than other criteria.

Treatment

One of the treatment methods which was utilized more often in the past, but is still justified in selected cases was surgical removal of the metastatic tumors. Moersch and Clagett (1961) published a report on 134 cases, 21 or 12.5 percent of which were breast primary. They pointed out that the nature and origin of the primary lesion was only of some prognostic import in individual cases for surgery, as all types could have long term survival. Many authors have advocated surgical removal of metastatic pulmonary tumors (Choksi, Tahita, and Vincent, 1972; Mountain, 1970; Smith, 1963) and one source stated that resection of metastatic lesions from the kidney, uterus or large bowel was followed by the greatest

degree of surgical success, but that breast, endocrine or melanoma primaries gave more discouraging results (Smith, 1963). Accepting this opinion, surgeons could only select relatively few for this form of therapy.

Choksi et al., (1972) believed that save for organs drained by the portal venous system, the pulmonary vascular bed formed the first effective filter for tumor emboli; thus he emphasized the importance and increasing incidence of pulmonary growths. They also noted that bronchoscopy prior to surgery for diagnostic purposes was often negative because the metastases were mainly peripheral, only infrequently involving the bronchus.

Clagett and Woolner (1964) claimed that surgical resection of solitary nodular deposits might be undertaken only if there were no other evidence of recurrent or metastatic disease. The survival rate, however, was a depressing 30 percent.

Mountain (1970) outlined the criteria of operability for patients with pulmonary metastases: ability to tolerate the surgical procedure, absence of disease at the primary site, and absence of extrapulmonary metastases. Since 15 to 25 percent of patients have lung involvement as their only site of distant spread, surgical consideration could be given some weight in selected cases. However, breast cancer metastatic to lung had a relatively poor post surgical tumor free interval, probably because there was a high incidence of co-existing mediastinal node involvement in these patients (60 percent). Choksi and his colleagues (1972) concluded that "a solitary metastasis, if not removed, will continue to grow and lead to a decreased resectability rate, and the possibility of

development of tertiary metastases". Metastatic lung tumors are not commonly irradiated because of the low tolerance (relatively) of pulmonary tissue to ionizing radiation; in addition, a troublesome fibrosis is a typical sequelae, and can effect pulmonary function if large areas are affected. Chemotherapy in combinations of drugs has produced regression of pulmonary lesions in many patients, but the response is difficult to assess since nodules may remain quiescent for long periods, and may regress or increase in size in response to concomitant factors other than chemotherapy effects, most of these are unknown.

In summary of non-lymphangitic pulmonary metastases, the deposits in the lungs produced only such changes in pulmonary function as were contingent and consequent upon replacement of alveolar tissue by the solid tumors. Surgical treatment has waned in light of chemotherapy and radiation, but the use of both of the latter is limited in metastatic breast carcinoma with pulmonary manifestations.

Lymphangitic Pulmonary Metastases

In contrast to the above, in lymphangitic carcinoma of the lung, an entity of which the pathology merits more detailed explanation; loss of pulmonary compliance and severe symptomatology were early features (Bates and Christie, 1964). Severe dyspnea, the most prominent symptom, antedated the radiological changes in many cases.

In lymphangitic metastases, tumor cells were carried to the lungs by the bloodstream, and after extravasating from the blood

vessels to the interstitium, reached the pulmonary lymphatics. The interstitium became thickened due to distention of the channels immediately behind the central lymphatic tumor emboli, due to tumor cells in the interstitium itself, or due to the pulmonary edema (Heitzman, 1973; 330-332). This interstitial pulmonary edema was thought to be a common cause of pleural effusion because of accumulated fluid.

A comprehensive study by Goldsmith, Bailey, Callahan and Beattie (1967) reported that 87/365 or 24 percent of breast cancer patients coming to autopsy had lymphangitic metastases. According to this report, the progressive pulmonary lymphatic involvement with tumor caused the reduction in the ability of the parenchyma to move in accordance with pressure changes in the pleural cavity (decreased pulmonary compliance), and pathologically presented as decreased tidal volume, vital capacity, inspiratory capacity and decreased expiratory reserve volume, all accompanying the extreme dyspnea or tachypnea. This same research found a higher incidence of pleural effusion (63 percent) in lymphangitic metastases as opposed to non-lymphangitic pulmonary metastases (41 percent).

Fischer and Hagerstrand (1965) discussed the pathology of this often unrecognized phenomenon. They debated whether thrombosis of the blood vessels should have been ascribed to carcinomatous growth in the peri-vascular lymphatics or to tumor fragments transported in the actual blood vessels. Of interest in the study was the fact that out of 97 cases, 20, approximately 20 percent, were breast cancer primary, and tumor growths were found in the pul-

monary lymphatics in 97/174 cases with all types of pulmonary metastases.

A typical symptom complex was dyspnea, cough, cyanosis, pleuritic pain, and general physical deterioration (Hauser and Steer, 1951). These were most likely caused by the pulmonary edema, fibrosis, decreased pulmonary compliance, and obliterative arteritis which were found (Heitzman, 1973). Mueller and Sniffen (1945) thought that the presence of masses of tumor cells in the dilated lymphatics was responsible for the peculiar radiographic picture and pattern - a network of increased lung density radiating from enlarged hilar lymph nodes and spreading through the lung fields, interspersed with numerous fine nodules.

More current thinking in lymphangitic carcinomatosis of the lungs was displayed by Janower and Blennerhassett (1971) and Trapnell (1964). They divided the chest radiographs of 23 cases (13 of them breast primaries) into three groups - mixed, lymphangitic, and normal. Autopsies demonstrated that in lymphangitic metastases one-half of the bulk of the increased tissue was due to tumor cells, and the other half to reactive fibrosis and inflammatory tissue. Other research scientists have emphasized that parenchymal nodular and lymphangitic pulmonary metastases quite often exist together in the same individual. Detection of this condition is not difficult owing to the symptomatology and characteristic radiograph picture. However, if the patient is in the early stages, and is asymptomatic, the radiologist must rule out several other disease processes that can mimic lymphangitic metastases radiographically. There are few studies concerning the

appropriate clinical management of this condition, and once interstitial blockage and dyspnea become progressively severe, treatment is symptomatic.

Summary

In summary, pulmonary metastases are a result of tumor emboli becoming lodged in the lung capillaries, and breaking through into the lung parenchyma or lymphatic vessels. There are various characteristic radiographic pictures of pulmonary metastases, and a wide variety of symptoms may ensue, particularly in the lymphangitic type. All forms of secondary lung tumors are potentially lethal because they can replace normal lung tissue, collapse areas, and in so doing upset the normal physiological function of pulmonary tissue.

PLEURAL EFFUSIONS

Malignant pleural effusion is another relatively common complication of disseminated breast carcinoma (De Wys, 1974). Fracchia, Knappa, Carey, and Furrow (1970) estimated that approximately one half of patients with systemic breast carcinoma developed pleural effusions, and that breast carcinoma was the tumor most frequently responsible for the complication. Effusions occurred more frequently in patients with pre-existing lung metastases, especially of the lymphangitic type (Goldstein et al., 1967).

Pathology

Pathologically, effusions of a malignant nature could be

divided into three types: (1) those due to irritation of serous membranes from solid tumor implants, with exfoliation of the tumor cells into the fluid; (2) obstruction of the small pleural vessels or lymphatics associated with large solid tumor masses, a type usually acellular; and (3) nodules of carcinoma beneath the visceral pleura breaking through a tear in the pleura, permitting carcinoma cells to escape into the cavity (Haagensen, 1971).

Symptoms

The cardinal symptoms were dyspnea, pain and cough (Haagensen, 1971). Porter (1965) reported that out of 76 cases in a series, 49 were ipsilateral, 41 contralateral to the breast primary, and 23 were bilateral. Both authors contended that malignant pleural effusions were due to lymphatic permeation through the chest wall, because effusions arising from hematogenous spread should theoretically have arisen equally often on either side.

Treatment

Pleural effusions are usually treated, if severe enough to be resolved by methods other than systemic chemotherapy, by thoracentesis with or without instillation of tumorcidal agents. Radiation or surgical resection are only rarely employed.

Leninger, Barker, and Langston (1969) remarked that the pathology behind pleural effusions was not well understood and that whether tumor cells per se exuded fluid or whether an exudative response was secondary to the tumor implant producing friction against the opposing pleura, was not clear. They recommended

intercostal catheter drainage followed by the administration of intrapleural chemotherapeutic agents and appropriate analgesics and antiemetics. They gave the following rationale for the efficacy of chemotherapy: "the finding of tumor implants on both the visceral or parietal pleura at autopsy suggests that chemotherapy not so much destroys tumor cells, but rather causes a chemical pleuritis that bonds the pleura together after the fluid has been withdrawn by a chest tube" (Leninger et al., 1969). However, this bond may not be advantageous; some clinicians prefer chemotherapy that destroys cells yet prevents this chemical pleuritis.¹ Tetracycline is tumorcidal yet does not cause this bonding.

Summary

Pleural effusions, then are common in disseminated breast carcinoma; the average survival period in untreated patients is approximately seven months; chemotherapy or radioactive isotopes introduced intrapleurally can do much to relieve the significant symptoms and morbidity that this complication can produce.

BONE METASTASES

Extent of the Problem

The story of the dissemination of breast carcinoma can be told virtually in terms of metastases to the skeletal system. Osseous involvement is the most common sequelae of breast cancer

¹Dr. Susan Mellette, personal communication.

dissemination, most frequently presents as the first sign of distant spread, and probably causes the most distressing symptomatology and complications of all forms of metastases. In females, the great majority of skeletal metastases were caused by breast cancer (Zimskund and Surver, 1958). In careful autopsy studies, skeletal lesions are found in approximately 85 percent of women dying from breast carcinoma (Galasko, 1972). The present day oncologist can expect osseous metastases to become clinically evident in from 50 to 60 percent of patients with breast cancer - these significant figures seek to introduce the seriousness of the problem.

The frequency of involvement of the different bones is quite variable, being a function of the methods of thoroughness of detection in a given series (Staley, 1956). Galasko (1972) reported the following bones and percentages of patients having metastases: dorsal spine, 72 percent; lumbar spine, 68 percent; pelvis, 66 percent; ribs, 62 percent; proximal femur, 44 percent; skull, 44 percent; and cervical spine, 26 percent. Hoskins (1971) reported on the records of 150 cases of disseminated breast carcinoma, with skeletal spread occurring in 53 percent of this total. Fully 30 percent of these appeared within the first year of primary surgery - an observation particularly common in post-menopausal women. However, osseous metastases could present five and even ten years after treatment of the primary breast tumor.

Long free intervals observed in some patients were probably due to the fact that a percentage of cells failed to survive where they lodged, or they could remain quiescent in novel loca-

tions for years before erupting into clinical metastases. Recently, there has been evidence that suggested that bone metastases were more likely to occur in patients who developed their disease at a relatively earlier age, compared to more elderly individuals (Staley, 1956).

Lastly, the fact that recent series of simple mastectomies had survival rates comparable to series of radical mastectomies suggested that distant bone metastases might have already occurred in many patients at the time of diagnosis and initial treatment (Sklaroff and Charkes, 1968).

Pathology

Whether radiographs revealed bone metastases depended considerable upon the manner in which the disease grows in bone. Haagensen (1971) described three types of metastases: the intertrabecular type left the trabeculae nearly intact but filled the marrow spaces in between them with carcinoma. In the osteolytic type, the bone trabeculae were destroyed by the carcinoma, radiographically lesions appeared as irregular areas of decreased density. In the osteoblastic type, the bone trabeculae were thickened, and coalesced forming osseous masses. They presented on radiographs as abnormally dense areas of bone; although very common in prostatic cancer, only about ten percent of metastatic breast cancer presented solely as this type (Haagensen, 1971).

Galasko (1972) emphasized that osteolytic and osteoblastic patterns occurred more or less simultaneously as net results of bone formation and bone destruction. He theorized that osteo-

sclerotic cells were responsible for the bone destruction, but after tumor surrounded the bone spicules, the osteoblasts disappeared and the tumor cells themselves destroyed the osseous tissue. If the latter was the case, some property of the metastatic cancer cells was responsible; what exact chemical was released and the biochemical transformations taking place at the tumor cell bone interface were not completely understood.

Bone metastases were more common in red marrow as opposed to yellow marrow (Hoskins, 1971; Haagensen, 1971; Robbins et al., 1972; Zimskund and Surver, 1958). This is another reason for the unequal distribution of metastases in the skeleton. Unfortunately, estimates of the proportional amount of bone metastases effected by the vertebral venous system as opposed to the amount by the systemic venous system are lacking. Hickey (1967) remarked that pain would not occur until the periosteum was effected, and that early in the course of metastatic disease in bone, cancerous tissue could be present in the soft tissue of bone marrow without bone alteration.

The pathological mechanism of metastatic bone spread was based on three considerations (Johnston, 1970). The first was that sites of bone metastases were not determined by blood flow alone - tumor emboli could recirculate and not localize to the first bone which they reached. Secondly, the morphologic patterns of skeletal vasculature - capillaries in a rich sinusoidal pattern within the red marrow - partially explained the high incidence of metastases to bone. Recall that arteriolar walls were more resistant to tumor invasion than were the capillaries (Johnston, 1970). Thirdly, other

factors were important such as the decreased metastatic rate in patients on anticoagulant therapy, the purported increased rate with cortisone, nature of the primary tumor, and suppression of the cell mediated immunity, favoring accelerated dissemination in the later terminal stages.

Symptoms and Detection

Early in their involvement, bone metastases are asymptomatic. Pain usually heralds positive radiographs; it usually is deep and worsened by activity, particularly weight bearing. Pathological fracture, with pain, deformity, and loss of function of the joint, is typically of late occurrence. Infrequently the patient presents with severe pain and no abnormality can be discerned by bone survey or scan.

Improvement in the methods of bone scanning has broadened the role of the technique so that presently earlier, smaller, and very often unsuspected lesions are being routinely localized (Verdon, Yano, and Anger, 1971). Clinicians have readily agreed that the use of radionuclides demonstrated osseous involvement frequently before radiographic changes occurred (Galasko, 1969; Lawrence and Horseley, 1974; Scott and Adams, 1974; Verdon et al., 1971).

The basic principles underlying bone scanning have been outlined (Bland, 1971; Hoffman and Marty, 1972). Scans were general and not specific for cancer, the methods being based on uptake of the radioactive tracers in actively growing bone and not on uptake by the cancer cells per se. New bone was laid down by

proliferating osteoblasts; within the matrix hydroxy apatite crystals formed which interacted with the tracers. Because the principles underlying tracer uptake applied equally well to benign disorders and tumor metastases, the scan findings should be considered in terms of an alteration in local bone metabolism rather than a positive indication of the presence or absence of metastatic cancer (Bland, 1971; Hoffman and Marty, 1972).

Bone biopsy, by trephining, described excellently by Haagensen (1971), is specific only if the bone truly has metastases and is not commonly used due to the fact that scanning covers a greater area, and although more likely to be equivocal, carries a lesser likelihood of complications.

Complications and Treatment

Pathological fractures eventually occurred in 50 percent of patients with radiographic evidence of osseous metastases (Schurman and Amstutz, 1973). Femoral fractures are the most common and carry the greatest amount of morbidity, chiefly because of the weight bearing properties of this bone. The average time interval between initial diagnosis and onset of neoplastic fractures was 58.6 months for the femur and 52.1 months for the humerus; thus they are a late sequelae of breast cancer. Beals and Snell (1963) reported on 32 patients with 60 femurs so involved; in his series, the femoral metastases occurred within two years of the diagnosis of breast cancer, but the fractures somewhat later. Pelvic lesions nearly always preceded femoral involvement, an observation noted by Schurman and Amstutz (1973), and Haagensen (1971).

Studying the radiographs and clinical picture, Beals and Snell stated that the fracture rate in metastatic femora was 40 percent, and impending breaks could be predicted by checking the size of the lesion, its precise location, and the degree of involvement of the cortex. Staley (1956) reported pathological fractures in 80/166 patients for a rate of 48 percent.

"A pathological fracture of a major long bone is a dramatic, distressing, and incapacitating manifestation of disseminated breast carcinoma" (Coran, Banks, Aliapoulios and Wilson, 1968). Excluding vertebral body collapse, fractures of the femur were the most common complication. According to Galasko (1972), the mean survival after a pathological fracture was ten months.

Various clinicians have attempted to search for some criteria that could presage the imminent fractures in femurs, so that prophylactic hip nailing could be done (Snell and Beals, 1964; Bouchard, 1945). The latter contended that pathological fractures were common in osteolytic metastases where there was marked pain and more than 50 percent of the cortex destroyed in any one area. He added that when metastases developed in regions of the skeletal system where the natural body weight, torsion, indirect forces, or muscular traction were more pronounced, pain was sharper and came on earlier, and pathological fractures were a distinct possibility.

A detailed description of the surgical management of pathological fractures was published by Koskinen and Nieminen, (1973). They pointed out that fractures of the diaphysis or trochanteric region were the most common. Three points were stressed: (1) it was difficult to give a reliable prognosis, so the patient should

be given optimal surgical consideration, (2) the bony union of a metastatic fracture appeared to be essentially effected by the tumor type and response to palliation (breast cancer appeared to be a type conducive to good bony union), and (3) the fracture fragments should contain enough apparently healthy bone in order to render a stable osteosynthesis probable (Koskinen and Niemen, 1973).

The type of orthopedic procedures commonly used were internal fixation with a intramedullary rod for shaft fractures; resection of the head and neck of the femur, a procedure not done as often as formerly; a Jewett or other nail or plate for inter-trochanteric fractures; and prosthetic replacement of the femoral head for trans or subcapital fractures (Poigenfurst, Marcove and Miller, 1968). They assessed success of the operation on the patient's ability to walk; 60 out of 112 did ambulate post surgery, but the procedure failed to restore ambulatory function in 40. Long stem prostheses were favored, because they maintained stability, restored function earlier, and carried the possibility of stabilizing the femoral shaft at the same time (Poingenfurst et al., 1968).

Knutson and Spratt (1970) reported survival periods for a surgical and non-surgical group, which was approximately 13 months; one-half of the former group improved their ambulation status post surgery, while no one in the latter group did so.

There are several important and distinct advantages of internal fixation of pathological fractures of the femur due to metastatic breast carcinoma:

1. relief of pain
2. potential for ambulation enhanced
3. radiotherapy treatment is facilitated
4. excellent reduction and fixation without splinting
5. facilitates nursing care
6. complications of the bedridden patient are avoided
7. transportation and patient handling made easier
8. incidence of bony union is increased
9. hospitalization stay is shorter

Where metallic fixation devices were considered applicable, one had to have a strong enough bone surrounding the fracture to support it (Leach and Torgenson, 1967). These same authors valued physical therapy procedures to expedite and assist in the treatment of patients with osseous disease.

In a retrospective study of 96 patients, Parrish and Murray (1970) described 64 complete fractures, three impending fractures, and 72 surgical procedures performed. They judged the response to treatment of metastatic skeletal fractures by the osteoblastic reaction in the lesions and by relief of pain, and insisted that the benefits of internal fixation and open reduction far outweighed effects the procedure might have had on growth or local extension of the lesion (Parrish and Murray, 1970).

The relatively new concept of prophylactic fixation of imminent or threatening pathological fractures has presented an exciting challenge to the orthopedic surgeon. Since one-half of patients with bone metastases will eventually develop a fracture, Beals, Lawton, and Snell (1971) prophylactically pinned 94 cases, noting that the metabolic stresses of elective surgery were less than the combined stresses of surgery and fracture. They experienced no mechanical failures, and the results were encouraging. The operation was considered when a well-defined lytic type lesion

of 2.5 cm. diameter or greater involved the cortex.

Prophylactic intramedullary nailing or prosthetic replacement offered the following advantages: patient was in a relatively better condition; the operative procedure was of lesser magnitude and was less shocking; pain, displacement of fragments, and an emergency situation created by the fracture were all avoided and prevented (Coran et al., 1968; Fidler, 1973).

Non-surgical treatment of osseous metastases included irradiation, hormonal manipulation, and chemotherapy. Eisen, Bosworth, and Ghossein (1973) stated that fewer patients would run the risk of development of collapsed vertebrae, cord compression, or painful metastatic disease if the whole spine were irradiated initially with 3,000 to 4,000 rads. The rationale was that a high percentage of patients that were initially treated for a single metastatic focus in the spine required subsequent treatment to another area for symptomatic disease (Eisen et al., 1973). Bhalla (1970) advised radiotherapy in combination with hormonal therapy for control of the metastatic deposits, if there were no neurological involvement. Collapsed vertebrae were treated symptomatically, sometimes with external support of bracing, although the latter were tolerated poorly by patients with extensive metastatic disease.

"When osseous metastases are predominant, survivals are indirectly threatened, e.g. by complicating factors such as hypercalcemia, pathological fractures, or paraplegia or quadriplegia" (Mellette, 1970). In a report concerning hormonal management of

bone metastases, one of the major premises was that estrogenic hormones administered in greater than physiologic amounts suppressed tumor growth in 30 percent of post-menopausal females. Androgens worked better on women more than five years or more post-menopause. The side effects of the latter, however, were common and distressing. For pre-menstrual women, oophorectomy would effect bone tumor regression in 30 to 35 percent of patients, and finally the positive objective response to adrenalectomy in patients with osseous metastases was about 37 percent.

These results were encouraging, even more so if the hormonal manipulation were combined with radiation. Unfortunately, chemotherapy does not control or affect regressions in bone metastases as well as it does for some soft tissue dissemination.

Summary

Bone metastases may cause significant morbidity due to pain, decreased range of motion, imminent or resultant fractures, and other complications. Common surgical procedures were outlined for each fracture type, and results of treatment of this nature have been promising. This section has described the diagnosis, complications, use of radioisotopes, and summarized the basic treatment and management approaches to this common site of dissemination in human breast cancer.

LIVER METASTASES

Incidence and Pathology

Metastases to the liver from breast carcinoma is one of the

three most common sites of metastases of this disease. Clinicians can expect the liver to be involved in breast carcinoma in approximately 50 percent of cases (Freid and Goldberg, 1943). Abrams, Spiro, and Goldstein (1950) reported a 61 percent metastatic rate to the liver; the rich vascularity and extent of parenchyma of this organ, as well as local mechanical and biochemical factors, probably all figure in causing the high rate of metastases. In fact, liver involvement could be the sole evidence of distant spread of the breast cancer (Oberfeld, Cady, Pazianos and Salzman, 1972).

The commonest pathogenesis was by true metastases from the systemic circulation; metastases via the portal vein were also a theoretical possibility. Microscopically, hepatic arterial embolization was difficult to identify because the rapidly ensuing intrahepatic metastases complicated the picture (Sherlock, 1968). If the liver parenchyma were grossly replaced or destroyed, there could be decreased physiological function which could be measured by liver function tests.

Diagnosis and Symptoms

The cardinal symptoms of liver spread were fullness after eating, anorexia, nausea, emesis, and early tobacco and coffee intolerance; hepatomegaly, general discomfort, ascites and constipation also occurred. Clinical jaundice of the obstructive type could occur if the metastatic growths impinged upon or blocked ducts.

Diagnosis of liver metastases can be difficult. Although

direct biopsy was the most reliable method, it was a major procedure in a patient already weakened by metastatic disease (DeWys, 1974). Needle aspiration biopsy was less taxing but failed to detect tumor in 30 to 40 percent of cases: the chance of obtaining a positive result increased with extent of metastases, size of liver, and the presence of a palpable mass in the abdomen.

Liver scanning with radioactive isotopes has become an invaluable adjunctive diagnostic tool in metastatic breast cancer. Unlike bone scanning, those hepatic areas with disease will be poorly functioning and will therefore take up less of the isotope, and will appear as an area of less density or as a "cold spot". Volpe et al., (1971) classified liver scans into eight categories for diagnostic purposes.

Covington (1970) discussed the accuracy of photoscans, emphasizing normal readings; and stressed that proof of accuracy of a positive scan was always needed by biopsy, operation, or autopsy which corroborated the photoscan in 87, 71, and 72 percent of separate series respectively for each method. The treatment of liver metastases is usually by hormonal therapy or chemotherapy techniques.

