Factors associated with weight gain in women with breast cancer during adjuvant chemotherapy

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Abstract

Breast cancer is second to lung cancer as the leading cause of cancer deaths for Canadian women, and is responsible for the greatest number of years of life lost. Most women with newly diagnosed early stage disease will be offered surgery and adjuvant chemotherapy or radiation therapy as curative treatment. Although chemotherapy will be an important part of these patients' care, the tendency for breast cancer patients to gain weight with some forms of adjuvant chemotherapy has been reported over the past two decades. In addition to the body image concerns and possible health risks related to weight gain, an association between increased weight and earlier disease recurrence has been reported. The main purpose of this prospective study was to determine if weight gain occurs in premenopausal women who receive adjuvant chemotherapy using Adriamycin and cyclophosphamide (AC) or radiation therapy, from baseline to completion of treatment at 12 weeks. A secondary purpose was to measure the major factors associated with energy balance, including energy intake, resting energy expenditure (REE) and physical activity. Body composition was also measured, using dual energy x-ray absorptiometry (DEXA), to describe the total and regional changes in lean and fat mass.

Nineteen women completed the study, including nine women treated with four 21-day cycles of chemotherapy, and 10 women treated with radiation therapy who served as a comparison group. Statistical analysis using repeated measures ANOVA revealed that women in both groups had no weight change, from pre- to post-treatment. There were however significant changes in body composition for both treatment groups. All women in the study

experienced a decrease in total lean mass (p=0.05) and lean mass in the leg region (p=0.02), an increase in percent body fat (p=0.04), and a trend for a gain in fat mass in the trunk region (p=0.08). In addition, there was a significant difference in the pattern of change in bone mass between groups from pre- to post-treatment (p=0.04). Women treated with chemotherapy tended to decrease bone mass (p=0.14), whereas there was a tendency for women treated with radiation therapy to increase bone mass, from pre- to post-treatment (p=0.15). There were no statistically significant differences between groups in any of the factors associated with energy balance. There were however trends for an increase in total energy expenditure (p=0.08) in both groups, and for a different pattern of change in carbohydrate intake between groups from pre- to post-treatment (p=0.08). Women treated with chemotherapy tended to decrease carbohydrate intake, whereas there was a tendency for women treated with radiation therapy to increase carbohydrate intake, from pre- to post-treatment.

Overall, the results of the study suggest that a shorter chemotherapy regimen using AC which uses a fewer number of antineoplastic agents and number of treatments than most protocols does not result in weight gain in premenopausal women with early stage breast cancer. Future research is recommended to investigate the loss of lean body mass in all women, with emphasis on more precise methods to measure physical activity, such as doubly labeled water. Furthermore, the tendency for bone loss in women treated with chemotherapy who experienced treatment-induced menopause requires further study to determine if there are any long-term consequences.

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Chapter I

Introduction:

Breast cancer is second to lung cancer as the leading cause of cancer deaths for women in British Columbia and because it tends to occur earlier in life than other cancers and major causes of death, such as cardiovascular disease, it has been shown to be the greatest cause of years of life lost (British Columbia Cancer Agency Annual Report, 1994-1995; Canadian Cancer Society, 1993). Approximately one-in-ten women living in this country will develop breast cancer in the course of their lifetime (Canadian Cancer Society, 1993). If current trends continue, an estimated 2000 new cases of breast cancer will be diagnosed in British Columbia alone in 1995 (British Columbia Cancer Agency Annual Report, 1994-1995). Most of these patients will have early stage disease (stage I or II) and will be offered surgery and adjuvant chemotherapy, radiation therapy, or a combination of chemotherapy and radiation therapy as curative treatment (British Columbia Cancer Agency, 1994). Although chemotherapy will be an important part of their care, the tendency for breast cancer patients to gain weight with some forms of adjuvant chemotherapy has now been reported over the past two decades (Camoriano et al, 1990; Denmark-Wahnefried et al, 1993; Foltz, 1985). First documented in the 1970's (Dixon et al, 1978; Donegan et al, 1978), weight gain is a surprisingly frequent side effect that has received much less attention than other side effects such as hair loss, nausea, vomiting, menopausal symptoms, mucositis and cytopenia (Denmark-Wahnefried et al, 1993; Huntington, 1985).

Findings from numerous studies indicate that weight gain occurs in 50-75% (Chlebowski et al, 1986; Foltz, 1985; Knobf, 1985; Levine et al, 1991) and up to as many as 96% (Denmark-Wahnefried et al, 1993; Heasman et al, 1985) of all early stage breast cancer patients treated with adjuvant chemotherapy. Weight gains of 2.5 to 6.2 kg appear most common, however weight gain greater than 10 kg is not unusual during adjuvant chemotherapy for stage II breast cancer (Camoriano et al, 1990). While some women may again lose the weight after completion of chemotherapy, many do not (Camoriano et al, 1990; Levine et al, 1991). As many as 13% of premenopausal women remain more than 10 kg heavier than pre-treatment weight two years after completion of chemotherapy (Camoriano et al, 1990).

In addition to possible health risks of weight gain, an association between increased weight and earlier disease recurrence has been reported (Denmark-Wahnefried et al, 1993; Foltz, 1985). Weight gain during the course of adjuvant chemotherapy was found by Camoriano et al (1990) to be associated with increased rates of recurrence and poorer survival. Similarly, the influence of body weight on prognosis after initial diagnosis has been studied. Most investigators conclude that obese patients with breast cancer are more likely to develop recurrent disease after mastectomy and are more likely to do so sooner than their nonobese counterparts (Bastarrachea et al, 1993). Bastarrachea (1993) confirmed an independent negative association between obesity and disease-free survival using multivariate techniques to adjust for differences in disease characteristics between 735 obese and nonobese women. Relative risk for disease recurrence among obese patients was 1.33 compared to the nonobese population. Although obesity was a rather weak prognostic factor compared to disease stage (1.51) and axillary lymph node involvement (2.51) the risk is similar in magnitude to the

expected benefits of adjuvant chemotherapy (20-30%) (Bastarrachea et al, 1993). Research by Ballard Barbash et al (1990) suggests that the amount of weight gained during adulthood may be even a stronger correlate of breast cancer risk than absolute measures of body mass because weight gain during adulthood results in greater adiposity which they contend predisposes women to breast cancer.

An adverse psychological impact of weight gain in breast cancer patients was found by Knobf et al (1983), who reported a significant negative correlation between the amount of weight gained and self-reported happiness in women with early stage breast cancer. A majority of the 87 patients who gained more than 4.5 kg reported their weight gain as being distressful (Knobf et al, 1983). Similarly, Monnin et al (1993b) reported that women with breast cancer who had gained 4.5 kg or more during and/or after adjuvant treatment were less satisfied with their weight and were more concerned about how to lose weight, than those women who had gained less weight. In support of these observations, other investigators have suggested that since weight gain occurs during a period of vulnerability, it may exert a deleterious psychological impact on a group of patients already suffering from a loss of self esteem and altered body image (Camoriano et al, 1990; Denmark-Wahnefried et al, 1993). Thus, it becomes important to identify factors that are associated with weight gain during adjuvant chemotherapy for breast cancer.

Purpose of the study:

Therefore, the main purpose of the present study was to determine whether weight gain occurs in premenopausal women with early stage breast cancer, who receive adjuvant chemotherapy using Adriamycin® and cyclophosphamide or radiation therapy, from baseline to completion of treatment at approximately 12 weeks. A secondary purpose was to measure major factors associated with energy balance in premenopausal women with early stage breast cancer, who receive adjuvant chemotherapy or radiation therapy from baseline to completion of treatment at approximately 12 weeks. A final purpose was to determine total and regional body composition and distribution of fat and lean mass in women with early stage breast cancer prior to and following adjuvant chemotherapy or radiation therapy.

Null hypotheses:

The null hypotheses for this study were:

Null hypothesis 1:

There will be no difference in the change in body weight from baseline to completion of treatment between premenopausal women with early stage breast cancer who receive either adjuvant chemotherapy or radiation therapy.

Null hypothesis 2:

There will be no difference in the major factors associated with energy balance, including energy intake, resting energy expenditure and physical activity from baseline to completion of treatment, between premenopausal women with early stage breast cancer who receive either adjuvant chemotherapy or radiation therapy.

Null hypothesis 3:

There will be no difference in body composition or distribution of fat and lean mass from baseline to completion of treatment between premenopausal women with early stage breast cancer who receive either adjuvant chemotherapy or radiation therapy.

Objectives:

In premenopausal women with early stage breast cancer treated with either chemotherapy or radiation therapy, the objectives of the present study were:

1. to assess change in body weight from baseline to completion of treatment at approximately 12 weeks, as determined by a medical balance beam scale and dual energy x-ray absorptiometry (DEXA).
2. to assess change in major factors associated with energy balance including energy intake, resting energy expenditure, and energy expenditure from physical activity from baseline to completion of treatment at approximately 12 weeks, as determined by 3-day food records, indirect calorimetry using a metabolic cart, and a 3-day activity diary, respectively.
3. to assess change in body composition and distribution of fat and lean body mass from baseline to completion of treatment at approximately 12 weeks, as determined by dual energy x-ray absorptiometry (DEXA).
4. to monitor disease and treatment factors that may have a confounding effect on change in body weight and body composition, such as age, demographics, stage of cancer, combination therapy and type of surgery, as obtained from the patient's medical chart.

Chapter II

Review of literature:

1. Weight gain and adjuvant treatment:

Unlike the common problem of unintentional and sometimes severe weight loss known as cancer cachexia in other cancer patient groups, breast cancer patients may gain weight during treatment. Some researchers have suggested that weight gain may be universal in breast cancer patients, regardless of adjuvant therapy (Camoriano et al, 1990; Denmark-Wahnefried et al, 1993). Camoriano et al (1990), Goodwin et al (1988), and Monnin et al (1993b) found no difference in weight gain between women receiving chemotherapy and no adjuvant chemotherapy, which supported the premise that weight gain may be an artifact of breast cancer. Goodwin et al (1988) however reported retrospective data from non-randomized trials from different decades, which showed considerably less weight gain compared to other studies (Camoriano et al, 1990; Denmark-Wahnefried et al 1993). If chemotherapy does not result in weight gain, it is difficult to explain the findings that lengthy multidrug regimens seem to result in the most substantial gain in weight (Denmark-Wahnefried et al, 1993). Also, it is unlikely that there would be differences in weight gain between adjuvant treatments, such as hormonal therapy using tamoxifen or radiation therapy, that have been identified (Denmark-Wahnefried et al, 1993; Hoskin et al, 1992). Women with breast cancer treated with adjuvant radiation therapy have not been shown to gain weight during treatment (Hoskin et al, 1992). Hoskin et al (1992)

reported that there was no difference in absolute weight during treatment in women who received postoperative radiation therapy (n=28). Other studies have reported marginal weight gain in women with breast cancer who do not receive adjuvant chemotherapy (Goodwin et al, 1988; Camoriano et al, 1990). Goodwin et al (1988) reported that women with node negative disease (n=307) gained 1.2 kg and women with node positive disease (n=139) gained 2.6 kg, without the use of adjuvant chemotherapy. Furthermore, Camoriano et al (1990) reported greater weight gain in postmenopausal women randomized to treatment with adjuvant chemotherapy and tamoxifen (3.6 kg) than to observation (1.8 kg). While the possibility that weight gain is completely independent of adjuvant chemotherapy cannot be excluded, available literature suggests that adjuvant chemotherapy is associated with weight gain in women with early stage breast cancer, and that this weight gain is greater than that experienced by women receiving adjuvant radiation therapy.

Weight gain in women with breast cancer receiving adjuvant chemotherapy appears to be related to several factors including the chemotherapeutic regimen used, duration of treatment, and menopausal status of the patient (Denmark-Wahnefried et al, 1993). Greater weight gain in women with breast cancer has been found to be associated with particular regimens that involve multiple agents. Support for this finding is demonstrated by Heasman et al (1985) who reported less weight gain (2.0 kg) in women treated with fluorouracil alone, compared to women treated with multiple antineoplastic agents cyclophosphamide, methotrexate, and fluorouracil (CMF) (3.7 kg) (Denmark-Wahnefried et al, 1993). A number of other treatments for breast cancer have been associated with weight gain. The findings from Hoskin et al (1992) suggest that significant weight gain occurs in women with breast cancer

treated with adjuvant hormonal therapy using tamoxifen, and that this effect is greater in premenopausal than postmenopausal women. The single antineoplastic agent megestrol acetate (Megace®) has received the greatest notoriety in association with weight gain and has consequently been used in the treatment of cachexia in cancer and AIDS patients (Von Roeen et al, 1994). However, Megace® has not been routinely used as adjuvant therapy for women with early stage breast cancer.

Oral regimens are also associated with greater weight gains when compared to infusion based chemotherapy (Denmark-Wahnefried et al, 1993). In addition, ongoing studies are evaluating the length of chemotherapy treatments. Existing data by Bonadonna et al (1985) indicate that women on a 12-month regimen gain more weight than those on shorter 6-month regimens using CMF adjuvant chemotherapy.

The menopausal status of the breast cancer patient also appears to be a factor in determining the magnitude of weight gain. Findings consistent with Bonadonna et al (1985), Camoriano et al (1990), Foltz (1985), Heasman et al (1985), Huntington (1985), and Knobf et al (1983) indicate that weight gain in patients on a variety of therapies for breast cancer is significantly less in older postmenopausal women compared with younger premenopausal women. While unproven, it is possible that the impact of adjuvant chemotherapy on ovarian function and premature amenorrhea may trigger increased fat accumulation and changes in fat distribution (Denmark-Wahnefried et al, 1993).

It has been suggested that steroid use in the treatment of breast cancer is the main cause of weight gain in treated patients. However, it is unlikely for two reasons. First, steroids including prednisone (Decadron®) are typically only used prophylactically in small doses and for

short duration prior to or following chemotherapy to minimize nausea and vomiting. Secondly, weight gain is not consistently reported with steroid use and weight gain occurs in women treated with non-steroid containing regimens (Camoriano et al, 1990; Subramanion et al, 1981). Thus, while the side effects of steroids include appetite enhancement and fluid retention (Canadian Pharmaceutical Association, 1990) which may play a role in weight gain in breast cancer patients, their use is not a prerequisite for weight gain (Camoriano et al, 1990). A summary of the research that has investigated variables related to weight gain in patients with breast cancer receiving adjuvant chemotherapy is provided in Table 1. Studies were also conducted by Chlebowski et al (1985), Goodwin et al (1988) and Hoskin et al (1992), however factors associated with weight gain either were not measured, or hormonal agents alone (ie. tamoxifen) were investigated.

Table 1: Variables related to weight gain in patients with breast cancer receiving adjuvant chemotherapy (adapted from Winningham et al, 1989)

Reference	N	Chemotherapy	Variable	Results*
Bonadonna et al (1985)	n=845[1,2]	CMF[3]	menopausal status	no
Camoriano et al (1990)	n=372 199[1] 173[2]	CFP CFP plus tamoxifen observation only	menopausal status age initial weight body mass index nodal status estrogen receptor level	no no no no no no
DeConti (1982)	n=53[4]	CMF CMF plus prednisone & tamoxifen	pre-treatment weight nodal status menopausal status estrogen receptor levels treatment[5] disease recurrence	no no no no **yes** no
Foltz (1985)	n=34[1,2]	CMF	activity depression dietary intake serum estradiol metabolic rate menopausal status	no no no **yes**[6] no **yes**
Heasman et al (1985)	n=237 190[1] 43[2] 4[4]	melphalan[3] cyclophosphamide CMF[3] CMF[3] plus ovarian ablation	treatment[5] disease recurrence pre-treatment weight menopausal status prednisone & ovarian ablation nodal status tumor size estrogen receptor status	**yes** no no no **yes** no no no
Hernandez et al (1983)	n=61 27[1] 34[2]	melphalan plus 5-fluorouracil, with or without tamoxifen	menopausal status estrogen receptor levels progesterone receptor levels pre-treatment weight tamoxifen	no no no no no

*no = not related to weight gain; yes = related to weight gain;
[1]premenopausal; [2]postmenopausal; [3]with or without prednisone;
[4]perimenopausal or unknown menopausal status; [5]some subjects received prednisone;
[6]functional relationship not clarified; [7]no statistical analysis performed;
CMF=cyclophosphamide, methotrexate, and 5-fluorouracil;
CAF=cyclophosphamide, doxorubicin, and 5-fluorouracil;
CFP=cyclophosphamide, 5-fluorouracil, and prednisone

Table 1: Variables related to weight gain in patients with breast cancer receiving adjuvant chemotherapy (Winningham et al, 1989) *continued...*

Reference	N	Chemotherapy	Variable	Results*
Huntington (1985)	n=29 10[1] 16[2] 3[4]	CMF CMF plus vincristine & prednisone	age menopausal status estrogen receptor status nodal status biochemical parameters treatment[5] decreased activity relapse potential	no no no no no no no[7] no
Knobf et al (1983)	n=87 15[1] 56[2] 16[4]	numerous combinations of cytoxan, L-Pam methotrexate, 5-fluorouracil, tamoxifen	age treatment[5] menopausal status	yes[7] possibly[7] yes[7]
Knobf (1985)	n=78[4]	cyclophosphamide	mild nausea	yes
Levine et al (1991)	n=32 14[1] 18[2]	CMF[3] CAF melphalan CAF with prednisone	treatment surgery menopausal status nodal status psychological functioning exercise level dietary intake	no no no no yes no no
Subramanian et al (1981)	n=87[1,2]	CMF CMF plus vincristine & tamoxifen	menopausal status treatment[5] disease status drug toxicity nodal status prednisone	no no no no yes no

*no = not related to weight gain; yes = related to weight gain;

[1]premenopausal; [2]postmenopausal; [3]with or without prednisone;

[4]perimenopausal or unknown menopausal status; [5]some subjects received prednisone;

[6]functional relationship not clarified; [7]no statistical analysis performed;

CMF=cyclophosphamide, methotrexate, and 5-fluorouracil;

CAF=cyclophosphamide, doxorubicin, and 5-fluorouracil;

CFP=cyclophosphamide, 5-fluorouracil, and prednisone; L-PAM=L-phenylalanine mustard

2. Factors associated with weight gain:

Based on nutritional theory of energy balance, potential factors responsible for weight gain include increased energy intake, decreased energy expenditure (composed of resting energy expenditure, thermic effect of feeding and physical activity) or a combination of both factors. Thus, to monitor energy balance, factors identified as both important and practical to measure in women with breast cancer include energy intake, resting energy expenditure, and physical activity.

2.1 dietary intake:

The most popular theory regarding weight gain during adjuvant chemotherapy is that it is caused by an increase in energy intake (Bonadonna et al, 1985; Camoriano et al, 1990; Denmark-Wahnefried et al, 1993; Heasman et al, 1985). Although possible, there is limited scientific evidence to support this view. Brewin (1980) first suggested an increased appetite in breast cancer patients. From the review of self-reports of 14 women receiving adjuvant chemotherapy, Brewin (1980) concluded that these women experienced food cravings similar to pregnancy, and increased their frequency of eating to diminish nausea. Similar findings were reported by Knobf (1985), and Mukhopadhyay and Larkin (1986) who reported that women with breast cancer ate to relieve nausea associated with the administration of adjuvant chemotherapy. Although these early investigations provide valuable insight, it is difficult to draw conclusions from studies with few subjects, particularly when no attempt was made to validate reports against dietary intake data (Denmark-Wahnefried et al, 1993). Heasman et al, (1985) and Huntington (1985) also support the theory that weight gain is a result of increased energy intake, based on data from larger samples of women. However, again both investigators

failed to validate patient reports with dietary intake data (Denmark-Wahnefried et al, 1993). Another reason for increased energy intake in breast cancer patients may be well-meaning dietary recommendations from health care providers and family members to increase caloric intake during chemotherapy (Foltz, 1985). Interestingly, a well distributed pamphlet at the British Columbia Cancer Agency includes the suggestion that "you may need 50% more protein than usual and 20% more calories during chemotherapy" (Canadian Cancer Society, 1992).

Conversely, the onset of nausea, vomiting, taste alterations and learned food aversions have been suggested to alter food intake during treatment (Grindel et al, 1989). Again, there is a lack of scientific evidence to support these claims. In addition, establishing the diagnosis, undergoing surgery and initiating treatment often require the patient to spend large amounts of time away from normal routines, including meals, which may alter dietary intake.

There are only three known published studies that have attempted to quantitate energy intake in women treated with adjuvant chemotherapy (Foltz, 1985; Grindel et al, 1989; Levine et al, 1991). Foltz (1985) and Grindel et al (1989) concluded that self-reported changes in diet did not relate to weight change. Foltz (1985) monitored weight change in 34 women with stage II breast cancer receiving six months of CMF chemotherapy. Dietary intake in addition to four other potential contributory factors, including physical activity, depression, serum estradiol and metabolic rate were measured (Foltz, 1985). Three 24-hour recalls were obtained on randomly selected days during the first 14 and last 14 days of treatment. No difference in energy intake was found between women who gained weight compared to those who maintained or lost weight during the course of therapy (Foltz, 1985). The author attributed the negative findings to the small sample size with inadequate power to detect differences, and

difficulties with accurate data collection (Foltz, 1985). The lack of difference may also have resulted from the limited measurement of a 24-hour period for dietary intakes. Furthermore, differences in energy intake pre- and post-treatment or in comparison to usual intake (which was not measured) may have explained why some women gained weight during treatment. Evaluation of dietary intake in the study by Levine et al (1991) is difficult because the methodology used to measure dietary intake was poorly described. More adequate methods to collect dietary intake data were recommended by the authors, which suggests there may have been important methodological limitations.

Grindel et al (1989) also measured dietary intake in breast cancer patients receiving adjuvant chemotherapy. Grindel et al (1989) compared the food intake patterns of women with breast cancer receiving adjuvant chemotherapy with those of healthy women to determine if significant alterations in food intake occurred during the first six months of treatment. The conflicting results of this study detected greater energy intakes and number of food servings in 19 women treated with CMF (and various other antineoplastic or hormonal therapies) compared to location and age-matched controls without breast cancer (Grindel et al, 1989). Energy intake data were calculated based on self-reported amounts of 56 food items over a 3-day reporting period completed four times during the six month period (Grindel et al, 1989). While the results are of interest, the study had important limitations which were identified by Denmark-Wahnefried et al (1993). The control group included healthy women, baseline dietary intake data were not collected, and the 3-day dietary records were not highly correlated with food frequency questionnaires.

Although it currently can not be concluded that increased caloric intake is the primary cause of weight gain, it remains an important factor to measure based on basic nutritional theory that argues that weight gain occurs in the presence of increased energy intake, decreased energy expenditure, or a combination of both factors.

Dietary intake methods to assess individual intake generally include 24-hour recalls, food records or diaries and diet histories, including food frequency questionnaires (Hankin, 1992). Food records require subjects to measure or estimate and record concurrently all foods consumed over a specified period, usually 3 to 7 days or multiple periods within a year (Hankin, 1992). The major strength of food records is that they do not rely on memory, as do the 24-hour recall and diet history methodologies. As a result, food records have been used by investigators as a reference or standard for assessing the relative validity of other dietary methods that are based on recall (Hankin, 1992). In addition, food records are relatively easy to administer in smaller samples, and involve reasonable cost in time and personnel.

The most accurate method of recording dietary intake involves weighing all ingredients in recipes, and in the food portions selected and any food not consumed (Hankin, 1992). Because weighing may be difficult for some subjects, household measuring utensils are used more frequently than scales to improve accuracy (Hankin, 1992).

It has been shown repeatedly that the day-to-day differences in dietary intake are as large or larger than the differences in intake between individuals (Hankin, 1992). Consequently, a longer period of reporting is needed to characterize the usual intake of an individual person than the usual diet of a group. Several investigators have studied the variability in multiple 24-hour recalls and food records to determine the number of days needed to achieve reliable

estimates of average nutrient intakes of individuals and groups (Basiotis et al, 1987; Hankin, 1992). Energy intake has been shown to require the least number of days to estimate true average intake for groups, with statistical confidence. Basiotis et al (1987) found that for measurement of energy intake, 3 days were needed to estimate within 10% of the true average group intake for both sexes, with 95% confidence. In contrast, to estimate dietary fat intake, 6 days were required; for calcium 7 and 10 days were required for females and males respectively; and for vitamin A as many as 44 and 39 were required for females and males, respectively (Basiotis et al, 1987).

The limitations of food records are several. Generally, persons who agree to participate are dedicated, highly motivated, literate subjects, and thus may not be representative of the general population. Also, subjects may modify their eating practices after a few days to reduce their workload (Hankin, 1992). Additional limitations of food records, and most other methods, are that the reporting period may be atypical to assess usual intake, the method may be inappropriate for people who consume almost all of their meals away from home, the method provides data only on the current diet, and lastly typical 3 to 7 day reporting periods are not likely to reflect the true variability in the diets of individuals (Hankin, 1992).

2.2 Resting energy expenditure:

Resting energy expenditure (REE) contributes the largest portion of total energy expenditure in sedentary adults, and includes the energy expended by the activity of internal organs and the energy required to maintain body temperature (Denmark-Wahnefried et al, 1993). In most normal adults, it accounts for 65% to 75% of total energy expenditure (Denmark-Wahnefried et al, 1993). Resting metabolic rate (RMR) or resting energy expenditure, often used synonymously with BMR, represent the actual measurement of energy expenditure in the resting and fasting state and tend to be 8-9% greater than BMR (Medical Graphics Corporation Reference Manual, St. Paul, MN). An 8% overestimation of metabolic rate has also been reported when resting metabolic rate was measured in outpatient conditions compared to inpatient conditions, which underscores the importance of standardized experimental conditions (Berke et al, 1992).

Resting energy expenditure can be measured by direct calorimetry, however this method is not practical and is rarely used in clinical settings. More often, resting energy expenditure is measured by indirect calorimetry which calculates energy expenditure from the measurement of oxygen consumption (VO_2) and carbon dioxide production (VCO_2) including or excluding nitrogen excretion. Indirect calorimetry is based on the assumption that all energy comes from the oxidation of carbohydrate, lipids, and proteins, and that the energy produced and the amounts of O_2 and CO_2 exchanged are constant. However, there is some variability in the gas exchange and energy values of different lipids and proteins, but the error from using approximations is small (less than 3%) (Medical Graphics Corporation Reference Manual, St. Paul, MN).

The Weir equation (Weir, 1949) is most often used for calculation of resting energy expenditure (refer to methodology, page 47).

The ratio of carbon dioxide produced to oxygen consumed at the cellular level is called Respiratory Quotient (RQ) (Medical Graphics Corporation Reference Manual, St. Paul, MN). The RQ for lipid is 0.70, for proteins 0.80, and for carbohydrate is 1.0, indicating that for carbohydrate metabolism, equal amounts of oxygen are consumed as carbon dioxide produced (Schultz et al, 1994). During indirect calorimetry the gross RQ, identified as the Respiratory Exchange Ratio (RER or R), is the result of the global metabolic activity of the body. The value of RER indicates the mixture of substrate oxidized, and is normally 0.85, with a range of 0.75 to 1.0 (Medical Graphics Corporation Reference Manual, St. Paul, MN).

The standard recommendations for measuring resting metabolic rate by indirect calorimetry include the following: the subject should be at rest for 30 minutes before beginning the study; the subjects should be fasted for 12 hours; measurements should be done early in the morning before eating to minimize the effect of diurnal variation of REE; the environment should be thermoneutral and quiet; and a minimum of 15-20 minutes of data collection are usually required to ensure the subject is in a steady state (Medical Graphics Corporation Reference Manual, St. Paul, MN). The findings of Weststrate (1993) indicate that the phase of the menstrual cycle does not significantly influence REE, however other authors have found higher values during the luteal phase. Reasons for the differences are not clear, but may be related to differences in experimental protocol, techniques used for measuring energy expenditure, the number of subjects studied, the frequency of measurements, or the method used to assess ovulation (Weststrate, 1993).

While attempts to measure dietary intake in breast cancer patients have been documented, other factors including physical activity and metabolic rate have received even less attention. Exploration of changes in metabolic rate in the study of weight gain related to adjuvant chemotherapy is logical in view of evidence linking lowered metabolic rates to the development of obesity. Resting energy expenditure measured in cancer patients has shown either an elevation or no change (Arbeit et al, 1984). Arbeit et al (1984) studied four patients pre- and post-tumor resection and found that each patient's resting energy expenditure decreased, and that the extent of the decrease was significantly correlated with the volume of the tumor. Generally, interest in this area has been focused on estimating energy requirements and/or measuring energy expenditure in people with advanced cancer.

Although some evidence exists that resting energy expenditure decreases after surgical removal of tumor, no viable study has measured changes in metabolism that may occur in women with early stage breast cancer receiving adjuvant chemotherapy following surgical management of their disease (Denmark-Wahnefried et al, 1993). Foltz (1985) attempted to measure metabolic changes in this population, but the assessment of resting energy expenditure was not conducted under the necessary conditions (at rest and fasting) and thus the validity of the findings must be questioned (Denmark-Wahnefried et al, 1993). Reliability concerns were supported by the relatively high energy expenditure data that were obtained (Foltz, 1985).

There are a variety of mechanisms by which adjuvant chemotherapy could potentially decrease basal needs. First, basal energy expenditure may be reduced significantly due to the impact of chemotherapy on overall cell death resulting in less energy required to maintain the host (Denmark-Wahnefried et al, 1993). Second, chemotherapy-induced menopause in younger

women may lead to hormonal changes which could ultimately affect basal energy needs (Denmark-Wahnefried et al, 1993). It is possible that hormonal changes could reduce metabolism either directly or indirectly through changes in fat-free mass (FFM) and fat deposition and distribution. Indeed, there is reason to believe that menopause triggers an overall increase in body fat (Denmark-Wahnefried et al, 1993).

Diet-induced thermogenesis or the thermic effect of feeding (TEF) is defined as the increase in metabolic rate following ingestion of food, and contributes approximately 10% of total daily energy expenditure. The importance of TEF in energy balance is controversial, since it only marginally contributes to total energy expenditure and conflicting reports exist as to whether thermic responses differ in obese compared to lean subjects (Denmark-Wahnefried et al, 1993). The contribution TEF may have in weight gain in women treated with adjuvant chemotherapy is unknown, since there have been no reported studies that have measured its effect.

2.3 Physical activity:

While some reduction of activity can occur following mastectomy as evidenced by the development of post-mastectomy rehabilitation programs (Foltz, 1985), adjuvant chemotherapy is thought to impose further restriction on activity of patients with breast cancer. Anecdotal evidence and clinical experience suggest that fatigue is prevalent in people with cancer, but it has not been well-studied. Breast cancer patients in particular may experience treatment-related fatigue because treatment is usually aggressive and prolonged, often utilizing both chemotherapy and radiation therapy. Meyerowitz et al (1979) used direct interviews to assess

the psychological implications of adjuvant CMF chemotherapy in 50 women with stage II breast cancer. The most frequent and marked effect of adjuvant chemotherapy was a reported decrease in both general and work-related levels of activity (Meyerowitz et al , 1979). Fatigue was the most commonly reported side effect, occurring in 96% (n=48) of women, and was described by women as being "generally slowed down" and "feeling tired all the time" (Meyerowitz et al, 1979).

The degree of impact that fatigue has on energy balance and subsequent weight gain is unknown. However, stronger evidence exists for a relationship between decreased physical activity and obesity than for increased dietary intake and obesity (Denmark-Wahnefried et al, 1993). The limited research conducted in breast cancer patients has focused on measuring changes in social activities, housekeeping, and wage-earning measures, rather than actual physical activity (Denmark-Wahnefried et al, 1993). Limited preliminary findings in this area have been conflicting. Silberfarb (1980) and Meyerowitz et al (1979) documented significant reductions in activity after radical mastectomy. Meyerowitz et al (1979) found that 32% (n=16) of subjects were less socially active and 38% (n=19) were unable to perform their usual activity at work. Further, 60% of those working outside the home lost at least 59 hours a year because of chemotherapy (Meyerowitz et al, 1979). In contrast, Foltz (1985) did not observe changes in these parameters. Clearly, the limited data suggesting a role of fatigue and decreased levels of physical activity indicate that this variable requires further investigation as a major factor in energy balance in breast cancer patients.

Physical activity accounts for 15% to 20% of the total energy expenditure in sedentary adults. Various methods to measure physical activity have been used, including calorimetry,

time motion analysis, job classification, activity diaries, doubly labeled water methodology, pedometers, electronic motion sensors, dietary assessment and questionnaire (Lamb et al, 1990; Schultz et al, 1994). The assessment of physical activity by questionnaire is currently the most popular and practical method of quantifying physical activity levels (Lamb et al, 1990). Many questionnaires have considered overall or habitual activity, which includes occupational activity. Others have focused on leisure time physical activity owing to the recognition of its dominating contribution to total physical activity of developed populations (Lamb et al, 1990). Research related to the measurement of physical activity and the many questionnaires developed to estimate it, has resulted primarily from interest in establishing a relationship between participation in physical activity and occurrence of illness, namely cardiovascular disease.

Questionnaires such as the Harvard Alumni, Pennsylvania Alumni, Baecke, Framingham, Five City Project, Lipid Research Clinic or Minnesota Leisure Time Instruments have been suggested for use in the study of weight gain in women with breast cancer (Baecke et al, 1982; Denmark-Wahnefried et al, 1993; Kannel et al, 1979; Sallis et al, 1985). Most of these popular instruments, along with the Tecumseh, Health Insurance Plan, British Civil Servants, Swedish, Paffenbarger, and Bouchard questionnaires were originally designed to assess usual or habitual activity over preceding months or years (Lamb et al, 1990). Their use was primarily to quantify participation in prior physical activity in large population studies based on interview-assisted or self-administered recall of physical activity. Therefore, their use is limited to studies with these particular objectives. In comparison, the measurement of current levels of physical activity in individuals or groups is poorly documented.

There is no accepted criterion method for assessing physical activity. Doubly labeled water (DLW) methodology is currently the most accurate and precise method for measuring total daily energy expenditure in free-living subjects, but it is prohibitive in large scale studies due to the cost of the isotopes as well as the need for specialized analytical equipment (Racette et al, 1995; Schultz et al, 1989). Practical measures associated with physical activity include formal daily records of activity (ie. activity diaries), heart rate monitoring, retrospective questionnaires of habitual activity patterns, energy intake, and other techniques (Bouchard et al, 1983). Two of these techniques, commonly referred to as the intake/balance technique and factorial method, were considered to be practical for use in the present study and are described below in further detail.

The intake-balance method, historically used as a criterion method in various studies (Acheson et al, 1980; Borel et al, 1984; Kalkwarf et al, 1989; Schultz et al, 1989) to assess construct validity, estimates energy expenditure indirectly as the difference between energy intake and change in body energy stores over a given period of time. Disadvantages of this technique arise because it requires accurate information on energy intake for the entire period of interest, and the measurement period must be long enough to detect changes in body energy stores (Kalkwarf et al, 1984). The factorial method, in contrast, is a commonly used technique for estimation of energy expenditure which requires that subjects keep a detailed diary of the nature and duration of their activity. Subsequently, the energy cost of each activity is determined experimentally by indirect calorimetry (Passmore et al, 1955), is obtained from literature values, or from a combination of both methods (Borel et al, 1984). In the factorial method, daily energy expenditure is estimated by determining the time spent in each activity

multiplied by the energy cost of the activity per kilogram body weight or by multiplication of the duration of each activity by a energy expenditure factor based on an intensity rating (Ainsworth et al, 1993). A list of energy cost or energy expenditure factors for common household activities, selected occupational tasks and popular recreational activities is available in the literature (Ainsworth et al, 1993; McKardle et al, 1991). Ainsworth et al (1993) published a comprehensive list of energy expenditure values including the compilation of the most commonly referenced and previously published and unpublished energy expenditure data, which was designed to be used with methods that include diary, recall or direct observation. The compendium includes energy expenditure data from the Tecumseh Occupational Questionnaire, Minnesota Leisure Time Physical Activity Questionnaire, McArdle, Katch, and Katch's physical activity list, the 7-Day Recall Physical Activity Questionnaire and the American Health Foundation's physical activity list (Ainsworth et al, 1993). The use of this compendium has the advantage of facilitating the coding of physical activity and promoting comparability across studies. Total energy expenditure per day by this method is calculated by the summation of energy expenditure in each activity performed during the 24-hour period (Borel et al, 1984).

The factorial method of recording physical activity has several advantages, including: the assessment of current levels of physical activity; the estimation of energy expenditure based on specific reported activities; and that information is not based on recall. Limitations of this method include the time commitment required of subjects to record activities. This may result in fewer entries in the activity diary to reduce the time required to record activities. Also, the

estimates of caloric expenditure for various activities represents averages that may vary considerably.

Bouchard et al (1983) evaluated the reliability of activity diaries by determining the test-retest reproducibility using a 3-day reporting period in 61 adults. Activity diaries were found to be a highly reproducible method as shown by an intraclass correlation of 0.96 ($p<0.01$) for mean kilocalorie energy expenditure (Bouchard et al, 1983). In addition to reliability, accuracy of activity diaries has been evaluated in subjects using doubly labeled water (Schulz et al, 1989), or energy intake adjusted for changes in body energy stores (Borel et al, 1984; Kalkwarf et al, 1989; Schulz et al, 1989) as a reference. Direct calorimetry has also been used as a criterion method, however application is limited to a laboratory setting where activity and environment are well regulated (Schulz et al, 1989). Schulz et al (1989) found that energy expenditure from self-reported activity diaries was not statistically different from DLW in free-living subjects. Accuracy of activity diaries was also reported by Kalkwarf et al (1989) who found energy expenditure from activity diaries to be within 2-6% of energy intake, as the reference energy expenditure, when individually measured and published energy costs of activities were used. Results of other studies, although different in the methodology to estimate energy expenditure, have lead to similar conclusions about the accuracy of the activity diary method (Acheson et al, 1980; Borel et al, 1984), although both smaller and larger differences have been reported (Kalfwarf et al, 1989). Further, Acheson et al (1980), Dauncey and James (1979), and Kalkwarf et al (1989) concluded that activity diaries were no less accurate than the more technical method of heart rate monitoring in estimating energy expenditure (Kalkwarf et al, 1989). Despite the advantages of the factorial method, the great individual variability in self-

reported activity limits use of activity diaries to groups, rather than individuals (Acheson et al, 1980; Borel et al, 1984; Kalfwarf et al, 1989; Racette et al, 1995).

3. Body composition:

The measurement of body composition has been used in clinical settings for a wide variety of uses. Quantification of body fat is useful to determine the response of subjects to a range of metabolic disorders and diseases including cancer, and to study the nature and treatment of obesity. The assessment of the change in body composition related to weight gain in women treated with chemotherapy identifies a new area of research. As a result, a review of the literature has revealed only one study which has measured body composition in women during treatment for breast cancer (Winningham et al, 1989).

Body composition can be measured in many ways. The best method will depend on the purpose of its use and the practical possibilities for measurement. Some common techniques include hydrostatic weighing or densitometry, skinfold thickness, and bioelectrical impedance. Densitometry is based on the measurement of body volume (most commonly using hydrostatic weighing) in relation to total body mass, to measure body density and thus percent body fat. It is common practice to convert the derived value for body density into an estimate of percent body fat, using the prediction equations of Siri (1956) or Brozek (1963). Although densitometry has been referred to as a "gold standard" for measurement of body composition, there are many inherent inaccuracies when using this method. Sources of error in measuring underwater weight include the typical fluctuations of the weighing system during immersion, and the measurement or estimation of residual lung volume and the volume of gas in the intestines (Brodie, 1988). More important sources of error in densitometry result from the

variability in the density of the FFM in terms of the proportions of all the fat-free constituents, and their densities (Martin and Drinkwater, 1991). Of all the contributors to variability in the fat-free density, it appears that bone presents the most serious error (Martin and Drinkwater, 1991). Also, densitometry may lack precision to detect small changes in fat (< 2-3%) and FFM (< 2.0-2.5 kg), that is required in intervention studies where there are expected differences in fat-free composition as well as body fat (Going et al, 1993).

The use of skinfold thickness to assess body composition is popular because it is simple, convenient and inexpensive. Disadvantages are that as with all indirect techniques, estimating percent body fat from skinfold thickness assumes constancy of the FFM, and furthermore relies on the assumptions and inaccuracies inherent in underwater weighing, upon which it was derived. Unfortunately, empirical data to support this central assumption of the constancy of the FFM are very limited (Martin and Drinkwater, 1991). There are also sources of error in the prediction of body fat from skinfold thickness measurements that have been identified in practice and from direct measurements of body composition using cadavers. These errors include the inaccuracies that arise from variability in skinfold compressibility, skin thickness (particularly with lean subjects and with aging), adipose tissue patterning, fat fraction in adipose tissue, and individual differences in subcutaneous fat in relation to internal fat (Brodie, 1988; Martin et al, 1985; Martin et al, 1992). Additional errors can result from the use of only a few measurement sites, untrained personnel or the selection of generalized prediction equations to estimate percent body fat, that may not be valid for populations with different characteristics.

The use of bioelectrical impedance (BIA) to measure body composition has the advantages of safety, portability, and speed and ease of use. The procedure has been shown to

be reliable, and valid in comparison to hydrostatic weighing, with improved measurement of body composition when population-specific regression equations are used (Brodie, 1988). However, there are several disadvantages of BIA including the overestimation of fat in lean subjects and underestimation of fat in overweight subjects, and the sensitivity of this measurement to changes in hydration (Abu Khaled et al, 1988).

Dual energy x-ray absorptiometry technology, although originally designed to measure bone mineral content, can also be used to estimate body composition (Going et al, 1993; Heymsfield and Matthews, 1993). After its initial development in the 1960's and 1970's, the first commercial DEXA system became available in 1987 (Heymsfield and Mathews, 1993; Lohman, 1992). Three DEXA systems are now in use in the United States, Canada, and Europe, manufactured by Hologic Incorporated (Waltham, MA), Lunar Radiation Corporation (Madison, WI), and Norland Corporation (Fort Atkinson, WI). Measurement of body composition using DEXA has been found to be highly reliable (Hansen et al, 1992; Lohman, 1992). Hansen et al (1993) reported that repeat DEXA measurements were highly correlated (r=0.97, p<0.001) in 100 healthy premenopausal women. Validation studies have drawn similar conclusions about the accuracy of DEXA. Percent body fat by DEXA has been found to be highly correlated with percent body fat from densitometry as well as other common techniques (Lohman, 1992; Hansen et al, 1993). Based on these findings of the high reliability and validity, DEXA methodology is presently being evaluated as an alternative criterion method to densitometry (Lohman, 1992).

DEXA measurements allow quantification of bone mineral, fat and nonbone fat-free soft tissues in a subject's entire body and in five pre-determined regions, allowing construction of a

three-component model of body composition (Aloia et al, 1995; Norland Corporation, Fort Atkinson, WI, 1992; Tataranni and Ravussin, 1995). The five body regions set by the manufacturer include head, trunk, abdomen, legs and arms (see diagram in Appendix A). As many as three new operator-selected body regions can also be created and analyzed using the manufacturer's software. The measurement of body composition using DEXA is unique in that it includes an estimate of bone mass, and, excludes bone mass in the quantification of lean mass. Thus, the most accurate terminology to describe lean mass using DEXA is nonbone fat-free soft tissue, although lean mass has been used throughout for simplicity.

DEXA methodology uses a stable x-ray generator to produce a broad spectrum beam that is K-edge filtered to produce two photon peaks (46.8 and 80 keV). As the photons pass through the subject, the low and high energy photons are detected by thin and thick NaCl crystals, respectively. Energy from the x-ray source directed through the body undergoes an attenuation or reduction in intensity that is related to the specific chemical compounds with which it interacts (Heymsfield and Matthews, 1993). Bone is differentiated from soft tissue based on the attenuation of the low and high energy photons (Norland Corporation, Fort Atkinson, WI, 1992). The industry standard for tissue estimation for fat is stearic acid, a fatty acid which closely approximates the triglyceride esters which make up mammalian fat in molecular composition and in photon attenuation properties. The standard for lean soft tissue is 0.6% sodium chloride in water as this saline solution closely approximates the photon attenuation properties of lean soft tissue such as muscle, blood and skin. The industry standard for tissue estimation for bone is hydroxyapatite (a crystalline form of calcium), which approximates mineral content of bone (Norland Corporation, Fort Atkinson, WI, 1992). In

practice, instruments are calibrated before daily use to be within 1.0% of industry standards to maintain accuracy.

Because the DEXA method is theoretically independent of compartmental assumptions it is advantageous compared to most traditional techniques for estimating body composition that rely on the assumption of chemical constancy of the FFM, which is not valid for many groups (Going et al, 1993). The safety of DEXA can be assessed in terms of the radiation dose received by the patient. The radiation dose required to scan the entire body is considered to be very low and is less than that of other radiologic methods currently used for bone and body composition assessment (Aloia et al, 1995; Heymsfield and Matthews, 1993; Lohman, 1992; Norland Corporation, Fort Atkinson, WI, 1992). The skin dose is approximately 10-30 Gy per scan (Heymsfield and Matthews, 1993). In comparison, skin exposure from other radiation sources such as a chest x-ray is 80-100 Gy. Overall, DEXA is a precise and safe method to measure body composition, and is easy to administer. It also allows for the estimation of bone mass and the detection of small changes in body composition which are not possible with other techniques.

Possible limitations of using DEXA to measure body composition include the degree to which measurements are sensitive to changes in hydration or differences in body thickness, which remain unknown at present (Roubenoff et al, 1993). In addition, further research is needed to determine if there are additional limitations that may emerge from comparing body composition data from densitometers that use different technology and software to compute percent body fat (Lohman, 1992; Roubenoff et al, 1993). The limited scan area of DEXA,

which may not be adequate for obese subjects, has also been a concern for some researchers (Tataranni and Ravussin, 1993).

4. Summary of literature:

In summary, a review of the literature identified only three studies, by Foltz (1985), Grindel et al (1989), and Levine et al (1991) that attempted to quantitate causative factors of weight gain (including nutritional factors), in women with breast cancer receiving adjuvant chemotherapy. However, each study was either lacking in the accurate measurement of factors influencing weight gain, or limited by the sample size or methodological design to draw meaningful conclusions. A recent review by Denmark-Wahnefried et al (1993) revealed the need for a well-designed and well-controlled study that could determine the effects of dietary intake, as well as other components of energy expenditure to gain a better understanding of why women gain weight during treatment with adjuvant chemotherapy.

5. Dietary intervention programs:

Weight gain is a common, yet poorly understood side effect that occurs in women with breast cancer. This weight gain may be problematic for premenopausal women in terms of self-image, quality of life, potential for chronic disease, and survival (Denmark-Wahnefried et al, 1993). Within the past decade, there has been increasing interest in weight loss interventions for patients with breast cancer (Winningham et al, 1989). As a result, interventions to prevent weight gain during adjuvant chemotherapy have been initiated (Camoriano et al, 1990; Carson, 1989; Denmark-Wahnefried et al, 1993). Weight management programs for women with breast cancer have generally emphasized diet, exercise and behaviour modification, and support groups, as a means of achieving and maintaining a healthy body weight (Carson, 1989; Canadian Cancer Society, 1992; Winningham et al, 1993). Currently available dietary information for women with breast cancer does not support the inclusion of specific amounts or types of fat, vitamins, minerals, or avoidance of particular substances such as caffeine or alcohol, beyond the general recommendations. However, issues regarding these specific items have been raised when considering diet advice for women with breast cancer (Carson, 1989). It is expected that research designed to determine the mechanisms leading to weight gain may improve upon current practices to allow clinicians the opportunity to provide optimal weight management strategies for women with breast cancer who gain weight during adjuvant treatment (Denmark-Wahnefried et al, 1993).

Chapter III

Pilot study:

Prior to the commencement of the present study a pilot study was conducted, which involved the collection of retrospective data from medical charts of premenopausal women who received adjuvant treatment for early stage breast cancer. The purpose of the pilot study was to document the expected difference in weight gain within and between chemotherapy and radiation therapy treatments. In addition, weight gain during adjuvant treatment was compared between the two most common chemotherapy protocols, which were AC and CMF. Weight gain for the purpose of the pilot study was defined as the increase in weight from baseline to the completion of treatment.

Fifteen medical charts from breast cancer patients who were treated with CMF chemotherapy in 1990 were randomly selected and reviewed. Of the total, five patients were excluded for the following reasons: treatment was delivered offsite (n=2), a previous breast cancer diagnosis (n=1), change in treatment protocol (n=1), or an inability to complete treatment (n=1). For comparison, a total of 37 random medical charts of patients who were treated with the newer AC chemotherapy protocol in 1993-1994 were reviewed. Ten patients were excluded for the following reasons: treatment was delivered offsite (n=6), postmenopausal status (n=2), change in treatment protocol (n=1), and an inability to complete treatment (n=1).

Results of this pilot study are summarized below in Table 2 and are provided in greater detail in Appendix B.

Table 2: Pilot study of weight gain in women with breast cancer receiving adjuvant chemotherapy

Variable	*AC[1] Chemotherapy (n=26)*		*CMF[2] Chemotherapy (n=9)*	
	PRE-TREATMENT	*POST-TREATMENT*	*PRE-TREATMENT*	*POST-TREATMENT*
Weight (kg)	64.0±11.9[3]	64.5±11.9	72.0±15.1	75.6±16.5*

[1]premenopausal women with early stage breast cancer treated with adjuvant chemotherapy using Adriamycin® and cyclophosphamide in 1993-1994 (four consecutive 21-day cycles)
[2]premenopausal women with early stage breast cancer treated with adjuvant chemotherapy using cyclophosphamide, methotrexate and fluorouracil in 1990 (nine consecutive 21-day cycles)
[3]mean±standard deviation
*significant ($p<.05$) difference between pre- and post-treatment, determined by paired samples *t* test

Mean weight gain was 3.6 kg (±4.8 kg) in women receiving CMF chemotherapy compared to a mean weight gain of 0.5 kg (±2.5 kg) in women receiving AC chemotherapy. Less weight gain in women treated with AC chemotherapy is consistent with the literature in that fewer drugs and shorter treatment lengths are associated with less weight gain. Further analysis of the data for women treated with AC chemotherapy indicates that 16 (59%) gained weight. Average weight gain over four cycles for women who gained weight was 2.0 kg (range 0.5 to 5.0 kg). Seven (26%) lost weight, and four (15%) maintained their pre-treatment weight. Follow-up weights were available for 22 women (81%) in the sample. Of the 22

patients, 13 (59%) were heavier than pre-treatment weight. Mean weight for the sample of 27 women treated with AC chemotherapy was 62.7 kg (±11.5 kg), mean height was 161 cm (±8 cm), mean body mass index (BMI) was 24.7 kg/m^2 (±4.1 kg/m^2) and mean age was 42 yrs (±6 yrs).

Twenty-six medical charts from breast cancer patients who were treated with adjuvant radiation therapy in 1990 were also randomly selected and reviewed. However, all charts lacked sufficient record of weight at either pre- or post-treatment, to allow for a meaningful summary of data.

From the pilot study, it became evident that weight gain is variable among patients and treatments. Weight may be gained during treatment and subsequently lost before (or after) completion, or weight gain may persist and continue well after completion of treatment for some patients. The present study was designed to investigate energy intake, resting energy expenditure, physical activity and body composition in premenopausal women who receive adjuvant treatment for early stage breast cancer.

Design:

The present study was done in collaboration with medical staff at the British Columbia Cancer Agency (BCCA), the Breast Cancer Tumor Group (a multidisciplinary team) and the Department of Nuclear Medicine at St. Paul's Hospital.

The research design was a non-randomized prospective descriptive design comparing weight gain in premenopausal women receiving chemotherapy or combination therapy, to women receiving radiation therapy. Premenopausal women were chosen because of the greater weight gains previously reported in this population and therefore the greater potential benefit from the research findings. The radiation therapy comparison group with a similar stage cancer and menopausal status was specifically chosen to minimize confounding factors including variability in age, disease state, physiological parameters, and psychological characteristics related to coping with the diagnosis of breast cancer and its treatment. The lack of evidence for identification of major factors associated with weight gain in women with breast cancer underscores the importance of a comparison group when studying the effects of chemotherapy on weight gain. The descriptive design used in the present study was advantageous to identify the major determinants of weight gain and to establish associations among key factors, without interfering with patient care.

Subjects were recruited from the British Columbia Cancer Agency breast cancer outpatient clinics based on eligibility criteria including premenopausal and perimenopausal women with early stage breast cancer, aged 25-49 years, who were advised to receive adjuvant chemotherapy (including combination therapy) or radiation therapy by their attending oncologist. The age range was limited to 25-49 years to reduce the variability in sample

characteristics and partly to allow for comparison of dietary intake to the corresponding Recommended Nutrient Intake (RNI) category of the same age range. An increase in the upper limit of 49 years of age, to 51 years, was made to accommodate the additional subjects who were perimenopausal. Additional eligibility criteria included no chronic illness, no long-term use of medications that promote weight gain (eg. steroids), and body weight within 2.0 kg of stated usual weight. Patients advised to receive both adjuvant chemotherapy followed by radiation therapy, referred to as combination therapy, were included to increase subject enrollment. These subjects represented an estimated two-thirds of all premenopausal women treated with adjuvant therapy for early stage breast cancer at BCCA outpatient clinics.

Patients did not receive any specific dietary instruction during the study, although there were patients who received dietary counseling by the investigator or other clinic nutritionists at the completion of the study. One woman treated with adjuvant chemotherapy required consultation with a clinic nutritionist during the study for management of treatment-related side effects.

All patients with a new diagnosis of breast cancer who were scheduled to attend daily breast clinics were screened for eligibility using the computerized database in the Cancer Agency Information System (CAIS). Potential subjects were identified from new patient appointment times, of which there were approximately 27 per week. Using the CAIS computer system, patients were screened for age (as a estimate of menopausal status), and for place of residence (to determine if patients lived in Vancouver or the Lower Mainland). During the 36 weeks of recruitment, a total of 972 subjects were individually screened for eligibility based on age and place of residence. This preliminary list of patients was used to identify eligible women

on their first visit to the BCCA. Further screening was performed at outpatient clinics to identify only those patients who would be treated at the Vancouver Clinic and those who spoke English, to allow for successful follow-up. To complete the screening process, a review of each patient's medical chart and a discussion with the attending nurse and/or oncologist was conducted to assess the suitability of the candidate to be interviewed, and to assess their ability to perform the requirements of the study (eg. recording accurate information and attending all appointments). Consecutive eligible patients were then interviewed for participation in the study. Due to practical reasons and time constraints of the project, subject recruitment was limited to an eight month period.

Adjuvant chemotherapy treatment was based on the protocol used most often for premenopausal women with early stage breast cancer at the British Columbia Cancer Agency. This protocol included four consecutive 21-day cycles of AC (Adriamycin® and cyclophosphamide). Each of the four chemotherapy treatments was delivered on day one (of the 21-day cycle), allowing for approximately three weeks for recovery between treatments. Treatment dosages were calculated by the attending oncologist based on the body surface area of each patient, estimated from the measured height (cm) and weight (kg). Adriamycin®, also known by its generic name of doxorubicin, was administered in doses of 60 mg/m^2 of body surface area, and cyclophosphamide was administered in doses of 600 mg per m^2 of body surface area.

The AC protocol proved to be more commonly used than adjuvant CMF which is administered for nine consecutive 21-day cycles. Based on data from October 1993 to March 1994 from the British Columbia Cancer Agency Department of Pharmacy, 83% (n=113) of

breast cancer patients received adjuvant AC chemotherapy compared to only 17% (n=23) who received CMF chemotherapy. When patients are given the opportunity to choose between treatments, the popularity of the AC protocol appears to be due to the shorter treatment length, despite the invariable hair loss that occurs with this treatment. The transition of the protocol for adjuvant chemotherapy for early stage breast cancer patients from CMF to AC represented a challenge in that most of the present literature reports weight gain associated with the use of the CMF protocol. This study provided an opportunity to assess body weight and body composition changes in response to current treatment protocols for high risk breast cancer patients treated with adjuvant chemotherapy at the British Columbia Cancer Agency.

Radiation therapy was based on approximately three and one half weeks to a maximum of five weeks of daily treatments (excluding weekends). The total radiation dose, measured in centi-Gray (cGy), was divided into 16 or more treatment sessions. In instances where there was a larger area of breast tissue to be treated, an additional dose of radiation (approximately 750 cGy) was administered in three additional treatments.

In the present study, women were who were treated with adjuvant chemotherapy, combination therapy or radiation therapy, were followed on an outpatient basis for a period of approximately 12 weeks from initiation of treatment. Assessment of body weight, energy intake, resting energy expenditure, physical activity and body composition were performed at baseline, defined as the time period following surgery but prior to adjuvant treatment, and at the completion of treatment. The final measurements corresponded to approximately 2 weeks following the last cycle of chemotherapy, or 7 to 9 weeks following completion of radiation therapy, for the respective groups. If chemotherapy was delayed due to treatment-related

toxicity, the final measurements were postponed accordingly, to accommodate the additional time interval. Three of the nine women treated with chemotherapy required a 1 to 2 week delay in treatment for this reason. One woman whose treatment was delayed was also required to receive a 20% reduction in the dose of Adriamycin® and cyclophosphamide. For women receiving combination therapy of chemotherapy and radiation therapy, post-treatment measurements were performed following completion of chemotherapy but prior to commencement of radiation therapy. Thus, most post-treatment measurements were obtained at 12 weeks from the start of treatment for both groups.

Women treated with adjuvant chemotherapy were prescribed standardized anti-emetic therapy pre-treatment, and were provided with standardized prescriptions for home use. The standard medications prescribed to control nausea and vomiting were ondansetron (Zofran®) and dexamethasone (Decadron®). Prochlorperazine (Stemetil®), dimenhydrinate (Gravol®), or metoclopramide (Maxeran®) were occasionally prescribed for individuals with poor tolerance to the standard medications or to offer a less expensive alternative. Ondansetron and Decadron® were administered orally or intravenously prior to treatment, at a dose of 8 mg and 4-8 mg, respectively. To control post-treatment side effects, 24-48 hour prescriptions were provided for both ondansetron and Decadron® (or alternate medications, if required), in the amounts of 8 mg and 4 mg, respectively. In this study, the use of the steroid Decadron® was at low doses, for the short term control of nausea and vomiting following the administration of chemotherapy.

In addition to the standardized pre- and post-treatment measurements outlined above, subjects were followed during chemotherapy and radiation therapy appointments at the British

Columbia Cancer Agency. This served to maintain close subject contact, encourage interest and understanding of the project, clarify self-reported information, schedule (or re-schedule) appointments, and to monitor the progress of individual subjects to maintain current patient records. For women treated with adjuvant chemotherapy, weight was also recorded at each cycle of chemotherapy at three week intervals (assuming no delay in treatment). Dietary intake, resting energy expenditure, physical activity, and body composition were not measured during treatment primarily for practical reasons. Also, REE and body composition were not expected to change considerably in this short term. Refer to Appendix C for an overview of the study design.

Social and medical information was recorded on a standardized data collection form to maintain consistency and accuracy. Variables obtained included age, weight history, medications including chemotherapy dosages, type of surgery, stage of cancer, number of positive lymph nodes for metastatic disease, estrogen receptor status and other factors (See Appendix D). Stage of cancer for the purpose of this study was defined as the clinical stage, rather than the pathological stage. This information was obtained from the standardized Tumor Node Metastasis (TMN) staging sheet in the patient's medical chart, which was completed by each patient's oncologist (see Appendix E).

In preparation for testing, detailed instructions for recording dietary and physical activity data were reviewed with each subject at both pre- and post-treatment. Written instructions to record dietary and physical activity data on specific calendar days were provided to each subject to avoid the bias of recording information on the day prior to measurement of REE, as this test required subjects to abstain from physical activity (in the preceding 48 hours)

and fast (for 12 hours) in preparation for testing. Written information on testing protocols was provided on each occasion, and informed consent was obtained at the time of enrollment in the study. At the completion of testing at pre- and post-treatment, subjects were given an explanation of their results, and were provided with a light meal and reimbursement for travel or parking expenses.

A total sample of 50 subjects was initially proposed for the study including an equal number of subjects treated with adjuvant chemotherapy and radiation therapy. The sample size calculation (see Appendix F) estimated that 12 subjects were required to detect a 4.5 kg weight gain; an amount of weight gain during chemotherapy which was previously reported by women to be distressful (Knobf et al, 1983). A greater number of subjects than the calculated estimate was proposed based on the estimated 2000 new breast cancer patients seen at Vancouver Clinic per year. The proposed sample size (n=50) was also consistent with or greater than previous research which has studied factors associated with weight gain in premenopausal women (Foltz, 1985; Huntington et al, 1985; Levine et al, 1991). Limitations in subject recruitment are summarized in Chapter Four.

The present study improves upon the limitations of previous studies in that weight and factors associated with weight gain were recorded prospectively, and included a comparison group of women with breast cancer treated with radiation therapy (Foltz, 1985; Geraghty, 1989; Goodwin et al, 1988; Heasman et al, 1985; Huntington, 1985; and Levine et al, 1991). In addition, the present study is the first known to include resting energy expenditure under standardized conditions and an additional measure of body composition (using DEXA) to assess total and regional fat, lean mass, and bone mass during adjuvant treatment. The study

design also made it possible to identify weight gain in women with breast cancer in relation to usual weight. This was important to rule out the possibility of an increase in body weight that may have been a result of a regain of weight previously lost at the time of diagnosis and/or surgery. Lastly, because women with breast cancer treated with adjuvant radiation therapy were included for comparison, the present study provided information on dietary intake, REE, physical activity and body composition for these patients, which is currently lacking in the literature.

Methodology:

The methodology used in the measurement of major factors associated with weight gain and body composition in the present study are outlined in detail below.

1. Anthropometric measurements:

Height was measured once at baseline, without shoes. Weight was documented at baseline and at approximately 12 weeks following the start of treatment using a medical balance beam scale (Healthometer, Continental Scale Corporation, Bridgeview, IL). At these same timepoints an additional indirect measurement of body weight was available from the body composition determination using DEXA (referring to the sum of lean body mass, fat mass and bone mass to represent total body weight). In addition, for women receiving chemotherapy, body weight was documented monthly during chemotherapy treatments using a medical balance beam scale. This weight was obtained by nursing staff to verify correct dosages of chemotherapeutic agents, which are administered in amounts relative to body weight. Weight measurements during chemotherapy were recorded (to the nearest 0.1 kg) on a standardized form in the patient's medical chart.

2. Dietary intake:

Energy intake obtained by 3-day food records was collected at baseline and at completion of treatment at approximately 12 weeks, using the adapted Food Record Form in Appendix G. Subjects were given detailed instructions to record their food intake. They were encouraged to use household measures and scales to weigh food or to refer to package labels and food portion diagrams to improve the estimation of portion sizes. All food records were reviewed with each subject to clarify food record entries and to obtain missing information, where necessary. Food records were numerically coded and independently analyzed for dietary intake, excluding any vitamin or mineral supplements or herbal preparations. Analysis was completed by a registered dietitian/nutritionist who was blinded to the treatment group and identity of each subject, as well as to whether food records were from the pre- or post-treatment collection period.

The food records were analyzed using a computerized nutrition software program (Nutritionist IV, Version 3.5, First Data Bank, San Bruno, CA) which included a database of 12,000 foods from the Canadian Nutrient File (CNF), USDA, manufacturer's product information, foreign composition tables and published nutritional analysis data. To improve the accuracy of the food record data, the following steps were taken. Nutritional analysis for particular foods that were difficult to match in the database was obtained directly from the manufacturers product labels or from an alternate computerized nutritional analysis program (Minnesota Nutrition Data System, version 2.6, University of Minnesota, School of Public Health, Minneapolis, MN). This latter program included 160,000 food variations differing in preparation method and ingredients, including over 7,000 brand name foods. In addition, in

instances where recipes were provided by subjects, individual ingredients and portion sizes were used to improve accuracy.