BRAIN METASTASES

Introduction and Pathology

Breast cancer is the most common neoplasm in females to metastasize to the brain (Furlow, 1961). Incidence of this complication varies with many factors - the true incidence is difficult

to calculate since the metastases are often asymptomatic. Vieth and Odom (1965) reported that from 15 to 37 percent of primary breast carcinomas eventually metastasize to the brain. Of all brain tumors, some 12 to 20 percent were of metastatic origin. Breast carcinoma accounted for 44/195 (22.6 percent - Simonescu, 1960); 222/560 (39 percent - Nisce, Hilaris and Chu, 1971); 51/313 (16.3 percent - Vieth and Odom, 1965); and 15.8 percent (Lang, 1967) of the metastatic tumors in various series. Breast cancer tumor emboli can reach the central nervous system by the pulmonary-systemic or the vertebral venous circulation, the latter was discussed in detail in the beginning of this literature review.

Pathogenesis

The location of the metastatic deposits was parietal, frontal, cerebellar, temporal, and occipital areas in order of decreasing frequency (Haar and Patterson, 1972). The predominant distribution of the single or multiple lesions tended to be in the area of the brain supplied by the middle cerebral artery.

Pathologically, CNS metastases from breast carcinoma demonstrated typical characteristics: they were very likely to be multiple rather than single: in fact the lesions were multiple in fully 80 percent of the cases; they were usually well demarcated from the surrounding brain parenchyma; they were encapsulated, and were often grayish in color. Lesions varied in size from a few millimeters to several centimeters (Fuller et al., 1970). Wilson and Fewer (1971) emphasized marked cerebral edema; there has been sufficient evidence that there might be considerable extensive

cerebral edema with gross ventricular displacement even though the actual tumor nodules were small (Furlow, 1961). The average interval between breast primary diagnosis and onset of brain metastases was 17 months, and only one-half of these cases were symptomatic (Lesse and Netsky, 1954).

Symptoms and Detection

The symptoms of metastatic involvement depended primarily upon the location of the lesions, and were due not only to the expanding lesions but also to the increased intracranial pressure which accompanied them. Persistent early headache usually preceded nausea, emesis, psychic changes, and localizing signs such as Jacksonian seizures, hemiparesis, speech disorders, visual field defects, and parietal lobe sensory changes (Fuller et al., 1970). Nisce et al., (1971) reported motor deficits in 75 percent; disorientation, lethargy, or coma in 41 percent; headaches in 33 percent; and sensory deficits in 28 percent of patients with brain metastases. Hyperreflexia can occur (increased DTR) especially in patients who experienced hemiplegia. As clinical symptoms were the same as those in primary brain tumor and other intracranial processes, a differential diagnosis was mandatory (Lesse and Netsky, 1954).

With the discovery and development of scanning with radioactive isotopes, the detection of brain metastases is much more reliable than formerly. The mechanism of scanning parallels closely that for bone metastases; that is, areas of suspected metastases show as areas of increased radioactive uptake on the

scan. Biopsy of a cerebral lesion carries significant risk, and is not commonly employed as a diagnostic procedure.

Treatment

The treatment of CNS metastases was either by neurosurgery, irradiation, or steroid therapy - frequently a combination of treatment approaches was employed. Several authors have supported surgical procedures for removal of a single metastatic focus (Haar and Patterson, 1972; Lang, 1967; Simonescu, 1960; Vieth and Odom, 1965; and Wilson and Fewer, 1971). Surgery might have been indicated to establish the diagnosis in a patient without evidence of a primary tumor (rare in breast carcinoma) or in a patient without evidence of dissemination except for the solitary brain tumor (Haar and Patterson, 1972). Other indications for neurosurgery were limited to a select group - reserved for rapid deterioration in a solitary lesion, obstruction to cerebrospinal fluid flow, or recurrence after a total course of radiation had been given (Fuller et al., 1970). Combining steroids and radiation with surgical procedures was recommended.

Lang (1967) stated "Surgery does increase longevity in patients with brain metastases, but it may not be long enough to make the procedure rewarding". Other surgeons are skeptical about a procedure which only could be considered in one-fifth of a population with CNS dissemination.

Recently, the trend has been toward **whole** brain irradiation, usually combined with steroid administration. Nisce et al., (1971) reported improvement in the functional status of one-half of the

patients with brain metastases; the average duration of the remission was six months for breast carcinoma patients.

One report concerned the improvement of the quality of survival after irradiation for brain metastases (Order, Hellman, Von Essen, and Kligerman, 1968). These authors did propose a functional classification of patients with brain metastases, which was used in the construction of Model A - Extent of Metastases Operational Model, for the purpose of data collection in this thesis.

Of seven primary breast tumors with CNS metastases, four improved their functional status for varying periods of time after radiation (Horton, Baxle, and Olson, 1971). The recommended dose was 3,000 rads to the entire cranium in split doses. Since the intracranial pressure could rise secondary to irradiation, steroids in sufficient doses were routinely given to counterattack this common sequelae to treatment. Since most clinicians have been reporting superior results with radiation and steroids, these procedures are now preferred over surgical intervention in the majority of cases.

Summary

In summary, dissemination of breast carcinoma to the CNS was one of the more common observations in this disease; from 15 to more than 30 percent of women with breast cancer will eventually suffer brain metastases. The symptomatology that was outlined was heightened by an aggressive and consistent rise in intracranial pressure. Although breast carcinoma cerebral metastases were

characteristically well demarcated and usually encapsulated, they were seldom amenable to surgical resection, chiefly because of their multiplicity. Once the neurological deficits and other distressing symptoms appeared, the oncologist could utilize steroids and radiation to relieve suffering and palliate the resultant disabilities.

EPIDURAL SPINAL CORD COMPRESSION

Spinal cord compression due to epidural metastases was one of the clinical syndromes that had become more commonly recognized in recent decades. Considering the great frequency with which breast carcinoma metastasizes to the vertebrae, it was surprising that this complication was not more common (Rubin, Mayer, and Poulter, 1969).

Metastatic tumors almost always compressed the cord from the epidural space - a result of vertebral body extension (Posner, Myers, Benua, and Lipton, 1971). Much less commonly, the tumor metastasized to the epidural space without directly involving the bone. True intraspinal metastases within the tracts and nerve ganglia of the cord substance were extremely rare. As the tumor spreads to the epidural space in the most common manner, the blood supply was compromised and a hemorrhagic infarction developed leading to a paraplegia or quadriplegia that was irreversible (Posner et al., 1971).

Symptoms and Detection

Prodromal pain may be present for days or weeks prior to

the other symptoms: weakness, sensory loss, ataxia, motor loss and finally autonomic dysfunction. Since compression could result in complete motor and sensory loss and loss of sphincter control, the syndrome could contribute to significant disability in the metastatic breast cancer patient. For this reason, clinicians usually considered the condition to be a medical emergency (Rubin et al., 1969).

The diagnosis of the epidural block was best made by myelography (Viola, 1971; White, Patterson, and Bergland, 1971). There has been considerable controversy regarding the proper treatment of spinal cord compression - the physicians must think in terms of preventing rather than attempting to restore or reverse the paraplegia. The literature has emphasized a combined attack of surgical laminectomy and decompression, radiation, and chemotherapy (Fager, 1967; Rubin et al., 1969).

Treatment

Most of the research concerning the proper management of spinal cord compression has been performed on mixed series of patients, which have included various primary tumors, most of them of the lymphoma group. Caution is advised in extrapolating results to cord compression due to metastatic breast carcinoma. Rubin and his associates agreed that high daily dose radiotherapy without the need for laminectomy or systemic chemotherapy affected improvement. They recommended a regime of 400 to 500 rads daily for three days, then 100 to 200 rads daily until improvement was maximal (Rubin et al., 1969).

There were those who believed radiation edema heightened and aggravated neurological symptoms; therefore, these clinicians supported surgical decompression and laminectomy with or without radiation (Viola, 1971; White et al., 1971). If surgery was elected, the spinal cord must be well decompressed and as much of the tumor removed as possible. White and his colleagues (1971) reporting the results of decompression laminectomy in 226 patients (16 percent were breast primaries), contended that when signs of neurological dysfunction occurred, surgery was the primary form of treatment, unless the tumor was highly radiosensitive. Due to the emergency nature of the situation, the role of chemotherapeutic agents in the treatment of spinal cord compression is limited.

Summary

Spinal cord compression from metastatic spread of the disease into the epidural space has become increasingly more recognized in disseminated breast carcinoma. The complication usually presented as a medical emergency due to the tremendous potential disability when the blood supply to the cord became compromised. At the present time, although radiation therapy appears to be preferred over surgery, the circumstances in which spinal cord compression by metastatic carcinoma can be treated solely by radiation therapy remain to be established.

DISTANT LYMPHATICS

One of the most common modes of distant metastases of breast carcinoma was spread within the lymphatic system to distant

nodes (Spiels and Withan, 1933). By the definition given in this thesis, distant lymphatic spread excluded metastases to ipsilateral axillary and internal lymph nodes of the mammary chain, but included metastases to the supraclavicular or cervical lymph nodes on either side, as well as any other distant lymph nodes (Cutler et al., 1969).

Viadana et al., (1973) in their study of 647 primary breast carcinomas, reported the cervical lymph nodes to be involved in 233 (36 percent); the thoracic lymph nodes in 359 (56 percent); the abdominal lymph nodes in 250 (38.5 percent) and the pelvic lymph nodes in 107 (16.6 percent) of cases. Clearly there was a greater frequency of metastases to the lymphatics anatomically closer to the breast.

The interrelationship between hematogenous and lymphatic dissemination played an integral role; either distant lymph node spread could occur as a result of direct retrograde growth through organ lymphatics or less commonly, the metastases could reach the area through the hematogenous route, and subsequently pierce the endothelial and lymphatic walls and commence metastatic growths in the contiguous lymphatics.

Symptoms and Detection

Involvement of the hilar or peribronchial lymphatics could produce cough and dyspnea; significant dysphagia could result if the periesophageal lymph nodes were involved (Sears, 1968). Esophageal manifestations typically occurred at the level of the carina, and treatment was by radiation or surgery (Conklin, 1964). Spread to the lymph nodes proximal to the vena cava could cause

the vena cava syndrome, characterized by face and neck edema, venous distention, and possible congestive heart failure (Sears, 1968).

Involvement of the scalene lymph nodes, which anatomically are in close proximity to the brachial plexus, effected on occasion neurological signs and symptoms referable to that plexus. Symptoms were also possible if the supraclavicular lymph nodes were extensively involved with metastatic tumor (Sears, 1968). Brachial plexus involvement typically produced pain, numbness or paresthesias, and motor or sensory loss which varied from minimal to severe.

Metastases to the abdominal or mesenteric lymph nodes produced symptoms or syndromes largely dependent on the number, size of the metastases, and extent of obstruction or compression of the organs or systems by the enlarged lymphatics. The pelvic lymph nodes were involved in less than 20 percent of cases (Viadana et al., 1973) and usually only as a late manifestation. Symptoms other than pain might be lacking until the pelvis was filled with tumor; genitourinary complications, such as blocked ureters and ensuing uremia, were rare but could occur.

Detection of distant lymphatic involvement will depend upon symptoms caused by the tumor filled lymphatics. Superficial lymph nodes can be detected clinically by palpation, but the deeper nodes, if involved, may escape detection if the patient is asymptomatic. The actual extent in terms of number and amount of tumor spread to distant lymphatics is generally discovered as an incidental finding in autopsy studies. Lymphangiography is of more

use in cancers having more predictable routes of deep lymphatic spread, such as testicular tumors. The treatment of metastatic lymph node carcinoma will depend on location, size and extent of symptomatology. Radiotherapy might be judicious for some areas, while systemic or regional chemotherapy more prudent in other sites. Rarely is surgery indicated.

In summary, distant lymph node spread was common, especially to the mediastinal lymphatics. One would do well to remember that most of the so called visceral spread of breast carcinoma was actually metastases to the contiguous lymph nodes in the abdomen or thorax, producing organ symptoms by virtue of pressure or obstruction.

OTHER METASTATIC SITES AND SYSTEMIC EFFECTS

Hypercalcemia

Elevated levels of calcium in the blood serum can have variable causes when found in the metastatic cancer with a breast primary. Steroid therapy, if long continued, in high doses, has been suggested as being contributory. Long term estrogen or other hormonal therapy could precipitate a hypercalcemic episode. Although the great majority of women suffering this potentially fatal complication also had extensive bone metastases, hypercalcemia could occur in patients without evidence of osseous dissemination.

Galasko (1972) reported 24/127 incidental (asymptomatic) hypercalcemia and 18/127 acute hypercalcemic crises in one series.

The incidence reported by Davis, Wisely, Ramirez, and Ansfield (1973) was 7.2 percent of 305 women with disseminated breast carcinoma; Galasko and Burns (1971) reported a 14 percent incidence in 130 patients. In the study of Davis et al., (1973), 13 developed the condition spontaneously, and eight did so following estrogen or androgen administration.

Pathologically, in osteolytic metastases, the balance between calcium deposition in bone and calcium mobilization from bone was upset. As complex processes destroyed the actual bone and the osseous cells underwent necrosis, calcium spilled into the circulation. Several mechanisms were probably responsible. If the excess calcium was excreted by the kidney, clinical hypercalcemia did not occur.

Symptoms and Detection

The symptoms according to the above authors were skeletal pain, gastrointestinal symptoms such as anorexia, nausea, emesis, and weakness, lethargy, or somnolence. The hypercalcemic episode could be fatal in up to one-third of patients experiencing the complication (Mannheimer, 1965).

Treatment

Treatment of hormone induced hypercalcemia responded well to withdrawal of the drug and diuresis, according to Mannheimer (1965). Corticosteroid therapy was sometimes used, but the disadvantages were its slower action, 20 to 30 percent non response rate, and side effects such as peptic ulcer. Mithramycin, an

antibiotic useful in certain testicular neoplasms, effected a lowered serum calcium within a matter of hours (Lehnhard, 1971; Slayton, Schnider, Elias, Morton, and Perlia, 1971). The symptoms, lethargy, bone pain, and GI disturbances, could be successfully treated by diet, diuresis, mithramycin, phosphates, or steroids.

Other Sites

According to Viadana et al., (1973) metastases to the following organs were expressed as a percentage of 647 primary breast cancers: stomach, 10 percent; pancreas, 12 percent; adrenals 38 percent; and ovaries 15 percent.

Advanced cachexia, often seen as a terminal syndrome in many cancer patients, was not as common in breast cancer. Briefly, cachexia was a syndrome manifested by weakness, anorexia, weight loss, and protein loss - characterized by wasting and atrophy of the body tissues in combination with hypermetabolism for the nutritional state of the individual. Theories have proposed that the carcinoma caused the inappropriate activation and inactivation of enzymes without a need or a plan, leading to an increased energy expenditure and metabolic rate despite semi-starvation.

COMPLICATIONS DUE TO TREATMENT

There are four major treatment approaches of breast carcinoma: surgical, radiologic, chemotherapeutic, and hormonal. Since most of the surgical complications are related to radical mastectomy for the primary tumor, they will not be considered here. Major surgery, excluding ablative hormonal procedures, which will

be treated under hormonal approaches, and outside of the removal of the rare solitary pulmonary or cerebral lesion, or prophylactic and reconstructive orthopedic procedures, does not play a large role in the treatment of metastatic breast carcinoma.

Hormonal Therapy

Regimes based on hormonal management have varied with the age and menstrual status of the patient, the disease free interval, and the sites of organ involvement (Kaufman, 1973; Mellette, 1970, 1975). Premenopausal patients were subjected to surgical or radiological castration; recent tests that employ estrogen binding protein screened those patients who would benefit from the procedure (approximately 30 percent). Kelley (1971) stated that patients responding to oophorectomy had a significantly better chance of responding favorably to further palliative measures - adrenalectomy, hypophysectomy, or androgen administration. Side effects of ablative oophorectomy were onset of the menopause with its associated symptoms; these were not usually troublesome for the patients.

Adrenalectomy produced objective responses in from 30 to 40 percent of cases (Fracchia, Randall, and Farrow, 1970; Mellette, 1970). They found that patients with CNS metastases, restrictive pulmonary or pleural spread, or severe liver involvement did not fare as well as patients with soft tissue or bone metastases. Patients might develop hypoadrenalism and could require exogenous administration of the lacking adrenal hormones. Combined adrenalectomy and oophorectomy was frequently performed;

fluid and electrolyte imbalances that occurred required prompt and proper attention (Ratzkowski, Adler, and Hochman, 1973).

Hypophysectomy had many proponents. In addition to having a suppressant effect on estrogen productivity, and thus upon the growth of the tumor, the procedure eliminated growth hormone and prolactin, which probably also had an effect on tumor growth. Complications included fluid and electrolyte imbalances and abnormalities, which could be controlled by cortisone; and occasional diabetes insipidus, treated by salt retaining steroids such as dexamethasone. Thyroxin must also be supplanted.

In post-menopausal patients, either estrogens or androgens were administered. Possible side effects of estrogen treatment were mild to severe, and included fluid retention, uterine bleeding, and possible hypercalcemia. The chronic effects of androgen treatment were fluid retention and possible hypercalcemia, in addition masculinization could occur; many patients found this difficult to tolerate. Additive hormonal therapy was popular not only for its efficacy but also because the agents employed did not cause bone marrow suppression (Hickey, 1967; Mellette, 1970).

Chemotherapy

Although breast cancer did not respond as dramatically as other cancers (i.e. leukemia, Hodgkin's Disease) to chemotherapy, significant palliation with remission lasting months or years could be obtained. The choice and sequence of agents was critical, because seldom was it possible to try sequentially several successive therapeutic agents in the treatment of one patient. The bone

marrow frequently became irreversibly depleted by cancer, chemicals used, and associated radiotherapy (Eckles, 1970). Newer and more effective choices of treatment sequences and combinations were developed. As a rule, hormonal measures were used and exhausted before chemotherapy was tried - the goal being the "most effective relief in the shortest time with the least morbidity" (Oberfield et al., 1972). Some of the more common chemotherapeutic agents and their side effects and complications are listed in Table 2.

Chemotherapy characteristically has been considered effective in inducing responses in those sites with a relatively long survival time, including bone, pulmonary nodular, soft tissue, pleural effusions, and minor liver involvement (Plotkin, Kagan, Nussbaum, and Reddi, 1973). Sievers and Donovan (1973) warned that over zealous chemotherapeutic management might induce objective regression, but frequently substituted morbidity secondary to the therapy exceeding that which existed as a result of the disease.

The much celebrated "Cooper regime" has been used by many clinicians treating disseminated breast carcinoma after hormonal therapy had been exhausted in the patient. The approach consisted in combinations of vincristine, cytoxan, 5 FU, methotrexate, and prednisone. Average response rates, even with two or three drug combinations were from 50 to 60 percent; there are wide variations among individual authors reporting results. The advantages of combination chemotherapy - appropriate agent selection and dosage against cell population - usefulness when the cells have become

Table 2

Common Chemotherapeutic Agents Used in Advanced
Breast Cancer; Acute and Delayed
Side Effects and Complications

Agent	Acute Side Effects	Delayed Toxicity
I. Alkylating Agents		
A. Cyclophosphamide	nausea, emesis	bone marrow depression. alopecia. hemorrhagic cystitis.
B. Thiotepa	none	bone marrow depression.
C. Melphalan	none	bone marrow depression.
II. Antimetabolites		
A. Methotrexate	diarrhea, hepatonecrosis and toxicity	oral, GI ulceration. bone marrow depression. cirrhosis.
B. Fluorouracil (5 FU)	nausea emesis.	oral and GI ulceration. stomatitis, diarrhea. bone marrow depression. pigmentation of skin.
III. Natural Products (Plant Alkaloids)		
A. Vincristine Sulfate	locally irritating	constipation, arreflexia ileus. peripheral neuropathy.
B. Vinblastine Sulfate	locally irritating nausea, emesis.	some bone marrow depression, alopecia. stomatitis, decreased reflexes.
IV. Antibiotics		
A. Adriamycin	locally irritating. nausea emesis.	bone marrow depression. total alopecia. stomati- tis. cardiomyopathy (EKG changes, usually in the T wave.)

resistant as a result of repetitive exposure to single agents - were weighed in light of appropriately lowered doses to avoid intolerable side effects (Plotkin et al., 1973). Mellette believed that theoretically at least, the side effects might be more tolerable still allowing for greater effectiveness.

Complications due to the treatment could be conveniently divided into systems exhibiting side effects; many of these were also pertinent to radiation sequelae. Hematologic complications were by far the most common (WBC and platelet depression, anemia) followed by gastrointestinal complaints (nausea, emesis, diarrhea, constipation, ulceration, anorexia). Other possibilities were neurologic, hepatic, genitourinary (tubular necrosis, nephritis, cystitis, and renal failure) and dermatologic (alopecia, pruritus, hyperpigmentation, rashes, and atrophy). Infection, sepsis, fever, and general symptoms such as fatigue and weakness were common; miscellaneous complications included pulmonary fibrosis, pneumonia, myopathies, sterility, and carcinogenesis.

The complications then due to hormonal and chemotherapeutic treatment in advanced breast carcinoma were numerous, and could be manifested wither generally or specifically in several somatic systems. Most commonly, the hematological and gastrointestinal systems were affected. Those areas having the greatest turnover of cells were most often the site of serious side effects of treatment. This concept seemed to parallel that of radiation therapy and its complications, where most of the damage was to those areas and organs having the most rapidly dividing cells; i.e. bone marrow, GI, gonads and skin.

THE ROLE OF PHYSICAL THERAPY IN THE METASTATIC CANCER PATIENT

Although many authors have written concerning the management of post surgical patients, including post mastectomy patients, few have outlined programs for the metastatic cancer patient. Current thought concludes that the physical therapy care administered to the advanced breast cancer patient does not differ significantly from the supportive care given to other metastatic patients. Unfortunately, the research in this area is almost entirely descriptive, and demonstrates programs applicable to all metastatic patients, but not to breast cancer patients in particular. Since supportive physical therapy procedures comprise a relatively conglomerate group of treatment approaches, no one method has grown to be followed as protocol for these patients with advanced disease. In general, patients with metastases from breast carcinoma will exhibit a myriad of disabilities and distinct symptoms, but general weakness, pain, malaise and weight loss are the most common ones that are encountered. Physical therapy is needed in the form of mild, gentle exercise, palliative pain relief by accepted modalities, and progressive ambulation activities with appropriate assistive devices.

Dietz (1969) stressed functional activities, especially ambulation, as pertinent to the effective patient management in the treatment of the metastatic patient. This approach frequently requires interdisciplinary care - the physical therapist being only one effective member of the team. Dietz (1969) suggested starting

patients weakened by metastatic cancer and its treatment - the anemia, nausea, and other systemic effects of chemotherapy and radiation contribute greatly to the general activity ability of the patient - with graded whole body exercises, and early ambulation. Although he was actually specifying ambulation and progressive mobilization for advanced leukemia patients, the concepts are applicable to the metastatic breast cancer patient.

Coran (1968) reported on 31 metastatic breast cancer patients presenting with pathological fracture of one of the major long bones. Various operative techniques are employed, with different appliances inserted depending on the location of the tumor, amount of tumor left at the fracture site, among other factors. Physical therapy regimes for post operative care are not typically specific for pathological fractures due to metastatic breast carcinoma; programs followed are those outlined for regular traumatic hip fractures. Proper modification, if deemed necessary due to cachexia, systemic effects of disease, age, other sites of metastases, and untoward complications of the treatment for the cancer, might be necessitated. An interesting and practical consensus of several authors was that weight bearing, i.e. on a postoperative Jewett nail, was commonly begun earlier on cancer patients with pathological fractures as compared to patients with regular traumatic fractures (Coran et al., 1968; Leach and Torgenson, 1967; Parrish and Murray, 1970). The rationale was to sacrifice a certain but limited amount of stability at the fracture site in favor of earlier ambulation and mobilization, because of the expected shorter life span of these patients.

A knowledge of the exact sites of bony metastases and their extent and type of involvement, i.e. osteoblastic vs. osteolytic, is imperative in making decisions concerning the activity level of the patient as well as in selection of treatment approaches of mobilization of the weakened patient. The physical therapist in particular must be cognizant of these matters, and safeguard against excessive or strenuous mobilization which might result in a pathological fracture.

Metastases of the vertebral column may cause incapacitating pain. This is effectively treated with radiation - the need for a lumbosacral corset or support or other variations of spinal orthoses is not great. Cancer patients suffering pain due to vertebral involvement as a whole do not tolerate the physical pressures of orthotic devices on already tender body surfaces (Parrish and Murray, 1970).