Energy intake for each subject was calculated based on the mean of the three days, expressed in kcal/d. An analysis of macronutrient intake, including carbohydrate, fat, protein and alcohol, in grams per day, and percent of total energy was also performed (see Appendix H). The present study was not designed to assess or describe micronutrient intake, although this information was available.

3. Energy expenditure:

3.1 Resting energy expenditure:

Resting energy expenditure was measured by indirect calorimetry using a metabolic cart (Deltatrac Metabolic Monitor, Summit Technologies, Mississauga, Ontario). All measurements were obtained on an outpatient basis, at baseline, and completion of treatment at approximately 12 weeks. Subjects were instructed to refrain from exercise in the 48 hours preceding the test and to preferably be driven by car or use public transit to travel to the laboratory the day of the test. Measurements were conducted in the morning by a trained technician under the necessary standardized conditions which included resting in a fasted state (12 hours).

The metabolic cart was calibrated against a reference mixture of oxygen and carbon dioxide gas prior to testing. Resting energy expenditure measurements were performed while subjects rested in the supine position in a darkened and quiet room following a 30 minute supervised and timed rest period. Oxygen consumption (VO_2) and carbon dioxide production

(VCO_2) were measured from breath samples collected from an overhead transparent canopy system. For the duration of the test, subjects remained awake but motionless.

To calculate resting energy expenditure, a minimum of 15 consecutive energy expenditure values were averaged. Energy expenditure values (kcal/24 h) corresponding to a respiratory quotient (RQ) of less than 0.85 were considered to reflect a true resting and fasted state. Resting energy expenditure was calculated based on the Weir equation (Weir, 1949). When using this equation (Weir, 1949) to calculate resting energy expenditure, a measured or average estimated value for urinary nitrogen excretion can be used. In the present study the following equation was used to calculate resting energy expenditure:

$$RMR = 5.68VO_2 + 1.59VCO_2 - 2.17\,N_u$$

(Datex Corporation, 1987; Weir, 1949)

where;
- RMR = resting metabolic rate in kcal/24 h
- VO_2 = measured oxygen consumption in ml/min
- VCO_2 = measured carbon dioxide production in ml/min
- N_u = urinary nitrogen excretion in g/24 h

A constant value for nitrogen excretion (approximately 14 g) was included in the calculation of resting energy expenditure using the Deltatrac manufacturer's software.

The measured value for REE was expressed in kcal/kg body weight, and kcal/kg lean body mass, to adjust REE values for the differences in total body mass and lean body mass of individual subjects. Kilocalorie expenditure per minute was also calculated from REE

(kcal/24hr) for use in the estimation of energy expenditure from physical activity, using entries reported in the physical activity diaries.

In the present study, resting energy expenditure was not coordinated with the menstrual cycle due to the possibility of chemotherapy-induced amenorrhea, and practical considerations for measurement. In addition, the thermic effect of feeding was not measured. This was primarily due to its limited relative contribution to total energy expenditure, and to avoid the additional burden to the subjects to adhere to the necessary standardized testing conditions which include the measurement of respiratory gas exchange over 4-6 hours following a test meal.

3.2 Physical activity:

Average energy expenditure from daily physical activity was estimated at baseline and completion of treatment, based on self-reports. Subjects were provided with a structured activity diary (see Appendix I) divided into six levels of increasing intensity for which subjects could categorize their activity. Subjects were instructed to record each activity, the time spent during the activity, as well as the number of hours of sleep, rest or household tasks over a 24 hour period for each of the three days.

The intensity of physical activity was based on METS (metabolic units). According to Ainsworth et al (1993), one MET is defined as the ratio of the associated metabolic rate for the specific activity divided by the resting metabolic rate. One MET is also defined as the energy expenditure for sitting quietly, which for the average adult is approximately 3.5 ml of oxygen/kg body weight/min or, 1 kcal/kg body weight/h (Ainsworth et al, 1993). The six

intensity levels for recorded physical activities included: 1) inactivity: 0.9-1.0 METS, 2) very light activity: 1.1-1.9 METS, 3) light activity: 2.0-2.9 METS, 4) moderate activity: 3.0-4.9 METS, 5) vigorous activity: 5.0-6.0 METS, and 6) very vigorous activity: >6.0 METS. To improve subject interpretation of the above categories, each intensity level rating was provided with corresponding examples for each category.

Completed activity diaries were reviewed by the investigator at the pre- and post-treatment testing appointments, to clarify entries and to ensure that 24-hours of activities were recorded for each day. Energy expenditure for reported activities was calculated based on the derived REE (kcal/min), multiplied by the energy cost of the activity (METS), multiplied by the duration of the activity (minutes). The use of the resting energy expenditure in kilocalories per minute (measured by indirect calorimetry) was included to improve the accuracy of the estimated energy cost of each activity (Ainsworth et al, 1993). Values for energy expenditure for reported activities were selected from a comprehensive compendium representing the compilation of eight common expenditure tables, which has been provided in Appendix I (Ainsworth et al, 1993). To calculate the mean total energy expenditure (kcal/d), energy expenditure values for rest and all physical activity for each 24-hour period were summed and the total for the three day period was divided by three to reflect a daily average. To differentiate resting energy expenditure (REE) from energy expenditure calculated from rest and physical activity, the latter has been referred to throughout as total energy expenditure (TEE). Total energy expenditure in the present study did not include the thermic effect of feeding, which accounts for approximately 10% of TEE. Thermic effect of feeding was not measured primarily for practical reasons, and due to its marginal contribution to TEE.

4. Body composition:

To measure whole body and regional changes in body composition, dual energy x-ray absorptiometry was used (XR-Series Bone Densitometer, Norland Corporation, Fort Atkinson, WI). Body composition measurements were performed at baseline and at 12 weeks from the start of treatment, which corresponded to the completion of chemotherapy. On both occasions, body composition and REE were measured during the same hospital visit. All measurements were performed by a trained technician using standardized procedures.

With the subject lying supine (with all metal objects removed), a series of transverse scans were made from head to toe of each subject. According to the manufacturer's specifications, subjects were positioned within a maximum scan area of approximately 88 X 181 cm. Body composition data were collected using an IBM personal computer, and the manufacturer's software (Norland Corporation, Fort Atkinson, WI, version 2.5.0, 1992). Scans were done with a standardized transverse scan speed of 18 cm/sec giving a total scan time of approximately 15 minutes, depending on the height of the individual subject.

Percent body fat by DEXA was calculated by dividing fat mass (kg) by total body mass (kg). A second computational method was used by DEXA to calculate percent body fat. This method calculated total density using a weighted average of the tissue densities of the three body compartments (lean mass, fat mass, bone mass), and applied the prediction equations of Siri (1956) and Brozec (1963) to estimate percent body fat. The value calculated for total density using this method, represents the underwater weighing equivalent of total body density that is traditionally used to estimate percent body fat by densitometry.

The two prediction equations for estimating percent body fat are as follows:

% body fat (Siri) = [(4.95/Total Density) - 4.50] * 100 (Siri, 1956)

% body fat (Brozec) = [(4.57/Total Density) - 4.142] * 100 (Brozec, 1963)

Total body mass (kg) calculated by the summation of lean body mass, fat mass and bone mass using DEXA was also used for comparison to body weight (kg) measured using a medical balance beam scale.

Additional technical information is provided in Appendix J.

At the completion of data collection and analysis all subjects received a summary of their individual results (see Appendix K), and an invitation to attend a presentation to discuss the results of the study.

5. Ethical Approval:

The study received ethical approval from The University of British Columbia Clinical Screening Committee for Research and Other Studies Involving Human Subjects, and from The British Columbia Cancer Agency Clinical Investigations Committee. Subjects provided informed consent prior to participation in the study. See Appendix L and Appendix M for the recruitment letter and consent form for the study, respectively. The original and amended Certificate of Approval from The University of British Columbia are provided in Appendix N.

6. Statistical analysis of the data:

Data analyses were performed on the data collected from the 19 subjects who completed the study. Statistical analyses were calculated using the software program, Statistical Package for the Social Sciences (SPSS, version 6.1). All data were entered into SPSS files from a standardized data form at the time of data collection. Prior to analysis, all entries were verified as correct by comparing the recorded data in each subject file to a printed copy of the data files entered in SPSS.

All results are presented as mean ± standard deviation, with the exception of frequency data, where indicated. Unpaired Student's *t* tests were used to test for statistical differences in baseline subject characteristics, including age, height, weight, body mass index, and body composition. To test the hypotheses, repeated measures analysis of variance (ANOVA) was used to compare repeated measures of body weight, energy intake, resting energy expenditure, physical activity, and total and regional body composition, obtained at pre- and post-treatment, for women treated with chemotherapy (including combination treatment) and radiation therapy. All statistical tests were performed to detect differences at $p<0.05$ level of significance, a priori (using two-tailed values).

The repeated measures ANOVA statistical analysis was an important analysis, as it was used to test the hypotheses. Significant group by time interactions were considered to be an important result, since this finding suggests that the pattern of change over time for the two treatment groups was different. However, because it has not been proven that adjuvant chemotherapy independently causes weight gain in women with breast cancer, significant time effects were considered important to demonstrate differences that occurred from pre-treatment

to post-treatment for all subjects. This analysis was to further investigate findings from Goodwin et al (1988) and Camoriano et al (1990) that suggest breast cancer itself, independent of adjuvant treatment, may be associated with weight gain. Consultation with a statistician was sought during the study for guidance on the above statistical calculations and interpretation.

Chapter IV

Results:

1. Subject recruitment:

At the completion of an eight month recruitment period in June 1995, 972 women were individually screened by computer for eligibility based on age (as an estimate of menopausal status) and place of residence. From this total, 43 women were interviewed for participation based on additional eligibility criteria which included women with early stage breast cancer who were advised to receive either adjuvant chemotherapy (including combination therapy) or radiation therapy at the Vancouver Clinic, and included only those women who spoke English. Women were also considered eligible for the study if they did not have any chronic disease or long-term use of medications that promote weight gain, and were within 2.0 kg of their usual weight. Eight of the 43 women who were interviewed were found to be ineligible. Of the remaining 35 eligible women, 19 women consented to participate, representing a recruitment rate of 54% or approximately one out of every two women interviewed. In the group of eligible women who declined participation (n=15), reasons included the following: there was a time conflict in scheduling pre-treatment measurements, including the involvement in other research projects (n=5), the distance to the testing site was too far to travel (n=5), treatment was arranged in the patient's community (n=2), the patient was not able to make the necessary time commitment for participation (n=2), or the patient was not available upon contact (n=1).

2. Subject characteristics:

The frequency distribution of variables influencing breast cancer status for women treated with either chemotherapy or radiation therapy is provided in Table 3. Variables include surgical treatment, chemotherapy protocol, menopausal status, lymph node status, and estrogen receptor (ER) status.

Table 3: Frequency distribution of variables influencing breast cancer status

Variable	*Chemotherapy (n=9)*	*Radiation Therapy (n=10)*	*p value*
Surgical treatment[1]:			
partial mastectomy	3	7	0.12
lumpectomy	4	3	
mastectomy	2	0	
Chemotherapy protocol[2]:			
AC[3]	8	0	
CMF[4]	1	0	
Menopausal status:			
premenopausal	7	8	0.91
perimenopausal	2	2	
Lymph node status:			
positive	5	0	0.01*
negative	4	10	
Estrogen receptor status:			
positive	5	3	0.08
negative	3	1	
unknown	1	6	

[1]partial mastectomy and lumpectomy were pooled for statistical analysis
[2]not appropriate for statistical analysis
[3]Adriamycin® and cyclophosphamide
[4]cyclophosphamide, methotrexate, and fluorouracil (5-FU)
*significant ($p<.05$) difference between chemotherapy and radiation therapy, as determined by Chi square

All women in the study were treated with primary surgery and were referred by their surgeon to the British Columbia Cancer Agency for assessment for adjuvant treatment. The majority of women (89%) in the study were treated with breast-conserving surgery of either partial mastectomy or lumpectomy (combined with axillary lymph node dissection), while two women treated with adjuvant chemotherapy were treated with a modified radical mastectomy. Partial mastectomy is a surgical treatment that removes some normal breast tissue surrounding the cancer. It is the most commonly performed surgery for the treatment of breast cancer, based on studies that have found that partial mastectomy followed by radiation provides a woman with the same chance of survival and control of the local cancer as does modified radical mastectomy (a surgical treatment that removes the breast) (Olivotto et al, 1995).

Of the 19 women who participated in the study, nine (47%) were treated with adjuvant chemotherapy, including eight subjects who received combination therapy of chemotherapy followed by radiation therapy. Post-treatment measurements for women treated with combination therapy were obtained at the completion of chemotherapy, but prior to the commencement of radiation therapy. All women treated with adjuvant chemotherapy were able to complete the prescribed therapy, although dosages and length between treatments were altered for some individuals. In the group of women treated with combination treatment, radiation therapy was included due to the conservative type of surgery performed. The remaining ten women (53%) in the present study were treated exclusively with adjuvant radiation therapy. The mean dose of radiation in treated patients was 4500 cGy in 18 treatments. All subjects treated with radiation therapy were able to complete the prescribed therapy.

One subject receiving chemotherapy made the decision to be treated with adjuvant chemotherapy using CMF, after all pre-treatment measurements were completed. Data for this subject have been included in the analysis, after determination that exclusion did not affect the significance of findings for change in body weight. Post-treatment measurements for this subject were performed at the standardized 12 week interval, although chemotherapy continued for an additional five cycles based on the CMF protocol which includes nine 21-day cycles.

Menopausal status of the subjects included 15 women (79%) who were premenopausal, and the remaining four women (21%) who were perimenopausal, meaning they had experienced fewer than normal menstrual periods and/or the onset of menopausal symptoms in the past year. The four perimenopausal women were distributed equally, with two in each of the treatment groups.

Adjuvant chemotherapy for early stage breast cancer is generally recommended for moderate risk cancer when the tumour is more than 2 cm; and/or the lymph nodes contain cancer; and/or there is some invasion of lymphatic or blood vessels or nerves of the breast (Olivotto et al, 1995). For this reason, there were a significantly greater number of women treated with adjuvant chemotherapy (56%) with positive lymph nodes, compared to women treated with adjuvant radiation (0%).

Estrogen receptor status was measured at the time of surgery from a sample of breast tissue, to determine if the women would benefit from hormonal therapy using the anti-estrogen drug, tamoxifen. In general, the higher the estrogen receptor level, the more responsive the tumor will be to tamoxifen (Olivotto et al, 1995). In the present study estrogen receptor status was similar between treatment groups. However, very small cancers (less than 0.5 cm) cannot

be tested by this method, and more women treated with radiation therapy in the present study had tumours in this size range.

All women in the present study were classified as having stage I breast cancer, based on clinical staging (see Appendix E).

In summary, the only statistically significant difference in variables influencing breast cancer status between treatment groups in the present study was lymph node status (p=0.01).

Table 4 provides a summary of pre-treatment anthropometric characteristics.

Table 4: Pre-treatment anthropometric characteristics of women with breast cancer receiving adjuvant treatment

Variable	*Chemotherapy (n=9)*	*Radiation Therapy (n=10)*	*All (n=19)*
Age (yrs)	43±6[1]	42±5	43±5
Height (cm)	163±5	165±6	164±5
Weight at initial visit[2] (kg)	61.9±8.7	67.1±8.4	64.5±8.7
Weight pre-treatment[2] (kg)	61.5±8.0	65.9±8.6	63.8±8.4
Stated usual body weight (kg)	61.9±7.5	65.6±7.8	63.8±7.7
DEXA body weight (kg)	61.5±8.2	66.1±8.7	64.0±8.5
Body mass index (kg/m^2)[2]	23.1±2.7	24.4±3.5	23.8±3.1
Lean body mass[3] (kg)	33.1±2.9	37.5±4.0*	35.4±4.1
Fat mass[3] (kg)	25.9±6.4	25.8±6.1	25.9±6.1
Bone mass[3] (kg)	2.5±0.2	2.8±0.3*	2.6±0.3
% body fat[3] (Siri)	32.8±7.0	30.2±5.6	31.4±6.2
% body fat[3] (Brozec)	31.6±6.4	29.1±5.2	30.3±5.8
% body fat[3] (DEXA)	41.6±6.4	38.8±5.4	40.1±5.9

[1]mean±standard deviation
[2]using a medical balance beam scale (two missing values at initial visit)
[3]using dual energy x-ray absorptiometry
*significant ($p<.05$) difference between chemotherapy and radiation therapy, analyzed by an independent samples Student's *t* test

In summary, age, height, body weight at the initial visit and pre-treatment, usual body weight, body mass index, fat mass, and percent body fat were not statistically different between women treated with chemotherapy or radiation therapy at baseline, although women treated with radiation therapy tended to be heavier. There were however, significant differences in lean body mass (p=0.01) and bone mass (p=0.02) between groups at baseline, when tested using an independent samples Student's t test.

Table 5 summarizes the frequency distribution of demographic variables, including marital status, occupation, and parity.

Table 5: Frequency distribution of demographic variables[1]

Variable	*Chemotherapy (n=9)*	*Radiation Therapy (n=10)*	*p value*
Marital status:			
Married or common law	5	9	0.21
Divorced	1	0	
Single	3	1	
Occupation:			
Unemployed	0	1	0.74
Administration	5	4	
Professional	2	2	
Other	2	3	
Children:			
Yes	6	7	0.88
No	3	3	

[1]analyzed by Chi square

Marital status of the study participants included 14 (74%) married or common-law, four (21%) single and one (5%) divorced, which represented all subjects. Eighteen women (95%) were employed at the time of recruitment, most of whom were working full-time. All subjects who were employed were on disability or sick leave during adjuvant treatment, although a few women continued to work part-time throughout treatment. Of the women employed outside the home, nine (50%) were working in secretarial or administrative positions, four (22%) in professional positions, with the remaining five women (28%) employed in other positions including typesetter (n=1), journalist (n=1), artist (n=1), librarian (n=1), and seamstress (n=1).

Thirteen (68%) of the participants had children, which was similar for both treatment groups. A majority of women with children had dependents living at home at the time of recruitment. The mean number of children for women treated with chemotherapy and radiation therapy was 1 and 2, respectively. The ethnic background of the study participants was mostly Caucasian, representing 90% (n=17) of the sample. The two other participants were Chinese and Korean.

The following sections of the results chapter provide an analysis of body weight, dietary intake, energy expenditure, and total and regional body composition using repeated measures ANOVA. Corresponding F and p values are provided for the group effect, time effect, and group by time interaction for each variable, regardless of significance.

3. Body weight:

Body weight measured by DEXA and a medical balance beam scale at pre- and post-treatment is shown in Table 6. There were no differences in body weight (by either methodology) between women treated with adjuvant chemotherapy or radiation therapy. Furthermore, no differences were observed between body weight measured pre- and post-treatment.

Table 6: Body weight of women with breast cancer receiving adjuvant treatment[1]

Variable	*Chemotherapy (n=9)*	*Radiation Therapy (n=10)*
DEXA weight pre-treatment[2] (kg)	61.5±8.2[3]	66.2±8.7
DEXA weight post-treatment[2] (kg)	61.3±7.5	66.4±9.4
Weight pre-treatment[4] (kg)	61.5 ±8.0	65.9±8.6
Weight post-treatment[4,5] (kg)	61.5±7.6	66.9±10.6
Weight 3 months post-treatment[6] (kg)	61.1±9.3	69.5±10.3

[1]analyzed by repeated measures ANOVA
[2]measured using DEXA (sum of lean body mass, fat mass and bone mass)
[3]mean±standard deviation (refer to Table 7 for F and *p* values)
[4]measured using a medical balance beam scale
[5]three missing values at post-treatment
[6]two missing values for chemotherapy and four missing values for radiation therapy at 3 months follow-up (no statistical analysis was performed on weight a 3 months post-treatment due to the high number of missing values)

The corresponding F and *p* values for body weight analyzed by repeated measures ANOVA are provided below in Table 7.

Table 7: Analysis of variance (F and p values) of body weight of women with breast cancer receiving adjuvant treatment

Variable	*Group effect F (p)*	*Time effect F (p)*	*Group by time interaction F(p)*
DEXA weight[1] (kg)	1.84 (0.19)[2]	0.01 (0.91)	0.04 (0.84)
Weight[3] (kg)	1.32 (0.27)	0.40 (0.54)	0.29 (0.60)

[1]measured using DEXA (sum of lean body mass, fat mass and bone mass)

[2]analyzed by repeated measures ANOVA

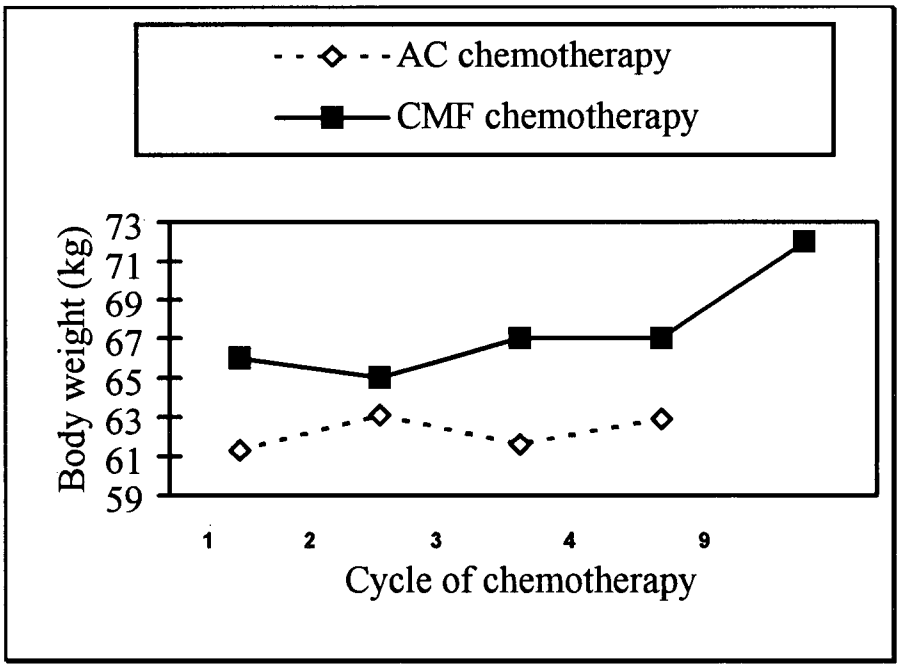
[3]measured using a medical balance beam scale (three missing values at post-treatment)

Overall, in the present study, seven women gained weight, seven lost weight, and five maintained weight within 0.5 kg of pre-treatment weight (using DEXA values). Four women treated with chemotherapy gained weight compared to three women treated with radiation therapy. Three women treated with chemotherapy lost weight compared to four women treated with radiation therapy. The remaining two women and three women treated with chemotherapy and radiation therapy, respectively, maintained weight during the study. According to the medical chart for the one subject who was treated with chemotherapy using the longer CMF regimen, there was steady and progressive weight gain.

Body weight at three months post-treatment was obtained from a standardized follow-up visit by an oncologist, which was arranged to assess progress and recovery from treatment. Due to the longer treatment length of adjuvant chemotherapy, follow-up weights for the two treatment groups represent different lengths of time from the start of treatment (see Appendix C for an overview of the study design). For women treated with radiation, the 3 month follow-up weight occurred at approximately 4-5 months from the start of treatment (depending on whether women received 3 or 5 weeks of therapy). For women treated with chemotherapy the 3 month follow-up weight occurred at approximately 6-7 months from the start of treatment (depending on whether adjuvant radiation therapy was administered). Due to the above methodological considerations, and the high number of missing values for weight at three months post-treatment, no statistical analysis was performed.

Figure 1 illustrates the change in body weight for women treated with adjuvant chemotherapy, using AC (n=8) and CMF (n=1). There was a marginal non-significant weight gain of 1.3 kg with adjuvant chemotherapy using AC which was calculated by the difference in weight from the first to the last cycle of chemotherapy. In contrast, the one women treated with adjuvant chemotherapy using the longer regimen of CMF gained 6.0 kg, with the greatest weight gain occurring after cycle five.

Figure 1: Change in body weight[1,2] of women with breast cancer receiving adjuvant chemotherapy



[1]includes eight women treated with AC chemotherapy (Adriamycin and cyclophosphamide) and one women treated with CMF chemotherapy (Adriamycin, cyclophosphamide and fluorouracil)
[2]includes five missing values at cycle 1 (n=2), cycle 2 (n=1), and cycle 4 (n=2) for AC chemotherapy

4. Dietary intakes:

Dietary intakes were estimated using a 3-day food record at pre- and post-treatment. As shown in Table 8, there was no statistically significant time effect, group effect, or group by time interaction in energy or macronutrient intake, in absolute measures (gms) or percent of total kilocalories. There was however a trend for a group by time interaction (p=0.08) for carbohydrate intake (gms) indicating that women treated with chemotherapy tended to decrease carbohydrate intake from pre- to post-treatment, whereas women treated with radiation therapy tended to increase carbohydrate intake over time.

Table 8: Dietary intakes[1] of women with breast cancer receiving adjuvant treatment

Variable	*Chemotherapy*		*Radiation Therapy*	
	PRE-TREATMENT (n=9)	*POST-TREATMENT (n=9)*	*PRE-TREATMENT[2] (n=9)*	*POST-TREATMENT (n=9)*
Energy (kcal)	1807±378[3]	1627±348	1577±375	1636±376
CHO[4] (gm)	232±52	201±55	205±49	226±63
Protein (gm)	76±17	74±20	63±16	66±17
Fat (gm)	60±19	56±12	52±21	48±19
Alcohol (gm)	4±7	3±5	5±8	5±6
CHO[4] (% total energy)	52±5	49±7	53±9	55±8
Protein (% total energy)	17±3	18±4	16±3	16±2
Fat (% total energy)	29±6	31±5	29±8	26±8
Alcohol (% total energy)	2±3	1±2	2±3	2±3
Number of entries[5]	61±17	54±19	64±15	58±17

[1] using 3-day food records
[2] one missing food record for radiation therapy group (pre-treatment only)
[3] mean±standard deviation (refer to Table 9 for F and p values)
[4] carbohydrate
[5] number of food items recorded in the 3-day food record

The corresponding F and *p* values for the dietary intake data analyzed by repeated measures ANOVA are provided below in Table 9.

Table 9: Analysis of variance (F and p values) of dietary intakes[1] of women with breast cancer receiving adjuvant treatment

Variable	*Group effect F (p)*	*Time effect F (p)*	*Group by time interaction F(p)*
Energy (kcal)	0.78 (0.39)[2]	0.62 (0.44)	1.08 (0.31)
CHO[3] (gm)	0.01 (0.92)	0.23 (0.64)	3.47 (0.08)
Protein (gm)	3.03 (0.10)	0.00 (0.99)	0.13 (0.72)
Fat (gm)	1.96 (0.18)	1.00 (0.33)	0.07 (0.80)
Alcohol (gm)	0.32 (0.58)	0.06 (0.80)	0.46 (0.51)
CHO[3] (% of total energy)	2.08 (0.17)	0.01 (0.94)	1.79 (0.20)
Protein (% of total energy)	1.95 (0.18)	0.64 (0.44)	0.92 (0.35)
Fat (% of total energy)	1.34 (0.26)	0.11 (0.74)	1.98 (0.18)
Alcohol (% of total energy)	0.40 (0.54)	0.01 (0.91)	1.53 (0.23)
Number of entries[4]	0.29 (0.60)	3.35 (0.09)	0.22 (0.65)

[1]using 3-day food records
[2]analyzed by repeated measures ANOVA
[3]carbohydrate
[4]number of food items recorded in the 3-day food record

Dietary data were compared to the Recommended Nutrient Intakes (RNI) for Canadians. For women aged 25-49 years, energy intake reported by both treatment groups was inadequate (ie. less than the recommended average energy requirement of 1900 kilocalories per day) (Health and Welfare Canada, 1990). The breakdown of macronutrient intake for carbohydrate, fat, protein, and alcohol (expressed as percent of total energy) was compared to the Nutrition Recommendations for Canadians. Carbohydrate intake was within the recommended range of 50-60% of total energy (Health and Welfare Canada, 1990), with the exception of the post-treatment carbohydrate intake for women treated with chemotherapy (49%). Fat intake was within the recommended level of less than 30% of total energy (Health and Welfare Canada, 1990), again with the exception of the post-treatment fat intake for women treated with chemotherapy (31%). Protein intake was greater than the recommended 13-15% of total energy (Health and Welfare Canada, 1990) in both treatment groups, at pre- and post-treatment. Intake of alcohol for both treatment groups did not exceed the maximum recommended intake of 5% of total energy (Health and Welfare Canada, 1990), although individual consumption was variable.

A summary of additional dietary intake data is provided in Table 10 and Table 11. Subjective responses as to whether women altered their dietary intake (ie. ate less, the same, or more than their usual amount) during the three day reporting periods at pre- and post-treatment are shown in Table 10. Refer to the Food Record form in Appendix G for questionnaire details.

Table 10: Subjective dietary intake data[1] of women with breast cancer receiving adjuvant treatment

	Chemotherapy		*Radiation Therapy*	
Variable	*PRE-TREATMENT (n=9)*	*POST-TREATMENT (n=9)*	*PRE-TREATMENT[2] (n=9)*	*POST-TREATMENT (n=10)*
Amount of food[1]:				
less than usual	1[3]	2	2	2
same as usual	8	5	5	7
more than usual	0	2	2	1

[1] refers to amount of food eaten during the 3-day food record reporting period (compared to usual)

[2]one missing food record for radiation therapy group (pre-treatment only)

[3]number of subjects

A majority of subjects in both treatment groups reported eating their usual amount of food at both pre- and post-treatment. In addition, there was a similar number of women in both treatment groups who reported eating both more than and less than their usual intake. No statistical analysis was performed on this subjective data.

A summary of subjective responses as to whether subjects altered their dietary intake as a result of eight specific factors is shown in Table 11. Refer to the Food Record form in Appendix G for questionnaire details.

Table 11: Factors associated with change of dietary intake[1] of women with breast cancer receiving adjuvant treatment

	Chemotherapy				*Radiation Therapy*			
Variable	*PRE-TREATMENT (n=9)*		*POST-TREATMENT (n=9)*		*PRE-TREATMENT[2] (n=9)*		*POST-TREATMENT (n=10)*	
Intake changed due to:	*more*	*less*	*more*	*less*	*more*	*less*	*more*	*less*
nausea	0[3]	1	1	2	0	1	0	0
appetite	2	1	1	4	1	2	0	1
advice from others	1	0	0	1	0	0	0	1
smell or taste of food	0	0	1	4	0	0	0	0
food offered by others	1	0	2	0	2	0	0	0
fatigue	2	1	0	2	1	2	0	1
lack of strength	2	0	2	1	1	0	0	0
feeling worried	1	2	0	3	0	1	0	0

[1] refers to amount of food eaten during the 3-day food record reporting period (compared to usual)
[2] one missing food record for radiation therapy group (pre-treatment only)
[3] number of subjects

More women treated with chemotherapy reported a change from their usual amount of food intake at post-treatment. For example, there were more women treated with chemotherapy who reported eating less food due to a change in "appetite", "smell or taste changes", or "feeling worried", compared to women treated with radiation therapy. No statistical analysis was performed on this subjective data.

5. Energy expenditure:

5.1 Resting energy expenditure (REE)

The results of resting energy expenditure measured by indirect calorimetry are presented in Table 12. Although no change was observed in REE (kcal/d) for both treatment groups, REE (kcal/LBM/d) increased from pre- to post-treatment, representing a significant time effect (p=0.03). There were no group effects or group by time interactions for REE.

Table 12: Resting energy expenditure (REE)[1] of women with breast cancer receiving adjuvant treatment

	Chemotherapy (n=9)		*Radiation Therapy (n=10)*	
Variable	*PRE-TREATMENT*	*POST-TREATMENT*	*PRE-TREATMENT*	*POST-TREATMENT*
REE (kcal/d)	1225±151[2]	1254±116	1294±112	1344±134
REE (kcal/min)	0.85±0.10	0.87±0.08	0.90±0.08	0.93±0.09
REE (kcal/kg body wt[3]/d)	20±2	21±1	20±2	20±2
REE (kcal/LBM[4]/d)	37±4	39±4	35±4	37±3**
RQ[5] (VCO_2/VO_2)[6]	0.84±0.06	0.80±0.05	0.82±0.06	0.80±0.07

[1]obtained by indirect calorimetry using a metabolic cart
[2]mean±standard deviation (refer to Table 13 for F and p values)
[3]using dual energy x-ray absorptiometry (DEXA), at pre- and post-treatment respectively
[4]lean body mass measured by dual energy x-ray absorptiometry (DEXA)
[5]respiratory quotient measured using respiratory gas exchange
Repeated measures ANOVA:
*group effect (chemotherapy different than radiation)
**time effect (pre-treatment different than post-treatment)
***group by time interaction (pattern of change over time different between groups)

The corresponding F and *p* values for the resting energy expenditure data analyzed by repeated measures ANOVA are provided in Table 13.

Table 13: Analysis of variance (F and p values) of resting energy expenditure (REE)[1] of women with breast cancer receiving adjuvant treatment

Variable	*Group effect F (p)*	*Time effect F (p)*	*Group by time interaction F(p)*
REE (kcal/d)	2.17 (0.16)[2]	2.55 (0.13)	0.18 (0.68)
REE (kcal/min)	2.09 (0.17)	3.30 (0.87)	0.23 (0.64)
REE (kcal/kg body wt[3]/d)	0.05 (0.83)	2.44 (0.14)	0.04 (0.84)
REE (kcal/LBM[4]/d)	2.24 (0.15)	5.40 (0.03)*	0.00 (1.00)
RQ[5] (VCO_2/VO_2)	0.39 (0.54)	1.59 (0.22)	0.24 (0.63)

[1]obtained by indirect calorimetry using a metabolic cart
[2]analyzed by repeated measures ANOVA
[3]using dual energy x-ray absorptiometry (DEXA), at pre- and post-treatment respectively
[4]lean body mass measured by dual energy x-ray absorptiometry (DEXA)
[5]respiratory quotient measured using respiratory gas exchange
*significant ($p<.05$) difference

5.2 Prediction of resting energy expenditure

A comparison of measured resting energy expenditure at baseline to energy expenditure predicted by the Harris Benedict equation (Harris et al, 1919) and Mifflin equation (Mifflin et al, 1990) is presented in Table 14. The mean predicted REE using the Harris Benedict and Mifflin equations for females were 1365 kcals and 1290 kcals, respectively, compared to the measured REE of 1261 kcals. Resting energy expenditure predicted using the Harris Benedict equation significantly overestimated measured REE (p=0.00), when all subjects (n=19) were included in the analysis. The predicted REE using the Harris Benedict equation was approximately 8% greater than measured REE by indirect calorimetry. There was no difference between measured REE by indirect calorimetry and predicted REE using the Mifflin equation (p=0.25).

Table 14: Comparison of measured[1] and predicted resting energy expenditure (REE) of women with breast cancer prior to adjuvant treatment

Resting energy expenditure	*Chemotherapy (n=9)*	*Radiation Therapy (n=10)*	*All subjects (n=19)*
Measured REE[1]	1225±151[2]	1294±112	1261±133
Predicted REE:			
Harris Benedict equation[3]	1338±70	1390±93	1365±85*
Mifflin equation[4]	1259±84	1319±107	1290±99

[1]pre-treatment resting energy expenditure, as determined by indirect calorimetry using a metabolic cart
[2]mean±standard deviation
[3]Harris Benedict equation for females; 665 + 9.6 (weight in kg) + 1.8 (height in cm) - 4.7 (age in yrs)
[4]Mifflin equation for females; 10 (weight in kg) + 6.25 (height in cm) - 5 (age in yrs) - 161
*significant (p<.001) difference between measured and predicted REE, using a dependent samples Student's t test

5.3 Total energy expenditure

Total energy expenditure from physical activity was estimated at pre- and post-treatment using a 3-day activity diary. Estimates of total energy expenditure (summation of resting energy expenditure and energy expended in physical activity), and the ratio of total energy expenditure to resting energy expenditure (activity factor) are shown in Table 15.

Table 15: Total energy expenditure (TEE) and energy expenditure from physical activity[1] of women with breast cancer receiving adjuvant treatment

	Chemotherapy		*Radiation Therapy*	
Variable	*PRE-TREATMENT (n=9)*	*POST-TREATMENT (n=9)*	*PRE-TREATMENT[2] (n=9)*	*POST-TREATMENT (n=9)[2]*
REE (kcal/d)	1225±151[3]	1254±116	1294±112	1344±134
TEE[4] (kcal/d)	1765±360	2027±348	2059±259	2140±335
Physical activity[5] (kcal/d)	542±251	772±392	780±192	796±277
Activity factor (TEE/REE)	1.4±0.2	1.6±0.4	1.6±0.1	1.6±0.2
Number of entries[6]	41±11	37±10	44±13	44±15

[1]using a 3-day activity diary

[2]one missing activity diary in radiation therapy group (pre-treatment only), therefore pre- and post-treatment measurements have been excluded from the statistical analysis using repeated measures ANOVA

[3]mean±standard deviation (refer to Table 16 for F and *p* values)

[4]not including thermic effect of feeding (TEF)

[5]number of kcalories expended in physical activity during 24 hours, determined by 3-day activity diary

[6]number of entries recorded in 3-day activity diary

Total energy expenditure and energy expenditure from physical activity were not significantly different between groups or over time, and there was no group by time interaction. However, there was a trend for a time effect (p=0.08) for TEE (kcal/d), indicating that all women in the present study tended to increase total energy expenditure from pre- to post-treatment. The activity factor (TEE/REE) and number of entries in the activity diary did not change significantly for either treatment group during the study, and there were no group by time interactions for these variables.

Corresponding F and p values for the repeated measures ANOVA for energy expenditure from physical activity are provided in Table 16.

Table 16: Analysis of variance (F and p values) of total energy expenditure (TEE) and energy expenditure from physical activity[1] of women with breast cancer receiving adjuvant treatment

Variable	*Group effect F (p)*	*Time effect F (p)*	*Group by time interaction F(p)*
REE (kcal/d)	2.17 (0.16)[2]	2.55 (0.13)	0.18 (0.68)
TEE[3] (kcal/d)	2.71 (0.12)	3.44 (0.08)	0.87 (0.37)
Physical activity[4] (kcal/d)	1.73 (0.21)	1.83 (0.20)	1.30 (0.27)
Activity factor (TEE/REE)	0.72 (0.41)	1.23 (0.29)	1.62 (0.22)
Number of entries[5]	0.72 (0.41)	2.03 (0.17)	0.24 (0.63)

[1]using 3-day activity diary (one missing activity diary in radiation group at pre-treatment only)
[2]analyzed by repeated measures ANOVA
[3]not including thermic effect of feeding (TEF)
[4]number of kcalories expended in physical activity during 24 hours, as determined by 3-day activity diary
[5]number of entries recorded in 3-day activity diary

The self-reported rating of amount of physical activity performed at pre- and post-treatment is shown in Table 17.

Table 17: Subjective physical activity data[1] of women with breast cancer receiving adjuvant treatment

Variable	*Chemotherapy (n=9)*		*Radiation Therapy (n=10)*	
	PRE-TREATMENT	*POST-TREATMENT*	*PRE-TREATMENT[2]*	*POST-TREATMENT*
Amount of activity:				
less than usual	8[3]	4	5	4
same as usual	1	4	4	3
more than usual	0	1	0	3
Activity rating:				
active[4]	0	3	4	9
moderate[4]	7	5	5	0
mild[4]	2	1	0	1
none[4]	0	0	0	0

[1]subjective ratings of physical activity, obtained using a 3-day activity diary
[2]one missing physical activity diary for radiation therapy group (pre-treatment only)
[3]number of subjects
[4]active (defined as "no change"); moderate ("able to perform some household and work activities"); mild ("able to care for self"); none ("bedridden")

A greater number of women in both treatment groups reported performing less than their usual level of physical activity, following both surgery and treatment. This trend was greatest for women treated with chemotherapy (89%), prior to treatment.

A majority of women in both treatment groups reported their level of physical activity as "moderate", meaning they were able to perform some household and work activities. In comparison to women treated with chemotherapy, a greater number of women treated with radiation therapy reported their level of physical activity at pre- and post-treatment as "active", meaning there was no change from usual. In addition, there were no women in the present study that reported their level of physical activity as "none", meaning they were bedridden.

Additional comments obtained from the physical activity diaries indicated that most women in the present study usually participated in regular exercise (eg. aerobic classes, bicycling, and brisk walking), recreational activities and household tasks. Refer to the Physical Activity Diary form in Appendix I for questionnaire details. No statistical analysis was performed on this subjective data.

6. Body composition:

The results of the body composition measurements using dual energy x-ray absorptiometry are provided in Table 18. There was a significant time effect for lean body mass (p=0.05), and percent body fat by all methods, including DEXA (p=0.04), Siri (p=0.04), and Brozec (p=0.05). There was also a significant group effect for lean body mass (p=0.01) and bone mass (p=0.01), both of which were higher in women treated with radiation therapy. A significant group by time interaction for bone mass (p=0.04) was also detected. There was a tendency for bone mass to decrease in women treated with chemotherapy, whereas women treated with radiation therapy tended to increase bone mass from pre- to post-treatment. However, further analysis by post hoc paired t tests revealed that the differences between pre- and post-treatment bone mass were not significant for women treated with either chemotherapy (p=0.14) or radiation therapy (p=0.15).

Table 18: Body composition[1] of women with breast cancer receiving adjuvant treatment

Variable	*Chemotherapy (n=9)*		*Radiation Therapy (n=10)*	
	PRE-TREATMENT (n=9)	*POST-TREATMENT (n=9)*	*PRE-TREATMENT[2] (n=10)*	*POST-TREATMENT (n=10)*
Total body weight[2] (kg)	61.5±8.1[3]	61.3±7.5	66.2±8.7	66.4±9.4
Lean body mass (kg)	33.1±2.9	32.4±3.6	37.5±4.0	36.9±3.7*,**
Fat mass (kg)	25.9±6.4	26.5±5.8	25.9±6.1	26.7±6.9
Bone mass (kg)	2.47±0.21	2.45±0.20	2.76±0.26	2.78±0.27*,***
DEXA[1] % body fat	41.6±6.4	42.9±6.3	38.8±5.4	39.8±5.4**
Siri % body fat	32.8±6.9	34.0±6.6	30.2±5.6	31.0±5.7**
Brozec % body fat	31.6±6.4	32.6±6.1	29.1±5.2	29.8±5.2**

[1]using dual energy x-ray absorptiometry
[2]sum of DEXA values for lean body mass, fat mass, and bone mass
[3]mean±standard deviation (refer to Table 19 for F and *p* values)
Repeated measures ANOVA:
*group effect (chemotherapy different than radiation)
**time effect (pre-treatment different than post-treatment)
***group by time interaction (pattern of change over time different between groups)

Corresponding F and *p* values for the repeated measures ANOVA for body composition data are provided below in Table 19.

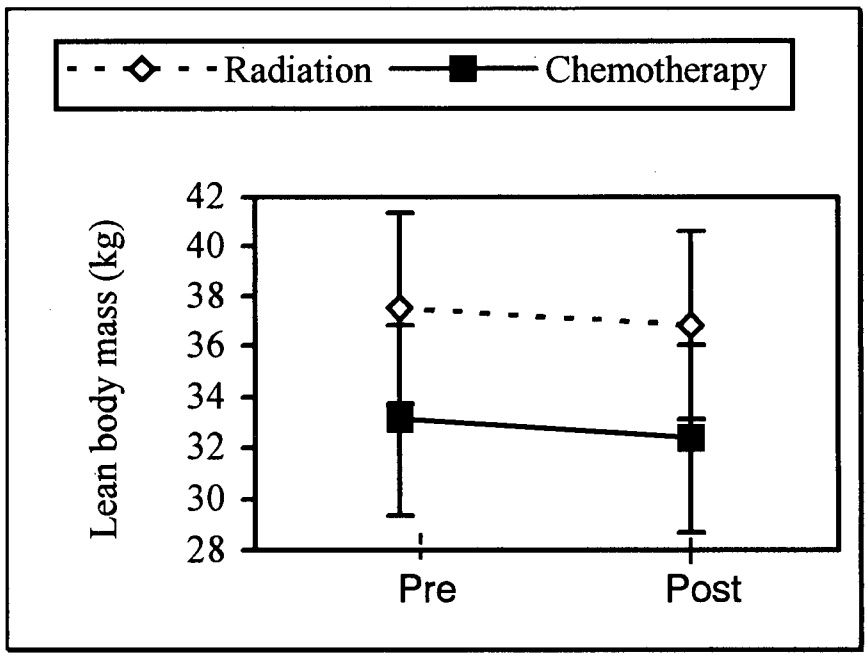
Table 19: Analysis of variance (F and p values) of body composition[1] of women with breast cancer receiving adjuvant treatment

Variable	*Group effect F (p)*	*Time effect F (p)*	*Group by time interaction F(p)*
Total body weight[2] (kg)	1.84 (0.19)[3]	0.01 (0.91)	0.04 (0.84)
Lean body mass (kg)	7.65 (0.01)*	4.41 (0.05)*	0.01 (0.93)
Fat mass (kg)	0.00 (0.98)	2.27 (0.15)	0.06 (0.82)
Bone mass (kg)	8.38 (0.01)*	0.07 (0.79)	5.12 (0.04)*
DEXA[1] % body fat	1.23 (0.28)	4.72 (0.04)*	0.05 (0.82)
Siri % body fat	1.00 (0.33)	4.75 (0.04)*	0.16 (0.70)
Brozec % body fat	1.00 (0.33)	4.49 (0.05)*	0.15 (0.70)

[1]using dual energy x-ray absorptiometry
[2]sum of DEXA values for lean body mass, fat mass, and bone mass
[3]analyzed by repeated measures ANOVA
*significant ($p<.05$) difference

Figure 2 displays the change in lean body mass from pre- to post-treatment, demonstrating the significant time effect (p=0.05), but lack of group by time interaction (p=0.93).

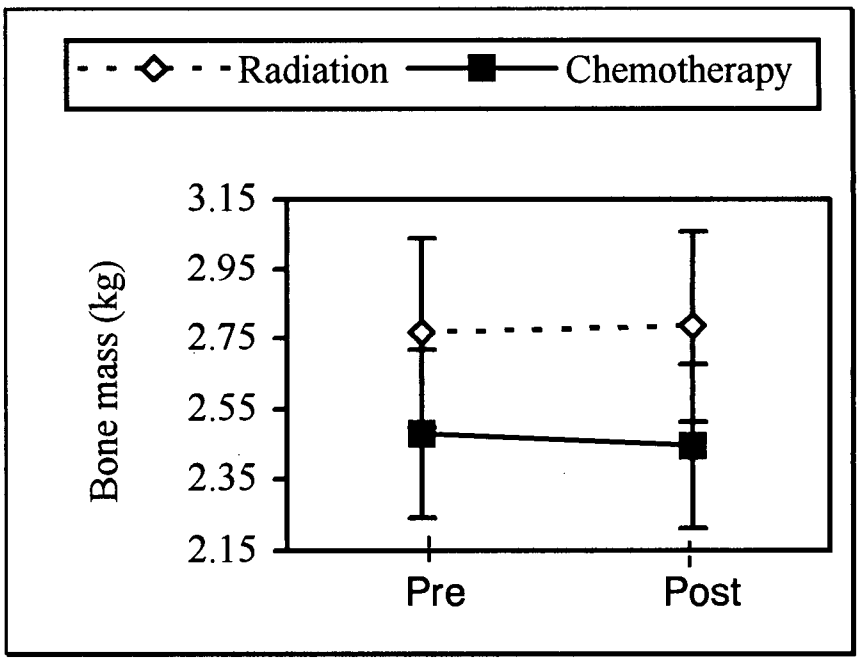
Figure 2: Change in lean body mass[1,2] of women with breast cancer receiving adjuvant treatment



[1]represents total lean mass measured by dual energy x-ray absorptiometry (DEXA)
[2]error bars represent the standard deviation of the mean

Figure 3 displays the group by time interaction for bone mass, indicating that women treated with chemotherapy tended to lose bone mass from pre- to post-treatment whereas women treated with radiation therapy tended to gain bone mass over time (p=0.04).

Figure 3: Group by time interaction for bone mass[1,2] of women with breast cancer receiving adjuvant treatment



[1]represents bone mass measured by dual energy x-ray absorptiometry (DEXA)
[2]error bars represent the standard deviation of the mean

The results of the body composition measurements were also analyzed for distribution of fat mass using DEXA. The five manufacturer pre-determined regions for analysis included head, trunk, abdomen, legs and arms (see Appendix A). These results are presented in Table 20.

There were no differences in fat distribution for any of the specified regions between groups or over time, and there was no group by time interaction. For this reason, the data were not further analyzed into additional operator-selected regions. There was however a trend for a time effect for trunk fat mass (p=0.08), indicating that all women tended to increase fat mass in the trunk region from pre- to post-treatment.

Table 20: Fat distribution[1] of women with breast cancer receiving adjuvant treatment

	Chemotherapy (n=9)		*Radiation Therapy (n=10)*	
Variable	*PRE-TREATMENT*	*POST-TREATMENT*	*PRE-TREATMENT*	*POST-TREATMENT*
head fat mass (kg)	0.7±0.1[2]	0.7±0.1	0.8±0.1	0.8±0.1
trunk fat mass (kg)	12.3±3.6	12.9±3.5	12.6±3.6	13.3±4.2
abdomen fat mass[3] (kg)	5.8±1.8	6.1±1.5	6.2±2.1	6.5±2.4
leg fat mass (kg)	9.9±2.1	9.8±2.0	9.6±2.2	9.8±2.4
arm fat mass (kg)	3.0±0.9	3.1±0.8	2.9±0.7	2.9±0.7

[1]fat mass of pre-determined regions using dual energy x-ray absorptiometry (DEXA)
[2]mean±standard deviation (refer to Table 21 for F and p values)
[3]abdominal fat mass is also included in trunk fat mass

Corresponding F and *p* values for the repeated measures ANOVA for distribution of fat mass are provided in Table 21.

Table 21: Analysis of variance (F and p values) of fat distribution[1] of women with breast cancer receiving adjuvant treatment

Variable	*Group effect F (p)*	*Time effect F (p)*	*Group by time interaction F(p)*
head fat mass (kg)	2.74 (0.12)[2]	0.14 (0.71)	1.11 (0.31)
trunk fat mass (kg)	0.04 (0.84)	3.37 (0.08)	0.01 (0.91)
abdomen fat mass[3] (kg)	0.18 (0.68)	2.64 (0.12)	0.03 (0.87)
leg fat mass (kg)	0.01 (0.91)	0.13 (0.72)	0.78 (0.39)
arm fat mass (kg)	0.31 (0.58)	1.08 (0.31)	0.66 (0.43)

[1]fat mass of pre-determined regions using dual energy x-ray absorptiometry (DEXA)
[2]analyzed by repeated measures ANOVA
[3]abdominal fat mass is also included in trunk fat mass

Changes in lean body mass in the five manufacturer pre-determined regions were also analyzed by repeated measures ANOVA, and are presented in Table 22. There was a statistically significant time effect for lean mass in the leg region (p=0.02), indicating that lean mass in the legs in both treatment groups decreased over time. There was also a statistically significant group effect for lean mass in the head (p=0.03), trunk (p= 0.01), leg (p=0.04) and arm regions (p=0.05). There were no significant group by time interactions, indicating that the pattern of change in lean body mass was not different between the two groups from pre- to post-treatment.

Table 22: Change in lean body mass[1] of women with breast cancer receiving adjuvant treatment

	Chemotherapy (n=9)		*Radiation Therapy (n=10)*	
Variable	*PRE-TREATMENT*	*POST-TREATMENT*	*PRE-TREATMENT*	*POST-TREATMENT*
head lean mass (kg)	3.1±0.2[2]	3.1±0.2	3.3±0.3	3.3±0.2*
trunk lean mass (kg)	15.4±1.6	15.3±2.2	17.7±1.7	17.5±2.0*
abdomen lean mass (kg)	7.5±1.0	7.6±1.1	8.4±0.8	8.3±1.0
leg lean mass (kg)	11.6±1.2	11.1±1.3	13.0±1.9	12.7±1.5*,**
arm lean mass (kg)	3.0±0.4	2.9±0.5	3.5±0.7	3.3±0.5*

[1]lean body mass of pre-determined regions using dual energy x-ray absorptiometry (DEXA)
[2]mean±standard deviation (refer to Table 23 for F and p values)
Repeated measures ANOVA:
*group effect (chemotherapy different than radiation)
**time effect (pre-treatment different than post-treatment)
***group by time interaction (pattern of change over time different between groups)

Corresponding F and *p* values for the repeated measures ANOVA for change in lean body mass are provided in Table 23.

Table 23: Analysis of variance (F and p values) of change in lean body mass[1] of women with breast cancer receiving adjuvant treatment

Variable	*Group effect F (p)*	*Time effect F (p)*	*Group by time interaction F(p)*
head lean mass (kg)	5.40 (0.03)[2]*	0.03 (0.86)	0.23 (0.64)
trunk lean mass (kg)	7.64 (0.01)*	0.42 (0.53)	0.04 (0.84)
abdomen lean mass (kg)	3.94 (0.06)	0.05 (0.83)	0.89 (0.36)
leg lean mass (kg)	4.82 (0.04)*	6.23 (0.02)*	0.75 (0.40)
arm lean mass (kg)	4.28 (0.05)*	2.12 (0.16)	0.49 (0.49)

[1]lean body mass of pre-determined regions using dual energy x-ray absorptiometry (DEXA)
[2]analyzed by repeated measures ANOVA
*significant ($p<.05$) difference

7. Retrospective review of medical charts:

To improve upon the methodological limitations of the small sample size of the present study, an additional review of medical charts was conducted. This retrospective review of medical charts included premenopausal women with early stage breast cancer who were diagnosed during the recruitment period of the present study. A total of 48 medical charts for women treated with adjuvant chemotherapy or radiation therapy were identified in the BCCA computer, using the study eligibility criteria. In most cases, these patients were initially screened for participation in the study but were not interviewed due to several factors, including

psychological, cultural or geographical factors, which would have limited participation in the present study.

From the total number of medical charts reviewed, there were 34 medical charts for women treated with adjuvant chemotherapy, including combination therapy. Fourteen of these medical charts were not suitable for analysis for the following reasons: chemotherapy was delivered offsite (n= 12), body weight was not recorded (n=1), or the patient was taking prescribed medication that promoted weight gain (n=1). As was found with the pilot study, all medical charts for women treated with adjuvant radiation therapy (n=13) lacked sufficient information for analysis. The majority of women treated with radiation therapy in the chart review lived outside of Vancouver or the Lower Mainland, spoke limited English, or chose treatment at a clinic in the United States, and as a result were not eligible for the present study.

In addition to documenting medical and demographic information from the medical charts, the chart review also served to investigate the potential number of eligible subjects that were not recruited. To be able to assess this, limiting factors to participation were examined. Women in the chart review who were treated with adjuvant chemotherapy essentially included women who were ineligible for the present study, and those women who declined participation (n=3). The reasons for ineligibility included living out-of-town (n=5), speaking limited English (n=4), or attending the breast clinic for a pre-operative consultation (n=2). There were also two women whose chemotherapy treatment was initiated before pre-treatment measurements could be obtained, and one woman who was initially considered ineligible because of an undetermined menopausal status. From the total of 20 women in the chart review, only three eligible women were never interviewed. Based upon a diary kept during recruitment, this was

determined to be a result of time conflicts of the investigator with subject testing (n=1), employment (n=1) or coursework (n=1). In summary, during the recruitment period, very few women who were eligible for participation in the present study were not interviewed.

The retrospective chart review also allowed for the comparison of the study sample to a larger number of women who were diagnosed with early stage breast cancer during the same time period. The results for the comparison of age, height, weight and body mass index (BMI) for subjects in the present study compared to those women who were included in the retrospective medical chart analysis are provided in Table 23. Mean age and height for the two groups were similar. Women in the chart review gained 1.9 kg, although this change in weight was not statistically significant. Body weight also did not change for women in the present study, based on the difference in weight from pre- to post-treatment measured using a medical balance beam scale. Body mass index (BMI) was similar for women in the chart review (25.4 kg/m^2) and the present study (23.1 kg/m^2). There were no statistically significant differences between groups when tested using an independent samples Student's *t* test.

Table 24: Comparison of anthropometric characteristics of women[1] with breast cancer receiving adjuvant chemotherapy

Variable	*Study subjects receiving AC and CMF Chemotherapy[2] (n=9)*	*Medical chart review subjects receiving AC Chemotherapy[3] (n=20)*	*p value[4]*
Height (cm)	163±5[5]	162±7	0.63
Age (years)	43±6	43±6	0.89
Weight pre-treatment (kg)	61.5±8.0	66.8±13.9	0.29
Weight post-treatment (kg)	61.5±7.6	68.7±14.3	0.17
Body mass index (m/kg^2)	23.1±2.7	25.4±5.1	0.11

[1]comparison of women in the study with retrospective data from patient medical charts
[2]includes AC chemotherapy using Adriamycin® and cyclophosphamide (n=8) and CMF chemotherapy using cyclophosphamide, methotrexate, and fluorouracil (n=1)
[3]includes AC chemotherapy using Adriamycin® and cyclophosphamide
[4]analyzed using an independent samples Student's *t* test
[5]mean±standard deviation

A comparison of frequency data for medical and demographic variables for the two groups is provided in Table 25. The majority of the women in the chart review were premenopausal women with clinical stage I breast cancer. All women were married, with children. Surgical treatment, menopausal status, lymph node status, and estrogen receptor status for the two groups were similar. A significantly greater number of women in the chart review were married (90%), compared to women in the present study (56%) (p=0.02). There was also a significantly greater number of women in the chart review (100%) with children, compared to the women in the present study (67%) (p=0.01).

Table 25: Frequency data of medical status and demographic characteristics of women with breast cancer receiving adjuvant chemotherapy

Variable	*Study subjects receiving AC and CMF Chemotherapy[1] (n=9)*	*Medical chart review subjects receiving AC Chemotherapy[2] (n=20)*	*p value[4]*
Surgical treatment[3]:			
partial mastectomy	3	6	0.06
lumpectomy	4	2	
mastectomy	2	12	
Menopausal status:			
premenopausal	7	17	0.63
perimenopausal	2	3	
Lymph node status:			
positive	5	10	0.78
negative	4	10	
Estrogen receptor status:			
positive	5	13	0.50
negative	3	3	
unknown	1	4	
Marital status:			
Married or common-law	5	18	0.02*
Divorced	1	0	
Single	3	2	
Children:			
Yes	6	20	0.01*
No	3	0	

[1] includes AC chemotherapy using Adriamycin® and cyclophosphamide (n=8) and CMF chemotherapy using cyclophosphamide, methotrexate, and fluorouracil (n=1)
[2] includes AC chemotherapy using Adriamycin® and cyclophosphamide
[3] partial mastectomy and lumpectomy were pooled for analysis
[4] analyzed by Chi square
*significant ($p<.05$) difference between women in the study and chart review

There were additional eligible subjects (n=15) that were interviewed for the study, but who declined participation. Medical information for these subjects was not entered into the British Columbia Cancer Agency database at the time of the retrospective chart analysis, and therefore these patients were not identified in the computer search. This group of women (who may be referred to as non-respondents) were similar to the study sample in medical and anthropometric characteristics. According to information obtained from each patient's medical chart, all women were premenopausal or perimenopausal with clinical stage I breast cancer. A majority of the non-respondents were treated with partial mastectomy, followed by either combination therapy using AC chemotherapy and radiation therapy, or radiation therapy. Mean age was 43 yrs (±6 yrs), mean height was 162 cm (±7 cm), and mean pre-treatment weight was 62.2 kg (±11.7 kg), which were similar to the study sample (n=19) who had a mean age of 43 yrs (±5 yrs), mean height of 164 cm (±5 cm), and mean weight of 63.8 kg (±8.4 kg).

8. Summary of results with reference to the study hypotheses:

Null hypothesis 1:

There will be no difference in the change in body weight from baseline to completion of treatment between premenopausal women with early stage breast cancer who receive either adjuvant chemotherapy or radiation therapy.

The null hypothesis was confirmed as there were no differences in body weight between treatment groups, from pre- to post-treatment.

Null hypothesis 2:

There will be no difference in the main factors associated with energy balance, including energy intake, resting energy expenditure and physical activity from baseline to completion of treatment, between premenopausal women with early stage breast cancer who receive either adjuvant chemotherapy or radiation therapy.

The null hypothesis was confirmed as there were no differences in any of the measured factors associated with energy balance between treatment groups, from pre- to post-treatment. However, there was a trend for the pattern of change in carbohydrate intake over time to differ between groups (p=0.08), with women with breast cancer treated with radiation therapy tending to have an increased intake, compared to a tendency for a decrease in carbohydrate intake in women treated with chemotherapy. There were also observed differences in dietary patterns between treatment groups, although these differences were not statistically analyzed. Subjective data indicated that more women treated with chemotherapy reported eating less than

their usual amount due factors associated with treatment, including a change in appetite, smell or taste of food, or feeling worried. There were no group differences in REE in kcal/d or kcal/kg, although there was an increase in REE (kcal/LBM/d) in both treatment groups from pre- to post-treatment (p=0.03) as a result of the significant loss of lean body mass in women treated with chemotherapy and radiation therapy. Lastly, there was a trend for increased total energy expenditure (p=0.08), including REE and energy expended in physical activity in both treatment groups from pre- to post-treatment.

Null hypothesis 3:

There will be no difference in body composition or distribution of fat and lean mass from baseline to completion of treatment between premenopausal women with early stage breast cancer who receive either adjuvant chemotherapy or radiation therapy.

The null hypothesis was rejected in the present study because of significant differences in body composition measured by dual energy x-ray absorptiometry. Differences included a decrease in total (p=0.05) and regional (p=0.02) lean body mass, and an increase in percent body fat (p=0.04) in both treatment groups from pre- to post-treatment. Regional changes in lean body mass included a decrease in lean mass in the leg region for both treatment groups, from pre- to post-treatment. There was also a significant difference between the pattern of change in bone mass between women treated with chemotherapy and radiation therapy from pre- to post-treatment (p=0.04), although there were no significant differences in bone mass over time for either treatment group using post hoc paired t tests.

The null hypothesis was confirmed with reference to fat distribution, as there were no differences between total or regional fat mass in any of the five measured regions, in women treated with either chemotherapy or radiation therapy, from pre- to post-treatment. However, there was a trend (p=0.08) for an increase in fat mass in the trunk region for all subjects, from pre- to post-treatment.

Chapter V

Discussion:

1. Major findings:

The main finding was that there was no change in body weight in premenopausal women with early stage breast cancer treated with either adjuvant chemotherapy, or radiation therapy. The second major finding was that there were significant changes in body composition for all women with breast cancer who received adjuvant treatment. These changes included a significant decrease in total and regional lean body mass, and an increase in percent body fat in both treatment groups from pre- to post-treatment. Regional change in lean body mass included a decrease in lean mass in the leg region for both treatment groups. Body composition findings also included a significant difference in the pattern of change in bone mass between treatment groups from pre- to post-treatment (p=0.04). There was a tendency for women treated with chemotherapy to lose bone mass (p=0.14), compared to a tendency for a gain in bone mass in women treated with radiation therapy (p=0.15), from pre- to post-treatment. There was also a trend (p=0.08) for an increase in fat mass in the trunk region for all subjects from pre- to post-treatment.

2. Other findings:

There were no significant differences in resting energy expenditure (kcal/d) between women treated with chemotherapy and radiation therapy or over time. However, there was an increase in REE derived from kcal/LBM/d for both treatment groups from pre- to post-treatment due to the significant decrease in lean body mass in both groups. An additional finding related to REE was the significant overestimation of REE by the Harris Benedict equation compared to measured REE using indirect calorimetry.

Other important findings in the present study were that there were no statistically significant differences between treatment groups or between pre- and post-treatment measurements of dietary intake or physical activity in women with breast cancer treated with adjuvant chemotherapy or radiation therapy.