The physical therapy needs of the metastatic cancer patient are increased tremendously by the concomitant diseases of the enlarging geriatric population (Zislis, 1970). The clinician often is treating the patients for generalized debility, weakness, and dysfunction which is a result of the combination of the disabilities of the cancerous process and accompanying major disease or syndromes, such as arteriosclerotic heart disease, obesity, diabetes, senility, and others. Even though the average age of the breast cancer patient is approximately 50 years, periods of survival are increasing, and more women will be living longer with their disease, and will approach age categories where they will be more likely to

develop additional conditions which will further tax the patient and contribute to disability.

Emphasis is on separating the resultant disabilities and relating it to their corresponding disease entities, a task not always possible in the cancer patient with multiple problems. For present purposes, physical therapy approaches concentrate on the general effects of chronic, debilitating illness syndromes as a whole - cancer and its related disability being one of the many causes of these syndromes (Dietz, 1969).

In summary, specialized physical therapy programs for the metastatic breast carcinoma patient are non existent in the literature; however, various authors have published loose guidelines which approach embryonic protocols, for pathological fractures of the long bones, lumbar disease, and most commonly for the general problems of all metastatic cancer patients. Since the therapeutic procedures presently play the biggest role in pathological fractures and their post operative management, more interest seems to be stimulated here. Further exploration will reveal additional clinical situations in metastatic cancer patients where physical therapy will be found advisable or necessary.

SUMMARY

The metastatic potential of breast carcinoma has been described with emphasis on the four major areas of involvement; the pulmonary, skeletal, hepatic, and central nervous systems. The chapter began with a review of the present classification of

breast carcinoma; the need for a systemic classification and categorization of metastatic disease was clearly indicated. Following this need specification, basic pathological considerations of the metastatic process related to breast cancer was depicted; the very propensity for breast cancer to disseminate both lymphatically and hematogenously was outlined. Standard theories of metastatic growth - the soil vs. the mechanical hypotheses were discussed in the light of the frequency of metastases to representative organs. Special importance was given to the role of the vertebral venous system in the spread of breast cancer to the spine, hip and pelvis, and shoulder girdle.

A short section discussed the present position of physical therapy in metastatic cancer; the limited number of outlined programs have the metastatic, advanced patient as a group as their target, and are sufficiently applicable, but not solely designed for metastatic breast cancer patients.

The bulk of this chapter consisted of systemic outlines of the incidence, diagnosis, physical signs and symptoms, major implications, and the treatment of the most common sites involved with metastatic breast carcinoma. A detailed account of the natural history of this disease was deemed necessary in order to relate specific metastatic characteristics with clinical disability, and it was for this reason that chapter two of this thesis was written.

Chapter 3

PROCEDURES

This chapter will outline the basic procedures used in data collection; data were compiled in an attempt to support the hypotheses given in Chapter One. The first two sections describe the procedures employed in the construction and approval of the two operational models which were conceived specifically for the purpose of this study. Following this, the methods of actual data collection, the subjects and materials used, are delineated. The methods used for the statistical analysis of the data are mentioned, and the chapter concludes with a short summary.

CONSTRUCTION AND PHYSICIAN APPROVAL FOR OPERATIONAL MODEL A

Model A, or the Extent of Metastases Operational Model for disseminated breast carcinoma, is given in its entirety in Appendix A. Included is the list of physicians who read and approved the model before data collection. This model is based on a foundation of scientific and clinical observations of the dissemination of human breast carcinoma. This model was developed to overcome the inadequacies of the UICC and AJCCS systems. The rationale for further classification has been demonstrated in Chapter Two of this paper.

The reader is referred to the introduction to Model A in Appendix A which offers a more precise explanation. Basically, a system was devised whereby a patient was graded on two levels for

each particular site of metastases: on severity of extent of the metastases, and on the severity of the symptomatology that was manifested as a result of the respective metastatic deposit.

Addendum I to Appendix A is a combined general description of the scale used to grade both extent of metastatic disease and severity of symptomatology as stated succinctly in the addendum introduction. One must view classification of a patient for each metastatic site as a dynamic and at best temporary phenomenon. The model has been constructed with this fact in mind; scores can be changed easily to describe the progression of the patient's state of disease.

Model A is divided into 15 groups, or sites of involvement and parameters of disease. Groups I through X inclusive, and Group XII are anatomical divisions where metastatic dissemination of breast carcinoma most commonly occurs; pulmonary, pleural, bone, hepatic, brain, peripheral nervous system, intraspinal, distant lymphatic, and skin and soft tissue areas are some of the many sites that are threatened by disease. Group XII was created as a collective area for other than major organ sites. The remaining groups include scores obtainable for complications of systemic disease, such as hypercalcemia (Group XI) and cachexia (Group XIII).

Group XIV, vincristine neurotoxicity, was deemed appropriate since this medication is commonly used as a chemotherapeutic agent in disseminated breast carcinoma, and the ensuing peripheral neuropathy that is possible can be potentially incapacitating. Group XV grades the complications due to treatment of the disease.

Because systemic manifestations of treatment can grossly and at times considerably influence functional performance, it was included as part of the model describing metastatic disease and its effects.

The model was subjected to extensive editing and revision. In August of 1975, copies were submitted to a panel of three medical oncologists and one oncology fellow for editing, suggestions, and final approval.

CONSTRUCTION AND THERAPIST APPROVAL OPERATIONAL MODEL B

Model B, or the Level of Functional Disability Operational Model, is given in its entirety, including the corresponding data collection form and list of members of the validation panel, in Appendix B. Unlike Model A, Model B was based on several established evaluation forms describing activities of daily living and/or general functional level of the patient. There are twelve groups or categories to the model, and they closely parallel those categories of the Barthel Index, a functional evaluation form used by many institutions to score patients on functional activity levels (Mahoney and Barthel, 1965). In the model prepared for this thesis, the format for scoring was reversed from the Barthel Index; higher scores represent greater levels of physical dysfunction. In most data evaluation forms, including the Barthel Index, the reverse is true - higher scores represent greater levels of physical functioning. Model B was formulated in this reversed manner in order that it could be properly correlated with Model A, where higher scores

signify greater amounts of metastatic disease and its accompanying symptomatology.

Different approaches describing physical dysfunction were combined to develop major categories of essential daily functioning: feeding, transfers, personal toilet, bathing, ambulation on levels and stairs, wheelchair activities, sitting tolerance, bed activities, bowel and bladder management, and dressing activities. For dressing activities, four separate groups were listed for various major articles of clothing.

Model B was formulated to distinctly demonstrate the level of dysfunction in the metastatic breast cancer patient, and in this sense is not really an ADL test or evaluation that is commonly employed by physical or occupational therapists. This model was also subjected to extensive revision, and in its final form was submitted to a panel consisting of nine registered physical therapists for final suggestions, editing, and approval.

SCORING OF THE MODELS

The scale used to grade patients on Model A for severity of extent of metastases and severity of symptomatology is from zero to four for both parameters. For extent of disease, a score of zero indicates that no metastases were present, whereas a score of four demonstrates severe, profound, involvement of the organ or system. Likewise, a zero score on the symptomatology parameter indicates no symptoms are present, whereas a score of four indicates and reports an extreme degree of symptomatology.

The two parameters for one particular site need not have the same score, although they often coincide. For example, lung metastases grade two (multiple nodules, moderate involvement) might be asymptomatic - grade zero on the symptomatology parameter. For some groups, such as Group VII, Peripheral Nervous System, and Group VIII, Intraspinal Metastases, the extent of disease is difficult if not impossible to grade clinically. Therefore, patients with metastases to these areas received scores on that group reflecting degree of symptomatology only.

For Model B, performance was graded according to a precisely defined system; the scale from zero to four used very closely parallels the zero to four scale used in the scoring of the parameters contained within Model A. For example, zero here implies no problem with the activity in question, and a score of four implies and reflects maximal assistance being required. The reader is referred to Appendix B for a complete description of this operational model.

METHODS OF PATIENT SELECTION

Thirty female tumor clinic patients with a proven diagnosis of metastatic breast carcinoma served as the sample in this study. They were selected from the patients being treated at the chemotherapy clinics, which are held in the Tumor Clinic, located in the Medical College of Virginia North Hospital. For a 49 day period, all metastatic breast cancer patients coming to clinic theoretically enjoyed an equal chance of being included in the

study. The period of data collection was from August 28 until October 15, 1975.

The tumor clinic is divided into two major divisions, or areas; the regular tumor clinic which serves anyone requiring care for cancer, mostly medically indigent persons; and the private tumor clinic where private physicians care for metastatic cancer patients. Each tumor clinic sees both ambulatory and non-ambulatory patients. This particular separation of patients into tumor clinic and private tumor clinic will be important during data analysis, and will be explained more fully in Chapter Four.

The method of patient selection was as follows: tumor clinic charts (records) were reviewed as the patients came through in the course of receiving treatment for their disease. The names and chart numbers of patients having breast carcinoma were recorded. If two metastatic breast cancer patients attended clinic on a particular day, both were evaluated for the study, providing they met the established criteria. If more than two patients attended the clinic and both met research criteria, a random selection of patients was made. The regular and private tumor clinics were screened for potential patients on alternate days; if no metastatic breast carcinoma patients attended one division on a particular day, the other division was screened on that day. The 30 subjects selected constitutes an acceptable random sample of all metastatic breast carcinoma patients attending the Medical College of Virginia tumor clinics during the established period of data collection.

Each tentative patient met the following simple criteria, or were dismissed from further evaluation: patient must be female,

have a proven diagnosis of breast carcinoma (sarcomas of the breast are excluded), and present with clinical evidence of disseminated disease (distant metastases), as defined in Chapter One. An obvious existing level of dysfunction was not considered as a necessary criteria for admission to the study. Subjects also did not have to exhibit severe metastatic involvement and/or constitutional symptomatology. Both the patient population and the sample therefore covered a considerable age range, as well as scope in amount and type of distant metastatic spread and physical dysfunction.

PROCEDURES IN PATIENT EVALUATION AND DATA COLLECTION

Preliminary Assessment

The initial screening was followed by a preliminary patient information survey which was obtained from the patient's tumor clinic record and medical record. The purpose of this survey was to check the medical record for adequate work-up, and to document that information which would assist in the evaluation of the patient on the operational models. In total 36 patients were reviewed at this stage of the data collection. If a patient's record demonstrated inadequate work-up, i.e. outdated diagnostic procedures, such as bone survey or liver scan performed more than three months prior to the date of evaluation, that patient was unacceptable for the study. Four charts were found deficient in this manner, and those patients were dropped from the study.

Following the record review, the author met personally

with the patient, and the purposes, methods, procedures, rationale, and use of the material to be gathered pertaining to the study were explained to the patient in laymen's terms. Informed consent was obtained in writing at this time. A copy of the consent form used follows Appendix E.

The preliminary patient information survey is outlined in Appendix C. Information pertinent to this phase of the study included name, age, hospital chart number, and address. Each patient was assigned a number to be used to identify her during all phases of the research. Also noted was the date of breast carcinoma diagnosis (or surgery), an important parameter used to divide patients relative to length of disease. The chart was reviewed noting the major sites of metastases, and dates of first evidence of disease at this site. This was done in order that the disease free interval¹ be estimated. The bulk of the preliminary information concerned sites and dates of surgical, radiation, hormonal, and chemotherapeutic management of the breast carcinoma metastases.

Then, the preliminary functional classification - performance status was determined, using representative categories. This classification is defined in Appendix D, and was developed in order to offer an easy, accessible, method of describing the functional

¹Defined, for purposes of this study, as the length of time between breast cancer diagnosis and the first evidence of distant metastatic disease.

level of the patient. This performance status grade, with modifications, is currently in use by the Cancer Rehabilitation Project of the Medical College of Virginia Hospitals. This study in part has attempted to validate the use of this classification in describing the performance status of cancer patients in general. Each patient was also classified according to the rehabilitation goals that would be chosen as part of the treatment plan. All patients by definition, fall into group B or C, as outlined in Appendix E. Lastly, the type of primary cancer was noted and recorded, if this information was available.

Patient Evaluation - Model B

The next phase of the data collection involved the evaluation and scoring of the patient on Model B, the Level of Functional Disability Operational Model. It was decided that Model A scoring would follow Model B scoring, and not the reverse. In this way, any bias concerning the functional state of the patient would be kept to a minimum. For example, if a patient was scored first on Model A and she achieved a high score reflecting a great amount of metastatic disease, one might tend to view or score her as being more potentially dysfunctional.

In total, 32 patients were reviewed and examined at this stage of the data collection. Two patients were found unusable for further progression through the study: the first due to voluntary withdrawal during the assessment of functional disability, and the second due to coexisting disease which rendered her unacceptable.

The equipment and space needed to conduct the Model B evaluation were provided by the tumor clinic. Several rooms were available for patient evaluation, when they were not being utilized for patient visits. Each was equipped with a standard hospital bed, a chair, and door. In one of these rooms, a patient toilet was located, equipped in the usual manner. Staircases for assessment on Group VII of Model B were within easy access. Any articles, i.e. comb, brush, towels, handcloth, etc. which were needed were graciously provided by the tumor clinic staff. For ambulatory patients, a comfortable chair and the nearby bed were the major equipment necessary.

This phase was begun with a period of conversation with the patient, lasting approximately 30 minutes. Major topics centered on the patient's feelings about her disease, and general ability to manage in the home situation. Much concerning the tentative functioning level and ability of these patients could be discerned during this preliminary interview. During this time the purposes and methods of the research were again explained to the patient.

The actual assessment and scoring of Model B, was done starting with Group I (feeding) and proceeding to the end. The patient was carried through many of the activities with modification; for example, the ability to reach the feet, back and extremities with a handcloth with appropriate washing motions was the procedure for assessment on Group V (Bathes Self). In addition to the actual objective scoring, the patients were very willing to outline areas where they needed assistance. Thus, the patient's verbal responses corroborated the objective results of the testing.

In almost all cases, a spouse, family member, or friend who knew the patient well accompanied her to the tumor clinic and was present during the evaluation; this person was helpful in corroborating the activity level of the patients. Each patient was scored according to the scale given in the introduction to Model B. At the conclusion of the evaluation, each group of the model was successively reviewed with the patient, to assure a reliable assessment of her level of dysfunction. The patient was then dismissed. All patients that were examined and evaluated for the study were thoroughly cooperative and several expressed interest in the outcome of the study.

Patient Evaluation - Model A

The next phase, the longest and most involved, was the scoring of the patient on Model A, the Extent of Metastases Operational Model. Thirty patients were carried through this stage of the data collection, and this constituted the sample size used in the study, N=30. The tumor clinic record and the medical record of the patient were again reviewed; if not already in the tumor clinic, the medical record was made available from the Department of Medical Records. This stage of the research project incorporated evaluation and precise assessment of the patient as a whole, with specific emphasis on the effects of the sites of the cancerous metastases in each patient.

Major metastatic sites being noted, the patient was scored according to the guidelines given in Model A (Appendix A). Radiographs were obtainable for most patients from the hospital X-ray

Department. Radiographs in the form of chest films, PA and lateral views, and the standard bone survey (skull, vertebral column, and pelvis) were most frequently necessary for complete patient assessment.

Chest radiographs displayed pulmonary metastases and pleural effusions, and these were graded according to criteria set forth in Model A. Dr. Harold Floyd of the Department of Radiology provided much initial and continuing assistance in the interpretation of these films. Unfortunately, radiograph interpretation is all too often equivocal, especially between two or more radiologists, and fine distinction and judgments are difficult and approximate. It is also true that pulmonary metastases may be present but not be demonstrated on radiographs.

Bone surveys were performed on all but four patients in the study, and these too were interpreted and graded according to criteria in Group IV of Model A. Not only the presence of metastases in the bone, but also the frequency of occurrence at each site, and predominant type of involvement were recorded. The frequency of metastases to various bone sites is a statistic of interest to physicians deciding which bones to survey for possible metastases. (Reader please consult Model A - Group IV). An excellent adjunctive diagnostic procedure was bone scanning, performed in 21 of the patients in the study. These reports were read and the results recorded and compared with those of the bone survey.

Liver involvement had been detected by various procedures; clinically, by palpation of a large nodular liver, diagnostically,

by use of the liver scan, or by liver function tests. Most of the patients having liver disease due to metastatic involvement were diagnosed by the liver scan. The advantages and disadvantages of this diagnostic procedure were discussed in Chapter Two.

Brain metastases were largely diagnosed by the brain scan, usually after the patient presented with some neurological symptoms that would suggest such a diagnosis. The medical record was carefully searched for symptoms referable to the liver or brain.

Documentation on areas of dissemination for the remainder of the model were largely a matter of patient record. In all areas, both major and minor, symptomatology for the corresponding site was based both on medical record documentation and subjective statements by the patient. The attending physician often helped in corroborating the degree of metastatic symptomatology exhibited by these patients. No patients presented with spinal cord compression. However, scoring on peripheral nervous system involvement with tumor was by severity of symptomatology produced by pressure or obstruction on the peripheral nerve; an anatomical score for extent of disease is difficult to interpret clinically for this category. Distant lymph node involvement is also difficult to discern in the clinical setting, unless the nodes involved were superficial and/or sufficiently large to be palpated directly. Skin and soft tissue metastases were easily appreciated clinically by inspection, measurement with a caliper, or palpation; this was done in conjunction with the physician during routine physical examination.

Other organ sites were indicated as being involved if so

mentioned or documented by patient history. The record was checked for chemotherapy regime - drugs, routes and dates of the agent were noted. Complications due to treatment and vincristine neurotoxicity, if present, were among the last parameters to be evaluated. In these parameters, subjective information was obtained from the patient concerning symptomatology due to treatment effects, and more objective evaluation, such as decreased blood counts and systemic symptoms due to chemotherapy or other treatment approaches, was obtained from the patient's medical and tumor clinic record.

After the medical record was thoroughly examined for pertinent information applicable to Model A, it was rechecked to insure that every metastatic site was detected, and indicated on the data collection form for Model A, and given an appropriate score. At this time, if necessary, radiographs, scan reports, and laboratory work, were all re-examined for accuracy. As a final step to this phase, the physician who examined and treated the patient on that day was consulted. With the physician, a brief review of the patient's progress, her extent of disease, effects of treatment, and any new developments were discussed in light of the data required for Model A. Any equivocal matter pertaining to scores for the various metastatic sites were cleared up at this time.

Formal data collection ended on October 15, 1975. After completion of the data gathering process, a folder for each patient (N=30) was compiled. This folder contained Model A and Model B data collection forms, signed consent forms, and preliminary patient information sheet.

The final phase of data collection was the follow up review to corroborate the clinical condition regarding metastatic disease for each patient. The tumor clinic record for each patient was again obtained, chiefly for the purpose of checking the dictation by the physician of the most recent tumor clinic visit by the patient. This dictation contained the most recent documentation of the patient's metastases and general condition. Any data that might have been overlooked was also collected at this time. If an additional diagnostic procedure had been ordered in the interim, this was studied. After all 30 records were re-reviewed, scores were tallied for the operational models, and data submitted for statistical analysis.

METHODS OF DATA ANALYSIS

Tables were constructed based on the collected data. Every patient received a total score on Model A and Model B, and these were the major quantitative items of interest that were tabulated. The major statistical test employed was the Pearson Product moment correlation coefficient, r , which related scores on Model A and scores on Model B for the 30 patients. Patients were divided into various groups depending on several variables. One division separated patients into one group comprised of women under the age of 60, and another group of patients over the age of 60. Correlation coefficients were compared, again based on Model A and Model B scores. All coefficients found by this analysis were subject to appropriate tests of significance.

Two separate groups were then formed of patients having their disease less than or more than 3.3 years (40 months). A second pairing was obtained by dividing the patients according to whether their disease free interval was less than or more than two years (24 months). A third pairing was based on duration of metastatic disease. Another division separated private from regular tumor clinic patients. For each of these groups mentioned above that was formed, Model A and Model B scores were compiled, and for each group a correlation coefficient was obtained, relating Model A with Model B. These were then analyzed for proper levels of significance.

In a fifth comparison, patients were also grouped according to major sites of metastatic involvement, and these results analyzed. In this way, a correlation coefficient was obtained relating Model A scores with Model B scores for all patients exhibiting lung metastases, another for all patients harboring pleural effusions, etc.

A frequency distribution of the 30 patients over six categories of functional status, as defined in Appendix D, is reported and tested by the Chi Square Goodness-of-Fit test. Finally, several additional tables and two figures outline variables such as chemotherapy, radiation, type of mastectomy, other surgical treatment, pathological classification, and frequency of metastases to various osseous sites.

SUMMARY

This chapter has outlined the methods, subjects, material, and procedures utilized in the undertaking of this research project. The construction, approval and validation of the two operational models used in data collection were summarized. The methods of patient selection for the study were delineated, along with an explanation of the criteria used to discard patients that were unacceptable for the study. The actual procedures in patient evaluation and data collection constituted five major phases performed in the following order:

1. initial screening to identify the metastatic breast cancer patients
2. preliminary patient evaluation and background information
3. consent having been obtained, patient evaluation and scoring on Model B
4. patient evaluation and scoring on operational Model A
5. reviewing of each tumor clinic and medical record to assure accurate collection of all necessary data.

The chapter concluded with a brief outline of the methods of data analysis.

Chapter 4

RESULTS OF THE STUDY

The results of the evaluation of the patient sample models and parameters discussed in Chapter Three will be summarized in the following order:

1. Total scores on Model A and Model B for all patients.
2. Model A and Model B divided by inclusive groupings for the following parameters: age, length of disease, length of disease free interval, duration of metastatic disease, and clinic attended.
3. Model scores and characteristics for six major individual sites of metastases.
4. Distribution of patients over six functional classification categories.
5. Related characteristics of the sample.
6. Frequency of specific disabilities.

MODEL A AND MODEL B TOTAL SCORES

Thirty patients were evaluated according to the method and sequence described in Chapter Three. These patients represented the population of all metastatic breast carcinoma patients attending the Medical College of Virginia Tumor Clinic over a specified time length. Table 3 gives the total Model A and total Model B scores for each of the patients in the sample. Model A scores

Table 3

Scores on Operational Models A and B
All Patients N = 30

Patient #	Model A Total Score	Model B Total Score	Patient #	Model A Total Score	Model B Total Score
1	38	46	16	19	3
2	24	18	17	13	8
3	13	0	18	7	1
4	24	20	19	27	11
5	30	2	20	23	9
6	10	5	21	12	1
7	17	8	22	5	1
8	11	5	23	15	10
9	31	33	24	30	24
10	9	6	25	11	3
11	22	14	26	13	13
12	6	2	27	15	2
13	10	2	28	21	6
14	13	7	29	12	5
15	21	5	30	8	7

Model A

Model B

Mean 17.0

9.33

Median 14.0

6.0

Correlation coefficient between Model A and Model B
For sample; $r = .7551$ significant at $p = .0001$

could theoretically range from zero to 160, depending on the number of sites of distant metastases; higher scores represent a greater extent of disease. Model B scores could range from zero to 60, depending on the extent of functional disability; higher scores represent a greater degree of physical dysfunction.

Scores on Model A ranged from five to 38, with a mean of 17.0 and a median of 14.0. Scores for Model B ranged from zero to 46 with a mean of 9.33 and a median of 6.0. Only two patients scored higher on Model B than they did on Model A; they were patient # 1, and patient # 9. The correlation coefficient, from this point on referred to as r , was .7551 for the patient sample. This is a highly significant correlation at $p = .0001$. The correlation coefficient computed for this sample, and for all other groups in this research, is one which relates scores attained on Model A with those attained on Model B.

MODEL A AND MODEL B SCORES AND CORRELATION COEFFICIENTS FOR SELECTED GROUPS

Age Factor

The sample was divided into groups based on selected variables of interest. The first of these, age, is depicted in Table 4. The age range of the full patient sample was 36 to 82, with a mean of 58.16 and a median of 59.5 years. Although this range is comparable to large series of breast carcinoma patients, the mean age is somewhat higher.