There were also important findings related to retrospective data obtained from medical charts of patients with breast cancer who completed adjuvant treatment. In the pilot study there was significantly greater weight gain in women treated with CMF chemotherapy, compared to women treated with AC chemotherapy. In contrast, there were no differences in weight between women in the present study compared to medical chart data from women who were treated with AC chemotherapy during the same time period. The two groups (those who participated in the study and those who were included in the chart review) differed only in that more women in the retrospective medical chart review than in the study sample were married, and had children.

Additional significant findings included group differences in bone mass, total lean body mass, and regional lean body mass in the head, trunk, legs and arms. These significant findings

were not considered important since the values represented combined pre- and post-treatment measurements for each treatment group. As a result, significant group effects are not included in the discussion of results.

3. Subject recruitment:

The number of women recruited for the present study (n=19) was less than that specified in the study protocol. Several factors limited subject recruitment. First, from the potentially large population of women with breast cancer, age and menopausal status most significantly limited recruitment opportunities, excluding approximately three-quarters of the women attending new patient clinics. Secondly, the number of women living outside of Vancouver or the Lower Mainland, and those women who spoke English as a second language also substantially limited the number of eligible participants. Further, because younger premenopausal women were targeted for participation, child care responsibilities and employment were important conflicts to arranging the necessary morning testing appointments. Other factors that limited recruitment were concurrent research studies with similar eligibility criteria, the need to measure patients at St. Paul's Hospital on only one specific day of the week, and the eventual opening of the Fraser Valley Cancer Centre (which reduced both the number of new patients visiting the Vancouver Cancer Centre and the waiting time for treatment). Despite these numerous limitations of recruitment, 19 subjects were successfully recruited in the present study, and all participants completed the study requirements.

Recruitment difficulties appear to have occurred in other studies involving women with breast cancer. During the same recruitment period as the present study, women with early stage breast cancer receiving adjuvant chemotherapy were also recruited for a randomized drug

trial for anti-emetic therapy. In an 18-month recruitment period (1993-1995) this concurrent research project at the British Columbia Cancer Agency recruited 28 premenopausal women (Lisa Unger, Clinical Nurse, personal communication, April, 1995). In addition, Grindel et al (1989) who studied dietary intake and taste alterations in women with breast cancer, reported recruitment of 26 women during a 20-month period, including seven women who were unable to complete the study. Furthermore, Geraghty (1989) recruited women with breast cancer to investigate the relationship of body weight, body composition, caloric intake and activity level in postmastectomy women on adjuvant chemotherapy. During a 12-month period, eight women were recruited, including three women who were unable to complete the study. In all of the above research studies involving women with breast cancer receiving adjuvant treatment, subject recruitment was prolonged and sample sizes were small.

4. Subject characteristics:

There were few differences in subject characteristics between treatment groups in the present study sample. A comparison of anthropometric characteristics revealed significant differences in lean body mass and bone mass between treatment groups at baseline. Women treated with radiation therapy had greater lean body mass and bone mass, compared to women treated with chemotherapy. These differences in body composition were likely the result of the non-randomized convenience sample.

All subjects were at their usual weight at the time of recruitment, which is an important strength of the present study. In addition, there were no differences in body weight measured using a medical balance beam scale and dual energy x-ray absorptiometry (DEXA), which attests to the reliability of measurement of this important variable.

Nodal status was the only statistically significant difference in subject medical and demographic characteristics between women treated with chemotherapy or radiation therapy. There was a greater number of women treated with adjuvant chemotherapy with positive lymph nodes, compared to women treated with radiation therapy. This difference was expected because positive lymph node status is a basic criterion for use of adjuvant chemotherapy (Olivotto et al, 1995).

Subjects in the present study were very similar in anthropometric, demographic, and medical characteristics to women with breast cancer treated with AC chemotherapy in the pilot study (n=27) and retrospective chart review (n=20). This suggests that the study sample may

have been representative of the larger population of premenopausal women with early stage breast cancer who are treated at the British Columbia Cancer Agency.

5. Weight gain during adjuvant chemotherapy:

Weight gain has been reported to occur in women with breast cancer, particularly among those treated with adjuvant chemotherapy (Denmark-Wahnefried et al, 1993). Mean weight gains of 2.9 kg, 5.0 kg, 5.9 kg, and 7.7 kg have been reported by Goodwin et al (1988), Bonadonna et al (1985), Camoriano et al (1990), and Huntington (1985) respectively, using a variety of chemotherapy protocols (and/or hormonal and other agents) in premenopausal women. In postmenopausal women treated with adjuvant chemotherapy mean weight gains of 1.8 kg, 3.0 kg, 4.3 kg, and 4.5 kg have been reported by Levine et al (1990), Bonadonna et al (1985), Heasman et al (1985) and Foltz (1985), respectively. Furthermore, weight gain in women with breast cancer has been reported in several other studies in which the results for both premenopausal and postmenopausal women have been combined (DeConti et al, 1982; Foltz, 1985; Heasman et al, 1985; Hernandez et al, 1983; Knobf et al, 1983; Levine et al, 1991; Monnin et al, 1993b). In contrast, findings from Camoriano et al (1990), Goodwin et al (1988), and Monnin et al (1993b) have revealed weight gain in breast cancer patients who did not receive adjuvant chemotherapy, suggesting that factors beyond the influence of chemotherapy play a role in weight gain in patients. The former studies however have been questioned for their methodological limitations. Camoriano et al (1990) and Goodwin et al (1988) used retrospective data and Monnin et al (1993b) reported results using a questionnaire of self-reported weight gain.

Various factors including age, menopausal status, treatment, nodal and estrogen receptor status, have been studied as potential determinants of weight gain, with few significant findings (see Table 1, page 11-12). Heasman et al (1985) found that the amount of weight gain during chemotherapy varied substantially according to treatment regimen, with the greatest weight gain occurring with multiple agents. DeConti et al (1982) and Heasman et al (1985) reported significant relationships between adjuvant treatment with CMF, and/or prednisone and/or tamoxifen with weight gain in women with breast cancer. Significant relationships have also been reported between weight gain and age and menopausal status (Knobf et al, 1983), nausea (Knobf, 1985), psychological functioning (Levine et al, 1991), and nodal status (Subramanian et al, 1981). In these studies, a significant increase in weight occurred in younger and premenopausal women, in patients who experienced nausea, and in patients with positive lymph nodes. Foltz (1985) reported a significant negative relationship between estradiol reduction and weight gain in premenopausal women, although a functional association was not clearly identified in the study.

Comparison of research that has investigated weight gain in women with breast cancer during adjuvant chemotherapy is difficult due to the differences in subject and medical characteristics, and methodologies. In addition, some studies have reported weight gain for subjects treated with multiple regimens (Camoriano et al, 1990; Heasman et al, 1985; Levine et al, 1991) and often the findings for premenopausal and postmenopausal women are not independently analyzed (Chlebowski et al, 1986; DeConti et al, 1982; Foltz, 1985; Heasman et al, 1985; Hernandez et al, 1983; Knobf et al, 1983; Levine et al, 1991).

Despite these limitations, a comparison of the present study to previous research has been made. In contrast to the majority of studies above, weight gain did not occur in the present study in premenopausal women with breast cancer treated with adjuvant chemotherapy. Although there was large individual variability in weight measured during the present study, women who gained weight and lost weight were distributed similarly within each of the treatment groups. As a result, there were no statistically significant differences in weight within or between treatments.

There are several possible reasons to explain the contradictory findings of the present study. First, the primary explanation is that the AC chemotherapy protocol, unlike several other regimens, does not result in significant weight gain in treated women. In theory, weight gain is less likely to occur with the AC protocol based on research that demonstrates less weight gain when using fewer anti-neoplastic agents (Chlebowski et al, 1986; Heasman et al, 1985), shorter treatment lengths (Bonadonna et al, 1985) and intravenous administration (Denmark-Wahnefried et al, 1993), which are all characteristics of the AC regimen. Second, the sample size in the present study was small due to numerous limitations in subject recruitment. It is possible that the AC protocol is associated with weight gain of less than 3.6 kg, which could not be detected with the current sample size (see sample size calculation in Appendix F). Third, subject characteristics could be partly responsible for weight maintenance in the present study. Participants were highly motivated, literate, well-educated volunteers, living in a large metropolitan area. In addition, subjects were informed of the study purpose which may have encouraged efforts to maintain a stable body weight due to the perceived negative consequences of weight gain. While some women were aware of the possibility of

weight gain prior to the study, for some women the study created awareness of an additional side effect of adjuvant treatment. Further, it is possible that some women chose to enroll in the study, at least partially, to prevent unwanted weight gain from occurring. Considering the high prevalence of dieting in women, it is not surprising that women with breast cancer already suffering from a loss of self-esteem and an altered body image (Camoriano et al, 1990; Denmark-Wahnefried et al, 1993), would be concerned about preventing weight gain. Despite these numerous possible influences on the study findings, there is strong support from data from the pilot study (n=27) and retrospective chart analysis (n=20) to suggest that the above factors may not have been operative in the present study, and that weight gain is not associated with chemotherapy using AC. Supportive findings from the above two studies that involved the review of medical charts (including a larger number of women), indicate that weight gain does not occur in women treated with AC chemotherapy. Further, the findings of the pilot study and chart review are thought to be accurate in that it is unlikely that the previously discussed sources of bias would occur in the review of medical charts.

According to the literature, premenopausal women with breast cancer have a tendency to gain more weight during adjuvant treatment than postmenopausal women. Because the present study examined factors associated with weight gain in premenopausal and perimenopausal women, no comparisons can be made.

There are no known studies that have investigated weight gain using AC chemotherapy, due to its limited use at present. Based on a survey of 13 major Canadian cancer treatment centres, a majority of the seven institutions that responded offered six months of CMF chemotherapy as the primary adjuvant systemic therapy for premenopausal women with node

positive breast cancer. Three of the seven institutions (43%) offered alternative regimens, of which two centres offered four 21-day cycles of AC chemotherapy (Dr. Susan O'Reilly, medical oncologist, BCCA). The common use of CMF chemotherapy in Canadian cancer centres supports previously published American literature from the past two decades that has reported weight gain in women with breast cancer treated with adjuvant chemotherapy using this regimen. The future trend may be that other major cancer treatment centres, in addition to the British Columbia Cancer Agency, will adopt the AC regimen as the primary adjuvant treatment for premenopausal women with high risk breast cancer. With further study in larger samples of women, an additional benefit to breast cancer patients may prove to be the absence of weight gain using this shorter regimen.

6. Dietary intake:

Many studies that have investigated weight gain have focused on measuring the prevalence and magnitude of weight gain and its relationship to recurrent disease (Camoriano et al, 1990; Chlebowski et al, 1986; Goodwin et al, 1988; Heasman et al, 1985; Knobf et al, 1983). As a result, few studies have measured factors associated with weight gain, including nutritional factors.

Three published studies by Foltz (1985), Grindel et al (1989) and Levine et al (1991), measured dietary intake in women with breast cancer receiving adjuvant chemotherapy. Foltz (1985) reported only difference scores for pre- and post-treatment energy intakes, which were not significantly different between women who gained and did not gain weight. Similarly, self-reported changes in diet measured by Levine et al (1991) did not relate to weight change. The only research that published actual energy intake data for women with breast cancer treated with chemotherapy was that of Grindel et al (1989). Energy intake in the present study was greater than that reported by Grindel et al (1989), who measured energy intake in women with breast cancer receiving chemotherapy compared to age-matched healthy controls. In their study women receiving adjuvant chemotherapy (using CMF and a variety of other anti-neoplastic and hormonal agents) reported mean energy intakes of 1377, 1384, 1325, and 1166 kcal, at 2, 6, 12, and 24 weeks from the onset of chemotherapy, respectively. Women with breast cancer consumed a significantly greater number of kilocalories and food servings than the control group. The substantially lower energy intake data in the Grindel et al (1989) study compared to the present study may have been a result of methodological differences in the estimation of energy intake. Grindel et al (1989) used a limited 56-item food diary which

involved inherent differences in coding and analysis from the present study. The chemotherapy protocol(s), timing of the measurement, and the duration of the two studies were also different.

In the present study, there were no differences in dietary intake in women with early stage breast cancer treated with adjuvant chemotherapy compared to a comparison group of women with breast cancer treated with adjuvant radiation therapy. Based on basic nutritional theory, this finding is supportive of the fact that weight gain did not occur in women in either treatment group. However, subjective dietary intake data in the present study suggested that there were differences in dietary patterns between treatment groups. More women treated with chemotherapy reported eating less than their usual amount due to a change in "appetite", "smell or taste of food", or "feeling worried" at post-treatment, compared to women treated with radiation therapy. Observations reported by Knobf (1985) indicate the occurrence of similar factors which altered the dietary intake of women with breast cancer treated with cyclophosphamide. Women reported nausea, taste changes and increased appetite as possible factors for weight gain during chemotherapy (Knobf, 1985). Changes in eating habits in 68% (n=53) of women were also reported by Knobf (1985). Forty-five percent (n=35) ate more often, 37% (n=29) reported eating more, and 11% (n=9) of subjects changed the type of food consumed. Subjects also reported eating more frequently to relieve nausea (Knobf, 1985). Alterations in taste and appetite in women undergoing chemotherapy for breast cancer were also reported by Grindel et al (1989).

Based on subjective information obtained from subject interviews and self-reported data, there was a trend for some women treated with radiation therapy to engage in efforts to "improve their eating habits" and "lose weight" by increasing dietary carbohydrate intake and

reducing dietary fat intake. These particular changes in dietary intake are supported by the trend (p=0.08) for a group by time interaction for carbohydrate intake (gms). A trend for positive dietary changes may be logical, in view of previously reported data that indicates that women with breast cancer are interested in dietary information to delay recurrence of the cancer and perhaps to prevent disease among susceptible family members (Monnin et al, 1993b). Similar observations were reported by Grindel et al (1989). Sixty-three percent (n=12) of women with breast cancer reported eating more nutritious foods, avoiding red meat and animal fat, eating more vegetables, and decreasing caffeine. In the present study, alterations in dietary intake patterns may have been more likely to occur in women treated with radiation therapy due to its shorter treatment length, compared to adjuvant chemotherapy.

Comparison of energy intake data to energy expenditure data in the present study reveals a negative energy balance in both treatment groups. With the exception of pre-treatment measurements for women treated with chemotherapy, mean energy expenditure for both treatment groups was greater than mean energy intake, by approximately 460 kcal/d. This difference may be a result of a bias of under-reporting of dietary intake, which has been demonstrated in many previous studies that has measured energy intake compared to DLW as the criterion (Bandini et al, 1990; Prentice et al, 1986; Schoeller et al, 1989). Further, the interpretation of under-reporting of dietary intake may be logical considering that there was weight maintenance in the present study sample.

In comparison to the Nutrition Recommendations for Canadians, total energy intake (kcal/d) of women in the present study was less than the estimated average requirement (Health and Welfare Canada, 1990). With the exception of women treated with chemotherapy at post-

treatment, macronutrient intakes (as a percentage of total energy) were within the Nutrition Recommendations for Canadians (Health and Welfare Canada, 1990). This was an unexpected finding due to the numerous potential influences on eating behaviour for women undergoing treatment for breast cancer. Possible toxic effects of chemotherapy include learned food aversions, nausea, vomiting and mucositis, which can disrupt nutritional patterns during treatment (Grindel et al, 1989). However, it has been suggested that improved medical management of treatment toxicities may limit the adverse effects of treatment on nutritional patterns.

Alternatively, it is possible that there were important differences in dietary intake between treatment groups or between pre- and post-treatment measurements in the present study that were not detected using diet records that included a limited number of days and/or time points. There is also the possibility that differences in dietary intake were not detected as a result of the small sample size. Furthermore, women may make changes to their diets earlier on in response to the diagnosis of breast cancer, which were not possible to detect during the reporting periods of the present study. Monnin et al (1993b) surveyed 103 women who had surgery for breast cancer to determine their nutritional concerns. In their study, a majority (43%) selected "shortly after breast surgery" as the most appropriate time to discuss nutritional concerns with a dietitian. Monnin et al (1993a) also reported that after diagnosis, some breast cancer patients make drastic dietary modifications, including excess consumption of certain foods, total elimination of one or more major nutrient sources, and megadoses of various supplements. In support of this, five women in the present study reported the use of nutritional

supplements, one women reported using alternative therapies, and three women reported consultation with a naturopath doctor or herbalist as a result of their diagnosis of breast cancer.

Women with breast cancer have identified "how to lose weight" as one of their main nutritional concerns following surgery and/or treatment (Monnin et al 1993b). In addition, more than half of women (a portion of which were treated with adjuvant chemotherapy) believed they were overweight and nearly 25% wanted to attend classes for weight reduction (Monnin et al 1993b). Thus, although the proposed study did not reveal weight gain in women with breast cancer treated with adjuvant chemotherapy or radiation therapy, other study findings suggest that women with breast cancer have concerns about their weight and body image and therefore may benefit from nutritional counseling for weight management.

7. Energy expenditure:

7.1 Resting energy expenditure

There is only one known published study that investigated resting energy expenditure as a potential determinant of weight gain in women with breast cancer treated with adjuvant chemotherapy (Foltz, 1985). Differences in metabolic rate were not significant (p=0.543), and because only difference scores for women who gained and did not gain weight were reported, comparison of the data is impossible. In addition, Foltz (1985) did not conduct measurements of metabolic rate under the necessary standardized conditions (ie. fasted state) and the values are therefore of limited use.

Resting energy expenditure in the present study was not significantly different between treatment groups or from pre- to post-treatment. Although REE (kcal/LBM/d) increased significantly in both treatment groups from pre- to post-treatment, this can be explained by the significant decrease in lean body mass in both treatment groups. There was no change in REE when it was expressed in kcal/d or kcal/kg.

Resting energy expenditure for all subjects in the present study (1261 kcal/d) was remarkably similar to a larger sample (n=39) of healthy women (1236 kcal/d), with a similar mean age (41 yrs), height (160 cm) and weight (64 kg) (Daly et al, 1985). This suggests that REE may not be altered in women with breast cancer treated with surgery.

7.2 Prediction of resting energy expenditure

The accurate prediction of energy requirements for healthy individuals has many important clinical applications, with the most obvious being use in weight management (Mifflin et al, 1990). In practice, assessment of energy expenditure has been used as a basic requirement for establishing caloric prescriptions to assist individuals to achieve and maintain a healthy body weight (Mifflin et al, 1990).

The prediction of resting energy expenditure by an equation is a simple and practical method which requires only the knowledge of a person's height, weight, age and sex. The most widely used predictive equation for estimating resting energy expenditure in clinical nutrition is the Harris Benedict equation (Harris et al, 1919). This equation was developed in 1919 on 136 men and 103 women, and was validated within ±5% throughout the 1950's (Mifflin et al, 1990). Several investigators (Daly et al, 1985; Owen et al, 1986, Roza et al, 1984), have reported an overestimation of resting energy expenditure in normal-weight and obese individuals using the Harris Benedict equation. More recently, investigators have questioned the continued use of the Harris Benedict equation in modern populations, with differences in body size and composition, levels of physical activity, diet, and the availability of improved equipment and technology to measure resting energy expenditure (Daly et al, 1985, Mifflin et al, 1990). To improve upon these limitations, Mifflin et al (1990) developed two sex specific prediction equations from a sample of 498 healthy normal-weight and obese men and women.

In the present study, the Harris Benedict equation significantly overestimated resting energy expenditure by 8%, which supports the findings of Daly et al (1985), Owen et al (1986), and Roza et al (1984) who reported average overestimations of 12%, 7-14%, and 14%,

respectively. However, a wide range of both under and overestimations of REE using the Harris Benedict equation have been reported in various populations (Daly et al, 1985). In the present study, the Mifflin equation (Mifflin et al, 1990) provided an accurate estimation of mean resting energy expenditure (within 2%) in premenopausal women with early stage breast cancer, treated with surgery. The mean of the absolute differences in measured and predicted REE for the entire sample (n=19) was 6.8%, compared to measured REE as the reference.

In summary, while direct metabolic measurements are still preferable in research settings, the Mifflin equation (Mifflin et al, 1990) may provide an inexpensive and simple alternative to estimate REE in situations where precise determination of REE is not required. With continued testing in other populations and larger samples, the Mifflin equation may provide an accurate estimation of REE for use in clinical practice among nutritionists.

7.3 Total energy expenditure

In the present study there were no significant differences in physical activity between treatment groups or from pre- to post-treatment in women with breast cancer treated with adjuvant treatment. The expected finding to support the significant decrease in lean body mass and trend for an increase in fat mass in the trunk region, was a decrease in physical activity in both treatment groups. To the contrary, further examination of the data revealed a trend towards increased total energy expenditure (including physical activity) in both treatment groups from pre- to post-treatment (p=0.08). In the present study, the number of entries in the physical activity diary was similar at pre- and post-treatment, suggesting that women did not reduce the number of entries to lessen their workload. It is possible that physical activity was accurately measured using the 3-day diary, but that the level of activity was less during treatment and increased following the completion of treatment (when measurement occurred). This may be particularly true for women treated with radiation therapy, since treatment was completed several weeks before post-treatment measurements were obtained. In support of this, Greenberg et al (1992) found that fatigue diminished over the three weeks following treatment in women with node-negative breast cancer (n=15) undergoing localized radiation therapy. In the present study, the calculation of energy expenditure in kcal/min (from measured REE using indirect calorimetry) allowed for greater accuracy in the estimation of the energy cost of various activities, compared to using average values from the literature.

There are also potential methodological limitations to explain the findings of physical activity data, including the use of a limited three day period and reliance on self-reported data. Inherent sources of error are incorporated into the process of recording physical activity. In the

present study, the mean number of entries was approximately 42 per day, or 1 entry every 35 minutes. This is considerably less than other studies in which activity was recorded every 1-3 minutes (Borel et al, 1984; Edholm et al, 1955) or every 10 minutes (Kalkwarf et al, 1989), and as a result the calculations of energy expenditure may have been less accurate. However, it is also recognized that a normal pattern of activity is unlikely to be maintained with such frequent recording as was used in the previous studies (Acheson et al, 1980; Kalkwarf et al, 1989). There were also potential inaccuracies in estimating energy expenditure as a result of errors in rounding numerical data, the use of average energy expenditure values from the compendium, and selection of activities from the compendium based on subjective ratings of intensity. The above potential sources of error limit the use of the obtained energy expenditure data to comparing groups, rather than individuals.

The present study findings are not easily compared to other investigators who measured physical activity using retrospective questionnaires, including different time points and lengths of measurement. In addition, direct comparison is difficult due to differences in chemotherapy protocols, and surgical treatment which may have affected the level of physical activity of subjects.

A review of literature reveals that there is a lack of well-conducted research which has measured physical activity in women with breast cancer, and existing studies have reported contradictory findings. Huntington (1985) reported weight gain in 50% of women treated with CMF and CMFVP (addition of vincristine and prednisone) to be a function of a decrease in activity level during treatment. This study however used retrospective questionnaires in only a few subjects (n=7) from the total sample (n=29), and did not support this finding with statistical

analysis. Knobf (1985) also reported decreased activity as a potential factor for weight gain in women treated with adjuvant chemotherapy, based on subjective patient responses. Foltz (1985) and Levine et al (1991) also measured activity in women with breast cancer. Foltz measured physical activity using The Psychiatric Status Schedule, even though it was recognized by the author that this tool may be too insensitive and unreliable as a measure of absolute activity (Foltz, 1985). Foltz (1985) found no significant differences in energy expenditure from physical activity between women treated with adjuvant chemotherapy who gained and did not gain weight. Similar to the REE data, only difference scores were reported, and therefore comparison to the present study is not possible. Levine et al (1991) also measured physical activity and concluded that self-reported exercise did not correlate significantly with weight gain, concurring with the results of Foltz (1985).

There is empirical and anecdotal support for decreased physical activity and a high prevalence of fatigue in women with breast cancer (Huntington et al, 1988; Grindel et al, 1989; Zemore et al, 1989). Zemore et al (1989) studied the social and emotional consequences of breast cancer and mastectomy in 87 Canadian women. The only problems that could be attributed to the cancer that occurred with any frequency were those resulting from reduced physical strength or stamina. In this study Zemore et al (1989) reported that women experienced difficulty in performing heavy housework and reduced participation in sports or other leisure activities. Further, fatigue has been the most commonly reported symptom in women with breast cancer (Greenberg et al, 1992; Meyerowitz et al, 1979; Zemore et al, 1989).

Fatigue has also been cited as one of the most frequent and discomforting side effects experienced by cancer patients receiving chemotherapy, and has also been associated with radiation therapy (Greenberg et al, 1992; Hislop et al, 1991; Winningham et al, 1994). Research on fatigue and cancer treatment has also identified surgery, anesthesia, pain, and use of narcotic analgesics and psychoactive drugs as potential etiologic factors (Winningham et al, 1994). These potential causes of fatigue associated with surgery may explain the trend for the majority of women in both treatment groups in the present study who reported "less than usual" as a subjective rating of their level of physical activity prior to treatment. In the present study, a greater number of women treated with radiation therapy reported no change in physical activity at pre- and post-treatment. Again, this may be in part a result of the shorter treatment length for radiation therapy, compared to chemotherapy, allowing for recovery from potential treatment-related influences on physical activity.

Despite the lack of conclusive evidence to support decreased physical activity as a causative factor in weight gain or loss of lean body mass in women with breast cancer treated with adjuvant treatment, clinical experience and the high prevalence of fatigue in these patients suggests that further investigation of this important variable is warranted. Future research should emphasize the use of more precise methods to measure physical activity, such as DLW; and include a comparison group of women with breast cancer who do not receive adjuvant chemotherapy for comparison.

8. Body composition:

Measurement of body composition in the present study revealed the significant loss of total and regional lean body mass and an increase in percent body fat in both treatment groups, despite weight maintenance in the study sample. There was also a trend for an increase in fat mass in the trunk region for all women from pre- to post-treatment (p=0.08). The present study was the first known to use DEXA to quantify total and regional fat and lean mass in women with breast cancer, and therefore no comparisons are possible. Supportive findings for the observed loss of lean body mass and the increase in percent body fat can be obtained from the study of Winningham et al (1989). Winningham et al (1989) measured percent body fat using skinfold measurements in otherwise healthy women with breast cancer undergoing adjuvant chemotherapy, who were randomized to a control group or exercise group that participated in 10-12 weeks of supervised moderate aerobic exercise. Their results indicated a tendency toward weight gain with adjuvant chemotherapy which consisted of actual fat gain, and loss of lean body tissue. While all women in their study gained weight, women in the control group who did not exercise had a significantly greater increase in percent body fat (2.19%), compared to a decrease in percent body fat (0.51%) in women who exercised (Winningham et al, 1989). There was also an increase in lean body mass (2.04 kg) in the exercise group, indicating a probable gain in muscle mass, because women in this group gained weight and lost body fat (Winningham et al, 1989). Women in the control group lost lean body mass (1.26 kg) which the authors theorize may contribute to a reduced functional capacity as well as a lower metabolic rate (Winningham et al, 1989). Measurement of body composition yields more precise data upon which to base interventions for weight management. Measures

of body composition are superior to height and weight tables based on actuarial data, or measures such as BMI, or waist-to-hip ratio that have limited value in assessing adiposity or obesity (Mifflin et al, 1990). Regional measures of body fat that can be obtained using DEXA offer an additional advantage to validate anthropometric dimensions as indices of abdominal fat. This is important due to the association of central fat with the risk of chronic diseases such as diabetes and coronary heart disease (Lohman, 1992).

Measurement of body composition using DEXA in the present study had the advantage of providing an estimate of bone mass (kg). The tendency for bone loss in women treated with chemotherapy (0.02 kg) and tendency for a gain in bone mass in women treated with radiation therapy (0.02 kg) was a unanticipated finding, which may have been a result of the few number of subjects in the analysis. Bone loss may also have occurred in women in the present study who were treated with chemotherapy due to treatment-induced menopause. Medical records reveal that all women in the study who were treated with chemotherapy, except one, experienced the onset of menopausal symptoms and/or the absence of menstrual periods during treatment. Although the time interval between measurements was relatively short (approximately 12 weeks), it is possible that bone loss could occur based on the well-established relationship between decreased bone mass and decreased estrogen seen in postmenopausal women. An alternative explanation for the tendency for a decrease in bone mass observed in the women who were treated with chemotherapy was the use of the steroids to control treatment-related side effects. This is less likely since the use of steroids was in small doses and for a short duration. Hormonal treatment using tamoxifen has been shown to slow the loss of calcium from the bones and reduce osteoporosis (Olivotto et al, 1995). In the

present study, women treated with radiation therapy did not receive tamoxifen, and therefore hormone therapy can not be used to explain the tendency for an increase in bone mass in this group. A progressive increase in physical activity may have contributed to an increase in bone mass in the comparison group of women treated with radiation therapy, particularly if activity was initially reduced at pre-treatment due to surgery. In support of this, Greenberg et al (1992) reported that women with early stage breast cancer who were treated with radiation scored lower in fatigue at three and 11 weeks post-treatment than they did following surgery.

Dual energy x-ray absorptiometry has been shown to be highly correlated to percent body fat obtained by underwater weighing or densitometry (Hansen et al, 1993; Lohman, 1992). The percent body fat values for DEXA and values predicted by Siri and Brozec are discrepant. There was approximately a nine percent difference in percent body fat measured by DEXA and that calculated by the Siri and Brozec equations. To evaluate this considerable difference in percent body fat using the two approaches, the following background information is provided. The predicted values for percent body fat using the Siri and Brozec equations are calculated by DEXA software using body density that is derived from the weighted amounts of fat, lean and bone (compared to total body weight), and the following constant values for the density of fat (0.915 g/cm^3), lean (1.072 g/cm^3) and bone (2.982 g/cm^3). It is logical that differences in percent body fat values would result from the use of different values for tissue densities, compared to the assumed values for fat (0.900 g/cm^3) and non-fat tissue (1.100 g/cm^3) that were used to establish the Siri equation. Density values used by DEXA were also different than the density values for fat (0.888 g/cm^3) and non-fat tissue (1.1033 g/cm^3) used to develop the Brozec equation. In addition, DEXA uses a constant value for the density of bone,

which has not been used in either the Siri or Brozec calculations. Thus, predicted percent body fat by the Siri and Brozec equations using the DEXA manufacturer's software have not been computed in the intended manner, which involves measuring body density by hydrostatic weighing (using different assumed constants). In contrast, to estimate percent body fat, DEXA measures the total amount of lean, fat and bone using the attenuation properties of standard composition references for lean tissue, fat and bone, and calculates percent body fat by the amount of fat mass compared to total body mass. Therefore, it is expected that there will be differences in the values calculated by these two methods, and comparison of percent body fat values provided by DEXA and its software is not logical. Prediction of percent body fat using the Siri and Brozec equations is calculated and provided by the DEXA software because many people have regarded underwater weighing as a gold standard for measuring body composition. In addition, published data are widely available using these equations, to which researchers may want to make comparisons.

9. Relevance of the study findings:

The lack of information and practical applications in the area of weight gain and adjuvant chemotherapy for women with breast cancer are well appreciated. New additions to the literature were possible in the quantification of energy intake, resting energy expenditure, physical activity, and body composition in premenopausal women with early stage breast cancer treated with either adjuvant chemotherapy (including combination therapy) or radiation therapy. Body composition analysis also allowed for an estimate of bone mass, which has not been previously measured in premenopausal women with breast cancer during treatment.

The relevance and intended use of the study findings was the identification of factors amenable to modification and the future design and implementation of weight management programs for women with breast cancer. However, in the present study weight gain was not found and subsequently measured factors were not found to be associated with weight gain. The additional information available from the measurement of body composition may be used to support the inclusion of increased physical activity in prevention strategies for women with breast cancer treated with adjuvant chemotherapy, to improve body image and minimize the loss of lean body mass and bone mass.

Chapter VI

Conclusion:

The present study did not support weight gain in a small sample (n=19) of premenopausal women with early stage breast cancer who received adjuvant chemotherapy or radiation therapy. Chemotherapy using AC did not result in significant weight gain, compared to other regimens, such as CMF, that use a greater number of antineoplastic agents and longer duration of treatment. The study also revealed a significant decrease in total and regional lean body mass and an increase in percent body fat in all women, despite weight maintenance in the study sample. There was also a trend (p=0.08) for an increase in fat mass in the trunk region for all women, from pre- to post-treatment. An unexpected finding of the present study was the tendency for a decrease in bone mass in women treated with chemotherapy and the tendency for an increase in bone mass in women treated with radiation therapy, which requires further investigation. The bone loss which may have resulted from treatment-induced menopause may have important implications for the long-term health of women who receive adjuvant chemotherapy for breast cancer. The findings of the present study must be evaluated within the context of the identified limitations. These include the small non-randomized convenience sample, the reliance on self-reported information from a limited number of measurements, and the short period of follow-up (ie. 12 weeks).

Recommendations:

1. Limitations of the study:

The main limitation was the small convenience sample. Due to the numerous limitations in subject recruitment the sample consisted of motivated volunteers, who were not randomized to the two treatment groups. The small sample size reduced the power of the statistical analysis to detect differences between groups, and therefore trends as well as *p* values were examined to interpret the results. The second major limitation of the study was the reliance on self-reported information for dietary intake and physical activity, which required detailed recording of information. It is possible that subjects may have modified their eating habits or activity patterns to reduce their workload in completing these tasks. The third major limitation was the limited number of measurements in the present study. Additional measurements of dietary intake and physical activity during treatment may have enabled more accurate interpretation and explanation of the existing findings. Although more frequent measurements were originally proposed, this was rejected due to the additional burden it would have imposed on the women in the study. An additional limitation of the study was the short period of follow-up between pre- and post-treatment. The final limitation which was not under the investigators control, was the gradual change in the chemotherapy protocol from CMF to AC. It would have been meaningful to study the commonly used CMF protocol for comparability to other studies. However, an advantage of the present study was that it allowed for the investigation of weight gain related to a less common chemotherapy protocol.

2. Future research:

The complexity and difficulty in measuring factors related to weight gain in women with breast cancer treated with adjuvant chemotherapy were appreciated in the present study. Future research in this area should include additional measurement intervals during treatment to be able to detect if there are any differences in treatment(s) that were not identified by the use of pre- and post-treatment testing. Measurement of body composition and inclusion of a comparison group of women with breast cancer who do not receive adjuvant chemotherapy is also highly recommended. In addition, until the mechanisms of weight gain and adjuvant chemotherapy are better understood, medical oncologists and researchers should carefully monitor and report weight gain in related studies.

Additional research is recommended on the relationship between various forms of exercise and the fat distribution patterns of women with breast cancer. Although exercise duration and intensity necessary to control body fat may be inappropriate and unsafe for clinical populations (including some women with breast cancer), an increase in physical activity should be further investigated as it is a potential method to reduce body fat that has many other positive health benefits. Studies which include the investigation of weight gain with the use of combination therapy (chemotherapy and radiation therapy) may also be an important area for future research.

3. Recommendations for women with breast cancer:

The present study did not reveal weight gain in premenopausal women who received adjuvant treatment for breast cancer. However, because all women experienced a loss of lean body mass and gain in body fat during the study period, a preliminary recommendation to women may be to increase physical activity to improve body image and minimize the loss of lean body mass, and possibly bone. This recommendation however must be considered with caution because an increase in physical activity may be too difficult and/or impractical for some women with breast cancer during adjuvant treatment. It would be important to emphasize to women that although actual weight loss would be gradual, exercise may induce greater lean body mass with a subsequent decline in body fat (Winningham et al, 1989).

Although there were no significant differences in dietary intake between pre- and post-treatment, several issues prompt careful reexamination of dietary and weight control advice to breast cancer patients. These include evidence of a link between breast cancer and dietary fat and obesity, public awareness of diet and cancer information, and reports of an inverse relationship between body weight and prognosis (Carson, 1989). In addition, many cancer patients seek advice on alternative nutritional therapies. Standard weight control advice to overweight individuals is to eat a varied diet, reduced in kilocaloires and fat, and increase exercise to achieve a healthy body weight. For women with breast cancer, factors such as assessment of recent weight change, present and recent treatment, and overall prognosis must be considered to assess whether weight reduction is appropriate (Carson, 1989). Dietary advice to women with breast cancer must be carefully considered with emphasis on healthy

dietary practices, since women who are at high risk apparently view diet as a key factor in cancer prevention and disease-free survival (Monnin et al, 1993b).

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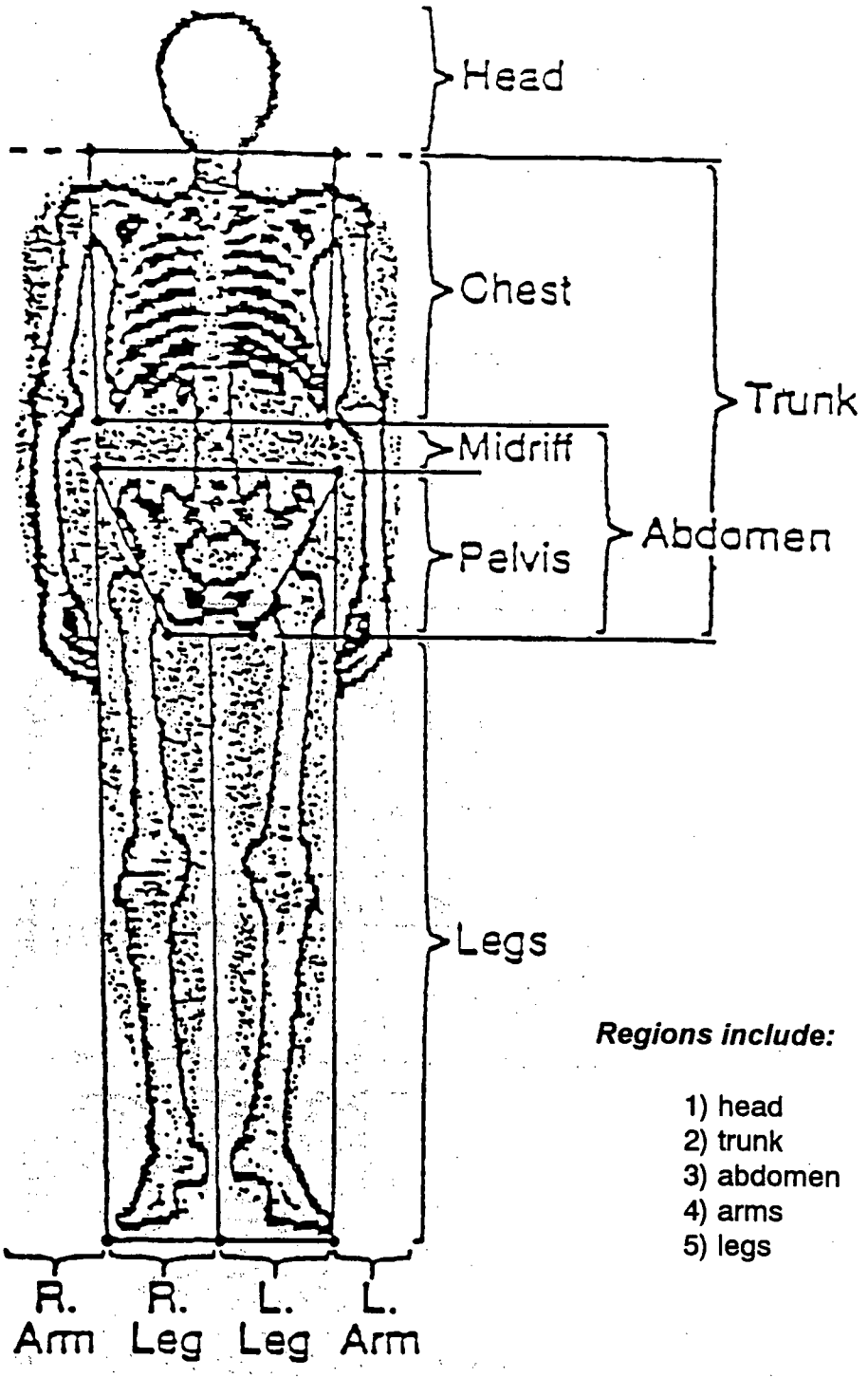
Pre-determined Dexa regions:



Regions include:

1) head
2) trunk
3) abdomen
4) arms
5) legs

Adapted from: XR-Series Bone Densitometer Operator's Guide (Norland Corporation, Fort Atkinson, WI, 1992).

Pilot study of weight gain during CMF[1] chemotherapy for breast cancer (n=10)

Subject Number	Weight (kg) at each cycle									Wt Gain[2] (kg)
	1	2	3	4	5	6	7	8	9	
1	53	53	55	N/R[4]	54	54	55.5	54	53	0.0
2	90	93	94.5	98	99	97.5	98.5	102	102.5	12.5
3	96	94	94	95	93	91	91	91	91	-5.0
4	60	61	60	60	62.4	62.5	63	63.5	63.5	3.5
5	57	59	59.5	60.5	61	61	61	61	60	3.0
6	76	79	79	79	79	79	80	80	81	6.0
7	63	63	60.5	61	61	65	64	N/R	65	2.0
8	82.3	84.5	86.5	89	86	88.5	87.5	88.5	89	6.7
9	N/R	72	72	72.5	72.5	73	73.5	76	75.5	3.5
10	71	72	72.5	74	73.5	75	75	75.5	75.5	4.5
Average weight gain during treatment[3] (kg)										3.7

[1]nine 21-day cycles of chempotherapy using cyclophosphamide, methotrexate, and 5-FU

[2]weight (kg) at cycle 1 - weight (kg) at cycle 9

[3]the sum of weight gained by each patient divided by the total number of patients

[4]N/R indicates that the weight was not recorded in the medical chart (< 1% missing values)

Pilot study of weight gain during AC[1] chemotherapy (n=27)

Subject Number	Weight (kg) at each cycle				Weight Gain[2] (kg)
	1	2	3	4	
1	47.0	48.0	49.5	49.0	2.0
2	60.0	N/R[4]	60.0	62.0	2.0
3	55.5	57.0	57.5	56.5	1.0
4	60.8	60.0	60.5	56.5	-3.5
5	78.5	77.0	74.5	76.0	-2.5
6	60.0	62.0	63.0	63.0	3.0
7	62.5	61.0	61.0	63.0	0.5
8	44.0	46.0	45.0	45.0	1.0
9	64.0	64.5	64.0	65.0	1.0
10	54.0	55.0	N/R	54.0	0.0
11	62.0	63.0	60.0	61.0	-2.0
12	89.5	90.5	88.5	89.0	-0.5
13	61.0	61.5	62.0	61.0	0.0
14	66.0	67.0	N/R	67.0	1.0
15	51.0	52.0	53.0	53.5	2.5
16	59.0	59.0	60.0	N/R	1.0
17	76.0	77.0	78.0	79.0	3.0
18	68.0	67.0	65.0	65.0	-3.0
19	63.5	63.5	63.5	65.0	1.5
20	61.0	62.8	64.0	65.0	4.0
21	59.0	59.0	N/R	58.5	-0.5
22	70.0	69.0	70.5	71.5	1.5
23	50.0	51.5	52.5	52.0	2.0
24	60.5	60.0	59.0	59.0	-1.5
25	70.0	71.5	70.5	70.0	0.0
26	76.0	71.5	70.5	70.0	0.0
27	95.0	99.0	98.5	100	5.0
Average weight gain during treatment[3] (kg)					0.8

[1]four 21-day cycles of chempotherapy using Adriamycin and cyclophosphamide
[2]weight (kg) at cycle 1 - weight (kg) at cycle 4
[3]the sum of weight gained by each patient divided by the total number of patients
[4]N/R indicates that the weight was not recorded in the medical chart (< 1% missing values)

Overview of Research Design:

	PRE-TEST		
	Radiation Therapy	**AC Chemotherapy Four-21 day cycles**	**Combination Therapy**
Week 1	Radiation	Cycle 1	Cycle 1
Week 2	Radiation		
Week 3	Radiation		
Week 4	Radiation	Cycle 2	Cycle 2
Week 5			
Week 6			
Week 7		Cycle 3	Cycle 3
Week 8			
Week 9			
Week 10		Cycle 4	Cycle 4
Week 11			
Week 12		POST-TEST	
Week 13			Radiation
Week 14			Radiation
Week 15			Radiation

PRE- and POST-TEST
weight, energy intake, metabolic rate, physical activity, body composition

Data Collection Form for Breast Cancer Patients

Personal data: **BCCA Doctor:**

Patient's name: _____ Clinic #: _____

Address: _____

_____

Phone number: _____ H _____ W

Date of birth: _____ Age (yrs): _____
month/day/year

Medical history:

Diagnosis: _____ date: _____

Stage of Cancer: ☐ I ☐ II _____

Type of surgery: ☐ modified radical mastectomy ☐ right ☐ left
☐ partial mastectomy
☐ lumpectomy
☐ axillary node dissection

Date of surgery: _____ Surgeon: _____

Node status: ☐ negative _____ ☐ positive _____

Estrogen receptor status: ☐ negative ☐ positive

Last menstrual cycle: _____

Demographics:

Marital status: _____ Children (ages): _____

Employment status: _____

Data Collection Form for Breast Cancer Patients, page 2

Anthropometric data:

Height (cm): _____

Weight at oncologist consultation: _____ kg date: _____

Usual Weight: _____ lbs. _____ kg

Recent change in weight: _____

Adjuvant treatment:

☐ radiation therapy

dose: _____ length: _____

☐ AC chemotherapy

dose: _____ mg adriamycin, _____ mg cyclophosphamide

Medications:

Pre-chemotherapy:

☐ Decadron/Dexamethasone ☐ IV ☐ oral ☐ 8mg or ☐ other _____

☐ Ondansetron/Zofran ☐ IV ☐ oral ☐ 8 mg or ☐ other _____

☐ Stemetil _____ ☐ Maxeran _____

☐ Other _____

Post-chemotherapy:

☐ Decadron/Dexamethasone _____ mg, schedule _____

☐ Ondansetron/Zofran _____ mg, schedule _____

☐ Stemetil _____ ☐ Maxeran _____

☐ Gravol _____ ☐ Other _____

Data Collection Form for Breast Cancer Patients, page 3

Weight:

Pre-test weight: _____ kg date: _____

Post-test weight: _____ kg date: _____

Weight for patients who are treated with chemotherapy:

Cycle I _____ kg _____ date _____ comments

Cycle II _____ kg _____ date _____ comments

Cycle III _____ kg _____ date _____ comments

Cycle IV _____ kg _____ date _____ comments

Weights for patients who are treated with radiation therapy:

Week 1 of treatment: _____ kg date: _____

Week 2 of treatment: _____ kg date: _____

Week 3 of treatment: _____ kg date: _____

Additional treatment (if necessary):

☐ combination therapy _____ date: _____

_____

_____

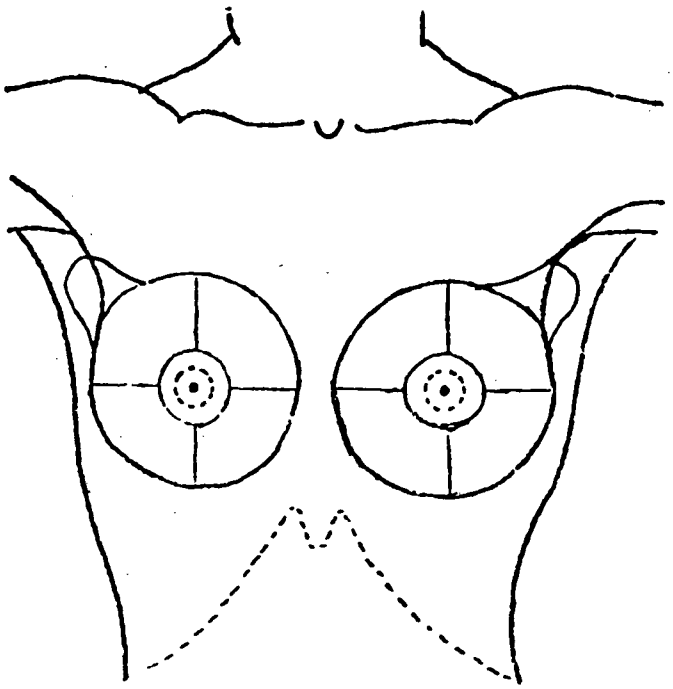
☐ Tamoxifen _____ date: _____

C.Kutynec, October 1994

BRITISH COLUMBIA CANCER AGENCY

BREAST

STAGING DIAGRAM



NOTE

1. "Central area" as shown by solid circle around the areola is defined as a 3 cm. radius from edge of the nipple.
2. Indicate scars on Staging Diagram.

Tumour palpable ☐ Tumour not palpable ☐

Size of breast tumour _____ cms

Measured by (a) Mammogram _____ (b) Caliper _____ (c) Other _____

Right breast ☐ Left breast ☐

Anatomical Subsite _____

Pathological Diagnoses _____

_____

PATIENT REFERRED: for initial planned management ☐ recurrence or metastatic disease ☐ post-treatment follow-up ☐ post-treatment unknown ☐

BASED ON: Assessment at BCCA ☐ BCCA Questionnaire ☐ Other ☐

CLINICAL - (CCABC 1960) IO I II III IV Unknown

TNM PRE-TREATMENT CLINICAL CLASSIFICATION (1987)

T - TX Tis T0 T1 T2 T3 T4 T4a T4b T4c T4d

N - NX N0 N1 N2 N3

M - MX M0 M1

TNM POST-SURGICAL HISTOPATHOLOGICAL CLASSIFICATION (1987)

BASED ON: Pathology Review at BCCA ☐ Other ☐

pT - pTX Tis pT0 pT1 pT2 pT3 pT4 pT4a pT4b pT4c pT4d

pN - pNX pN0 pN1 pN1a pN1b pN2 pN3

pM - pMX pM0 pM1

DISTANT METASTASES

	Clinical	Path
Pulmonary	☐	☐
Osseous	☐	☐
Hepatic	☐	☐
Brain	☐	☐
Marrow	☐	☐
Other	☐	☐
Distant Lymph Nodes	☐	☐

pTNM PATHOLOGICAL CLASSIFICATION

pT - Primary Tumour

The pathological classification requires the examination of the primary carcinoma with no gross tumour at the margins of resection. A case can be classified pT if there is only microscopic tumour in a margin.
The pT categories correspond to the T categories.

NOTE When classifying pT the tumour size is a measurement of the invasive component. If there is a large in-situ component (eg 4 cm) and a small invasive component (eg 0.5 cm) the tumour is coded pT1 a. Dimpling of the skin, nipple retraction or other skin changes, except those in T4, may occur in T1, T2 or T3 without affecting the classification.

pN - Regional Lymph Nodes

pNX The extent of invasion cannot be assessed

pN0 No evidence of invasion of regional nodes

pN1 Evidence of invasion of movable homolateral axillary lymph nodes
pN1a) Micrometastasis 0.2 cm or less in node(s)
pN1b) Gross metastasis in node(s)

pN2 Evidence of invasion of homolateral axillary lymph nodes fixed to one another or to other structures

pN3 Evidence of invasion of homolateral internal mammary lymph nodes.

REGIONAL LYMPH NODES

The regional lymph nodes are:

1. Axillary (ipsilateral) and interpectoral (Rotter's nodes): lymph nodes along the axillary vein and its tributaries, which may be divided into the following levels:
   i) Level I (low-axilla): lymph nodes lateral to the lateral border of pectoralis minor muscle.
   ii) Level II (mid-axilla): lymph nodes between the medial and lateral borders of the pectoralis minor muscle and the interpectoral (Rotter's) lymph nodes.
   iii) Level III (apical axilla): lymph nodes medial to the medial margin of the pectoralis minor muscle including those designated as the subclavicular, infraclavicular, or apical.

NOTE: Intramammary nodes are coded as axillary lymph nodes.

2. Internal Mammary (Ipsilateral): lymph nodes in the intercostal spaces along the edge of the sternum in the endothoracic fascia.

Any other lymph node metastasis is coded as a distant metastasis (M1), including supraclavicular, cervical, or contralateral internal mammary lymph nodes.

pM - Distant Metastasis

The pM categories correspond to the M categories

INITIAL PLANNED MANAGEMENT

Includes all cases where referral to an Agency facility was part of the treatment plan, even though delayed by chemotherapy or other causes.

Stage **CCABC PRETREATMENT CLINICAL (1960)**

I0 No palpable disease

I Primary freely movable on pectoral fascia, muscle, or chest wall. Skin involvement, including ulceration, may be present but must be in direct continuity with the tumour and no extension wide of the tumour itself.

II As Stage I but there are palpable mobile lymph nodes in the axilla on the same side 2.5 cm or less.

III **Either** (a) the skin invaded or fixed over an area wide of the tumour itself but limited to the breast, **or**, (b) the tumour fixed to underlying fascia/muscle but not to chest wall. Homolateral-axillary nodes, if present, must be mobile.

IV The growth has extended beyond the breast area as shown by:
a) Axillary nodes not mobile or >2.5 cm
b) Tumour fixed to chest wall
c) Supraclavicular or infraclavicular node involvement
d) Involvement of skin wide of breast
e) Opposite breast involved with metastatic disease
f) Distant metastases
g) Inflammatory carcinoma

Paget's disease of the nipple only is Stage I unless nodes present.

RULES FOR TNM CLASSIFICATION

The classification applies only to carcinoma.

In the case of multiple simultaneous tumours, the tumour with the highest T category should be identified.

TNM CLINICAL CLASSIFICATION (1987)

TX Primary tumour cannot be assessed

T0 No evidence of primary tumour

Tis Carcinoma in-situ: intraductal carcinoma, or lobular carcinoma in-situ, or Paget's disease of the nipple with no tumour

NOTE: Paget's disease associated with a tumour is classified according to the size of the tumour

T1 Tumour 2 cm or less in greatest dimension

T2 Tumour more than 2 cm but not more than 5 cm in greatest dimension

T3 Tumour more than 5 cm in greatest dimension

T4 Tumour of any size with direct extension to chest wall or skin

NOTE: Chest wall includes ribs, intercostal muscles and serratus anterior muscle but not pectoral muscle.

T4a Extension to chest wall

T4b Oedema (including peau d'orange), or ulceration of the skin of the breast, or satellite skin nodules confined to the same breast

T4c Both 4a and 4b, above

T4d Inflammatory carcinoma

NOTE: Inflammatory carcinoma of the breast is characterized by diffuse brawny induration of the skin with an erysipeloid edge, usually with no underlying palpable mass. If the skin biopsy is negative and there is no localized, measurable primary cancer, the T category is pTX when pathologically staging a clinical inflammatory carcinoma (T4d).

N - Regional Lymph Nodes

NX Regional lymph nodes cannot be assessed (eg previously removed)

N0 No regional lymph node metastasis

N1 Metastasis to movable ipsilateral axillary node(s)

N2 Metastasis to ipsilateral axillary node(s) fixed to one another or to other structures

N3 Metastasis to ipsilateral internal mammary lymph node(s)

M - Distant Metastasis

MX Presence of distant metastasis cannot be assessed

M0 No distant metastasis

M1 Distant metastasis (includes metastasis to supraclavicular lymph nodes)

Estimation of sample size

Continuous data with independent groups (formula 20.2) Cherney et al (1992)

$$n = \frac{(SD_1^2 + SD_2^2)\,(Z_{1-\beta} + Z_{1-\alpha/2})^2}{(X_2 - X_1)^2}$$

Where values $Z_{1-\beta}$ and $Z_{1-\alpha/2}$ can be found in Table 20.2 (page 342) (Cherney et al, 1992). The SD_1 and SD_2 for women receiving chemotherapy and no chemotherapy are 3.1 kg and 1.5 kg, respectively. The difference of interest, $(X_2 - X_1)$, is 4.5 kg based on patients who reported this weight gain as distressful[9]. A p value of 0.05 and ß value of 0.1 have been used.

Based on the limited information available, data from Foltz (1985) and Heasman et al (1985) were averaged to estimate SD_1. Foltz (1985) reported a mean weight gain of 10.0 lbs (4.5 kg) with a standard deviation of 6.1 lbs (2.8 kg) in those women whom gained weight during 6 months of CMF chemotherapy on a 28 day cycle (n=24). Heasman et al (1985) reported a mean weight gain of 3.65 kg and a SD of 3.39 kg in a sample of patients who received CMF chemotherapy (n=112). The average SD is 3.1 kg. The SD_2 for women receiving no chemotherapy has been estimated. The absence of an untreated control group in a majority of studies involving premenopausal patients creates difficulty in quantifying weight change in this population. In addition, conflicting findings have been reported in patients who do not receive adjuvant chemotherapy (Denmark–Wahnefried et al, 1993).

According to formula 20.2 the sample size is:

$$n = \frac{(3.1^2 + 1.5^2)\,(1.28 + 1.96)^2}{(4.5)^2}$$

$$= \frac{(11.86)\,(10.50)}{20.25}$$

$$= \frac{124.53}{20.25}$$

$$= 6 \text{ in each group (12 total)}$$

Using a difference in weight of 4.0, 3.6, 3.5, 3.0, 2.5, and 2.0 kg between chemotherapy and radiation treatments results in an estimated sample size of 8, 9, 10, 14, 20, and 31, respectively.

Guidelines for keeping a Food Record

A food record is a detailed description of each food or drink item taken over 24 hours of a day. An accurately completed food record can provide valuable information about the nutritional content of an individual's usual diet.

To assess your food record correctly, you must provide enough detail to clearly describe the foods and drinks that you have recorded. The guidelines below describe the information that is important for you to record. Please read the guidelines before you start.

Please keep a record of everything that you eat or drink on the attached forms for THREE (3) days in a row.

1. **THE PORTION SIZE (QUANTITY) NEEDS TO BE ACCURATELY RECORDED.** Please don't guess if you can measure!

   It may be helpful to measure how much your regular glasses, cups and bowls contain before you start. You can describe portion sizes in as many ways as you like. The attached food pictures are provided to help with the portion sizes.

   For example, you might record:

Volume	1 cup or 8 oz or 250 ml of 2% milk 1 tablespoon or 15 ml of peanut butter or cream cheese 1 teaspoon or 5 ml of sugar or honey
Size	One 2 " (inch) by 3/4 " by 3/4 " piece of cheddar cheese 1 medium egg, poached 1 small apple One 2 inch diameter digestive biscuit 1 medium bran muffin
Weight	2 oz or 60 grams (gms) of lean hamburger meat or chicken or fish (use labels on package to help you)

2. A DETAILED DESCRIPTION OF FOOD ITEMS IS ESSENTIAL.

Include as much information as you can about the foods that you eat. Be specific about the type of food, brand name if applicable and the content of mixed dishes.

For example:

If you have cookies, please indicate what type (eg. chocolate chip), what brand (eg. Dare or homemade) as well as the size (eg. two inches). If you have milk, indicate whether it is skim milk, 2% or whole milk as well as the amount (eg. 4 oz or ½ cup).

Describe mixed foods as if you were writing a recipe. Everyone has their own way of making everyday foods--please provide details of how you prepare your food.

For example:

If you make a cheese sandwich, do you use margarine or butter?
Do you add mayonnaise or Miracle Whip™, or lettuce or tomato slices?
What type of cheese and bread did you use?
How much of each item did you use?

Attaching recipes for items such as casserole dishes or labels from prepackaged foods such as frozen dinners is helpful. If you didn't make the food yourself, describe the contents as best you can. For example, if you ate 1 cup of tuna casserole, specify if it was about 1/2 macaroni, and 1/4 tuna and 1/4 peas and celery and cream sauce.

3. RECORD IMMEDIATELY AFTER EACH MEAL AND SNACK

Take your food record with you if you go out to eat. Please keep track throughout the day. Otherwise, it is easy to forget exactly what you have eaten.

Sample Food Record

Time	Food or drink item(s)	Quantity
12:30 pm	*Macaroni and cheese*	
	-cooked macaroni noodles	*1 cup*
	-homemade cheese sauce	*1/2 cup*
	(made with butter, flour, cheddar	
	cheese and 2% milk)	
	Tomato juice, canned	*4 oz glass*
	Whole wheat dinner roll	*1 - 2" diameter*
	Margarine (soft tub or brand name eg. Becel™)	*2 tsp.*

When you have completed your 3 day food record, please indicate:

A) WHETHER THIS WAS A USUAL DIET FOR YOU:

☐ yes, this record describes my usual diet _____

☐ no, this was not my usual diet, because _____

_____

_____

I WOULD USUALLY EAT: _____

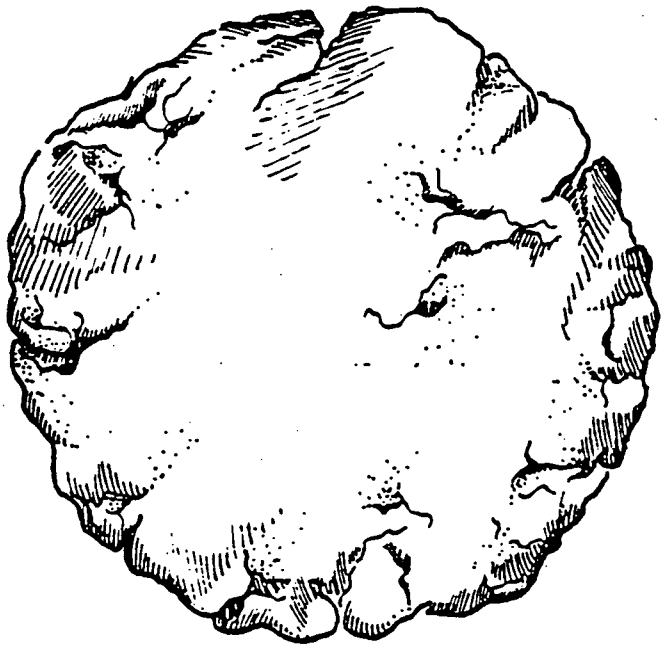
_____

_____

_____

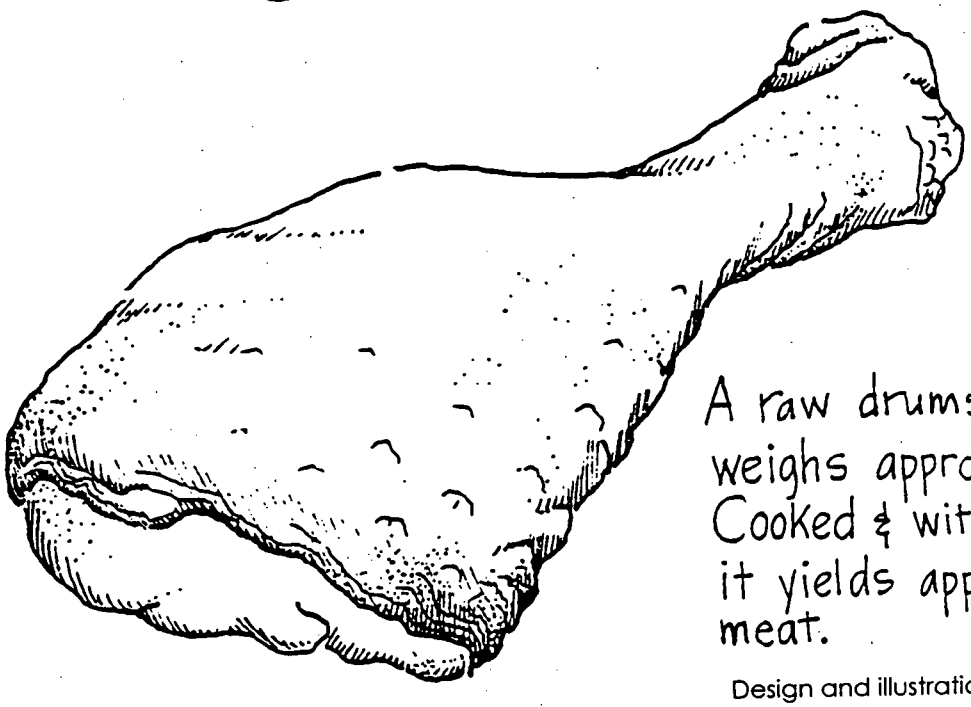
_____

A ¼" thick piece of cheese this size weighs approx. 1 oz.