Correlation of Model A and Model B. Sixteen patients were under the age of 60, this group was designated Group Y, its members

Table 4

Analysis of Scores on Operational Models A and B - Division by Age

Group Y Patients Under Age 60				Group O Patients Over Age 60			
Patient #	Age	Model A Score	Model B Score	Patient #	Age	Model A Score	Model B Score
22	36	5	1	2	60	24	18
19	42	27	11	14	60	13	7
25	45	11	3	21	60	12	1
10	47	9	6	27	61	15	2
13	47	10	2	9	62	31	33
18	51	7	1	16	62	19	3
23	51	15	10	6	63	10	5
11	52	22	14	24	65	30	24
15	52	21	5	30	65	8	7
1	53	38	46	20	68	23	9
4	53	24	20	8	72	11	5
3	54	13	0	29	76	12	5
7	54	17	8	12	79	6	2
28	56	21	6	26	82	13	13
5	58	30	2				
17	59	13	8				

N = 16 Mean 50.52 17.687 8.937
 Median 52 16.0 6.0

N = 14 Mean 66.78 16.214 8.933
 Median 64 13.0 6.0

r = .7199 p = .0019

r = .8269 p = .0005

Difference between Group Y and Group O means; for Model A not significant, t = .4682; for Model B not significant, t = .0011 Alpha = .05

having a mean age of 50.62, a median of 52, and a range from 36 to 59. This mean and range are compatible to large series of breast carcinoma patients. The mean score for Model A for Group Y was 17.687, and for Model B, 8.937. The correlation between Model A and Model B scores for Group Y (patients younger than age 60) was $r = .7199$, a value significant at $p = .0019$.

Group O was comprised of patients aged 60 or over; 14 patients made up this particular group. Ages and model scores for these patients are shown in the right half of Table 4. The mean age was 66.78 years, with a median of 64 years. The mean score for Model A was 16.214; and for Model B, 8.933 for this group. The computed correlation coefficient was $r = .8629$, and was significant at $p = .0005$.

Comparison of Age Group Means. A statistical test was employed to determine if the differences between Group Y and Group O means for Model A and Model B were significant. For Model A, a student's t test was performed on the difference between Group Y and Group O means; $t = .4682$, which was not significant at $\alpha = .05$, and 28 degrees of freedom. Likewise, for Model B, the same test yielded a t value of .0011, which was not significant at $\alpha = .05$.

The test for homogeneity of correlation coefficients was applied in order to determine if the coefficients found differ significantly for the two groups. This test transposes the r 's algebraically into the normally distributed Fischer's Z value. For $r = .7199$ and $r = .8269$ for Groups Y and O respectively, the difference was not significant; $Z = .66058$ and $\alpha = .05$.

Length of Disease Factor

The patient sample was also divided into two groups based on length of disease, which was the period from the date of diagnosis or radical mastectomy, to the date of the evaluation for the study, expressed in months and years. For most patients, the date of radical mastectomy, or in cases where this surgery was not performed, the date of primary detection or treatment was taken as the approximate date of diagnosis of breast carcinoma. Since for most patients, the exact date of detection is unknown, we assume that the date of primary treatment is a reasonable estimate of this parameter.

Table 5 shows the scores for Model A and Model B divided into two groups, based on length of disease. Group S, the left side of Table 5, was composed of patients having their disease less than 3.3 years; $N = 13$. The range in length of disease was from five months (.42 years) to 39 months (3.25 years) with a mean of 21.4 months (1.78 years) and a median of 20 months (1.66 years). The average scores for Model A and Model B for Group S were 14.38 and 7.54 respectively. By inspection, these scores are somewhat lower than the average scores for the total sample; $r = .6948$ was significant at $p = .0083$.

Group L patients, their length of disease and model scores, are described in the right half of Table 5. This group numbered 17 patients; mean length of disease was 72 months (six years), with a range of 43 months (3.5 years) to 120 months (ten years). The average Model A score was 19.0 and the average Model B score

Table 5

Analysis of Scores on Operational Models A and B - Division by Disease Period Since Diagnosis

Group S Patients Having Disease < 3.3 Years (40 months)					Group L Patients Having Disease ≥ 3.3 Years (40 months)				
Patient #	Length of Disease* Months (Years)		Model A Score	Model B Score	Patient #	Length of Disease* Months (Years)		Model A Score	Model B Score
4	5	(.42)	24	20	25	43	(3.58)	11	3
12	8	(.66)	6	2	28	44	(3.66)	21	6
22	10	(.83)	5	1	5	45	(3.75)	30	2
2	12	(1)	24	18	21	45	(3.75)	12	1
10	14	(1.16)	9	6	3	46	(3.83)	13	0
11	20	(1.66)	22	14	9	57	(4.75)	31	33
13	20	(1.66)	10	2	17	60	(5)	13	8
8	25	(2.1)	11	5	19	60	(5)	27	11
16	27	(2.25)	19	3	29	72	(6)	12	5
27	27	(2.75)	15	2	24	73	(6.08)	30	24
26	33	(2.75)	13	13	23	85	(7.08)	15	10
15	39	(3.25)	21	5	7	87	(7.25)	17	8
30	39	(3.25)	8	7	14	87	(7.25)	13	7
					1	93	(7.75)	38	46
					18	96	(8)	7	1
					6	111	(9.25)	10	5
					20	120	(10)	23	9
N = 13 Mean 21.46 (1.78)					N = 17 Mean 72 (6)				
Median 20 (1.66)					Median 72 (6)				
14.38 7.54					19.0 10.53				
12 5					15 7				

r = .6448 p = .0083

r = .7794 p = .0004

Difference between Group S and Group L means; for Model A not significant, t = 1.5198; for Model B not significant, t = .7869 Alpha = .05

*Years in parentheses

was 10.53. By inspection they are slightly higher than the average scores for the full patient sample (Table 3). The correlation between model scores for Group L was .7794, a value significant at $p = .0004$.

In relation to Model A, the person having breast carcinoma less than 3.3 years scored on the average 4.6 points below the woman having her disease longer than 3.3 years. The difference, however, was not significant at $\alpha = .05$; $t = 1.5198$. In reference to Model B, the patient having breast carcinoma less than 3.3 years attained a score three points lower than that attained by a woman having her disease longer than 3.3 years. Here too the difference was not significant; $t = .7869$.

As in the previous table, a test for homogeneity of correlation coefficients was applied to $r = .6948$ (Group S) and $r = .7794$ (Group L). The difference between the correlations was not significant at $\alpha = .05$ level; $Z = .45100$. In summary, then, both groups - those having their disease less than 3.3 years or more than 3.3 years - reported significantly high correlation coefficients, that for Group L being slightly higher, but the difference between them was not significant.

Disease Free Interval Factor

The sample was divided to determine if the length of the disease free interval had any effect upon the mean scores of Model A and Model B or the relationship between the two models. The disease free interval, that period between diagnosis and time of evidence of first distant recurrence, is a factor that has been

correlated in the past with longer survival times, lesser morbidity, better response to various treatments, and overall brighter prognosis for various types of cancer.

Table 6 gives the scores for patients based on whether the disease free interval is less than two years (Group F) or longer than or equal to two years (Group G). Each group contained 15 patients. The left side of the table shows analyses of model scores for Group F; of immediate interest is the fact that for two patients, there was no DFI (disease free interval), or in effect, there was distant spread at the time of initial diagnosis for these patients. The mean value for the DFI was only 8.4 months (.70 years) for this group, with the median of 5 months (.42 years) being more indicative of the brevity of the period without clinically active disease. This is in sharp contrast to Group G, where the DFI averaged over four years. (See Table 6).

For Group F, the mean Model A score was 16.6, and the mean Model B score was 9.73. This is a peculiar finding, the former being smaller and the latter larger than the respective full sample means for the models. However, they differ very little from these means. For Group F, $r = .8417$ was highly significant at $p = .0002$; this was higher than the correlation found for Group G ($r = .6599$).

Group G, depicted in the right half of Table 6, describes the scores for those patients with a DFI longer than or equal to two years. The DFI ranged from 24 months (2.0 years) to 81 months (6.75 years), with an average of 48.66 months (4.05 years) and a

Table 6

Analysis of Scores on Operational Models A and B - Division by Disease Free Interval

Group F Patients Having Disease Free Interval < 2 Years (24 months)				Group G Patients Having Disease Free Interval ≥ 2 Years (24 months)			
Patient #	Disease Free Interval* Months (Years)	Model A Score	Model B Score	Patient #	Disease Free Interval* Months (Years)	Model A Score	Model B Score
1	0 (0)	38	46	21	24 (2.0)	12	1
27	0 (0)	15	2	30	30 (2.5)	8	7
2	1 (.08)	24	18	19	31 (2.58)	27	11
22	2 (.17)	5	1	5	39 (3.25)	30	2
4	3 (.25)	24	20	17	41 (3.42)	13	8
8	4 (.33)	11	5	23	44 (3.67)	15	10
26	4 (.33)	13	13	24	44 (3.67)	30	24
12	5 (.42)	6	2	3	48 (4.0)	13	0
10	10 (.83)	9	6	9	54 (4.5)	31	33
15	12 (1.0)	21	5	20	56 (4.67)	23	9
25	12 (1.0)	11	3	7	57 (4.75)	17	8
13	15 (1.25)	10	2	6	60 (5.0)	10	5
16	15 (1.25)	19	3	14	60 (5.0)	13	7
11	20 (1.67)	22	14	29	61 (5.1)	12	5
28	23 (1.92)	21	6	18	81 (6.75)	7	1
N = 15 Mean 8.4 (.70) Median 5 (.42)				N = 15 Mean 48.66 (4.05) Median 48 (4.0)			
		16.6	9.73			17.4	8.734
		15	5			13	7

r = .8417 p = .0002

r = .6599 p = .0074

Difference between Group F and Group G means; for Model A, t = .255 not significant at alpha = .05; for Model B, t = .262 not significant at alpha = .05

*Year given in parentheses

median of 48 months (4.0 years). The means for Model A and Model B scores were 17.4 and 8.734 respectively. Here the situation is the reverse of that for Group F; now the Model A mean is larger and the Model B mean smaller than the full sample means (17.0 and 9.33). Again, however, the difference is only slight. For this group, $r = .6599$, which was significant at $p = .0074$.

The t test revealed that the differences between Group F and Group G means for the operational model scores were not significant at the .05 level; the test statistics were $t = .255$ for Model A and $t = .262$ for Model B. Lastly, the test for homogeneity of correlation coefficients was performed; $Z = 1.0637$, was not significant at $\alpha = .05$, even though at first glance there appears to be a considerable difference between the correlation coefficients obtained for the two groups.

Duration of Metastatic Disease

Although not specifically used to test the hypotheses outlined in Chapter One, the duration of metastatic disease is one concept which is closely related to the disease free interval. If for each patient the disease free interval is subtracted from the total length of disease, the result is the duration of metastatic disease for that patient. Table 7 gives the scores for patients based on the duration of the clinical metastatic process. The left half of Table 7 lists the scores for Group M, those patients having a duration of metastatic disease less than 1.5 years. The mean duration was 6.5 months (.54 years) with a median of 5.5 months (.46 years). The average Model A and Model B scores were

Table 7

Analysis of Scores on Operational Models A and B - Division by Duration of Metastatic Disease

Group M Patients Having Metastatic Disease < 1.5 Years (18 months)				Group N Patients Having Metastatic Disease ≥ 1.5 Years (18 months)			
Patient #	Duration of* Metastatic Disease Months (Years)	Model A Score	Model B Score	Patient #	Duration of* Metastatic Disease Months (Years)	Model A Score	Model B Score
11	0 (0)	22	14	17	19 (1.58)	13	8
3	2 (.17)	13	0	28	21 (1.75)	21	6
4	2 (.17)	24	20	8	21 (1.75)	11	5
12	3 (.25)	6	2	21	24 (2.0)	12	1
9	3 (.25)	31	33	27	27 (2.25)	15	2
10	4 (.33)	9	6	14	27 (2.25)	13	7
13	5 (.42)	10	2	15	27 (2.25)	21	5
5	6 (.5)	30	2	24	29 (2.42)	30	24
22	8 (.67)	5	1	26	29 (2.42)	13	13
30	9 (.75)	8	7	19	29 (2.42)	27	11
29	11 (.92)	12	5	7	30 (2.5)	17	8
2	11 (.92)	24	18	25	31 (2.58)	11	3
16	12 (1.0)	19	3	23	41 (3.42)	15	10
18	15 (1.25)	7	1	6	51 (4.25)	10	5
				20	64 (5.34)	23	9
				1	93 (7.75)	38	46
N = 14 Mean 6.5 (.54) Median 5.5 (.46)				N = 16 Mean 35.2 (2.93) Median 29 (2.42)			
15.71 8.14				18.125 10.19			
16 6.5				15 9.5			

r = .8266 p = .0005

r = .8707 p = .0004

Difference between Group M and Group N means; for Model A not significant at alpha = .05, t = .7767; for Model B not significant at alpha = .05, t = .5505

*Years given in parentheses

15.71 and 8.18 respectively; these do not differ markedly from the full patient sample means in Table 3. For this group, $r = .8266$, significant at $p = .0005$.

The right half of Table 7 lists the scores for Group N, those patients having a duration of metastatic disease longer than 1.5 years. This duration ranged from 19 months (1.58 years) to 93 months (7.75 years) with an average of 35.2 months (2.93 years) and a median of 29 months (2.42 years). Patients in this group had clinically evident metastatic disease approximately five times longer than patients in Group M. For Group N, the average Model A score was 18.125 and Model B score 10.19. A high correlation coefficient was also found for this group; $r = .8707$ was significant at $p = .0004$. Even though a patient having metastatic disease longer than 1.5 years scored more than two points higher on the extent of metastases model than the patient having metastatic disease less than 1.5 years, the difference was not significant at $\alpha = .05$, ($t = .7767$). Nor was the difference between Group M and Group N means for level of functional disability significant at this level, ($t = .5505$). The difference between the correlation coefficients for the two groups was not significant.

Clinic Factor

The sample was divided into two groups according to the tumor clinic the patient attended; the analysis is given in Table 8. The left half of this table shows scores for Group P, the 13 private tumor clinic patients. They averaged 15.38 on Model A and 7.0 on Model B, scores slightly below the full sample

Table 8

Analysis of Scores on Operational Models A and B - Division by Clinic Attended

Group P Private Tumor Clinic Patients			Group R Regular Tumor Clinic Patients		
Patient #	Model A Score	Model B Score	Patient #	Model A Score	Model B Score
6	10	5	1	38	46
8	11	5	2	24	18
10	9	6	3	13	0
11	22	14	4	24	20
16	19	3	5	30	2
18	7	1	7	17	8
19	27	11	9	31	33
20	23	9	12	6	2
23	15	10	13	10	2
25	11	3	14	13	7
26	13	13	15	21	5
28	21	6	17	13	8
29	12	5	21	12	1
			22	5	1
			24	30	24
			27	15	2
			30	8	7
N = 13	Mean 15.38 Median 13.0	7.0 6.0	N = 17	Mean 18.23 Median 15.0	10.9 8.0
r = .5657	p = .0420		r = .8009	p = .0002	

Difference between Group P and Group R means; for Model A, $t = .929$ not significant at $\alpha = .05$; for Model B, $t = 1.052$ not significant at $\alpha = .05$

means, at inspection it can be seen that the medians agreed with the full sample more closely. The correlation coefficient found was .5657, lower than any computed for any of the other groups in this discussion, but still significant at $p = .0420$.

Scores are shown in the right half of Table 8 for Group R, the 17 regular tumor clinic patients. The mean Model A score here was 18.23, and Model B score 10.9, both slightly higher than the full sample means of the respective models. A higher coefficient between models was found here; $r = .8009$ was significant at $p = .0002$.

A patient in the private tumor clinic scored on Model A an average of about three points below a patient from the regular tumor clinic. Concerning the score for functional disability (Model B), again a patient from the private tumor clinic scored approximately three points below a patient from the regular tumor clinic. Neither of these differences between means was significant at accepted levels.

The test for homogeneity of correlation coefficients was applied to the two groups; in spite of a difference (arithmetically) of over .2 between the r 's for Groups P and R, the difference was not significant ($Z = 1.0637$).

SCORE ANALYSES AND CORRELATION COEFFICIENTS FOR SIX MAJOR SITES OF METASTASES

Mean model scores, appropriate correlations, total and mean sites of metastases, and other characteristics will be outlined for the following major sites of metastases: lung, pleura,

bone, liver, brain, distant lymphatic, and skin and soft tissue.

Lung Metastases

Patients having lung metastases from their breast carcinoma are listed in Table 9. This group was comprised of 11 (36.67%) subjects; of those 11, four (36.4%) exhibited unilateral metastases, and seven (63.6%) bilateral pulmonary metastases. The total sites of metastases is that number obtained by adding all major and minor sites of clinical metastases. For the full patient sample the mean was 2.86, with a range of one site to five separate anatomical sites of tumor involvement. (Bone metastases, for example, was counted as one major site of spread, regardless of the number of bones involved). The full sample mean was computed so that the total number of metastatic sites could be compared between groups. For example, patients with lung metastases had a mean of 3.45 sites of involvement, somewhat higher than the full sample mean. This simply means that patients with lung metastases from breast carcinoma tend to have more areas of involvement in comparison to the full sample. The difference between the means for this parameter was not significant.

The mean Model A score and Model B score were 16.54 and 8.54 respectively, with an $r = .8189$ ($p = .0024$). A difference between means t test was done, using the full sample means as a comparison, to determine if patients with lung metastases scored significantly lower than the full sample on Models A and B. For this statistic, $t = .1466$ for Model A and $t = 1.01$ for Model B, neither figure was significant. The test of homogeneity of cor-

Table 9

Model Scores and Total Sites of Metastases for
Patients With Lung Metastases - Group LM

Patient #	Involvement		Model A Score	Model B Score	Total Sites Of Metastases
	Unilat.	Bilat.			
1	X		38	46	5
7		X	17	8	5
12	X		6	2	3
13		X	10	2	2
15		X	21	5	3
16		X	19	3	3
18	X		7	1	4
20		X	23	9	3
28		X	21	6	3
29	X		12	5	4
30		X	8	7	3

N = 11

Mean 16.54 8.54 3.45
 Median 17.0 5.0 3
 Mode 3

Lung Metastases Patients N = 11 r = .8189 p = .0024

All others N = 19 r = .7029 p = .0011

Difference between full sample mean and Group LM mean; for Model A, t = .1466 not significant at alpha = .05; for Model B, t = 1.01 not significant at alpha = .05

relation coefficients was performed comparing the r for lung metastases group with the full sample r , .7551. The difference was not significant at the accepted level ($Z = .41966$, $\alpha = .05$).

Pleural Effusions

Those patients with pleural effusions are listed in Table 10. This group, designated PD, contained nine (30%) members; seven (77.78%) of whom had unilateral involvement, and two (22.22%) of whom had bilateral involvement. The mean number of sites of metastases was 2.88, comparing favorably with the full sample mean of 2.86.

A patient with pleural effusion scored almost six points below the full sample mean on Model A (11.11 versus 17.0). The difference was significant at $\alpha = .10$ where $t = 2.0014$, but not at the .05 level. In addition, although the average patient with pleural effusions scored almost four points below the full sample mean on Model B (5.44 versus 9.33) the difference was not significant at either level, $t = 1.1175$. The correlation coefficient for Group PD was .3649, quite low, and significant only at $p = .3356$. Possible reasons for this low value will be discussed in Chapter Five. Since there were less than ten observations in Group PD, no comparison can be made between $r = .3699$ and the full sample correlation coefficient.

Bone Metastases

Bone metastases were harbored by 25 (83.34%) of the patient sample. Model scores and total sites of metastases are given in

Table 10

Model Scores and Total Sites of Metastases for
Patients With Pleural Effusions - Group PD

Patient #	Involvement		Model A Score	Model B Score	Total Sites of Metastases
	Unilat.	Bilat.			
6	X		10	5	3
10	X		9	6	2
12	X		6	2	3
14	X		13	7	2
16	X		19	3	3
17	X		13	8	2
18	X		7	1	4
23		X	15	10	4
30		X	8	7	3

N = 9

Mean 11.11 5.44 2.88
Median 10.0 6.0 3
Mode 3

Pleural Effusion Patients N = 9 r = .3649 p = .3356

All others N = 21 r = .7734 p = .0001

Difference between full sample mean and Group PD mean; for Model A, $t = 2.0014$ significant at $\alpha = .10$, not significant at $\alpha = .05$; for Model B, $t = 1.1175$ not significant at $\alpha = .05$

Table 11; in addition, the fifth column lists the total number of bony sites involved, by anatomical division. The latter ranged from one to nine bony sites, or areas, involved with metastases; with a mean of 6.36, a median of four, and a mode of three. The total number of sites of metastases had a mean of 2.84, not significantly different from the full sample mean of 2.86.

The mean score on Model A was 18.48 and on Model B, 10.28. Neither of these scores was significant when compared to the full sample means and a t test for the difference between means was employed. By inspection, the means for Group BONE were only slightly higher than the full sample means on both models. An $r = .7398$ was found for this group, significant at $p = .0001$. A test for homogeneity of correlation coefficients, again comparing the r for patients with bone metastases with the r of $.7551$ revealed no significant difference ($Z = .1259$) at accepted levels.

Liver Metastases

Metastases to the liver were found in ten (33.3%) women from the patient sample. This percentage compared well with the frequency of metastases to the liver in large series of breast carcinoma patients. Model scores, and total sites of metastases are listed in Table 12 for this group. The mean value for the total sites of metastases was 3.6, with a median of four. By inspection this value is higher than the full sample mean of 2.86; patients with liver metastases, had, on the average, one more site of involvement than the full sample. The difference, however, is not significant.

Table 11

Model Scores and Total Sites of Metastases for
Patients With Bone Metastases - Group BONE

Patient #	Model A Score	Model B Score	Total Sites of Metastases	No. of Bony Sites Involved
1	38	46	5	9
2	24	18	3	6
3	13	0	1	5
4	24	20	5	2
5	30	2	2	8
6	10	5	3	1
7	17	8	5	7
8	11	5	2	3
9	31	33	2	8
10	9	6	2	2
11	22	14	1	9
14	13	7	2	1
15	21	5	3	3
16	19	3	3	7
17	13	8	2	4
18	7	1	4	1
19	27	11	4	7
20	23	9	3	5
21	12	1	2	3
24	30	24	2	8
25	11	3	2	3
27	15	2	4	3
28	21	6	3	5
30	8	7	3	3
26	13	13	3	2

N = 25	Mean 18.48	10.28	Mean 2.84	6.36
	Median 17.0	7.0	Median 3.0	4.0
			Mode 2.0	3.0

Bone Metastases Patients N = 25 r = .7398 p = .0358

All others N = 5 r = .8997 p = .0001

Difference between full sample mean and mean for Group BONE; for Model A, t = .6417 not significant at alpha = .05; for Model B, t = .3295 not significant at alpha = .05

Table 12

Model Scores and Total Sites of Metastases for
Patients With Liver Metastases - Group LIV

Patient #	Model A Score	Model B Score	Total Sites of Metastases
1	38	46	5
2	24	18	3
4	24	20	5
7	17	8	5
21	12	1	2
22	5	1	2
23	15	10	4
24	30	24	2
27	15	2	4
29	12	5	4

N = 10	Mean 19.2	Mean 13.5	Mean 3.6
	Median 16.0	Median 9.0	Median 4
			Modes 2, 4 and 5

Liver Metastases Patients	N = 10	r = .9514	p = .0001
All others	N = 20	r = .5435	p = .0127

Difference between full sample mean and mean for Group LIV; for Model A, $t = .6852$ not significant at $\alpha = .05$; for Model B, $t = 1.0093$ not significant at $\alpha = .05$

The mean scores for Model A and Model B were 19.2 and 13.5 respectively. The woman with liver metastases scored on the average two points higher on the extent of metastases operational model, and fully four points higher on the level of functional disability operational model, in comparison to the full sample means. The differences were not significant at $\alpha = .05$ ($t = .6852$ for Model A and 1.0093 for Model B).

The correlation coefficient was $r = .9514$, which was highly significant at $p = .0001$. In reporting a non-statistical comparison, all patients without liver metastases had an r of $.5435$, at $p = .0127$.

The coefficient for Group LIV at $.9514$ was the highest obtained for any division or group in this research. The test for homogeneity was applied, using the full sample correlation coefficient of $.7551$. A Z value of 2.031 was obtained; the difference between coefficients was significant at $\alpha = .05$. The patients with liver metastases, then, had a significantly higher correlation between extent of metastases and level of functional disability than the full sample correlation.