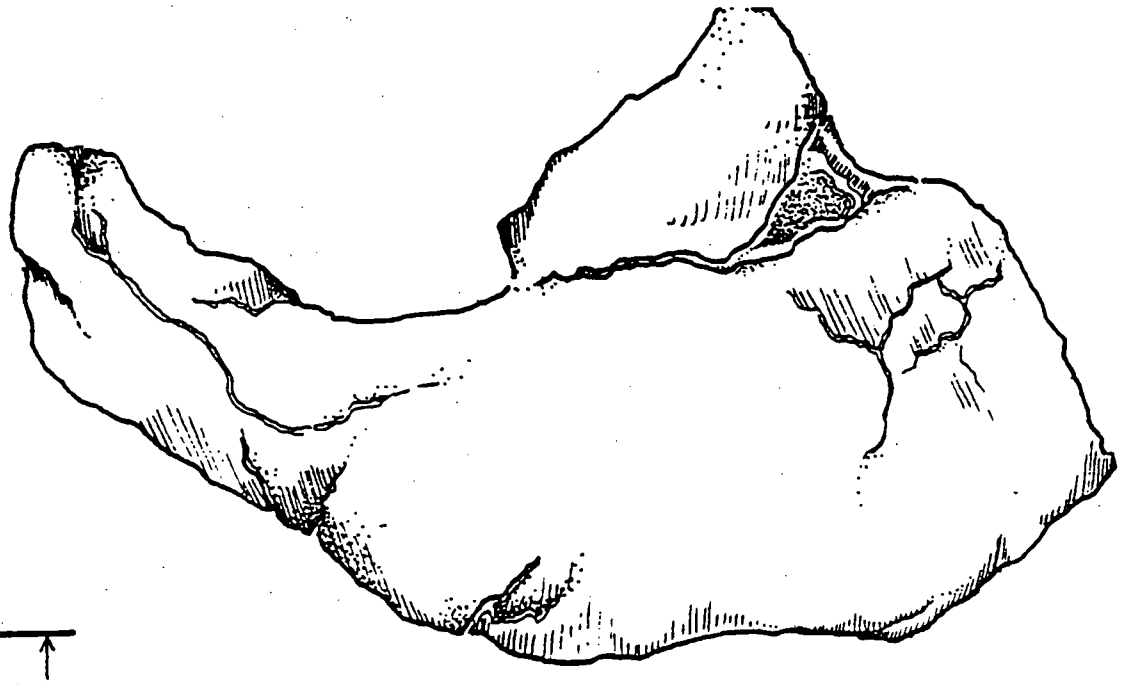
A ¾" thick patty of raw meat this size weighs approx. 4 oz. (3 oz. cooked)

A ½" thick patty of raw meat this size weighs approx. 3 oz. (2½ oz. Cooked)

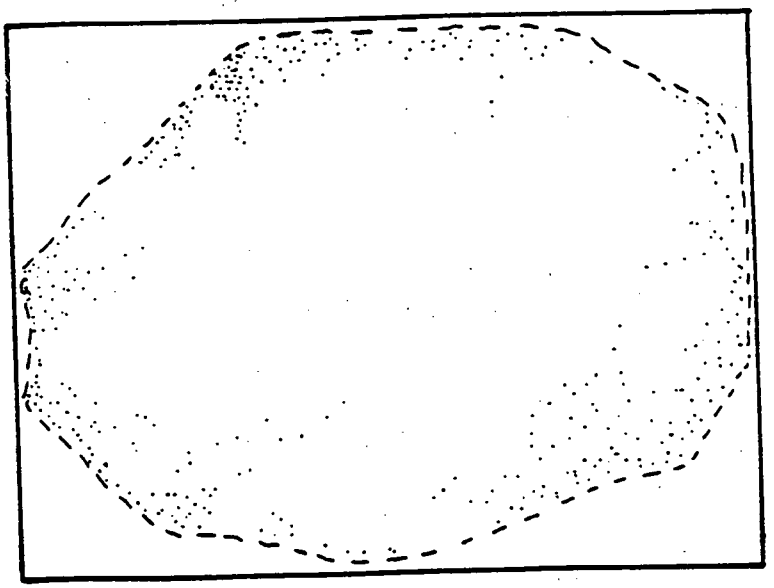


A raw drumstick this size weighs approx 4 oz. Cooked & with skin removed, it yields approx. 2 oz. of meat.

Design and illustration by C. Condruck, 1990



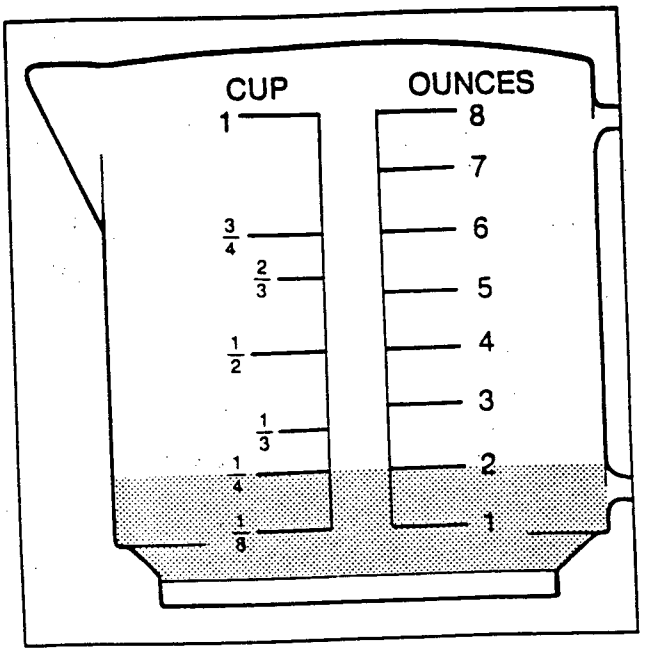
A ¾" thick, raw pork chop this size weighs approx. 4 oz.
(3 oz. cooked)

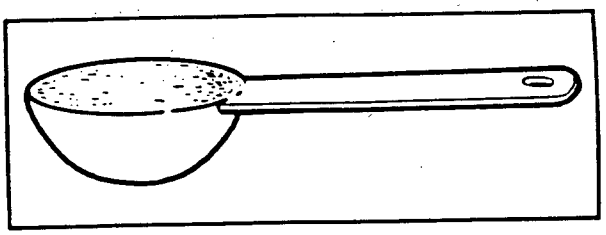


A ¼" thick slice of cooked meat or fish that will fit into the box above weighs approx. 1 oz.

2 slices of cooked meat or fish this size will weigh approx. 2 oz.

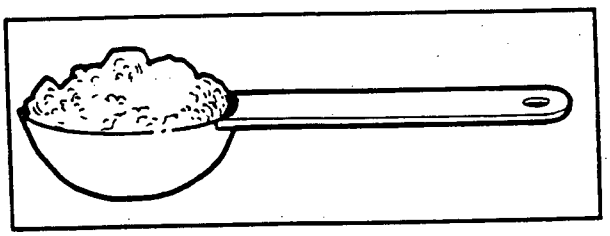
Measuring Utensils





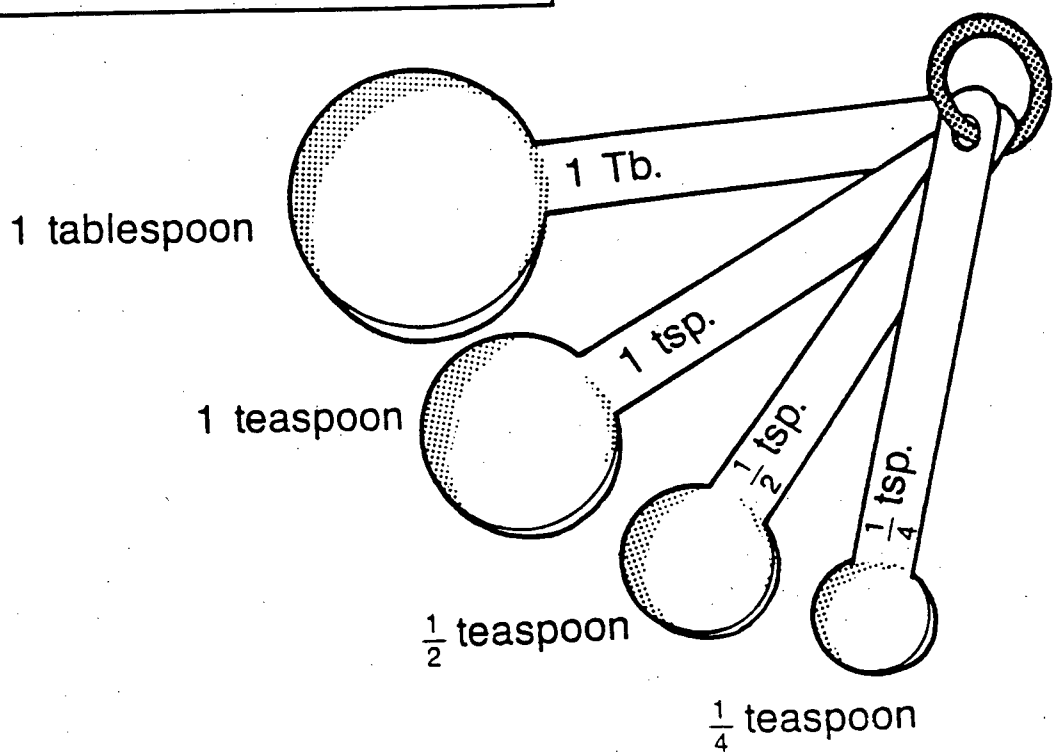
A

A = "level" tablespoon



B

B = "heaping" tablespoon



Food Record

Clinic Number Day of Week Date (dy/mon/yr)

Time of meal		Food and drink items	Quantity
Hour & minute	Eaten at home or away	Use a separate line for each item. Describe carefully as if writing a recipe.	Specify each measure. Eg. gm, oz, tsp or cup

Adapted from Reid, D. Folate and zinc status in hemodialysis patients. MSc thesis, UBC, 1990.

After keeping a record of your food intake for 3 days, please answer the following questions:

1. The amount of food I ate during the past 3 days is:

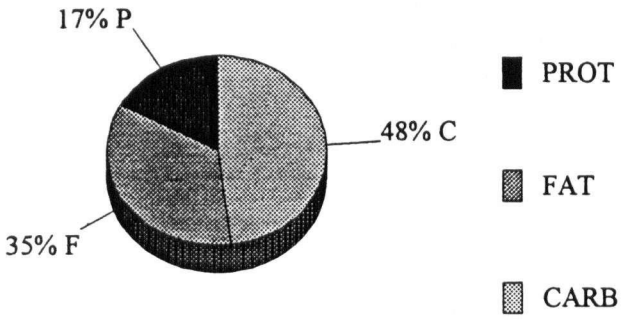
   ☐ less than my usual amount
   ☐ about the same as my usual amount
   ☐ more than my usual amount

2. Please indicate whether you changed the amount you ate (ie. ate more than usual or ate less than usual) because of the following factors:

		ate less than usual	ate more than usual	does not apply
a)	"I changed the amount I ate to take away the feeling of nausea"	☐	☐	☐
b)	"I changed the amount I ate because my appetite was not as good as usual"	☐	☐	☐
c)	"I changed the amount I ate based on the advice from health care workers or family and friends"	☐	☐	☐
d)	"I changed the amount I ate because the smell or taste of food was different"	☐	☐	☐
e)	"I changed the amount I ate because of food prepared/offered by family and friends"	☐	☐	☐
f)	"I changed the amount I ate because I was feeling fatigued"	☐	☐	☐
g)	"I changed the amount I ate to keep my strength up"	☐	☐	☐
h)	"I changed the amount I ate because I was feeling down or worried"	☐	☐	☐

Dietary Analysis

RNI-FEMALE-25 TO 49 YEARS
RESEARCH STUDY



Minerals

	Your Intake	Goal Amount	Goal %
Sodium	2718 mg	1.0 mg	**** %
Potassium	2780 mg	1.0 mg	**** %
Iron	18.32 mg	13.0 mg	141 %
Calcium	1008 mg	700.0 mg	144 %
Magnesium	295.6 mg	200.0 mg	148 %
Phosphorus	1226 mg	850.0 mg	144 %
Zinc	8.375 mg	9.0 mg	93 %
Copper	1.236 mg	1.0 mg	124 %
Manganese	3.812 mg	1.0 mg	381 %
Selenium	0.053 mg	1.000 mg	5 %
Fluoride	15659 Ug	1.0 Ug	**** %
Chromium	0.078 mg	1.000 mg	8 %
Iodine	- Ug	160.0 Ug	- %
Molybdenum	19.28 Ug	1.0 Ug	1928 %

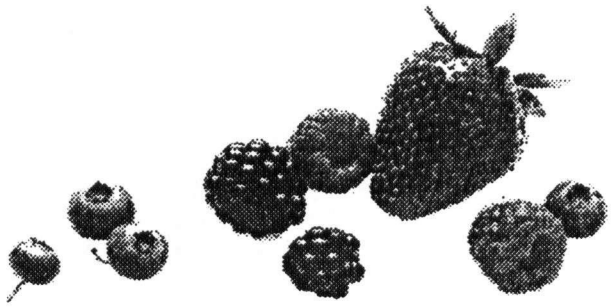
Nutritionist IV v.4.0 First DataBank

Macronutrients

	Your Intake	Goal Amount	Goal %
Calories	1915 Cals	2000 Kc	96 %
Protein	86.18 Gm	44.0 Gm	196 %
Carbohydrate	243.1 Gm	275.0 Gm	88 %
Fat	78.9 Gm	66.7 Gm	118 %
Saturated Fat	23.14 Gm	22.2 Gm	104 %
Mono Fat	20.07 Gm	22.2 Gm	90 %
Poly Fat	12.37 Gm	22.2 Gm	56 %
Other Fat	23.32 Gm		
Cholesterol	356.7 mg	1.0 mg	5670 %
Dietary Fiber	16.85 Gm	1.0 Gm	1685 %
Sugar	60.2 Gm		

Vitamins

	Your Intake	Goal Amount	Goal %
Vitamin A	1448 RE	800.0 RE	181 %
Thiamin B1	1.918 mg	.8 mg	240 %
Riboflavin B2	1.67 mg	1.0 mg	167 %
Niacin B3	16.52 mg	14.0 mg	118 %
Pyridoxine B6	1.726 mg	1.0 mg	173 %
Folate	338.8 Ug	175.0 Ug	194 %
Cobalamin B12	2.132 Ug	2.0 Ug	107 %
Vitamin E	13.91 mg	- mg	232 %
A-Tocopherol	27.2 mg	1.0 mg	2720 %
Pant. Acid	4.212 mg	1.0 mg	421 %
Biotin	31.39 Ug	1.0 Ug	3139 %
Vitamin C	155.2 mg	30.0 mg	517 %
Vitamin D	2.943 Ug	2.5 Ug	118 %
Vitamin K	205 Ug	1.0 Ug	**** %



Activity Diary

An accurately completed diary describing the types and amounts of physical activity you participate in over three days will be used to measure your level of activity before, during, and after treatment.

FOR THREE (3) DAYS IN A ROW, RECORD:

1. ALL ACTIVITIES such as exercise (eg. walking) and home activities (eg. dish washing), child-care activitites, self-care activities and work-related activities, as well as resting, sitting, lying and sleeping.
2. RECORD EACH ACTIVITY UNDER THE APPROPRIATE INTENSITY LEVEL. For example, sitting quietly reading a book would be recorded under "very light activities" on the attached forms. See the sample physical activity diary below.
3. RECORD THE AMOUNT OF TIME (in minutes or hours) spent at each of the activities you list; the total hours for each day should add up to 24 hours.
4. USE A SEPARATE PAGE FOR EACH DAY. If you require additional space for any of the days, use the extra page provided.

Sample Physical Activity Diary:

Description of Activity	**Amount of Time (minutes or hours)**
Inactivity:	
sleep	*8 hours*
lying quietly, awake	*45 minutes*
Very light activities:	
sitting, reading a book or newspaper	*1 hour*
sitting, eating	*15 minutes*
Light activities:	
light cleaning, dusting, vacuuming	*30 minutes*
dressing	*10 minutes*
Moderate activities:	
child care, sitting and bathing, dressing	*30 minutes*

Sample List of Physical Activities:

Inactivity:

- *sleeping*
- *bathing, sitting*
- *lying quietly, reclining (eg. watching television)*
- *lying quietly, in bed, awake*
- *sitting quietly, (eg. riding in car, listening to music, watching a movie)*
- *reclining, talking or talking on the telephone*
- *reclining, reading*
- *reclining, writing*

Very Light Activity:

- *sitting, reading a book or newspaper, etc.*
- *sitting, talking or talking on the telephone*
- *sitting, playing cards, playing a board game*
- *sitting, eating*
- *sitting, writing, desk work*
- *sitting, studying, general, including reading and/or writing*
- *sitting, meetings, general*
- *sitting, light office work (eg. chemistry lab, light use of handtools, watch repair, light assembly/repair)*
- *typing, electric, manual or computer*

Light Activity:

- *implied standing (eg. folding or hanging laundry, packing)*
- *making bed*
- *walking, less than 2.0 mph, level ground, strolling, household walking, very slow*
- *ironing*
- *washing dishes, general*
- *cooking or food preparation, general*
- *cleaning, light (eg. dusting, straightening up, vacuuming, changing linen, carrying out trash), moderate effort*
- *sweeping floors*
- *sitting or standing, grooming (eg. washing, shaving, brushing teeth, urinating, putting on make-up)*
- *dressing, undressing*
- *standing, light (eg. bartending, store clerk, assembling, filing, xeroxing)*
- *walking, 2.0 mph, level, slow pace*
- *walking, pushing or pulling stroller with child*
- *standing, playing with children*

Sample List continued...

Moderate Activity:

- *walk/run, playing with children, moderate*
- *child care (eg. sitting/kneeling, dressing, bathing, feeding, occasional lifting), light*
- *child care (eg. standing/dressing, bathing, occasional lifting), light effort*
- *walking, carrying infant or 15 lbs. load (eg. suitcase), level ground*
- *walking, for pleasure, work break, walking the dog*
- *walking, 2.5 mph, firm surface*
- *walking, 3.0 mph, level, moderate pace*
- *walking, 3.5 mph, level, brisk*
- *food shopping, with grocery cart*
- *cleaning house, general*
- *cleaning, heavy (eg. wash car, wash windows, mop, clean garage), vigorous effort*
- *bicycling, stationary, very light effort*
- *bicycling, <10 mph, general leisure, to work or for pleasure*
- *weight lifting, light workout, general*

Vigorous Activity:

- *bicycling, stationary, general*
- *bicycling, stationary, moderate effort*

Very Vigorous Activity:

- *bicycling, 10–11.9 mph, general, leisure, slow, light effort*
- *bicycling, 12–13.9 mph, leisure, moderate effort*
- *bicycling, stationary, moderate effort*
- *swimming, freestyle, slow, moderate or light effort*
- *swimming, leisurely, not lap swimming, general*
- *walking, carrying load upstairs, general*

Activity Diary: Day 1

Name | Clinic Number | Date (dy/mon/yr)

Description of Activity	**Amount of Time (minutes or hours)**
Inactivity (eg. sleeping, lying quietly or watching television):	
Very light activities (eg. sitting, eating or reading):	
Light Activities (eg. cooking, dressing, walking at a slow pace):	
Moderate Activities (eg. general cleaning, food shopping with cart):	

Vigorous Activities (eg. scrubbing floors, gardening, golf):

_____

_____

_____

Very vigorous Activities (eg. skiing, running, hiking):

_____

_____

_____

Total hours (should equal 24 hours): _____

Activity Diary, continued

When you have completed the 3 day activity diary, please indicate:

A) WHETHER THIS WAS A USUAL AMOUNT OF ACTIVITY FOR YOU:

☐ **yes**, this diary describes my usual activity

☐ **no**, this was not my usual activity, because _____

_____

_____

_____

MY USUAL ACTIVITY WOULD INCLUDE: _____

_____

_____

_____

B) OVERALL, FOR THE THREE DAYS YOU KEPT A DIARY WAS THE AMOUNT OF ACTIVITY :

☐ less than usual
☐ about the same as usual
☐ more than usual

C) LASTLY, RATE YOUR ACTIVITY LEVEL BY CHECKING ONE OF THE BOXES BELOW:

☐ active/no change
☐ moderate (able to perform some household/work activities)
☐ mild (able to care for self)
☐ none (bedridden)

APPENDIX 1. Compendium of Physical Activities.

01009	8.5	Bicycling,	Bicycling, BMX or mountain
01010	4.0	Bicycling,	Bicycling, <10 mph, general, leisure, to work or for pleasure (T115)
01020	6.0	Bicycling,	Bicycling, 10–11.9 mph, leisure, slow, light effort
01030	8.0	Bicycling,	Bicycling, 12–13.9 mph, leisure, moderate effort
01040	10.0	Bicycling,	Bicycling, 14–15.9 mph, racing or leisure, fast, vigorous effort
01050	12.0	Bicycling,	Bicycling, 16–19 mph, racing/not drafting or >19 mph drafting, very fast, racing general
01060	16.0	Bicycling,	Bicycling, >20 mph, racing, not drafting
)1070	5.0	Bicycling,	Unicycling
J2010	5.0	Conditioning exercise,	Bicycling, stationary, general
02011	3.0	Conditioning exrecise,	Bicycling, stationary, 50 W, very light effort
02012	5.5	Conditioning exercise,	Bicycling, stationary, 100 W, light effort
02013	7.0	Conditioning exercise,	Bicycling, stationary, 150 W, moderate effort
02014	10.5	Conditioning exercise,	Bicycling, stationary, 200 W, vigorous effort
02015	12.5	Conditioning exercise,	Bicycling, stationary, 250 W, very vigorous effort
02020	8.0	Conditioning exercise,	Calisthenics (e.g., pushups, pullups, situps), heavy, vigorous effort
02030	4.5	Conditioning exercise,	Calisthenics, home exercise, light or moderate effort, general (T 150) (example: back exercises), going up & down from floor
02040	8.0	Conditioning exercise,	Circuit training, general
02050	6.0	Conditioning exercise,	Weight lifting (free weight, nautilus or universal-type), power lifting or body building, vigorous effort (T 210)

APPENDIX 1. Continued

02060	5.5	Conditioning exercise,	Health club exercise, general (T 160)
02065	6.0	Conditioning exercise,	Stair-treadmill ergometer, general
02070	9.5	Conditioning exercise,	Rowing, stationary ergometer, general
02071	3.5	Conditioning exercise,	Rowing, stationary, 50 W, light effort
02072	7.0	Conditioning exercise,	Rowing, stationary, 100 W, moderate effort
02073	8.5	Conditioning exercise,	Rowing, stationary, 150 W, vigorous effort
02074	12.0	Conditioning exercise,	Rowing, stationary, 200 W, very vigorous effort
02080	9.5	Conditioning exercise,	Ski machine, general
02090	6.0	Conditioning exercise,	Slimnastics
02100	4.0	Conditioning exercise,	Stretching, hatha yoga
02110	6.0	Conditioning exercise,	Teaching aerobic exercise class
02120	4.0	Conditioning exercise,	Water aerobics, water calisthenics
02130	3.0	Conditioning exercise,	Weight lifting (free, nautilus or universal-type), light or moderate effort, light workout, general
02135	1.0	Conditioning exercise,	Whirlpool, sitting
03010	6.0	Dancing,	Aerobic, ballet or modern, twist
03015	6.0	Dancing,	Aerobic, general
03020	5.0	Dancing,	Aerobic, low impact
03021	7.0	Dancing,	Aerobic, high impact
03025	4.5	Dancing,	General
03030	5.5	Dancing,	Ballroom, fast (disco, folk, square) (T 125)
03040	3.0	Dancing,	Ballroom, slow (e.g., waltz, foxtrot, slow dancing)
04001	4.0	Fishing and hunting,	Fishing, general
04010	4.0	Fishing and hunting,	Digging worms, with shovel
04020	5.0	Fishing and hunting,	Fishing from river bank and walking
04030	2.5	Fishing and hunting,	Fishing from boat, sitting
04040	3.5	Fishing and hunting,	Fishing from river bank, standing (T 660)
04050	6.0	Fishing and hunting,	Fishing in stream, in waders (T 670)
05080	1.5	Home activities,	Sitting, knitting, sewing, light wrapping (presents)
05090	2.0	Home activities,	Implied standing-laundry, fold or hang clothes, put clothes in washer or dryer, packing suitcase
05095	2.3	Home activities,	Implied walking-putting away clothes, gathering clothes to pack, putting away laundry
05100	2.0	Home activities,	Making bed
05110	5.0	Home activities,	Maple syruping/sugar bushing (including carrying buckets, carrying wood)
05120	6.0	Home activities,	Moving furniture, household
05130	5.5	Home activities,	Scrubbing floors, on hands and knees
05140	4.0	Home activities,	Sweeping garage, sidewalk or outside of house
05145	7.0	Home activities,	Moving household items, carrying boxes
05146	3.5	Home activities,	Standing-packing/unpacking boxes, occasional lifting of household items light-moderate effort
05147	3.0	Home activities,	Implied walking-putting away household items-moderate effort
05150	9.0	Home activities,	Move household items upstairs, carrying boxes or furniture
05160	2.5	Home activities,	Standing-light (pump gas, change light bulb, etc.)
05165	3.0	Home activities,	Walking-light, noncleaning (ready to leave, shut/lock doors, close windows, etc.)
05170	2.5	Home activities,	Sitting-playing with child(ren)-light
05171	2.8	Home activities,	Standing-playing with child(ren)-light
05175	4.0	Home activities,	Walk/run-playing with child(ren)-moderate
05180	5.0	Home activities,	Walk/run-playing with child(ren)-vigorous

04050	6.0	Fishing and hunting,	Fishing in stream, in waders (T 670)
04060	2.0	Fishing and hunting,	Fishing, ice, sitting
04070	2.5	Fishing and hunting,	Hunting, bow and arrow or crossbow
04080	6.0	Fishing and hunting,	Hunting, deer, elk, large game (T 710)
04090	2.5	Fishing and hunting,	Hunting, duck, wading
04100	5.0	Fishing and hunting,	Hunting, general
04110	6.0	Fishing and hunting,	Hunting, pheasants or grouse (T 680)
04120	5.0	Fishing and hunting,	Hunting, rabbit, squirrel, prairie chick, raccoon, small game (T 690)
04130	2.5	Fishing and hunting,	Pistol shooting or trap shooting, standing
05010	2.5	Home activities,	Carpet sweeping, sweeping floors
05020	4.5	Home activities,	Cleaning, heavy or major (e.g., wash car, wash windows, mop, clean garage), vigorous effort
05030	3.5	Home activities,	Cleaning, house or cabin, general
05040	2.5	Home activities,	Cleaning, light (dusting, straightening up, vacuuming, changing linen, carrying out trash), moderate effort
05041	2.3	Home activities,	Wash dishes-standing or in general (not broken into stand/walk components)
	2.3	Home activities,	Wash dishes; clearing dishes from table-walking
05050	2.5	Home activities,	Cooking or food preparation-standing or sitting or in general (not broken into stand/walk components)
05051	2.5	Home activities,	Serving food, setting table-implied walking or standing
05052	2.5	Home activities,	Cooking or food preparation-walking
05055	2.5	Home activities,	Putting away groceries (e.g., carrying groceries, shopping without a grocery cart)
05056	8.0	Home activities,	Carrying groceries upstairs
05060	3.5	Home activities,	Food shopping, with grocery cart
05065	2.0	Home activities,	Standing-shopping (non-grocery shopping)
05066	2.3	Home activities,	Walking-shopping (non-grocery shopping)
05070	2.3	Home activities,	Ironing
05185	3.0	Home activities,	ous Child care: sitting/kneeling-dressing, bathing, grooming, feeding, occasional lifting of child-light effort
05186	3.5	Home activities,	Child care: standing-dressing, bathing, grooming, feeding, occasional lifting of child-light effort
06010	3.0	Home repair,	Airplane repair
06020	4.5	Home repair,	Automobile body work
06030	3.0	Home repair,	Automobile repair
06040	3.0	Home repair,	Carpentry, general, workshop (T 620)
06050	6.0	Home repair,	Carpentry, outside house (T 640), installing rain gutters
06060	4.5	Home repair,	Carpentry, finishing or refinishing cabinets or furniture
06070	7.5	Home repair,	Carpentry, sawing hardwood
06080	5.0	Home repair,	Caulking, chinking log cabin
06090	4.5	Home repair,	Caulking, except log cabin
06100	5.0	Home repair,	Cleaning gutters
06110	5.0	Home repair,	Excavating garage
06120	5.0	Home repair,	Hanging storm windows
06130	4.5	Home repair,	Laying or removing carpet
06140	4.5	Home repair,	Laying tile or linoleum
06150	5.0	Home repair,	Painting, outside house (T 650)
06160	4.5	Home repair,	Painting, papering, plastering, scraping, inside house, hanging sheet rock, remodeling (T 630)
06170	3.0	Home repair,	Put on and removal of tarp-sailboat
06180	6.0	Home repair,	Roofing
06190	4.5	Home repair,	Sanding floors with a power sander
06200	4.5	Home repair,	Scrape and paint sailboat or powerboat
06210	5.0	Home repair,	Spreading dirt with a shovel
06220	4.5	Home repair,	Wash and wax hull of sailboat, car, powerboat, airplane
06230	4.5	Home repair,	Washing fence
06240	3.0	Home repair,	Wiring, plumbing
07010	0.9	Inactivity, quiet	Lying quietly, reclining (watch television), lying quietly in bed-awake

APPENDIX 1. Continued

07020	1.0	Inactivity, quiet	Sitting quietly (riding in a car, listening to a lecture or music, watch television or a movie)
07030	0.9	Inactivity, quiet	Sleeping
07040	1.2	Inactivity, quiet	Standing quietly (standing in a line)
07050	1.0	Inactivity, light	Recline-writing
07060	1.0	Inactivity, light	Recline-talking or talking on phone
07070	1.0	Inactivity, light	Recline-reading
08010	5.0	Lawn and garden,	Carrying, loading or stacking wood, loading/unloading or carrying lumber
08020	6.0	Lawn and garden,	Chopping wood, splitting logs
08030	5.0	Lawn and garden,	Clearing land, hauling branches
08040	5.0	Lawn and garden,	Digging sandbox
08050	5.0	Lawn and garden,	Digging, spading, filling garden (T 590)
08060	6.0	Lawn and garden,	Gardening with heavy power tools, tilling a garden (see occupation, shoveling)
08080	5.0	Lawn and garden,	Laying crushed rock
08090	5.0	Lawn and garden,	Laying sod
08095	5.5	Lawn and garden,	Mowing lawn, general
08100	2.5	Lawn and garden,	Mowing lawn, riding mower (T 550)
08110	6.0	Lawn and garden,	Mowing lawn, walk, hand mower (T 570)
08120	4.5	Lawn and garden,	Mowing lawn, walk, power mower (T 590)
08130	4.5	Lawn and garden,	Operating snow blower, walking
08140	4.0	Lawn and garden,	Planting seedlings, shrubs
08150	4.5	Lawn and garden,	Planting trees
08160	4.0	Lawn and garden,	Raking lawn (T 600)
08170	4.0	Lawn and garden,	Raking roof with snow rake
08180	3.0	Lawn and garden,	Riding snow blower
08190	4.0	Lawn and garden,	Sacking grass, leaves
08200	6.0	Lawn and garden,	Shoveling, snow, by hand (T 610)
08210	4.5	Lawn and garden,	Trimming shrubs or trees, manual cutter
08215	3.5	Lawn and garden,	Trimming shrubs or trees, power cutter
08220	2.5	Lawn and garden,	Walking, applying fertilizer or seeding a lawn
11020	2.3	Occupation,	Bookbinding
11030	6.0	Occupation,	Building road (including hauling debris, driving heavy machinery)
11035	2.0	Occupation,	Building road, directing traffic (standing)
11040	3.5	Occupation,	Carpentry, general
11050	8.0	Occupation,	Carrying heavy loads, such as bricks
11060	8.0	Occupation,	Carrying moderate loads up stairs, moving boxes (16–40 pounds)
11070	2.5	Occupation,	Chambermaid
11080	6.5	Occupation,	Coal mining, drilling coal, rock
11090	6.5	Occupation,	Coal mining, erecting supports
11100	6.0	Occupation,	Coal mining, general
11110	7.0	Occupation,	Coal mining, shoveling coal
11120	5.5	Occupation,	Construction, outside, remodeling
11130	3.5	Occupation,	Electrical work, plumbing
11140	8.0	Occupation,	Farming, baling hay, cleaning barn, poultry work
11150	3.5	Occupation,	Farming, chasing cattle, nonstrenuous
11160	2.5	Occupation,	Farming, driving harvester
11170	2.5	Occupation,	Farming, driving tractor
11180	4.0	Occupation,	Farming, feeding small animals
11190	4.5	Occupation,	Farming, feeding cattle
11200	8.0	Occupation,	Farming, forking straw bales
11210	3.0	Occupation,	Farming, milking by hand
11220	1.5	Occupation,	Farming, milking by machine
11230	5.5	Occupation,	Farming, shoveling grain
11240	12.0	Occupation,	Fire fighter, general
11245	11.0	Occupation,	Fire fighter, climbing ladder with full gear
11246	8.0	Occupation,	Fire fighter, hauling hoses on ground
11250	17.0	Occupation,	Forestry, ax chopping, fast
11260	5.0	Occupation,	Forestry, ax chopping, slow
11270	7.0	Occupation,	Forestry, barking trees
11280	11.0	Occupation,	Forestry, carrying logs
11290	8.0	Occupation,	Forestry, felling trees
11300	8.0	Occupation,	Forestry, general
11310	5.0	Occupation,	Forestry, hoeing