Brain Metastases

Metastases to the central nervous system, excluding the spinal cord, were found in seven (23.34%) patients in the sample. This percentage compares well and is within the range reported in large series of breast carcinoma patients. The model scores and total sites of metastases are summarized in Table 13. The mean total sites of metastases was 3.43 , somewhat higher, but not sig-

Table 13

Model Scores and Total Sites of Metastases for
Patients With Brain Metastases - Group BR

Patient #	Model A Score	Model B Score	Total Sites of Metastases
1	38	46	5
2	24	18	3
7	17	8	5
9	31	33	2
13	10	2	2
19	27	11	4
28	21	6	3

N = 7	Mean 24.0	Mean 17.71	Mean 3.43
	Median 24.0	Median 11	Median 3
			Modes 2, 3 and 5

Brain Metastases Patients N = 7 r = .9061 p = .0057

All others N = 23 r = .5695 p = .0047

Difference between Group BR mean and full sample mean; for Model A, t = 1.9445 significant at alpha = .10, but not significant at alpha = .05; for Model B, t = 1.7377 significant at alpha = .10, but not significant at alpha = .05

nificantly, than the full sample mean.

Patients with brain metastases had a mean Model A score of 24, and an identical median. The mean and median Model B scores were 17.71 and 11 respectively. By inspection these values are larger than those for the full sample means of 17.0 and 9.33. A person with brain metastases scored on the average seven points higher on Model A and 8.37 points higher on Model B when compared to all patients.

A t test was used to inspect these differences. On Model A, the difference between means for Group BR and the full sample was significant at $\alpha = .10$ ($t = 1.9445$) but not at $\alpha = .05$. Likewise, for Model B means, the difference between that for Group BR and that for all patients was significant at $\alpha = .10$ ($t = 1.7377$) but not at $\alpha = .05$.

For Group BR, $r = .9061$ for the seven patients. This, like the reported r for Group LIV, was highly significant at $p = .0057$; the p value would be higher if there were a greater number of observations in Group BR. This correlation coefficient is slightly higher than that for all patients, and is considerably higher than the coefficient for all patients without brain metastases, $r = .5695$. Neither of these differences are apparently significant. In fact, since there are less than ten observations in Group BR, no statistical comparison can be made between its correlation and that for all patients.

Metastases to Distant Lymphatics, Skin and Soft Tissue

The last group in the present discussion was formed by

combining patients who had developed distant lymph node metastases or spread to the skin or soft tissue. This major group was designated Group LYM, and was made up of 15 (50%) women from the sample (Table 14). Of these, five (33.3%) had distant lymphatic involvement, five (33.3%) had skin or soft tissue involvement, and another five (33.3%) harbored metastases to both areas. The mean total sites of metastases was 3.4, identical to that for brain metastases patients. Although higher than the full patient sample of 2.86, the difference was not significant.

The mean Model A and Model B scores were 16.67 and 8.933 respectively, slightly lower than those for all patients. A *t* test was performed using the means for Group LYM and those for the full sample, and the difference between means tested for significance. For Model A, $t = .1201$, and for Model B, $t = .1184$, neither being significant at the $\alpha = .05$ level.

For patients in Group LYM, $r = .7177$ was significant at $p = .0029$. This value is consistent with the high correlation coefficients found for all groups examined in this research. This signifies that patients with distant lymphatic and/or skin and soft tissue metastases show a high correlation between Model A scores (extent of metastatic disease) and Model B scores (level of physical disability). The test for homogeneity between correlation coefficients was applied, using $r = .7177$ for Group LYM and the full sample r of $.7551$. The difference was not significant at $\alpha = .05$ ($Z = .2359$), which is expected since the difference between the coefficients is arithmetically small.

Figure 2 demonstrates the frequency of metastases to six

Table 14

Model Scores and Total Sites of Metastases for
Patients With Distant Lymphatic and/or Skin
and Soft Tissue Involvement - Group LYM

Patient #	Distant Lymphatic Involvement	Skin and Soft Tissue Involvement	Model A Score	Model B Score	Total Sites of Metastases
1	X		38	46	5
4	X	X	24	20	5
5		X	30	2	2
7	X		17	8	5
12	X		6	2	3
14		X	13	7	2
15	X	X	21	5	3
18		X	7	1	4
20		X	23	9	3
22		X	5	1	2
23	X	X	15	10	4
25	X		11	3	2
26	X	X	13	13	3
27	X	X	15	2	4
29	X		12	5	4

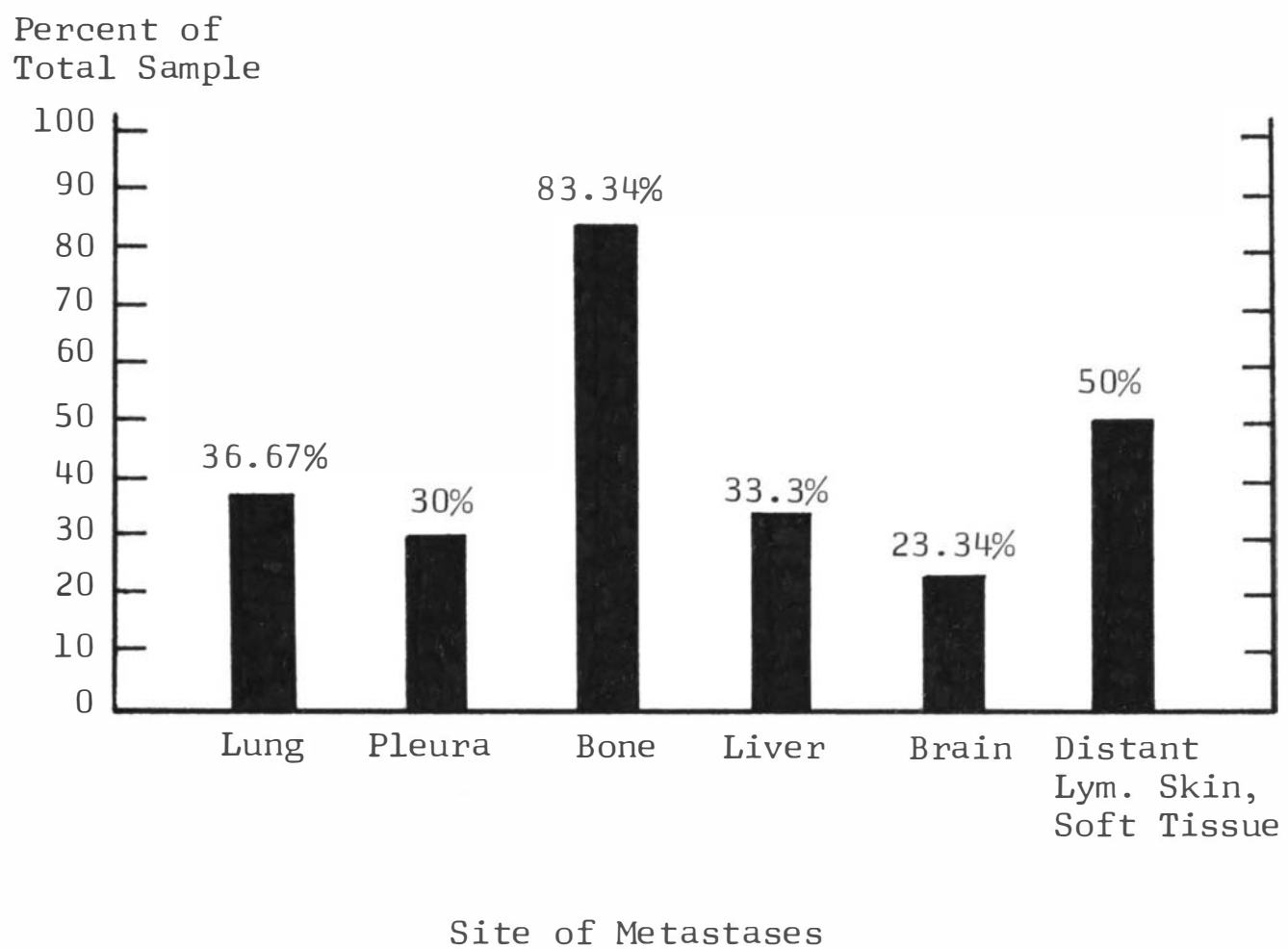
Mean 16.67 8.93 3.4
 Median 15.0 5 3
 Modes 2, 3
 and 4

Patients with Distant Lymphatic and/or Skin and Soft Tissue
 Involvement N = 15 r = .7177 p = .0029

All others N = 15 r = .8096 p = .0004

Difference between Group LYM means and full sample means; for
 Model A, t = .1201 not significant at alpha = .05; for Model B,
 t = .1184 not significant at alpha = .05

Figure 2



Percentage of Patients Having
Metastases to the Six Major Sites

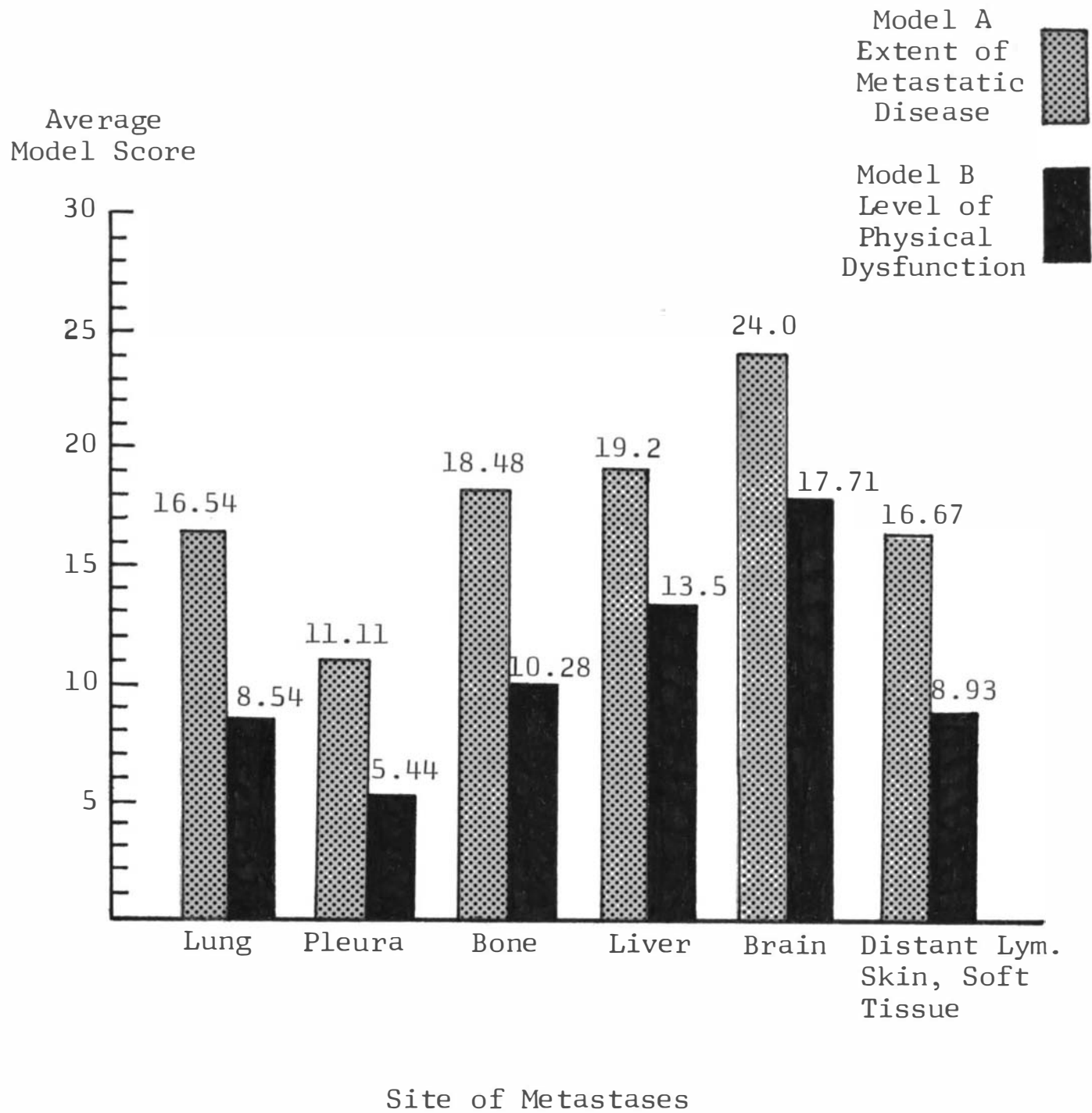
major sites of tumor involvement. By inspection, bone metastases is the most common site of disseminated disease, followed by skin, soft tissue, or distant lymphatic; lung metastases; liver metastases; pleural effusions; and brain metastases in order of decreasing frequency. Figure 3 illustrates the average model scores for both models for the six major sites of tumor involvement.

FREQUENCY DISTRIBUTION OF PATIENTS OVER SIX CATEGORIES OF FUNCTIONAL ABILITY

In order to support or refute the hypothesis that the 30 patients in the sample will be distributed evenly over a six category functional classification system, a description of the performance status required for each level was necessary. Appendix D succinctly outlines the criteria for each classification, and depicts pertinent definitions. The reader should note that the patient classified in category one is completely functional; the totally dysfunctional and completely dependent patient would be classified in category six. The six levels represent a progression through functional disability levels. This schema was devised to afford a quick reference to the functional level of any given patient.

Each patient in the sample was classified, but the decision as to the proper category was often equivocal. For this reason, an upper limit of function was defined as that potential level of function representing the highest category for that particular patient. For example, for a patient alternately functioning at level one and two, one would be the upper limit. Conversely, the

Figure 3



Average Model Scores for the Six Major Sites of Metastatic Tumor Involvement

lower limit of function was that level representing the lower level for that particular patient. A patient alternately functioning at level two and three would have three as the lower limit. For the 14 equivocal patients, the upper and lower limits are given in columns six and seven of Table 17. For the remaining 16 patients whose levels were not equivocal, the upper limit is equal to the lower limit.

Table 15 summarizes the number of patients in each category according to both upper limit of function (Part I) and lower limit of function (Part II). It was hypothesized that the patients would be distributed evenly over the performance status categories. A Chi square Goodness-of-Fit test applied to both parts revealed a significant deviation from this proposed frequency; the level of Chi square was 11.07, and values for both the upper and lower limits of function exceeded that value, meaning that the patients could not be distributed evenly over the categories. The significance of this finding will be discussed in Chapter Five.

RELATED DESCRIPTIVE SAMPLE CHARACTERISTICS

Characteristics of the patient sample which are relevant to the total understanding of the patient with metastatic breast cancer are delineated in this section. Patterns of bone metastases are important in deciding on appropriate diagnostic procedures to determine extent of involvement in the skeletal system. The tables describe data which supports the contention that the study sample is a random representative sample of the population

Table 15

Frequency Distribution Over Six Categories
of Performance Status - Functional Classification

Part I Upper Limit of Function		Part II Lower Limit of Function	
Classification	No. of Patients	Classification	No. of Patients
1	7	1	3
2	4	2	10
3	12	3	9
4	4	4	3
5	2	5	3
6	1	6	2

Chi square = 16

Chi square = 12.4

Reject Hypothesis of even
distribution of patients
(E = 5)

Reject Hypothesis of even
distribution of patients
(E = 5)

Significant Chi square value = 11.07 at alpha = .05

of patients with metastatic breast carcinoma attending the Medical College of Virginia Tumor Clinics. In addition, the functional status and rehabilitation goals of the patient are tabulated; these items are discussed more fully in Chapter Five.

Bone Metastases Patterns

Of particular interest was the frequency of metastases to various bony sites, which is summarized in Table 16. Metastases were most common in the vertebral column, particularly in the lumbar and thoracic vertebrae. These sites led all others in percentage of patients having bony metastases. Most large series of patients reported similar frequencies to the various bony sites (Galasko, 1972; Hoskins, 1971). The majority of these patients exhibited a mixture of both osteoblastic and osteolytic bony metastases. Most authors have not divided the femur or pelvis into separate anatomical components to report frequencies of metastases. In this research, however, the pelvis was subdivided into five areas (wing of ilium, ischium, acetabulum, pubic bone, and sacrum) and the femur into three areas (head and neck, intertrochanteric, and subtrochanteric) for further classification. By inspection one can note that the ilium and ischium make up the majority of metastases to the pelvis, the acetabulum and sacrum being of less importance in bony spread, as found by this investigation.

Also noted is the observation that most femoral metastases occurred in the head and neck (32%) and in the intertrochanteric

Table 16

Frequency of Metastases to Specific Bony Sites*

Bony Site	No. of Patients	Percent of Patients Having Bony Disease, N = 25
Lumbar Vertebrae	15	60%
Thoracic Vertebrae	15	60%
Ribs	13	52%
Wing of Ilium	10	40%
Skull	9	36%
Ischium	8	32%
Femur-Head and Neck	8	32%
Femur-Intertrochanteric	7	28%
Acetabulum	6	24%
Pubic Bone	6	24%
Sacrum	4	16%
Shoulder girdle (clavicle, scapula, upper humerus)	4	16%
Femur-Subtrochanteric	2	8%
Cervical Vertebrae	2	8%
Sternum	1	4%

N = 25

*Detected by bone survey, bone scanning, or both

region (28%) - the subtrochanteric area and the shaft of the femur (8%) being much less common sites of metastatic spread. The role of the vertebral venous system in the distribution of metastases to the spine and pelvis, as well as proximal femur, has been discussed at length in Chapter Two.

Of patients with bone metastases, two suffered pathological fractures: patient # 9 - a fracture through the right humerus, and patient # 28 - a fracture of the right femoral neck. The former was treated by closed reduction and the latter by surgical insertion of an Austin Moore prosthesis. Only one patient (# 9) had hypercalcemia.

General Patient Information

Table 17 summarizes general patient information that was found in examining the patient sample. The eight columns depict the following information, from left to right: patient identification number, proximal (breast, ipsilateral axillary or internal mammary) radiation, distant radiation, whether oophorectomy or adrenalectomy was performed, upper limit of functional classification, lower limit of functional classification, and rehabilitation goal.

From this table, 56.67 percent of the patient sample had radiation therapy to the breast, ipsilateral axillary nodes or internal mammary nodes. The supraclavicular nodes were usually, but not always, included in the treatment field of these patients. Also, 66.67 percent had radiation therapy to distant metastatic sites, such as osseous, dermal, or lymphatic metastases. Only two

Table 17

General Patient Information Part I

Patient # (1)	Radiation		Oophor. (4)	Adren. (5)	Functional Classification		Rehab. Goal (8)
	Proximal* (2)	Distant (3)			Upper Limit (6)	Lower Limit (7)	
1	X	X	X	X	6	6	C
2		X	X	X	4	4	B
3	X				1	2	B
4		X			4	5	C
5	X	X	X	X	2	3	B
6		X			3	3	B
7	X	X	X		3	3	B
8		X			2	3	C
9	X				5	6	C
10	X	X	X		3	3	B
11		X			4	4	B
12					1	2	B
13	X	X	X		2	3	B
14			X	X	3	3	B
15	X	X			2	2	B
16		X			1	2	B
17	X	X			3	3	B
18			X		1	2	B
19	X	X	X		3	3	C
20	X	X			3	3	B
21					1	2	B
22	X		X		1	1	B
23	X			X	3	4	C
24	X				5	5	C
25		X	X		1	1	B
26	X				4	5	C
27		X			2	3	B
28	X	X			2	2	B
29		X			2	2	B
30	X	X			3	4	B

*Breast, axillary nodes or internal mammary nodes

patients did not receive any form of radiation therapy.

An oophorectomy was performed in 11 (36.67%) patients, while an adrenalectomy was performed on five (16.67%). The two are sometimes combined into one surgical operation, and while an oophorectomy is commonly done alone in pre-menopausal patients, only once was an adrenalectomy performed without simultaneous or previous sterilization (patient # 23). The number of patients in each of six functional classifications has been summarized in Table 15. Columns six and seven of Table 17 illustrate the category for each patient.

Column eight lists the rehabilitation goal for each patient, chosen if that patient were to hypothetically receive physical therapy treatment. Appendix F gives an explanation of the criteria for these goals. For purposes of this research, all patients were either classified as Goal B (supportive) or Goal C (palliative). There were 22 (73.34%) patients in Class B and eight (26.67%) patients in Class C.

Other sites of metastases not included in the six major sites discussion were variable, each site exhibited by only a few patients. Three women (10%) had peripheral nerve involvement: patient # 4 - in the sacral plexus; patient # 6 - in the right sixth cranial nerve; and patient # 20 - in the left twelfth cranial nerve. That none of these patients had brachial plexus involvement is probably due to the small sample size; generally peripheral nerve impingement is more common here due to lymphatic metastases to the scalene and supraclavicular nodes. The mesenteric lymph

nodes were clinically involved in one patient (#23), producing signs of intestinal obstruction and abdominal discomfort. One patient (# 19) had metastases to the retina of the eye, treated by radiation; another developed a metastasis to the periorbital region, also treated by radiation. The former is becoming more common (Fuller et al., 1970) and being recognized earlier.

Two patients had ovarian metastases, patient # 19 - to the left ovary, and patient # 25 to both ovaries. These were incidental findings discovered by a pathologist receiving tissue specimens from oophorectomies, and do not represent true clinical metastases.

Table 18 summarizes the following patient sample information in six columns: from left to right: patient identification number, type of breast surgery, whether a bone survey or scan was performed, whether chemotherapy was used in treatment, and the pathological type of breast carcinoma. The breakdown for type of surgery was as follows: radical mastectomy, 20 (66.67%); modified radical mastectomy, one (3.34%); simple mastectomy, two (6.67%); lumpectomy, two (6.67%); and biopsy only, five (16.67%).

Bone surveys were performed in 26 (86.67%) patients, and bone scans in 21 (70%) patients. Of interest is the fact that in ten bone surveys performed, no evidence of metastases was found, but metastases were subsequently detected by scanning techniques. Therefore, in 10/21 (47.62%) scans performed, there were false negative bone surveys for one or more bony areas. This clearly indicates the value of scanning in clinical determination of bone

Table 18

General Patient Information Part II

Patient # (1)	Type of Breast Surgery (2)	Bone Survey (3)	Bone Scan (4)	Chemo-therapy Treatment (5)	Breast Carcinoma Pathological Type (6)
1	Biopsy	Yes	No	Yes	IDC
2	RM	Yes	Yes	Yes	IDC
3	RM	No	Yes	Yes	IDC
4	RM	Yes	Yes	Yes	Medullary
5	Biopsy	Yes	Yes	Yes	Lobular
6	RM	Yes	No	Yes	Unavailable
7	RM	Yes	Yes	Yes	IDC
8	MRM	Yes	Yes	Yes	IDC
9	RM	Yes	Yes	No	IDC
10	RM	Yes	No	Yes	IDC
11	RM	Yes	Yes	Yes	IDC
12	Biopsy	No	No	No	IDC
13	RM	Yes	Yes	Yes	Medullary
14	RM	Yes	Yes	Yes	IDC
15	RM	Yes	Yes	Yes	IDC
16	RM	Yes	Yes	Yes	IDC
17	RM	Yes	Yes	Yes	IDC
18	RM	Yes	Yes	Yes	Unavailable
19	LUM	Yes	Yes	Yes	IDC
20	RM	Yes	No	Yes	IDC
21	RM	Yes	Yes	Yes	IDC
22	Biopsy	No	Yes	Yes	IDC
23	Biopsy	Yes	Yes	Yes	IDC
24	RM	Yes	No	Yes	IDC
25	RM	Yes	No	Yes	IDC
26	LUM	Yes	No	Yes	IDC
27	SM	Yes	No	Yes	IDC
28	SM	Yes	Yes	Yes	Mucoid
29	RM	Yes	Yes	Yes	IDC
30	RM	No	Yes	Yes	IDC

Abbreviations

- IDC - Infiltrating Ductal Carcinoma
- RM - Radical Mastectomy
- MRM - Modified Radical Mastectomy
- LUM - Lumpectomy
- SM - Simple Mastectomy

metastases.

All but two patients were receiving or had received some form of chemotherapy. Not indicated in the table was the observation that ten (37.3%) patients received estrogen therapy and one (3.34%) patient received androgen therapy. Vincristine was administered at one time or another to 11 (36.67%) patients. Neurotoxicity was observed in seven, or 63.64 percent of these patients; in three this was of a minimal nature, and in four the level of neurotoxicity was of a moderate degree. The frequency of use of the major therapeutic drugs in the patient sample was not tabulated.

Lastly, column six of Table 18 lists the pathological types of breast carcinoma; this information was unavailable for two (6.67%) patients. Twenty-four (80%) of the patient sample had infiltrating ductal carcinoma, two (6.67%) had medullary carcinoma, one (3.34%) lobular, and one (3.34%) colloid carcinoma. These figures compare favorably with those given by Haagensen (1971), who found 75 percent infiltrating ductal carcinomas in a large patient series, and similar percentages for the other pathological types. This column is of interest mainly because it gives support to the observation that the 30 patient sample size in this study constitutes an accepted random sample, since its distribution according to pathological type of carcinoma closely approximates that of large series of breast carcinoma patients.

FREQUENCY OF SPECIFIC DISABILITIES

Table 19 describes the frequency of disability in the

Table 19
 Frequency Distribution of Disabilities in
 Model B Groups

Functional Group	No. of Patients Exhibiting Dysfunction	Percent
I. Feeding	3	10 %
II. Transfer General	13	43.3 %
III. Personal Toilet	10	33.3 %
IV. Transfer, Use of Toilet	7	23.3 %
V. Bathing	18	60 %
VI. Ambulation on Levels	24	80 %
VII. Ambulation on Stairs	27	90 %
VIII. Wheelchair Management*	-	-
IX. Sitting Activities	13	43.3 %
X. Bed Activities	10	33.3 %
XI. Dressing		
A. Upper Body	5	16.7 %
B. Lower Body	11	36.7 %
C. Hose and Shoes	12	40 %
D. Bedclothing	3	10 %
XII. Bowel and Bladder Continence	4	13.4 %

*No patients in this study employed a wheelchair as an assistive device.

various Model B groups. From this table, the physical therapist can identify areas where the patient with metastatic breast carcinoma is most likely to exhibit dysfunction. The data indicated that if the total patient sample, 27 (90%) experienced at least some disability in ascending or descending stairs, and 24 (80%) were dysfunctional to some degree in ambulating on level surfaces. More than one half (60%) of the patient sample experienced difficulty with bathing. Less than one half of the patient sample exhibited dysfunction in each of the remaining groups. More patients tended to have difficulty with lower body clothing and hose and shoes in comparison to upper body clothing or bedclothing. Relatively few patients exhibited dysfunction in feeding activities or in bowel and bladder continence.

SUMMARY

Chapter Four has summarized the results of a descriptive study of 30 patients with disseminated breast carcinoma. The major items of interest were total and mean scores for operational Model A - Extent of Metastases, and total and mean scores for Operational Model B - Level of Functional Disability. These were first determined for the full sample, and subsequently for groups based on age, length of disease, disease free interval, duration of metastatic disease, and tumor clinic attended.

For each group, including the full sample, a correlation coefficient was computed, between the mean score for Models A and B. Appropriate statistical tests of significance were employed to

test the correlation coefficients, and the difference between means for the various groups. The results were placed in table form and summarized within the chapter.

In a similar manner, mean model scores and correlation coefficients were computed for the following six major metastatic sites: lung, pleura, bone, liver, brain, and distant lymphatic - skin and soft tissue; the results tabulated, and the the proper statistical tests employed. The distribution of the patient sample over a six category classification of performance levels measuring functional ability was outlined and the Chi square Goodness-of-Fit Test applied. The chapter ended with a discussion of pertinent general patient information that was collected in the course of this study.

Chapter 5

CONCLUSIONS AND RECOMMENDATIONS

Chapter Five is divided into three parts in order to outline and discuss the conclusions, interpretations, and recommendations of this research project. The first part describes the conclusions and interpretation of the data that was gathered; here the hypotheses proposed in the introduction of the thesis (Chapter One) are tested for acceptance or rejection. The second part of the chapter gives recommendations for further study and research in breast carcinoma, based on the findings of the study, and relates them to physical therapy needs and practices. The chapter ends with a review of the study and short summary of the thesis as a whole.

CONCLUSIONS AND INTERPRETATIONS

Full Sample Correlation

The first hypothesis (H_{01}) stated that there would be no or a negative statistical correlation between the extent of metastases in the metastatic breast carcinoma patient, as measured by Model A, and the level of functional disability, as measured by Model B. Since the correlation coefficient was .7551, which was significant at $p = .0001$, we can, based on the data, reject the null hypothesis and accept the alternate, H_{a1} , which states that there is a positive correlation between the extent of metastatic disease and the level of functional disability. In summary, a

high statistical correlation was found, suggesting that the amount of metastatic disease in a typical patient with disseminated breast carcinoma will relate strongly to the amount of functional disability she will display. The converse of this statement can also be accepted, that the amount of functional disability found in a patient with metastatic breast carcinoma will relate strongly to the amount of metastatic disease that is present. A cursory glance at Table 3 demonstrates that as scores on Model A increase, scores on Model B tend to increase also.

Division by Age, Length of Disease, Disease Free Interval, Tumor Clinic

Age. Another major hypothesis (H_3) in reality has two parts. One examines age (older or younger than age 60) and the other examines length of disease (longer than or less than 3.3 years), and their relationship to model means. H_3 stated that those patients over the age of 60 and those patients living longer than 3.3 years with their disease will not exhibit any greater amounts of disability (i.e. attain a higher score on Model B). In examining Table 4 once again, patients over age 60 (Group O) did not attain a higher Model B score in comparison to patients under age 60 (Group Y). The t test applied to the difference between means was not significant. This finding tends to support H_3 ; we can conclude that patients under or over age 60 showed little difference in the amount of functional disability as measured on Model B.

This finding might be explained by the fact that the mean age of Group O was only 66.78, and that only four patients were over 70 years of age. This represents a group of people barely over the age of 65, and many disabilities due to increased age, which would inflate Model B scores, were not found. One might also postulate that patients over age 60 simply do not carry a greater risk of increased morbidity from their breast carcinoma. One can also suggest that tumor growth might be less aggressive in older patients. The correlation coefficients did not differ significantly, although patients over age 60 showed a higher r , suggesting that what disabilities that they do have might be more closely related to the amount of metastatic disease present.

This mean age for all patients was 58.16, somewhat higher than most studies. However, the average of 50 reported in most series is the age of onset of breast carcinoma, so the mean age of all the patients with the disease will be expectedly higher - the additional years probably due to patients living longer with their disease due to improved treatment methods.

Length of Disease. To test the second part of H_03 - that of length of disease effect, Table 5 must be examined. The hypothesis stated that patients living longer than 3.3 years with their disease will not show increased disability. For Group L, the mean Model B score was 10.53, which is somewhat higher than the full sample mean, and three points higher than the Group S mean. A t test applied to the difference between means was not significant. This finding

also tends to support H_{03} , therefore we accept the null hypothesis of no difference, and conclude that by this data, patients having their disease over 3.3 years do not show significantly greater levels of functional disability. Conclusion from the two separate parts of the hypothesis is to accept H_{03} and reject H_{a3} .

Table 5 does indicate that those patients having their breast carcinoma longer (Group L) tend to have more metastatic disease as expressed by Model A scores, but this difference is not significant. However, the trend appears to be toward new sites of metastases developing as the length of disease increases. Those patients in Group L correlate slightly higher between Model A and Model B than those patients in Group S. Although the difference is not significant, one can speculate that as a patient has her disease longer, the disabilities she does have will relate more closely to her extent of metastatic disease. This might imply that as patients live longer with their disease, disabilities will be a greater reflection of the metastatic process within the body.

Disease Free Interval, Duration of Metastatic Disease. Table 6 divides patients according to disease free interval. Although none of the accepted statistical tests proved significant differences between Groups F and G, the following interpretation may be made: patients with a DFI longer than two years had a lower r than those with a DFI of less than two years. It is postulated that Group F patients develop more disease and its concomitant dysfunction, and that the level of dysfunction is better related to

the amount of metastatic disease. One hypothesis is that patients with disease free intervals of longer than two years might have their metastatic disease a shorter period, on the whole, and not sufficiently long to produce or affect significant increases in levels of physical dysfunction. This might explain the lower Model B score and slightly lower correlation coefficient found here.

Data from Table 7 do not support this hypothesis. Of the 15 patients having a disease free interval of more than two years, ten had their metastatic disease longer than 1.5 years, and only five had their metastatic disease less than 1.5 years. This suggests that patients with long disease free intervals also tend to have a longer duration of metastatic disease. It is possible though that those patients with shorter disease free intervals can develop more disease and disability even in the relatively shorter duration of metastatic disease.

Those patients who had a longer duration of metastatic disease tend to have somewhat more metastatic disease than those patients with a shorter duration. This finding is expected since a patient with breast cancer runs the risk of developing new areas of involvement as the duration of metastatic disease increases. Increases in functional disability are expected in conjunction with this phenomenon. In the present study this was reflected in the higher Model B scores found in patients experiencing a longer duration of metastatic disease.

Tumor Clinic. Table 8, summarizing scores according to tumor clinic attended, also demonstrated some interesting findings. Again, none of the tests of statistics employed showed any significant differences between Groups P and R. The lower coefficient ($r = .5657$) for private patients suggests that this group of patients do not relate as highly between amount of disease and amount of physical dysfunction. Apparently, factors, such as type of treatment, length of disease, psychological parameters, motivation and others serve to modify this correlation. Unfortunately, the present study cannot precisely define all the variables upon which private and regular tumor clinic patients would differ.

Another finding from Table 8 merits further attention: that Group R patients tended to have slightly more metastatic disease and greater levels of functional disability than Group P patients. A postulation is that regular tumor clinic patients often present with more advanced disease, larger primary tumors, and longer lengths of disease, among other factors, which would alter their clinical course to the point where they would be more likely to have more disease and disability. On the other hand, patients in Group P might be managed somewhat differently, and probably enjoy more consistent medical follow up, reflected by lower Model A and Model B scores. Lastly, Group R has a disproportionate number of medically indigent patients, the sociological and psychological ramifications of which might possibly be reflected in scores attained on Models A and B.

Major Sites of Metastases

Tables 9 through 14 describe scores and coefficients for six designated major sites of metastases. This data is relevant to the following null hypothesis (H_{02}): for the patient demonstrating a specified site of metastases (i.e., lung, bone, brain, etc.) there would be no or a negative correlation between the extent of metastases (Model A) and the level of physical disability (Model B). By further examination, this hypothesis can be tested individually for each of the major sites.

Each group reported high correlation coefficients, with the exception of patients having pleural effusions. For all other groups, the r was greater than .7 and significant at accepted levels. The conclusion then is to reject the null hypothesis (H_{02}) and accept its alternate hypothesis, H_{a2} : there is a positive correlation between extent of metastases as measured on Model A and level of physical disability, as measured on Model B for selected sites of metastases. Because the various sites showed different correlation coefficients and variable mean model scores, a summary and interpretation of the results for each site follows.

Lung Metastases. Patients with lung metastases correlated highly between Model A and Model B ($r = .8189$), thus this group supports the rejection of H_{02} . Clinically bilateral metastases were found more often than unilateral metastases in this group. Mean model scores did not differ significantly from those for the full sample.

This suggests that patients with lung metastases are characteristically representative of patients with disseminated breast carcinoma as a whole. None of the present patient sample exhibited lymphangitic metastases, the symptomatology of which might have increased both model scores. The patient with lung metastases averaged a slightly larger number of overall sites of metastases, which suggests that these patient are likely to have more sites involved than the average patient or the patient without lung metastases. The data do not allow one to conclude that lung metastases only occur after several other sites have been seeded with tumor. A study which documents the order of occurrence of metastatic sites would be needed to make assumptions or conclusions of this nature.

Pleural Effusions. Patients having pleural effusions showed the smallest coefficient relating extent of metastatic disease and level of physical dysfunction, $r = .3649$. However, the value is still positive, although significant at only $p = .3356$. Due to this low p value, the conclusion is to accept the null hypothesis (H_0) and reject H_a . Patients with pleural effusions do not correlate at an accepted significance level between extent of disease and level of functional disability. The reasons for this lower coefficient could be possibly explained in light of the significantly lower Model A scores - Group PD patients tended to have significantly less metastatic disease than the full sample, and this did not relate as well to the level of functional disability.

Another reason for the low coefficient might be the fact that the patient with a pleural effusion averaged 2.88 metastatic sites, which did not much exceed the full sample average. These patients, having relatively less extensive disease, and relatively fewer sites involved, would not be expected to correlate highly with levels of functional disability. Since most of the patients had only unilateral involvement and were not strongly symptomatic, one can postulate that much of the disability (Model B) might be due to the influence of other major sites of metastatic involvement.

Lastly, patients with pleural effusions as the sole or major areas of involvement usually do quite well clinically. This would explain the corresponding lower Model B scores that were observed here. Another postulation is that pleural effusions occur earlier in the course of the breast cancer's history, before many other sites are seeded, and long before significant symptomatology from other areas could affect a greater degree of physical dysfunction.

Bone Metastases. Patients with bone metastases (Table 11) correlated .7398 between Model A and Model B, thus also lending support to H_a_2 , that there is a positive correlation between extent of metastases and level of physical disability for major metastatic sites. Since 25 patients exhibited this phenomenon, this group could be viewed as closely representative of the full sample. That the model means were only slightly higher than the full sample probably reflects the slight increase in symptomatology and disa-

bility brought on by distressing bone pain.

Patients with bone metastases most frequently reported only two major metastatic sites (bone being one of them), while other groups usually reported three sites involved. The mean of 2.84 is comparable to that for all patients; patients with bone metastases are not likely, then, to have several additional areas involved with metastases, as compared to other groups. In the clinical situation, physicians and other health personnel often find that in a patient developing bone metastases, long periods of time may pass before any other areas of distant spread make their presence known. With effective treatment, the onset of additional metastases may be delayed even longer. Perhaps this effect also has a bearing on the lower mean for total sites of metastases that was observed here.

Galasko (1972) stated that 85 percent of patients dying from breast carcinoma have bone metastases at autopsy. The figure in this research, 83.34 percent, closely approaches this theoretical and observed percentage. That the research figure is somewhat higher than that expected clinically (50 to 60 percent) is probably due to the increased use of both bone scanning techniques and corroborative bone surveys. To conclude that there are a disproportionate number of patients with bone metastases in this patient sample would be erroneous; rather the fact that the observed percentage approximates the theoretical found at autopsy lends support to the contention that the present 30 patient sample is a good representation of the total population of patients with

metastatic breast carcinoma.

Patterns of osseous metastases to various bony sites were summarized in Table 16 and discussed in Chapter Four. Galasko (1972) and Staley (1956) reported frequencies comparable to those observed in this research. Of particular importance to the physical therapist are metastases to the femur which carry a fracture rate of 50 percent. The fact that only one patient (out of 17 with femoral metastases) suffered a pathological fracture probably indicates that an insufficient number of patients have had their femoral metastases long enough to develop a fracture. Also, prompt radiation and other supportive measures and treatment for symptomatic patients with femoral metastases have probably contributed to the lower incidence of pathological fractures in the present patient sample.

Liver Metastases. Patients with liver metastases were observed to have the largest correlation coefficient, $r = .9514$, significant at $p = .0001$. The conclusion from this group is to reject H_0 and accept H_a . Interestingly enough, patients not having liver metastases only correlated .5435 between Model A and Model B. The correlation for Group LIV was significantly different from that for all patients. The conclusion is that patients with liver metastases show a significantly higher correlation between extent of disease and level of physical dysfunction; women in this group exhibit disability that is more clearly related to their state of metastatic disease. One explanation for this phenomenon might be

found in the fact that the mean total sites was 3.6 - patients with liver metastases were likely to have several additional areas involved with tumor. The added areas, taking into account the degree of involvement and symptomatology, add to the overall Model A and Model B scores and serve to inflate the correlation coefficients.

Patients with liver metastases might have relatively increased symptomatology (jaundice, nausea and emesis, abdominal discomfort) which could significantly affect the patient's level of functioning, and perhaps in a larger series of patients, disproportionately change the level of physical dysfunction. Lastly, the data would suggest that liver metastases usually occur when several additional sites are involved simultaneously or previously; however, that two patients presented with liver metastases as their first sign of distant recurrence provides contradictory data to this contention.

Brain Metastases. The brain metastases group (N = 7) also attained a high correlation between Model A and Model B scores, $r = .9061$. For this group, the decision is to reject the null hypothesis (H_0) and accept the alternate (H_a) of a positive correlation between the extent of disease and the level of physical disability. As with Group LIV, those patients not having brain metastases (N = 23) only correlated .5695 between Model A and Model B. This suggests that for a given number of patients, those who have brain metastases are more likely to show a higher correlation between

extent of metastases and level of physical dysfunction than those patients who do not demonstrate such metastases.

Several investigators (Fuller et al., 1970; Lesse and Netsky, 1954; Vieth and Odom, 1965) have suggested that cerebral metastases occurred later in the course of breast carcinoma and after the disease was fairly widespread. Because the mean number of metastatic sites involved was 3.43, larger than the full sample mean of 2.86, the implication is that patients with brain metastases are also likely to have several other sites of metastases.

This likelihood is given further support if one examines the significantly higher mean scores on Model A and Model B, in comparison to the full sample means. The hypothesis that there is no difference between means for Both Model A and Model B compared to the full sample must be rejected. The mean Model A score, 24, probably represents the influence of extent of metastases and severity of symptomatology from the relatively large numbers of sites of metastases in this group, and may not be a true reflection of the brain metastases per se. This same explanation may apply to Model B, where the influence of a heightened mean of 17.71 might be due to the combined effect of the greater number of sites of metastases, each contributing considerably to the level of functional disability. Also, the two patients with the highest Model A and B scores of all patients both had brain metastases, and their high scores within a small number of observations (seven) served to considerably inflate the means for both models for this group.

In retrospect, only two of the seven patients (# 1 and # 2) demonstrated moderate to severe physical dysfunction due mainly, it was believed, to the neurological effects of the brain metastatic deposits. The remainder of the patients in this group demonstrated scores that suggested less severe levels of physical disability.

The difference between means being tested at $\alpha = .10$, one can conclude that patients with brain metastases have a significantly greater extent of metastatic disease, and exhibit significantly greater levels of physical dysfunction, as measured on Model A and Model B scores respectively. This conclusion is based on a comparison with the means on Model A and Model B of all patients combined.

Distant Lymphatic, Skin and Soft Tissue Metastases. Patients having metastases to the distant lymphatics, and/or skin and soft tissue, comprise the last major group upon which the null hypothesis (H_0) was tested. This group, described in Table 14, had an r of .7177, significant at $p = .0029$. Therefore, the data indicate that the H_0 must be rejected, and the alternate hypothesis, H_a be accepted for this group - there is a positive statistical correlation between the extent of metastases and the level of physical dysfunction for that group of patients harboring metastases to the distant lymph nodes and/or skin and soft tissue.

Group LYM had a mean of 3.4 total sites of metastases, suggesting too that these patients were likely to have several

other areas of metastatic involvement. However, the difference between this mean and that for all patients was not significant. By examining the means for both models, it cannot be concluded that patients in this category have a greater extent of metastatic disease nor a greater level of functional disability.

Clinicians should remember that a patient could possibly have widespread lymphatic involvement which is asymptomatic, and therefore not detected clinically. For this reason, it is reasonable to assume that the incidence of distant lymphatic involvement (33.3%) reported in this patient sample might in reality be higher.

In summary, for all six major metastatic sites, positive statistical correlations were found, thus the null hypothesis, H_0 , of no relationship between extent of disease and level of physical dysfunction in the metastatic breast carcinoma patient was rejected, and the alternate hypothesis was accepted.

Functional Classification - Performance Status

The six category functional classification used to group patients according to the level of physical function was described in Table 14, Chapter Four, and outlined completely in Appendix D. A Chi square Goodness-of-Fit test was applied to test the null hypothesis that there was an even distribution of the 30 patient sample over the six functional classifications. This test was performed for both the upper and lower limits of function for the patient sample. In both cases, the computed Chi square values exceeded the theoretical value of 11.07. Therefore, the null

hypothesis is rejected and its alternate accepted: the patients are distributed unevenly over the six levels describing performance status.

The patients were clearly heterogenous in terms of functional ability and performance status. A large series of breast carcinoma patients would perhaps be distributed more evenly over the six categories of performance. The reasons for the uneven distribution of the present sample are only postulations. At inspection, the greatest concentration of patients appeared to be in categories two and three, suggesting that most patients with disseminated breast carcinoma are able to care for all personal needs, carry on most normal daily activities, and return to at least part time employment, duties, or age appropriate tasks. For both upper and lower limits of function, over two thirds of the patients fell within categories one to three, demonstrating that they are capable of the level of function described above.

From this data, one can speculate that most patients with disseminated breast carcinoma, evaluated at various periods of their disease, will not be severely dysfunctional. The data provided from this representative sample surely would indicate this conclusion. However, the sample was composed of outpatients only, and did not include any acutely ill patients, nor any patients in the very terminal stages of cancer. This would partly explain the fact the patients were not evenly distributed over the classification schema, as well as the fact that the majority were not severely dysfunctional.

In inspection of Table 15 once again, the finding is that less than one third of the patients were classified in levels four, five, or six. This suggests that only a minority of patients will require assistance in their daily activities, or protective conditions or modified environments, or suffer a loss of independence.

Physical therapy procedures, then, would most likely be concentrated within this group of patients; less than one third of all outpatients with metastatic breast carcinoma. They would be the target of programs designed to increase the level of functional ability through exercise, mobilization, or appropriate modality treatment. Within this group would probably be pre-terminal and terminal patients, as well as those with pathological fractures due to bone metastases, those with liver metastases, those patients with brain metastases, and those patients having their disease a significant length of time, and finally, quite probably those patients with shorter disease free intervals.

In summary, a top priority group could be identified within the sample, making up less than one third of the patients studied, whose members will be more likely to require assistance in daily functional activities. It is this group toward which the physical therapist would direct more intensive rehabilitation efforts to bring these patients to higher levels of functioning.

Rehabilitative Goals

Two points merit further interpretation in addition to the information afforded by Tables 17 and 18. Column eight of Table 17

lists the rehabilitation goal for each patient. Almost three fourths (73.34%) of the patient sample were classified as having a supportive goal for their proposed rehabilitation program. Since these patients are controllable for varying periods of time, intensive rehabilitation efforts, including physical therapy, should be offered to this group. The present data support the contention that distant metastatic spread does not necessarily presage a steady downhill course or even significant levels of physical dysfunction. Rather the physical therapist should be alert to promptly assess and treat those disabilities that do arise in the course of the disease, thus assisting in keeping the patient functional throughout the controllable period of her disease.

Only one fourth (26.67%) of the patients, those in Class C, could be classified as terminal or pre-terminal; this too is a subjective judgement since a number of these patients can be brought to a supportive goal level. For those outpatients with metastatic breast cancer in Class C, the rehabilitation goal is palliative. Here would be included the palliative care, both physical and psychological, afforded to the dying patient. One can conclude that only a minority of breast carcinoma outpatients treated by the physical therapist will require palliative care; probably the greater need, at least in expenditure of time, will be among patients having supportive rehabilitative goals. This is not to deny the smaller number of patients in Class C the services of a professional physical therapist when needed.

Frequency of Specific Disabilities

There was a wide variation in the frequency with which the patient sample demonstrated dysfunction in the 12 functional activity groups of Model B. Table 19 lists the number and percentages of patients showing disability in the different functional activity categories.

That most patients showed dysfunction to some degree in ambulation on stairs and level surfaces probably reflects the systemic effects of the metastatic disease and its treatment. However, since over 80 percent of the patient sample had bone metastases, which were most common in the spine, pelvis, and proximal femur, the pain and limitation of motion in the affected joints could be expected to limit the breast cancer patient's ambulatory status. Dyspnea and other pulmonary symptoms related to lung metastases or pleural effusions may also contribute to the patient's inability to tolerate moderately stressful ambulation activities.

A considerable number of patients exhibited dysfunction in bathing activities. Approximately 40 percent showed dysfunction in either dressing activities associated with lower body garments, and hose and shoes; sitting activities; or general transfer activities. Dressing the lower half of the body, transfers, and bathing involve considerable reaching, stooping, and flexion of the trunk and hip. Since the spine, pelvis, and proximal femurs are more commonly affected with bone metastases, and are apt to be painful upon movement, more patients could be expected to exhibit some level of disability in activities requiring active movement

of these joints.

Correspondingly fewer patients reported disability in feeding activities, personal toilet activities, or dressing activities with upper body garments or bedclothing - all activities primarily involving use of the upper extremities. That 13 patients experienced disability in sitting activities is apparently more a function of decreased sitting tolerance than actual difficulty with activities performed from the seated position. Most patients reported that they were more comfortable lying down than sitting.

This is not to postulate that the state of the patient's bone metastases solely determines the areas where dysfunction is displayed, but only to suggest the bone involvement due to breast cancer can severely limit the patient in functional activities, particularly those involving movement of the lower extremities. If the patient has severe liver or brain metastases, symptoms from these sites will probably override the effect of osseous metastases in causing functional disability. Pain and symptomatology due to metastatic sites other than bone possibly have a more general effect on the patient's activity level, thus manifesting disability over a wider range of functional activities.

Implications for physical therapy can be developed from these findings. The data suggest that metastatic breast cancer patients requiring physical therapy treatment will most likely exhibit problems with ambulation and functional activities involving the use of the lower trunk and lower extremities. Physical therapists are advised to be cognizant of these areas; they can

then prescribe activities and equipment designed to improve the ambulation tolerance and functional level in these patients. Assistive devices, particularly walkers, canes, and self help equipment, often may be necessary. That fractures of the lower extremities due to metastatic cancer are more common than in the upper extremities substantiates the contention that more attention will be given to the former area by the physical therapist treating the breast cancer patient with disseminated disease. However, general fatigue, extensive metastatic disease, systemic symptomatology, and treatment effects can result in disability in all functional activities - suggesting that the physical therapist always consider the total patient in evaluation and treatment.

RECOMMENDATIONS

Several recommendations for additional research are generated by the results of this study. The major implication of the data presented is that additional research is necessary in all areas of metastatic breast carcinoma. Some of these areas are strictly medical, but others bear a more direct relationship to physical therapy approaches.

Clinical Versus Autopsy Studies

A study which would compare metastases that are detected clinically with those found at autopsy would be of tremendous value to physicians, so that areas where improved clinical diagnostic procedures are needed can be documented. Since the present

study is a clinical one, some of the incidences of metastases to selected sites or groups could be compared favorably to existing autopsy studies (Shields and Withan, 1973; Viadana et al., 1973).

Identification of Factors Affecting Mean Model Scores

A larger series of patients could be evaluated on Models A and B to determine if the results found in this research could be repeated and validated. In particular, a larger number of observations of women over the age of 60 (or 65) would be helpful to determine if these patients actually do have greater extents of metastatic disease or greater levels of functional disability. Methodical procedures are needed within the models to remove those factors other than metastatic deposits which might influence a score on level of functional disability. In this way scores could be corrected for increased disability due to advancing age.

Of interest would be to document the ages of those patients having a disease free interval of longer than two years, and compare the average age with those patients having a disease free interval of less than two years. This procedure can also be performed for length of disease groups, on groups divided by duration of metastatic disease, and on private versus regular tumor clinic patients. In this way the average ages of various groups could be compared; some groups might contain a disproportionate number of patients over the age of 60 (or 65) which in other studies might be found to influence the level of disability that is exhibited.

Further research could apply the same general procedure, with modifications, to the various metastatic sites, to determine if certain sites contain a disproportionate number of patients with longer periods of disease, shorter disease free intervals, longer durations of metastatic disease, or private (versus regular) tumor clinic patients. Any of these factors, all studied in the present research project, could singly or in combination effect the mean scores attained on Model A or Model B for the various metastatic groups. Studies of this nature would identify factors, such as the exact length of the DFI, which could statistically alter the amount of metastases or level of disability in a particular metastatic site. By virtue of this, physical therapists could more closely evaluate selected groups, as defined by the factors discovered, for pertinent disabilities and implement appropriate treatment programs.

Treatment and Diagnostic Evaluation Procedures

Relative to medical treatment, the frequency of use of the various chemotherapeutic agents employed in the patient sample would be of interest in order to relate this incidence to model scores. One could then determine if the choice of chemotherapeutic drugs has any definitive effect upon the patient's level of physical dysfunction. Since all but two patients received some type of chemotherapy, and most of this number developed at least some side effects due to treatment, this information would also be of importance in more specific studies. A study which would

offer correlation coefficients of various groups divided on levels of severity of side effects to chemotherapy is an example of determining how treatment effects the amount of disease and the level of disability. In addition, specific documentation of the symptoms and their degree of severity in vincristine neurotoxicity are especially needed to clinically corroborate existing investigations. This then can be related to mean scores on the operational models used in the present study. Unfortunately, an in depth exploration of the neurotoxic effects of vincristine was beyond the scope of this research project.

Another area for potential exploration would be documentation of the methods of diagnosis of specific bony metastatic sites; whether by scan, bone survey, or both. This is needed to support ongoing research which measures the reliability of scans and surveys, in order to discern which techniques are more diagnostically reliable for specific osseous sites.

Recommendations for Physical Therapists

Of particular desire would be studies which would document the types of physical therapy procedures currently used for patients with metastatic disease or, if possible, for metastatic breast cancer patients in particular. Conceivably this avenue of research would outline approaches for various types of metastases, so that procedures applicable to patients experiencing specific symptomatology could be enumerated. Studies of this type are lacking in the literature. The present research established sim-

ply that patients with metastatic breast cancer exhibit functional disability, and that this disability could be related to the amount of metastatic disease harbored within these patients. A summary of the physical therapy treatment employed would also alert the physical therapist to potential areas of dysfunction. This of course assumes that the treatments administered reflect trouble spots in the patient's functional level. Therapists could, if results were adequately documented, then more closely monitor the clinical course of patients having metastatic disease in higher risk areas, (such as liver and brain), those metastatic sites more prone to be associated with significant physical dysfunction.

It was found that patients with metastatic breast cancer more frequently exhibited disability in functional activities requiring movements of the lower trunk and lower extremities. Further research into specific programs which would assist patients in ambulation and lower body mobilization are needed to support the contention that the physical therapy need is greater in these areas.

From existing data, physical therapists are advised to be cognizant of the patient with disseminated breast carcinoma who might be more likely to develop physical dysfunction that would necessitate professional physical therapy attention. Patients having their disease longer than 3.3 years, patients having a DFI of less than two years, patients with liver or brain metastases, and patients with large lytic lesions in the proximal femur might be

included in this group.

The final recommendation is that the two operational models developed for this research be employed in evaluating metastatic cancer patients with primary tumors other than breast. The main function of a study of this nature would be to test the validity of the models. Two types of cancer that could easily be tested on the existing models, with minor modifications, would be carcinoma of the lung and hypernephroma of the kidney. Both types give rise to widespread metastases, although the behavior of these tumors regarding metastatic spread is not as diverse, and typically not as many sites of distant spread are involved as in disseminated breast carcinoma. Nonetheless, a patient sample could be selected and evaluated for extent of metastatic disease and level of functional disability. Correspondingly fewer categories on Model A would be scored, especially in kidney cancer, reflecting fewer anatomical sites of metastases.

In both lung and kidney cancer, brain and osseous metastases would be particularly frequent; metastases to the skin, soft tissue, and probably liver would not be as frequent. Model B would probably need little modification if used to evaluate patients with lung or kidney primaries, since it measures general functional activity, non-specific for breast cancer patients. Other forms of cancer could be tested using the models, deleting metastatic groups or categories of dysfunction that would not be relevant to the type of cancer in question.

THESIS SUMMARY

Thirty female outpatients with metastatic breast carcinoma were evaluated using two operational models constructed for the purpose of assessing and assigning a quantitative score for (A) extent of metastatic disease and (B) level of functional disability. These patients were drawn from the population of patients with disseminated breast carcinoma attending the medical oncology clinics at the Medical College of Virginia Tumor Clinics for a 49 day period in 1975. The data from this patient sample were used to test several hypotheses.

Each patient underwent an initial screening procedure designed to clearly identify those patients with disseminated disease. This was followed by a preliminary evaluation involving related background information. The selected patient sample was then evaluated and scored on the operational models.

The numerical data were tabulated and statistically analyzed for the full patient sample and subsequently for inclusive groupings using the following parameters: age, length of disease, length of disease free interval, duration of metastatic disease, clinic attended, and major metastatic sites. In addition, the distribution of the patient sample over functional classification categories, the frequency of specific disabilities, and related sample characteristics were tabulated and analyzed.

A summary of the major findings of this research project are enumerated below:

1. There is a positive statistical correlation between the extent of metastatic disease and the level of disability and physical dysfunction for the full sample of patients with metastatic breast carcinoma.

2. Those patients over the age of 60, and those patients having their disease longer than 3.3 years do not exhibit significantly greater levels of functional disability than those patients under the age of 60 or those patients having their disease less than 3.3 years.

3. The length of the disease free interval, the duration of metastatic disease, and the tumor clinic attended did not have a significant effect on the extent of metastases or the level of physical dysfunction in these patients.

4. For each of the six major metastatic sites (lung, pleura, bone, liver, brain, and distant lymphatic or skin and soft tissue), there was a positive statistical correlation between the extent of metastatic disease and the level of physical dysfunction. The value for r exceeded .7 and was significant for each group except Group PD - those patients with pleural effusions.

5. Patients with pleural effusions had significantly less metastatic disease in comparison to the full patient sample. These patients also correlated the lowest between extent of metastases and level of functional disability.

6. Patients with liver metastases showed the highest correlation coefficient of any of the other groups; this value was significantly different from the full patient sample correlation

coefficient.

7. Patients with brain metastases had significantly greater amounts of metastatic disease, and significantly greater levels of functional disability in comparison to all patients combined.

8. Patients with pleural effusions or bone metastases were less likely to have several additional anatomical sites involved with metastatic tumor.

9. Patients with lung, liver, brain, or skin and soft tissue - distant lymphatic involvement were more likely to have several additional anatomical sites involved with metastatic tumor.

10. There was a statistically uneven distribution of patients over a six category functional classification schema, the majority of patients not being severely dysfunctional.

11. Approximately three fourths of the patients with metastatic breast carcinoma would have the supportive goal selected for their rehabilitation needs.

12. Approximately one fourth of the patients could be classified as terminal or preterminal and would have the palliative goal selected for their rehabilitation needs.

13. Less than one third of the patient sample could be classified in performance status levels which would indicate that they need assistance of some kind to care for their personal needs, carry on normal daily activities, or return to part time employment, duties, or age-appropriate tasks. The physical therapy needs for this group are correspondingly greater.

14. The remainder (over two thirds) were found to be functioning at performance status levels which would indicate that they did not require assistance of some kind to care for their personal needs, carry on normal daily activities, or return to part time employment, duties, or age appropriate tasks. The physical therapy needs for this group are correspondingly less.

15. More than one half of the patient sample demonstrated some degree of dysfunction in ambulation on stairs or level surfaces and in bathing activities. Patients with metastatic breast cancer most frequently exhibited disability in functional activities requiring movements of the lower trunk and lower extremities.

The present research hopefully will assist the professional physical therapist in the rational and proper evaluation and treatment of the patients with disseminated breast cancer. Additional studies can be expected to increase the present knowledge of the most common cancer in women, and supplement approaches to care for these patients.

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APPENDICES

APPENDIX A

MODEL A

EXTENT OF METASTASES OPERATIONAL MODEL
DISSEMINATED BREAST CARCINOMA

Introduction: The major objective of this model is to describe the natural history of breast carcinoma in regards to its dissemination and development of metastatic deposits. In the process it is hoped that a semi-mathematical approach to the description of extent of metastases in the woman with disseminated mammary carcinoma will be realized. This novel approach to classification of patients with metastatic cancer can then be related to functional disability in the patient as manifested in a test for functional level in activities of daily living. The latter is outlined in Model B, the Level of Functional Disability Operational Model.

This present model deliberately excludes any primary tumor characteristics; or the spread, symptomatology, or condition of homolateral axillary lymph nodes, homolateral pectoralis major or minor muscles, edema of the arm, degree of skin fixation of the primary tumor, or degree of skin edema. These characteristics are not considered to be distant metastases, and are therefore not classified in a model describing disseminated disease.

A detailed description of the model used for the data collection is followed by the score sheet that was used for each patient in the study. Groups marked with an asterisk were those that were given a score; often symptom lists, locations where applicable, and treatment are included for completeness and accuracy for the proper interpretation of the data.

Group I - Pulmonary Metastases.

*A. Extent of Disease.

- 0 no metastases.
- 1 single parenchymal nodule.
- 2 multiple unilateral or bilateral parenchymal nodules.
- 3 multiple amorphous, infiltrative lesions, diffuse, miliary metastases.
- 4 lymphangitic metastases. massive consolidation and atelectasis.

*B. Symptomatology.

0 asymptomatic.		0 absent.
1 minimal.		1 minimal.
2 mild-moderate.	<u>or</u>	2 moderate.
3 moderately severe to severe.		3 severe.
4 very severe-extreme.		4 extreme.

C. List of Possible Symptoms.

- a. cough.
- b. dyspnea.
- c. tachypnea.
- d. sputum production.
- e. hemoptysis or bloody sputum (rare).

D. Treatment.

- a. symptomatic.
- b. chemotherapy.
- c. radiotherapy.
- d. hormonal therapy.
- e. other treatment, combination therapy.

Group II - Pleural Metastases. Pleural Effusions.

*A. Extent of Involvement.

- 0 no metastases; no pleural effusion present.
- 1 small effusion and/or pleural thickening present ipsilateral to the breast primary.
- 2 moderate effusion is present ipsilateral or contralateral to the breast primary.
- 3 a large, severe, extensive and incapacitating effusion present on either side, or a bilateral pleural effusion.
- 4 massive effusion with atelectasis.

*B. Symptomatology.

0 asymptomatic.		0 absent.
1 minimal symptoms.		1 minimal.
2 mild to moderate.	<u>or</u>	2 moderate.
3 severe, considerable.		3 severe.
4 very severe to extreme.		4 extreme.

C. Symptom List.

- a. dyspnea.
- b. cough.
- c. pain.

D. Treatment.

- a. thoracentesis with drainage.
- b. thoracentesis plus intrapleural chemotherapy.
- c. quinacrine or tetracycline therapy.
- d. prolonged drainage with thoracic tubes.
- e. thoracentesis with infusion of ^{198}Au or ^{32}P .
- f. thoracotomy and pleurectomy (rare).
- g. systemic chemotherapy.

Group III - Other Effusions (pericardial, ascites).

*A. Extent of Involvement.

- 0 none.
- 1 small effusion or minimal ascites.
- 2 moderate effusion or moderate ascites.
- 3 large, severe effusion or ascites.
- 4 massive effusion or massive ascites.

*B. Degree of Symptomatology.

- | | | |
|---------------------------|-----------|-------------|
| 0 asymptomatic. | | 0 absent. |
| 1 minimal symptoms. | | 1 minimal. |
| 2 mild to moderate. | <u>or</u> | 2 moderate. |
| 3 severe, considerable. | | 3 severe. |
| 4 very severe to extreme. | | 4 extreme. |

C. Treatment.

- a. pericardiocentesis or abdominal drainage.
- b. pericardiocentesis or abdominal tapping and drainage plus intrapericardial or intraperitoneal chemotherapy.
- c. continued drainage with intrapericardial or intraperitoneal tubing.

Group IV - Bone Metastases.

- | | |
|-----------------------------|---|
| *A. Ribs. | *I. Femur - intertrochanteric. |
| *B. Skull. | *J. Femur - subtrochanteric. |
| *C. Pelvis - wing of ilium. | *K. Vertebrae - lumbar spine. |
| *D. Pelvis - acetabulum | *L. Vertebrae - thoracic. |
| *E. Pelvis - ischium. | *M. Vertebrae - cervical. |
| *F. Pelvis - pubic bone. | *N. Shoulder girdle (clavicle, humerus, scapula). |
| *G. Sacrum. | |
| *H. Femur - head and neck. | |

Grade for each of the above:

- 0 no evidence of metastases.
- 1 metastatic spread detected or suspected by scanning technique or barely discernible on radiographs as one or two isolated osteoblastic or osteolytic bone reactions.
- 2 moderate involvement of the bone in question, with varying degrees of lysis or blastic activity. Cortex is typically not involved or is only minimally so; radiographs are positive.
- 3 considerable to severe involvement of bone - involvement of approximately one half of the bone or bones in question; diffuse fairly widespread bone reaction and activity visible on the radiographs.
- 4 severe involvement of bone or bones in question, destructive blastic or lytic reaction in well over one half of the bone; widespread and multiple areas involved, pathological fracture of hip or one of the long bones.

*Type of Involvement (Overall).

- 0 evident by scan only, or suspected because of pain.
- 1 intertrabecular, or primarily osteoblastic.
- 2 mixed pattern, osteoblastic predominating.
- 3 mixed pattern, osteolytic predominating.
- 4 predominately osteolytic.

*Symptomatology (Pain, decreased ROM, tenderness, swelling).

- | | | |
|--------------------------------|-----------|------------------------|
| 0 asymptomatic. | | 0 absent. |
| 1 minimal. | | 1 minimal. |
| 2 mild to moderate. | <u>or</u> | 2 moderate. |
| 3 moderately severe to severe. | | 3 severe. |
| 4 extreme, profound. | | 4 extreme or profound. |

Treatment.

- a. irradiation.
- b. chemotherapy.
- c. hormonal therapy (additive or ablative).
- d. combination of two or more of the above.

Group V - Liver Metastases.

*A. Extent of Disease.

- 0 metastases not present.
- 1 single discrete lesion or nodule, or minimal disease detected via liver scan, but not clinically evident.
- 2 multiple nodules; intermediate degree of liver involvement.

- 3 diffuse involvement with considerable hepatomegaly.
- 4 liver crowded with metastases; parenchyma almost totally replaced; massive hepatomegaly.

*B. Severity of Symptomatology.

- | | | | | |
|---|--|-----------|---|--------------------|
| 0 | no symptoms, asymptomatic. | | 0 | absent. |
| 1 | minimal. | | 1 | minimal. |
| 2 | mild to moderate. | <u>or</u> | 2 | moderate. |
| 3 | moderately severe to severe. | | 3 | severe. |
| 4 | extreme, profound,
potentially fatal. | | 4 | extreme, profound. |

C. Symptom List secondary to liver involvement.

- a. pain.
- b. anorexia.
- c. nausea and emesis.
- d. coffee and tobacco intolerance.
- e. distressing hepatomegaly.
- f. jaundice.

D. Treatment.

- a. general chemotherapy.
- b. intraarterial infusional chemotherapy.
- c. hormonal therapy.
- d. surgery.
- e. combined treatment approach.

Group VI - Brain Metastases.

*A. Extent of Disease.

- 0 metastases not present.
- 1 single discrete metastatic focus (unilateral).
- 2 multiple lesions are present.
- 3 meningeal or dural involvement or one or two large (greater than three cm.) discrete lesions. Cerebellar metastases.
- 4 combination involvement of cerebrum, cerebellum, or meninges etc. with multiple lesions. Diffuse and severe brain spread of the carcinoma.

*B. Combination of Severity of Symptomatology and Functional Level.

- 0 no neurological findings. Normal activity present.
- 1 Class I. Intellectual and physically able to work and perform other normal daily activities. Minimal sympto-

matology - one or two neurological findings may be present but only to a minor degree.

- 2 Class II. Patient is usually intellectually intact, but will have some physical or other limitations which although will allow him to be home and perform some daily activities, nursing care may be required. Moderate symptomatology is exhibited - between two and four symptoms present to a moderate degree.
- 3 Class III. Patient exhibits major neurological findings, more than four, with symptoms that are fairly severe in degree; patient will require hospitalization, medical care, and supervision. Patient will need considerable assistance in most daily activities.
- 4 Class IV. Several neurological signs are present with a very severe or profound degree of symptomatology. Patient is typically comatose. This is a serious or grave neurological state requiring hospitalization; patient is nearly or completely dependent.

C. Symptom List. (Local tumor effects and/or increased intracranial pressure effects).

- a. hemiparesis.
- b. lethargy or coma.
- c. disorientation; intellectual impairment.
- d. sensory deficits.
- e. headaches.
- f. nausea and/or emesis.
- g. slurred speech or aphasia.
- h. seizures.
- i. ataxia; gait disturbances.
- j. other cerebellar signs or involvement.
- k. paresthesias; numbness and tingling.
- l. other (nystagmus, visual field defects, cranial nerve).

D. Treatment.

- a. corticosteroids.
- b. irradiation.
- c. surgical procedures.
- d. chemotherapy.
- e. hormonal therapy (other).
- f. combination of two or more of the above.

Group VII - Peripheral Nervous System Involvement.

- A. Brachial Plexus Involvement from scalene and hilar or supraclavicular lymph node metastases.
- B. Other Peripheral Nerve Involvement.

*C. Symptomatology, Severity of Involvement.

- 0 asymptomatic.
- 1 mild or minimal pain; minimal motor or sensory loss.
- 2 moderate pain, or motor or sensory loss.
- 3 severe degree of pain, and/or motor or sensory loss.
- 4 extreme symptomatology. Severe pain and/or complete motor or sensory loss.

D. Treatment.

- a. irradiation.
- b. chemotherapy.
- c. hormonal therapy.
- d. combination of two or more of the above.

Group VIII - Intraspinal Metastases - Spinal Cord Compression.

A. Level.

- a. cervical spine.
- b. thoracic spine.
- c. lumbar or sacral spine.

*B. Degree of Severity of Symptoms.

- 0 no discernible motor, sensory, or bowel function impairment.
- 1 mild or minimal dysfunction or symptomatology.
- 2 moderate degree of dysfunction or symptomatology secondary to cord compression. Patient can ambulate with considerable assistance.
- 3 marked, severe degree of dysfunction (motor, sensory, or bowel), secondary to cord compression. Patient is non-ambulatory but some motor function is present.
- 4 complete sensory and motor loss below the level of compression.

C. Symptom List.

- a. sensory deficits or losses. Pain and temperature, position sense, vibratory sense, fine touch, deep touch.
- b. motor paralysis. Varying degrees of motor loss distal to the level of compression. May be unilateral, bilateral, and affect single or groups of muscles.
- c. loss of sphincter control - bowel incontinence.

D. Treatment.

- a. irradiation.

- b. prednisone or other corticosteroid.
- c. surgical laminectomy and decompression.
- d. combination of the above, including chemotherapy.

Group IX - Distant Lymph Nodes.

A. Site of Involvement.

- a. contralateral axillary lymph nodes.
- b. supraclavicular or scalene lymph nodes on either side.
- c. cervical lymph nodes on either side.
- d. abdominal (mesenteric) lymph nodes.
- e. mediastinal and paraesophageal lymph nodes.
 - 1. esophageal stenosis, mildly symptomatic.
 - 2. esophageal obstruction, partial or complete, with dysphagia.
- f. pelvic or inguinal lymph nodes.
- g. other distant nodes.

*B. Extent of Involvement.

- 0 no distant lymphatic involvement.
- 1 one regional site of lymphatic involvement from the list above.
- 2 two isolated sites of involvement of the lymphatics.
- 3 three or more sites of involvement from the list above.
- 4 severe and extensive involvement of the distant lymph nodes, especially peritoneal and abdominal.

*C. Severity of Symptomatology.

- 0 asymptomatic.
- 1 minimal or very mild symptoms from the lymph node spread.
- 2 moderate symptomatology in specific organs due to pressure or obstruction.
- 3 severe degree of symptomatology; specific organ symptoms present with considerable patient distress. Several sites are typically involved.
- 4 very severe organ specific symptoms or syndromes due to pressure, obstruction, or extension of the tumor masses in the lymphatics.

D. Treatment.

- a. chemotherapy.
- b. irradiation.
- c. surgery.
- d. hormonal therapy.
- e. combination of two or more of the above.

Group X - Skin and Soft Tissue.

A. Includes single or multiple subcutaneous nodules, ulcerations, and infiltrations into soft tissue or structures.

*B. Extent of Disease.

- 0 no skin or soft tissue involvement.
- 1 one or two isolated, small (one-two centimeters) nodules or ulcerations, or soft tissue infiltrations. Minimal involvement.
- 2 two or three medium size (two-three centimeters) nodules, ulcerations, or soft tissue infiltrations. Moderate involvement.
- 3 several large (greater than three centimeters) nodules, ulcerations, or soft tissue infiltrations. Severe involvement.
- 4 widespread, very severe involvement with skin nodules, ulcerations, or soft tissue infiltrations.

*C. Overall Severity of Involvement of Symptoms.

- 0 none, asymptomatic.
- 1 minimal.
- 2 moderate.
- 3 severe.
- 4 extensive, very severe.

D. Treatment.

- a. chemotherapy.
- b. irradiation.
- c. surgery
- d. hormonal therapy.
- e. combination of two or more of the above.

Group XI - Hypercalcemia.

*A. Severity of Symptoms.

- 0 normal serum calcium, no symptomatology.
- 1 minor or mild. Slightly elevated serum calcium, usually asymptomatic, minimal signs may be present.
- 2 moderate. There is a moderate degree of elevation of serum calcium with definite but moderate clinical symptoms that are fairly easily controlled.
- 3 severe. Very high levels of serum calcium with severe constitutional symptoms. Immediate and intensive therapy is imperative.
- 4 profound. Extreme serum calcium levels with coma.

B. Symptom List.

- a. nausea and emesis.
- b. coma or lethargy.
- b. dryness of the mouth.
- d. confusion.
- e. kidney failure.
- f. other symptoms.

C. Treatment.

- a. mithramycin.
- b. phosphates.
- c. steroids.
- d. forced fluid intake and low calcium diet.
- e. combination therapy.

Group XII - Other Organ Sites.

- A. Hematogenous dissemination and actual organ involvement with metastatic carcinoma from a breast primary.
Locations:

- a. adrenals.
- b. ovaries.
- c. stomach.
- d. pancreas.
- e. retina of the eye.
- f. thyroid.
- g. other.

- *B. The organ specific symptoms or syndromes for each site are:

- 0 none. metastases are not present.
- 1 minor organ involvement and/or symptomatology.
- 2 moderate organ involvement and/or symptomatology.
- 3 severe involvement and/or symptomatology.
- 4 profound degree of involvement, with organ failure.

C. Treatment.

- a. chemotherapy.
- b. irradiation.
- c. surgical procedure or procedures.
- d. hormonal therapy.
- e. combination of two or more of the above.

Group XIII - Cachexia and Systemic Symptomatology.

- *A. Severity of the Syndrome.

- 0 no evidence of cachexia or systemic symptoms.
- 1 mild or minor. Less than ten pound weight loss with minor anorexia, fever, or fatigue.
- 2 moderate. Between ten and 20 pound weight loss, moderate anorexia, fever, or fatigue, and distress, and moderate protein or nitrogen imbalance.
- 3 severe. Between 20 and 35 pound weight loss, muscular atrophy, pallor, troublesome anorexia, fever, or fatigue, and severe protein imbalance.
- 4 end stage cachexia, profound systemic symptoms.

Group XIV - Vincristine Neurotoxicity.

*A. Extent of Involvement.

- 0 no toxic effects due to therapy; patient not receiving vincristine.
- 1 minimal. constipation, minor paresthesias, insomnia, numbness and tingling, depression of deep tendon reflexes.
- 2 mild-to-moderate. constipation, some loss of bowel motility, moderate paresthesias and numbness and tingling, loss of deep tendon reflexes, mild general pain, mild general weakness (distal), easy fatigability, insomnia.
- 3 considerable toxicity, mild confusion, incoordination, generalized pain, extraocular palsy, paralytic ileus, distressing paresthesias and numbness and tingling, wrist or foot drop, moderate distal weakness.
- 4 severe. paralysis, hallucinations, disorientation, psychosis, delusions, ileus, permanent wrist or foot drop, inability to ambulate or severe gait abnormalities, generalized muscular weakness and atrophy, but even in severe cases is usually distal.

Group XV - Other Complications due to Treatment; those due to surgery, chemotherapy, hormonal therapy, radiation therapy, or other treatment administered for the neoplastic process. Consult Addendum II - Complications Due to Treatment - General Description, for specific detail.

*A. Severity of Symptoms

- 0 no complications or adverse effects.
- 1 minimal severity.
- 2 mild to moderate severity.
- 3 severe complications or symptoms.
- 4 extremely severe to profound complications or symptoms.

B. Treatment.

- a. none.

- b. modification of dosage of drug or withdrawal of drug.
- c. alternate therapy administered.
- d. supportive therapy and other treatment methods.

DATA COLLECTION FORM FOR MODEL A
DISSEMINATED BREAST CARCINOMA
EXTENT OF METASTASES OPERATIONAL MODEL

Group I - Pulmonary Metastases

- *A. Extent of Disease _____
- *B. Symptomatology _____
- C. Symptom List _____
- D. Treatment _____

Group II - Pleural Metastases; Pleural effusion.

- *A. Extent of Involvement _____
- *B. Symptomatology _____
- C. Symptom List _____
- D. Treatment _____

Group III - Other Effusions (Pericardial, Ascites)

- *A. Extent of Involvement _____
- *B. Degree of Symptomatology _____
- C. Treatment _____

Group IV - Bone Metastases.

- | | |
|-------------------------------------|--|
| *A. Ribs _____ | *J. Femur - subtrochanteric _____ |
| *B. Skull _____ | *K. Vertebrae - lumbar _____ |
| *C. Pelvis - wing of ilium _____ | *L. Vertabrae - thoracic _____ |
| *D. Pelvis - acetabulum _____ | *M. Vertebrae - cervical _____ |
| *E. Pelvis - ischium _____ | *N. Shoulder girdle (clavicle, humerus, scapula) _____ |
| *F. Pelvis - pubic bone _____ | |
| *G. Sacrum _____ | |
| *H. Femur - head and neck _____ | |
| *I. Femur - intertrochanteric _____ | |
| *Type of Involvement _____ | |
| *Symptomatology Degree _____ | |

Treatment _____

Group V - Liver Metastases.

- *A. Extent of Disease _____
- *B. Severity of Symptomatology _____
- C. Symptom List _____
- D. Treatment _____

Group VI - Brain Metastases.

- *A. Extent of Metastases _____
- *B. Combination Severity of Symptomatology and Functional Level _____
- C. Symptom List _____
- D. Treatment _____

Group VII - Peripheral Nerve Involvement (Brachial Plexus Involvement).

- A. Area of Involvement _____
- B. Symptom List _____
- *C. Symptomatology, Degree of Severity _____

Group VIII - Intraspinal Metastases. Spinal Cord Compression.

- A. Level _____
- *B. Degree of Severity of Symptoms _____
- C. Symptom List _____
- D. Treatment _____

Group IX - Distant Lymph Nodes

- A. Nodes Involved _____

*B. Extent of Involvement _____

*C. Severity of Symptomatology _____

D. Treatment _____

Group X - Skin and Soft Tissue

A. Specified Area of Involvement _____

*B. Extent of Disease _____

*C. Severity of Symptomatology _____

D. Treatment _____

Group XI - Hypercalcemia.

*A. Severity of Symptoms _____

B. Symptom List _____

C. Treatment _____

Group XII - Other Organ Sites.

A. Location _____

*B. Organ Specific Symptoms or Syndromes for each site:

C. Treatment _____

Group XIII - Cachexia and Systemic Symptomatology.

*Severity of the syndrome _____

Group XIV - Vincristine Neurotoxicity.

*A. Level of Neurotoxicity _____

B. Treatment _____

Group XV - Complications Due to Treatment.

*A. Severity of Symptoms _____

B. Treatment _____

VALIDATION PANEL - MODEL A

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Galen Wampler, M.D.

Ellen Spremulli, M.D.

ADDENDUM I TO APPENDIX A

SEVERITY OF EXTENT OF METASTASES AND THEIR SYMPTOMS -
GENERAL DESCRIPTION

Introduction: Symptomatology from organ involvement in metastatic breast carcinoma can be changed appreciably by various treatment regimes. Therefore, the classification of any one patient in regard to extent of symptoms should be viewed as a dynamic and fluid process - and really only applicable to the period of evaluation; it may change radically within relatively short periods of time. In other words, the condition of the patient may vary considerably with treatment, general physical condition, natural history of the site and characteristics of the metastatic deposit in question, and a host of other factors. Extent of metastases and symptomatology need not always agree for all sites. For example, severe lung involvement may not cause severe symptomatology.

- 0 Metastatic disease is not present. There is no evidence of metastases in the organ, group, tissue, or system in question.
- 1 There is minimal involvement of metastases in the organ, tissue, group, or system in question. The involvement is very apt to be asymptomatic i.e. bone or liver metastases detected via radio-nuclide scanning but not clinically evident. If symptoms are present, they are minimal and inconsequential, and are usually tolerated well by the patient.
- 2 Mild-Moderate. A moderate degree of symptomatology is present, which is tolerated only fairly by the patient. Examples are pain, loss of range of motion, loss of sensation, GI disturbances, and moderate specific organ symptoms. The symptoms caused by extent of disease in this category are usually well controlled on an outpatient basis.
- 3 Severe. A significant and distressing degree of involvement of an organ, tissue, group, or system is present, usually producing severe symptomatology, which will require intensive treatment and, typically, hospitalization. Examples include marked pain requiring powerful analgesic management, dyspnea precluding unrestrained activity, collapse of a vertebrae, severe bone pain, considerable cachexia, and other severe specific organ symptoms.
- 4 Extreme-Profound. Extreme (and in some instances, end stage) degree of symptomatology requiring institutionalization or other special care, and constant nursing or attention to meet the needs of increasing total dependency. Various target organ effects, including total failure of that organ to fulfill its specified function, may occur singly or concomitantly; for example, severe

liver failure; severe dyspnea from pulmonary metastases; profound neurological signs from cerebral metastases; pathological fractures of pelvis or long bones; or progressive spinal cord compression.

ADDENDUM II TO APPENDIX A

COMPLICATIONS DUE TO TREATMENT - GENERAL DESCRIPTION

Introduction: Complications due to treatment may be hematologic, gastrointestinal, neurologic, hepatic, genitourinary, or dermatologic. Also, infections and fever may occur, as well as other general and miscellaneous symptoms. The cause of these complications can be directly or indirectly related to concomitant therapy such as endocrine surgery or hormonal therapy, radiation therapy including radioisotopes, systemic or local chemotherapy for metastatic disease, other surgical procedures, and other forms of therapy. Symptoms may vary from mild to profound.

- 0 There are no adverse effects or symptoms due to chemotherapy, radiotherapy, hormonal therapy, or other treatment. A classification of "0" is also given if patient is not receiving the therapy in question.
- 1 Minimal severity. Complications due to treatment are producing conditions and/or symptomatology that are minimal in nature, are tolerated fairly well by the patient, and do not require dosage or other modification in treatment.
- 2 Mild severity. Complications and symptoms produced by the treatment in question are moderate or mild in degree, and are tolerated with some distress on the part of the patient. Complications will usually require dosage or other modification of treatment regime.
- 3 Severe. Complications and symptomatology produced by the treatment are severe in nature, and are poorly tolerated with considerable distress on the part of the patient. This classification usually will demand that the treatment or therapy be withdrawn or interrupted.
- 4 Extremely severe or profound complications have ensued which under certain circumstances may be irreversible. Patient is profoundly ill or is in serious medical condition.

APPENDIX B

MODEL B

LEVEL OF FUNCTIONAL DISABILITY OPERATIONAL MODEL

Major Objective: to assess the functional disabilities of the metastatic breast cancer patient. The model is divided into twelve major groups, each describing an essential daily activity. Performance on each of these functional activities will be scored according to the scale and definitions given below. Since this model defines the categories more precisely, there should be little disagreement regarding the level of disability for each category for a particular patient.

LEVELS OF FUNCTIONAL DISABILITY

- 0 Independent: safe in an unstructured environment with or without universal equipment.
- 1 Functional: independent within a structured environment and/or with non universal equipment.
- 2 Minimal Assistive: requires safety guarding and/or verbal cues.
- 3 Moderate Assistive: patient requires contact guarding.
- 4 Maximal Assistive; Dependence: patient attempts to help; is completely dependent in the activity.

DEFINITION OF TERMINOLOGY

- a. unstructured environment: community.
- b. structured environment: contained or modified and/or supervised.
- c. universal equipment: portable, i.e. wheelchair, braces, prosthetics, splints, slings, ambulatory aids (walker, cane, crutches, etc.), other.
- d. non-universal equipment: not easily portable, such as parallel bars or hospital bed, lifts, etc.

- e. verbal cues: verbal commands or instructions.
- f. safety guarding: stand by supervision.
- g. contact guarding: physical assistance.

Group I - Feeding

- 0 Patient is completely independent in all feeding activities.
- 1 Functional. Patient can eat if the meal is on a table or tray before her, and can handle all eating utensils satisfactorily.
- 2 Minimal assistive. Patient typically needs assistance in cutting up food, use of some utensils, or spreading butter.
- 3 Moderate assistive. Patient requires considerable contact guarding in feeding activities.
- 4 Patient cannot feed herself, maximum assistance or total dependence.

Group II - Transfer wheelchair to bed and back, or regular chair to bed and back.

- 0 Patient is totally independent or activity does not apply.
- 1 Functional. Transfers to and from a wheelchair or chair from a standard height bed. Structured environment.
- 2 Minimal assistive with various aspects of the transfer.
- 3 Moderate assistive.
- 4 Maximal assistive to total dependence. Patient can attempt to help, but cannot perform transfer without maximal assistance of one or more persons.

Group III - Personal toilet and hygiene activities (excluding bowel and bladder).

- 0 Complete independence in this activity.
- 1 Functional. Patient is able to wash hands and face, take care of hair, shaving needs, etc. Females can handle makeup and other appropriate personal toilet needs.

- 2 Minimal assistive.
- 3 Moderate assistive: approximately one half of the activity or one half of the effort behind the activity is performed by the patient.
- 4 Maximal assistive - near total dependence regarding tasks.

Group IV - Transfer to and from and use of the toilet.

- 0 Complete independence, or activity does not apply.
- 1 Functional. Patient gets on and off the toilet, adjusts clothing, cleanses self, and prevents soiling of self or clothing. If bedpan is used, the patient is able to get on and off, use, clean, and put away the bedpan within the structured environment.
- 2 Minimal assistance required in use of the toilet or bedpan.
- 3 Moderate assistive.
- 4 Maximal assistance is required, either to get to the toilet or use the bedpan; patient is completely or nearly completely dependent in the activity.

Group V - Bathes Self.

- 0 Independent in activity.
- 1 Functional. Patient uses bathtub, shower, or takes complete sponge bath. Direction and modification of the activity may be required.
- 2 Minimal assistive.
- 3 Moderate to considerable assistive - up to one half of activity or effort is performed by the patient herself.
- 4 Maximal assistive to complete dependence on others for bathing activities.

Group VI - Ambulation on level surfaces.

- 0 Independent; universal equipment may be used.
- 1 Functional ambulation. Patient can ambulate within a structured environment with or without universal or non-

universal equipment.

- 2 Minimal assistive. Patient frequently needs safety guarding/ambulation tolerance fair to good.
- 3 Moderate assistive. Patient requires physical assistance to ambulate/ambulation tolerance poor to fair.
- 4 Patient can ambulate with very maximal assistance for only a few steps/patient is non-ambulatory.

Group VII - Ambulation on Stairs.

- 0 Independent.
- 1 Functional in ascending or descending stairs.
- 2 Minimal assistive, requiring safety guarding. Patient is typically prone to early or easy fatigue.
- 3 Moderate assistive. Patient typically can, with assistance, ascend and descend stairs once a day maximum.
- 4 Maximal assistive or dependent. Very maximal assistance needed to ascend one or two steps/patient not able to perform activity.

Group VIII - Wheelchair Activities. (Does not apply if patient is ambulatory).

- 0 Independent in all wheelchair activities.
- 1 Functional. Maneuvers wheelchair on levels with occasional supervision or modification of activity.
- 2 Minimal assistive.
- 3 Moderate assistive. Considerable assistance is needed for the patient to mobilize the wheelchair.
- 4 Maximal assistive. For all practicality, patient is not able to maneuver the wheelchair.

Group IX - Sitting tolerance and activities.

- 0 Independent. Patient sits indefinitely; can mobilize self from the sitting position.

- 1 Functional. Patient tolerates sitting up most of waking hours, and performs most activities from the sitting position satisfactorily.
- 2 Minimal assistive. Patient tolerates sitting up for approximately one half of the day. Needs minimal assistance as defined for activities in the sitting position.
- 3 Moderate assistive. Patient tolerates sitting up for short periods, an hour or so once or twice a day. Needs moderate assistance as defined for activities in the sitting position.
- 4 Patient cannot tolerate sitting up; is confined to bed.

Group X - Bed Activities.

- 0 Independent in all bed activities.
- 1 Functional. Within the structured environment, patient is able to sit up, turn from prone to supine, and from supine to prone; can turn self at night, and is able to position self to comfort.
- 2 Minimal assistive. Safety guarding and/or verbal cues needed for bed mobility activities.
- 3 Moderate assistive. Patient will typically perform up to one half of bed mobility activities herself; in addition to physical assistance an overhead trapeze bar is frequently needed.
- 4 Maximum assistive to complete dependence.

Group XI - Dressing Activities.

- A. Upper Body Garments. (Shirt, blouse, jacket, pullover garments).
 - 0 Independent.
 - 1 Functional. Needs occasional guidance and supervision within the structured environment.
 - 2 Minimal assistance required.
 - 3 Moderate assistance needed.
 - 4 Maximal assistance; patient cannot perform activity; completely dependent.

- B. Lower Body Garments (trousers, pants, shorts, skirts).
Scored from zero to four as above.
- C. Hose and Shoes (Tie shoes, loafers, slippers).
Scored from zero to four as above.
- D. Underclothing and/or bedclothing (Pajamas, nightgowns, simple bedjackets).
Scored from zero to four as above.

Group XII - Bowel and Bladder Management.

- 0 Patient always continent of bladder and bowel.
- 1 Patient is functional in bowel and bladder control. Is able to take an enema or suppository with supervision; controls bowel and bladder day and night.
- 2 Minimal assistive. Patient has accidents on occasion; is too weak to control functions fully.
- 3 Moderate assistance as defined in using any aids, such as enemas or suppositories or other devices, to control bowel and bladder function. Accidents are frequent, especially at night.
- 4 Patient is incontinent of either bowel or bladder function or both.

DATA COLLECTION FORM FOR MODEL B
LEVEL OF FUNCTIONAL DISABILITY OPERATIONAL MODEL

- Group I - Feeding. _____
- Group II - Transfer to wheelchair or regular chair to and from
bed. _____
- Group III - Personal Toilet and Hygiene Activities. _____
- Group IV - Transfer to and from and Use of the Toilet. _____
- Group V - Bathes Self. _____
- Group VI - Ambulation on Level Surface. _____
- Group VII - Ambulation on Stairs. _____
- Group VIII - Wheelchair Activities. _____
- Group IX - Sitting Tolerance and Activities. _____
- Group X - Bed Activities. _____
- Group XI - Dressing Activities.
- A. Upper Body Garments. _____
 - B. Lower Body Garments. _____
 - C. Hose and Shoes. _____
 - D. Bedclothing. _____
- Group XII - Bowel and Bladder Continence. _____

VALIDATION PANEL - MODEL B

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Mary Miller, RPT

APPENDIX C

PRELIMINARY PATIENT INFORMATION PREPARATORY TO DATA COLLECTION

SHORT DATA BASE

Name: _____ Hospital Chart Number: _____

Date: _____ Age: _____

Address: _____

Date of Breast Cancer Diagnosis: _____

Date of Radical Mastectomy or other Breast Surgery: _____

Known Metastases (further breakdown will be outlined on the Extent of Metastases Operational Model):

Site: _____ Date: _____

Other Surgical Procedures Used:

_____ Date: _____

Radiation Procedures Used:

_____ Date: _____

Chemotherapy Treatment:

Agent: _____ Date: _____

Hormonal Treatment

Additive (Estrogens or Androgens):

Agent: _____ Date: _____

Ablative:
 Oophorectomy: _____ Date: _____

Adrenalectomy: _____ Date: _____

Hypophysectomy: _____ Date: _____

Preliminary Functional Classification (Performance Status)

1 _____
 2 _____
 3 _____
 4 _____
 5 _____
 6 _____

Tentative Rehabilitation Goals (See Rehabilitation Goals and Their Criteria)

A _____
 B _____
 C _____

Type of Primary Cancer

1. Infiltrating Ductal Carcinoma
2. Lobular Carcinoma in Situ
3. Medullary (Circumscribed) Carcinoma
4. Inflammatory Carcinoma
5. Papillary Carcinoma
6. Mucoid (Colloid) Carcinoma
7. Paget's Disease, Carcinomatous change
8. Other

APPENDIX D

PERFORMANCE STATUS - FUNCTIONAL CLASSIFICATION

1. Patient is able to care for personal needs and to carry on normal daily activities and to return to previous employment or previous household duties and functions, or previous age appropriate tasks (i.e. elderly versus children); patient has returned to premorbid status.
2. Patient is able to care for personal needs and carry on normal daily activities and to return to alternative employment or alternative household duties or functions or previous age appropriate tasks within the limits of disability.
3. Patient is able to care for personal needs and carry on normal daily activities and return to part time (less than half time) employment or part time household duties and functions, or part time age appropriate tasks.
4. Patient is able to live at home and care for most personal needs, and to carry on some normal daily activities, and engage in a limited and minimal amount of employment (less than part time), household duties and functions, or very minimal age appropriate tasks under protective conditions. Some assistance will be required and there is a loss of independence to some degree.
5. Patient is able to perform very limited self care but requires considerable assistance in all daily activities. Considerable care will probably be needed. Patient is unable to be employed, perform household duties and functions, or perform age appropriate tasks. There is a serious loss of independence in all areas.
6. Patient has virtually lost all independence in her disposition, is unable to care for herself, and requires the equivalent of institutional or hospital care. Constant medical and nursing care are required as the patient approaches the terminal stage of her disease.

Definitions:

Care for personal needs: Patient is able to take the responsibility for her own self care regarding bodily functions, personal hygiene, and related routine tasks.

Normal daily activities: Those activities regarding ordinary daily functions that the patient routinely performs as a matter of habit, custom, or desire.

Employment duties pertain to employed persons, working daily for a salary or wage.

Household duties and functions pertain to persons managing a household as the activity that takes the greater part of the day.

Age appropriate tasks are those activities not included under employment or household duties and functions, such as the play activities of children or the normal daily activities of the aged.

APPENDIX E

REHABILITATION GOALS AND THEIR CRITERIA

A. Restorative Goal

- Criteria: - the total tumor has been removed or eradicated by surgery, irradiation, chemotherapy, or hormonal methods.
- there is no evidence of residual or recurrent disease.
 - there is sufficient reason to believe that the prognosis is good.
 - there is possible residual disability from the primary tumor or its treatment (i.e. post mastectomy lymphedema; loss of an extremity due to surgical amputation).

Rehabilitation Meaning: The patient in all likelihood can be restored to premorbid or very near premorbid performance levels. Special therapies with planned and graded rehabilitation goals for the patient can do much to assist him or her in realization of full functional potential.

B. Supportive Goal

- Criteria: - there is residual tumor remaining after surgery or other treatment methods.
- there is evidence of regional or distant spread.
 - although the prognosis is uncertain, the patient is still potentially controllable for a varying period of time.

Rehabilitation Meaning: The patient can be restored to a premorbid or near premorbid level of performance for a varying period of time. Modification of performance levels will be necessary in light of realistic rehabilitation goals. Distant metastatic spread of the disease does not necessarily or automatically guarantee a steady downhill course or even significant disability. However, by proper and adequate training and treatment, there will be elimination of as much disability as possible, and intensive rehabilitation should be offered to the patient.

C. Palliative Goal

- Criteria: - there is widespread metastatic disease present.

Rehabilitation Meaning: Increasing disability may occur from progressing disease with associated decrease in performance capacity, but appropriate provision of therapeutic treatment

will eliminate some of the complications that might otherwise ensue. The experienced and competent oncologist who can discover and treat disseminated disease with alacrity may make all the difference between controlled versus uncontrolled disease. The patient needs support through the pre-terminal and terminal period and aid in reaching the highest level of functioning that is possible in light of the disability that is present.

DEPARTMENT OF PHYSICAL THERAPY
SCHOOL OF ALLIED HEALTH PROFESSIONS
VIRGINIA COMMONWEALTH UNIVERSITY

CONSENT FORM

I hereby grant permission to Stephen A. Gudas, RPT to evaluate my performance in daily routine chores, ability to eat and dress, and performance in walking, mobility, and other self care activities. The purpose and procedures used have been adequately and fully explained to my satisfaction. There will be no discomfort or pain involved in this evaluation, however, I understand that I may freely and voluntarily withdraw my participation in the evaluation process at any time. I also give the student permission to use the results of the functional ability evaluation for use in writing his research thesis. I also understand that at no time will my name be used to identify me in the course of this research.

person authorizing consent

WITNESS

DATE: _____