08230	1.5	Lawn and garden,	Watering lawn or garden, standing or walking
08240	4.5	Lawn and garden,	Weeding, cultivating garden (T 580)
08245	5.0	Lawn and garden,	Gardening, general
08250	3.0	Lawn and garden,	Implied walking/standing-picking up yard, light
09010	1.5	Miscellaneous,	Sitting, card playing, playing board games
09020	2.0	Miscellaneous,	Standing-drawing (writing), casino gambling
09030	1.3	Miscellaneous,	Sitting-reading, book, newspaper, etc.
09040	1.8	Miscellaneous,	Sitting-writing, desk work
09050	1.8	Miscellaneous,	Standing-talking or talking on the phone
09055	1.5	Miscellaneous,	Sitting-talking or talking on the phone
09060	1.8	Miscellaneous,	Sitting-studying, general, including reading and/or writing
09065	1.8	Miscellaneous,	Sitting-in class, general, including note-taking or class discussion
09070	1.8	Miscellaneous,	Standing-reading
10010	1.8	Music playing,	Accordion
10020	2.0	Music playing,	Cello
10030	2.5	Music playing,	Conducting
10040	4.0	Music playing,	Drums
10050	2.0	Music playing,	Flute (sitting)
10060	2.0	Music playing,	Horn
10070	2.5	Music playing,	Piano or organ
10080	3.5	Music playing,	Trombone
10090	2.5	Music playing,	Trumpet
10100	2.5	Music playing,	Violin
10110	2.0	Music playing,	Woodwind
10120	2.0	Music playing,	Guitar, classical, folk (sitting)
10125	3.0	Music playing,	Guitar, rock and roll band (standing)
10130	4.0	Music playing,	Marching band, playing an instrument, baton twirling (walking)
10135	3.5	Music playing,	Marching band, drum major (walking)
11010	4.0	Occupation,	Bakery, general
11320	6.0	Occupation,	Forestry, planting by hand
11330	7.0	Occupation,	Forestry, sawing by hand
11340	4.5	Occupation,	Forestry, sawing, power
11350	9.0	Occupation,	Forestry, trimming trees
11360	4.0	Occupation,	Forestry, weeding
11370	4.5	Occupation,	Furriery
11380	6.0	Occupation,	Horse grooming
11390	8.0	Occupation,	Horse racing, galloping
11400	6.5	Occupation,	Horse racing, trotting
11410	2.6	Occupation,	Horse racing, walking
11420	3.5	Occupation,	Locksmith
11430	2.5	Occupation,	Machine tooling, machining, working sheet metal
11440	3.0	Occupation,	Machine tooling, operating lathe
11450	5.0	Occupation,	Machine tooling, operating punch press
11460	4.0	Occupation,	Machine tooling, tapping and drilling
11470	3.0	Occupation,	Machine tooling, welding
11480	7.0	Occupation,	Masonry, concrete
11485	4.0	Occupation,	Masseur, masseuse (standing)
11490	7.0	Occupation,	Moving, pushing heavy objects, 75 lbs or more (desks, moving van work)
11500	2.5	Occupation,	Operating heavy duty equipment/automated, not driving
11510	4.5	Occupation,	Orange grove work
11520	2.3	Occupation,	Printing (standing)
11525	2.5	Occupation,	Police, directing traffic (standing)
11526	2.0	Occupation,	Police, driving a squad car (sitting)
11527	1.3	Occupation,	Police, riding in a squad car (sitting)
11528	8.0	Occupation,	Police, making an arrest (standing)
11530	2.5	Occupation,	Shoe repair, general
11540	8.5	Occupation,	Shoveling, digging ditches
11550	9.0	Occupation,	Shoveling, heavy (more than 16 lbs · min^{-1})
11560	6.0	Occupation,	Shoveling, light (less than 10 lbs · min^{-1})
11570	7.0	Occupation,	Shoveling, moderate (10–15 lbs · min^{-1})

APPENDIX 1. Continued

11580	1.5	Occupation,	Sitting-light office work, in general (chemistry lab work, light use of handtools, watch repair or micro-assembly, light assembly/repair)
11585	1.5	Occupation,	Sitting-meetings, general, and/or with talking involved
11590	2.5	Occupation,	Sitting; moderate (heavy levers, riding mower/forklift, crane operation)
11600	2.5	Occupation,	Standing; light (bartending, store clerk, assembling, filing, xeroxing, put up Christmas tree)
11610	3.0	Occupation,	Standing; light/moderate (assemble/repair heavy parts, welding, stocking, auto repair, pack boxes for moving, etc.), patient care (as in nursing)
11620	3.5	Occupation,	Standing; moderate (assembling at fast rate, lifting 50 lbs, hitch/twisting ropes)
11630	4.0	Occupation,	Standing; moderate/heavy (lifting more than 50 lb, masonry, painting, paper hanging)
11640	5.0	Occupation,	Steel mill, fettling
11650	5.5	Occupation,	Steel mill, forging
11660	8.0	Occupation,	Steel mill, hand rolling
11670	8.0	Occupation,	Steel mill, merchant mill rolling
11680	11.0	Occupation,	Steel mill, removing slag
11690	7.5	Occupation,	Steel mill, tending furnace
11700	5.5	Occupation,	Steel mill, tipping molds
11710	8.0	Occupation,	Steel mill, working in general
11720	2.5	Occupation,	Tailoring, cutting
11730	2.5	Occupation,	Tailoring, general
11740	2.0	Occupation,	Tailoring, hand sewing
11750	2.5	Occupation,	Tailoring, machine sewing
11760	4.0	Occupation,	Tailoring, pressing
11766	6.5	Occupation,	Truck driving, loading and unloading truck (standing)
12090	13.5	Running,	Running, 8 mph (7.5 min · mile^{-1})
12100	14.0	Running,	Running, 8.6 mph (7 min · mile^{-1})
12110	15.0	Running,	Running, 9 mph (6.5 min · mile^{-1})
12120	16.0	Running,	Running, 10 mph (6 min · mile^{-1})
12130	18.0	Running,	Running, 10.9 mph (5.5 min · mile^{-1})
12140	9.0	Running,	Running, cross-country
12150	8.0	Running,	Running, general (T 200)
12160	8.0	Running,	Running, in place
12170	15.0	Running,	Running, stairs, up
12180	10.0	Running,	Running, on a track, team practice
12190	8.0	Running,	Running, training, pushing wheelchair, marathon wheeling
12195	3.0	Running,	Running, wheeling, general
13000	2.5	Self-care,	Standing-getting ready for bed, in general
13009	1.0	Self-care,	Sitting on toilet
13010	2.0	Self-care,	Bathing (sitting)
13020	2.5	Self-care,	Dressing, undressing (standing or sitting)
13030	1.5	Self-care,	Eating (sitting)
13035	2.0	Self-care,	Talking and eating or eating only (standing)
13040	2.5	Self-care,	Sitting or standing-grooming (washing, shaving, brushing teeth, urinating, washing hands, put on make-up)
13050	4.0	Self-care,	Showering, toweling off (standing)
14010	1.5	Sexual activity,	Active, vigorous effort
14020	1.3	Sexual activity,	General, moderate effort
14030	1.0	Sexual activity,	Passive, light effort, kissing, hugging
15010	3.5	Sports,	Archery (nonhunting)
15020	7.0	Sports,	Badminton, competitive (T 450)
15030	4.5	Sports,	Badminton, social singles and doubles, general
15040	8.0	Sports,	Basketball, game (T 490)
15050	6.0	Sports,	Basketball, nongame, general (T 480)
15060	7.0	Sports,	Basketball, officiating (T 500)

11770	1.5	Occupation,	Typing, electric, manual or computer
11780	6.0	Occupation,	Using heavy power tools such pneumatic tools (jackhammers, drills, etc.)
11790	8.0	Occupation,	Using heavy tools (not power) such as shovel, pick, tunnel bar, spade
11791	2.0	Occupation,	Walking on job, less than 2.0 mph (in office or lab area), very slow
11792	3.5	Occupation,	Walking on job, 3.0 mph, in office, moderate speed, not carrying anything
11793	4.0	Occupation,	Walking on job, 3.5 mph, in office, brisk speed, not carrying anything
11795	3.0	Occupation,	Walking, 2.5 mph, slowly and carrying light objects less than 25 lbs
11800	4.0	Occupation,	Walking, 3.0 mph, moderately and carrying light objects less than 25 lbs
11810	4.5	Occupation,	Walking, 3.5 mph, briskly and carrying objects less than 25 lbs
11820	5.0	Occupation,	Walking or walk downstairs or standing, carrying objects about 25–49 lbs
11830	6.5	Occupation,	Walking or walk downstairs or standing, carrying objects about 50–74 lbs
11840	7.5	Occupation,	Walking or walk downstairs or standing, carrying objects about 75–99 lbs
11850	8.5	Occupation,	Walking or walk downstairs or standing, carrying objects about 100 lbs and over
11870	3.0	Occupation,	Working in scene shop, theater actor, backstage, employee
12010	6.0	Running,	Job/walk combination (jobbing component of less than 10 min) (T 180)
12020	7.0	Running,	Jogging, general
12030	8.0	Running,	Running, 5 mph (12 min · mile^{-1})
12040	9.0	Running,	Running, 5.2 mph (11.5 min · mile^{-1})
12050	10.0	Running,	Running, 6 mph (10 min · mile^{-1})
12060	11.0	Running,	Running, 6.7 mph (9 min · mile^{-1})
12070	11.5	Running,	Running, 7 mph (8.5 min · mile^{-1})
12080	12.5	Running,	Running, 7.5 mph (8 min · mile^{-1})
15070	4.5	Sports,	Basketball, shooting baskets
15075	6.5	Sports,	Basketball, wheelchair
15080	2.5	Sports,	Billiards
15090	3.0	Sports,	Bowling (T 390)
15100	12.0	Sports,	Boxing, in ring, general
15110	6.0	Sports,	Boxing, bunching bag
15120	9.0	Sports,	Boxing, sparring
15130	7.0	Sports,	Broomball
15135	5.0	Sports,	Children's games (hopscotch, 4-square, dodgeball, playground apparatus, t-ball, tetherball, marbles, jacks, arcade games)
15140	4.0	Sports,	Coaching: football, soccer, basketball, baseball, swimming, etc.
15150	5.0	Sports,	Cricket (batting, bowling)
15160	2.5	Sports,	Croquet
15170	4.0	Sports,	Curling
15180	2.5	Sports,	Darts, wall or lawn
15190	6.0	Sports,	Drag racing, pushing or driving a car
15200	6.0	Sports,	Fencing
15210	9.0	Sports,	Football, competitive
15230	8.0	Sports,	Football, touch, flag, general (T 510)
15235	2.5	Sports,	Football or baseball, playing catch
15240	3.0	Sports,	Frisbee playing, general
15250	3.5	Sports,	Frisbee, ultimate
15255	4.5	Sports,	Golf, general
15260	5.5	Sports,	Golf, carrying clubs (T 090)
15270	3.0	Sports,	Golf, miniature, driving range
15280	5.0	Sports,	Golf, pulling clubs (T 080)
15290	3.5	Sports,	Golf, using power cart (T 070)
15300	4.0	Sports,	Gymnastics, general
15310	4.0	Sports,	Hacky sack
15320	12.0	Sports,	Handball, general (T 520)
15330	8.0	Sports,	Handball, team
15340	3.5	Sports,	Hang gliding
15350	8.0	Sports,	Hockey, field
15360	8.0	Sports,	Hockey, ice

APPENDIX 1. Continued

15370	4.0	Sports,	Horseback riding, general
15380	3.5	Sports,	Horseback riding, saddling horse
15390	6.5	Sports,	Horseback riding, trotting
15400	2.5	Sports,	Horseback riding, walking
15410	3.0	Sports,	Horseshoe pitching, quoits
15420	12.0	Sports,	Jai alai
15430	10.0	Sports,	Judo, jujitsu, karate, kick boxing, tae kwan do
15440	4.0	Sports,	Juggling
15450	7.0	Sports,	Kickball
15460	8.0	Sports,	Lacrosse
15470	4.0	Sports,	Moto-cross
15480	9.0	Sports,	Orienteering
15490	10.0	Sports,	Paddleball, competitive
15500	6.0	Sports,	Paddleball, casual, general (T 460)
15510	8.0	Sports,	Polo
15520	10.0	Sports,	Racketball, competitive
15530	7.0	Sports,	Racketball, casual, general (T 470)
15535	11.0	Sports,	Rock climbing, ascending rock
15540	8.0	Sports,	Rock climbing, rapelling
15550	12.0	Sports,	Rope jumping, fast
15551	10.0	Sports,	Rope jumping, moderate, general
15552	8.0	Sports,	Rope jumping, slow
15560	10.0	Sports,	Rugby
15570	3.0	Sports,	Shuffleboard, lawn bowling
15580	5.0	Sports,	Skateboarding
15590	7.0	Sports,	Skating, roller (T 360)
15600	3.5	Sports,	Sky diving
15605	10.0	Sports,	Soccer, competitive
15610	7.0	Sports,	Soccer, casual, general (T 540)
15620	5.0	Sports,	Softball or baseball, fast or slow pitch, general (T 440)
15630	4.0	Sports,	Softball, officiating
15640	6.0	Sports,	Softball, pitching
15650	12.0	Sports,	Squash (T 530)
15660	4.0	Sports,	Table tennis, ping pong (T 410)
17130	8.0	Walking,	Up stairs, using or climbing up ladder (T 030)
17140	4.0	Walking,	Using crutches
17150	2.0	Walking,	Walking, less than 2.0 mph, level ground, strolling, household walking, very slow
17160	2.5	Walking,	Walking, 2.0 mph, level, slow pace, firm surface
17170	3.0	Walking,	Walking, 2.5 mph, firm surface
17180	3.0	Walking,	Walking, 2.5 mph, downhill
17190	3.5	Walking,	Walking, 3.0 mph, level, moderate pace, firm surface
17200	4.0	Walking,	Walking, 3.5 mph, level, brisk, firm surface
17210	6.0	Walking,	Walking, 3.5 mph, uphill
17220	4.0	Walking,	Walking, 4.0 mph, level, firm surface, very brisk pace
17230	4.5	Walking,	Walking, 4.5 mph, level, firm surface, very, very brisk
17250	3.5	Walking,	Walking, for pleasure, work break, walking the dog,
17260	5.0	Walking,	Walking, grass track
17270	4.0	Walking,	Walking, to work or class (T 015)
18010	2.5	Water activities,	Boating, power
18020	4.0	Water activities,	Canoeing, on camping trip (T 270)
18030	7.0	Water activities,	Canoeing, portaging
18040	3.0	Water activities,	Canoeing, rowing, 2.0–3.9 mph, light effort
18050	7.0	Water activities,	Canoeing, rowing, 4.0–5.9 mph, moderate effort
18060	12.0	Water activities,	Canoeing, rowing, >6 mph, vigorous effort
18070	3.5	Water activities,	Canoeing, rowing, for pleasure, general (T 250)
18080	12.0	Water activities,	Canoeing, rowing, in competition, or crew or sculling (T 260)

15670	4.0	Sports,	Tai chi
15675	7.0	Sports,	Tennis, general
15680	6.0	Sports,	Tennis, doubles (T 430)
15690	8.0	Sports,	Tennis, singles (T 420)
15700	3.5	Sports,	Trampoline
15710	4.0	Sports,	Volleyball, competitive, in gymnasium (T 400)
15720	3.0	Sports,	Volleyball, noncompetitive; 6–9 member team, general
15725	8.0	Sports,	Volleyball, beach
15730	6.0	Sports,	Wrestling (one match = 5 min)
15731	7.0	Sports,	Wallyball, general
16010	2.0	Transportation,	Automobile or light truck (not a semi) driving
16020	2.0	Transportation,	Flying airplane
16030	2.5	Transportation,	Motor scooter, motor cycle
16040	6.0	Transportation,	Pushing plane in and out of hangar
16050	3.0	Transportation,	Driving heavy truck, tractor, bus
17010	7.0	Walking,	Backpacking, general (T 050)
17020	3.5	Walking,	Carrying infant or 15-lb load (e.g., suitcase), level ground or downstairs
17025	9.0	Walking,	Carrying load upstairs, general
17026	5.0	Walking,	Carrying 1- to 15-lb load, upstairs
17027	6.0	Walking,	Carrying 16- to 24-lb load, upstairs
17028	8.0	Walking,	Carrying 25- to 49-lb load, upstairs
17029	10.0	Walking,	Carrying 50- to 74-lb load, upstairs
17030	12.0	Walking,	Carrying 74+-lb load, upstairs
7035	7.0	Walking,	Climbing hills with 0- to 9-lb load
7040	7.5	Walking,	Climbing hills with 10- to 20-lb load
7050	8.0	Walking,	Climbing hills with 21- to 42-lb load
7060	9.0	Walking,	Climbing hills with 42+-lb load
7070	3.0	Walking,	Downstairs
7080	6.0	Walking,	Hiking, cross country (T 040)
7090	6.5	Walking,	Marching, rapidly, military
7100	2.5	Walking,	Pushing or pulling stroller with child
7110	6.5	Walking,	Race walking
7120	8.0	Walking,	Rock or mountain climbing (T 060)
18090	3.0	Water activities,	Diving, springboard or platform
18100	5.0	Water activities,	Kayaking
18110	4.0	Water activities,	Paddleboat
18120	3.0	Water activities,	Sailing, boat and board sailing, windsurfing, ice sailing, general (T 235)
18130	5.0	Water activities,	Sailing, in competition
18140	3.0	Water activities,	Sailing, Sunfish/Laser/Hobby Cat, keel boats, ocean sailing, yachting
18150	6.0	Water activities,	Skiing, water (T 220)
18160	7.0	Water activities,	Skimobiling
18170	12.0	Water activities,	Skindiving or scuba diving as frogman
18180	16.0	Water activities,	Skindiving, fast
18190	12.5	Water activities,	Skindiving, moderate
18200	7.0	Water activities,	Skindiving, scuba diving, general (T 310)
18210	5.0	Water activities,	Snorkeling (T 320)
18220	3.0	Water activities,	Surfing, body or board
18230	10.0	Water activities,	Swimming laps, freestyle, fast, vigorous effort
18240	8.0	Water activities,	Swimming laps, freestyle, slow, moderate or light effort
18250	8.0	Water activities,	Swimming, backstroke, general
18260	10.0	Water activities,	Swimming, breaststroke, general
18270	11.0	Water activities,	Swimming, butterfly, general
18280	11.0	Water activities,	Swimming, crawl, fast (75 yards · min^{-1}), vigorous effort
18290	8.0	Water activities,	Swimming, crawl, slow (50 yards · min^{-1}), moderate or light effort
18300	6.0	Water activities,	Swimming, lake, ocean, river (T 280, T 295)
18310	6.0	Water activities,	Swimming, leisurely, not lap swimming, general
18320	8.0	Water activities,	Swimming, sidestroke, general
18330	8.0	Water activities,	Swimming, synchronized
18340	10.0	Water activities,	Swimming, treading water, fast vigorous effort

APPENDIX 1. Continued

18350	4.0	Water activities,	Swimming, treading water, moderate effort, general
18360	10.0	Water activities,	Water polo
18365	3.0	Water activities,	Water volleyball
18370	5.0	Water activities,	Whitewater rafting, kayaking, or canoeing
19010	6.0	Winter activities,	Moving ice house (set up/drill holes, etc.)
19020	5.5	Winter activities,	Skating, ice, 9 mph or less
19030	7.0	Winter activities,	Skating, ice, general (T 360)
19040	9.0	Winter activities,	Skating, ice, rapidly, more than 9 mph
19050	15.0	Winter activities,	Skating, speed, competitive
19060	7.0	Winter activities,	Ski jumping (climb up carrying skis)
19075	7.0	Winter activities,	Skiing, general
19080	7.0	Winter activities,	Skiing, cross-country, 2.5 mph, slow or light effort, ski walking
19090	8.0	Winter activities,	Skiing, cross-country, 4.0–4.9 mph, moderate speed and effort, general
19100	9.0	Winter activities,	Skiing, cross-country, 5.0–7.9 mph, brisk speed, vigorous effort
19110	14.0	Winter activities,	Skiing, cross-country, >8.0 mph, racing
19130	16.5	Winter activities,	Skiing, cross-country, hard snow, uphill, maximum
19150	5.0	Winter activities,	Skiing, downhill, light effort
19160	6.0	Winter activities,	Skiing, downhill, moderate effort, general
19170	8.0	Winter activities,	Skiing, downhill, vigorous effort, racing
19180	7.0	Winter activities,	Sledding, tobogganing, bobsledding, luge (T 370)
19190	8.0	Winter activities,	Snow shoeing
19200	3.5	Winter activities,	Snowmobiling

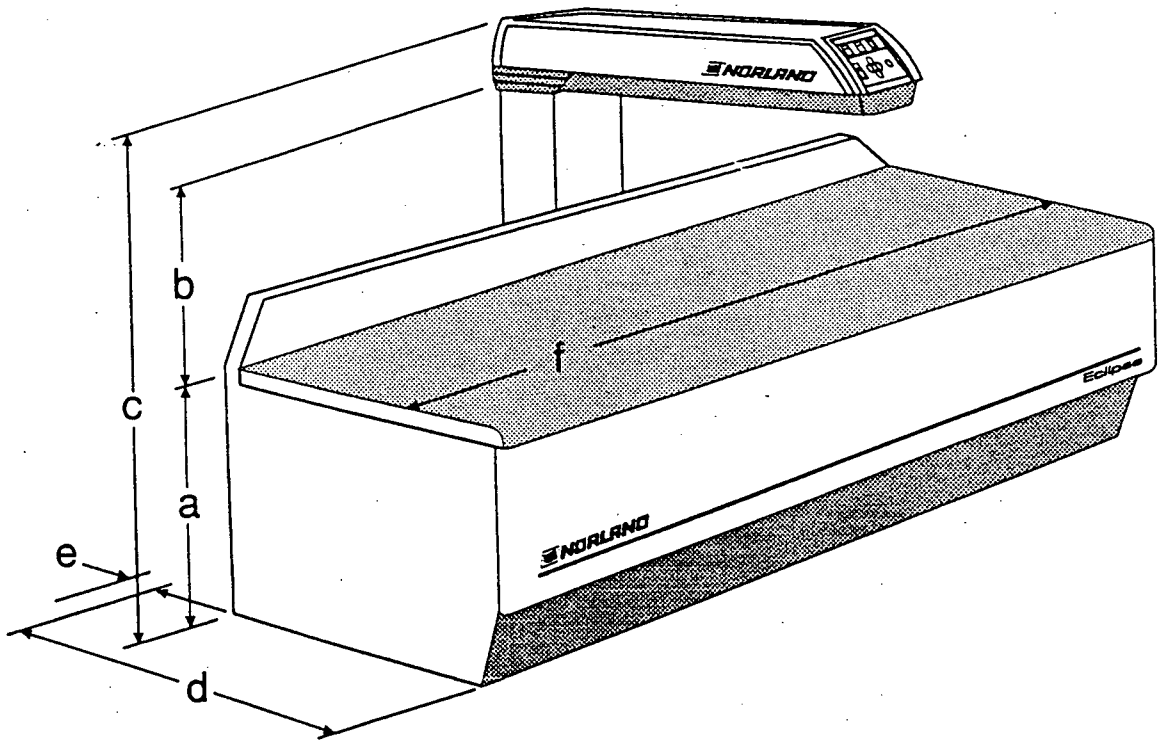
Eclipse System Specifications

This section lists specifications and features unique to the Norland Eclipse scanner. All specifications subject to change without notice.

Scan Window Dimensions	90cm x 64cm (35.4" x 25.2"). Patient Surface: 181cm (71.25") L x 88cm (34.6") W x 66cm (26") H. System: 181cm (71.25") L x 122cm (48") W x 131cm (51.8") H. Tabletop-to-arm distance: 40cm (15.75").
Weight	264 kg (580 lbs).

Eclipse System Dimensions

a	Scanning Platform Height	66cm (26")
b	Maximum Patient Clearance	40cm (15.75")
c	Overall Scanner Height	131cm (51.8")
d	Overall Scanner Width	122cm (48")
e	Minimum Wall Clearance	2.5cm (1")
f	Overall Scanner Length	181cm (71.25")



Source: XR-Series Bone Densitometer Operator's Guide (Norland Corporation, Fort Atkinson, WI, 1992).

Soft Tissue Composition Numeric Results: Whole Body

When a *Results Page 1* display is requested for a Whole Body scan, XR software automatically locates the arms, legs, head and trunk regions and performs calculations.

The image is presented, along with values for the following quantities:

- Total Bone Mineral Content (TBMC), in grams
- Total Soft Tissue Mass (TSTM), in grams
- Total Body Mass (TBM), in grams
- %FAT
- % Total Bone Mineral Content/Lean Body Mass (%TBMC/LBM)

The *Results Page 1* display also contains any appropriate trending or reference graphs. An example *Results Page 1* screen is seen in Figure 1.

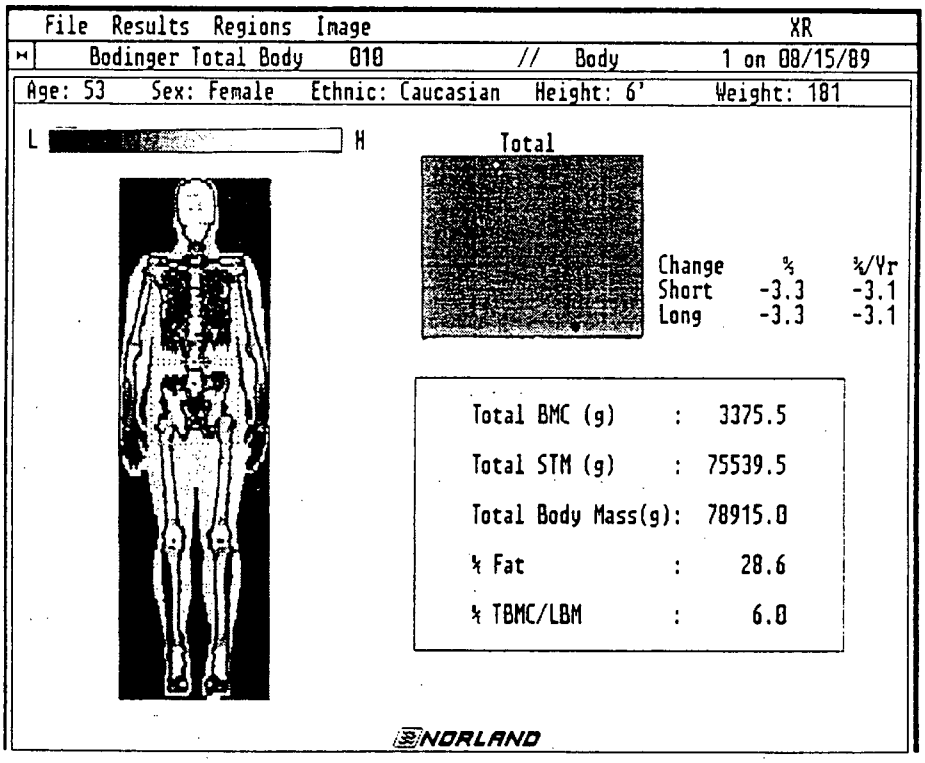


Figure 1 - Example Whole Body Results Page 1 screen

Quantities Estimated

Soft Tissue calculations are performed for the following quantities:

STM	= Soft Tissue Mass, in g
TBM	= Total Body Mass, in g
	= TBMC + TOTAL STM
TBMC	= Total BMC, in g
TSTM	= Total STM, in g
LBM	= Lean Body Mass, in g
	= TBMC + TSTM - FAT MASS
LSTM	= Lean STM, in g
	= TBM - (BMC + FAT MASS)
% TBMC/LBM	$= \frac{TBMC}{LBM} * 100$
FAT MASS	= TBM - (BMC + LSTM), in g
% FAT	$= \frac{FAT\ MASS}{TBM} * 100$

Nutrition Research Study

Thank you for your patience in waiting for your results. The following is a summary of the information that was collected on your two visits to St. Pauls's Hospital and from the information you recorded in the food record and activity diary. Please be reminded that any information resulting from the study is confidential. As a participant your data will be represented using a code number rather than your name in all reports of the completed study.

Measurement	Before Treatment	After Treatment
1. *Dietary intake:*		
total calories	2170	1630
% carbohydrate	52	60
% protein	12	15
% fat	32	22
% alcohol	4	3
2. *Physical activity:*		
calories/day	2175	2675
3. *Metabolic Rate:*		
calories/day	1300	1425
4. *Body Composition:*		
lean tissue (lbs.)	83	78
fat (lbs.)	65	70
% body fat (DEXA)	42	45
% body fat (Siri)	33	36
5. *Weight:*		
lbs.	154	155

1 dietary intake as calculated from 3-day food records;
the recommended percents are: 55-60% carbohydrate, 10-15% protein, and less than 30% fat
2 calories expended from physical activity as calculated from activity diaries
3 resting metabolic rate as calculated by respiratory gas exchange
4 body composition calculated using dual energy x-ray absorptiometry (DEXA) at St. Paul's Hosptial; DEXA values are higher than traditional measurements because all fat in the body is included;
Siri equation typically calculates lower values for % body fat and is commonly referred to in the literature

The study requires the following measurements.

1. Body weight will be measured during treatment appointments at the British Columbia Cancer Agency.

2. Calorie consumption will be measured based on a record of all food and fluid consumed for three days during each of the two test periods, which will require approximately 30 minutes of recording time at each of the two occasions.

3. Measurement of resting energy expenditure will be completed at St. Paul's Hospital laboratory after a 12 hour overnight fast, and will require collection of breath samples over a period of 15 minutes for an estimated total testing time of 1 hour (allowing for travel time and test preparation).

4. Body composition will be measured twice during the study at St. Paul's Hospital, using x-ray technology, in which you will need to allow approximately 30 minutes on both occasions.

5. Lastly, to estimate energy expended during daily activities, you will be required to record physical activity in a 3-day diary during both of the test periods which will require approximately 30 minutes at each of the two occasions.

The estimated total time commitment for participation in the study is approximately 6 hours, a large part of which will be spent lying or resting comfortably during measurements or recording information.

As a result of participation you will receive information about whether your metabolism and/or body composition changes due to the specific treatment you receive. The information from the group as a whole will aid in the design of weight management strategies for premenopausal women who gain weight during treatment for breast cancer.

Your interest in the study and consideration is greatly appreciated. With your permission I will be contacting you by telephone to discuss the study in further detail.

Sincerely,

Cheri Kutynec, RDN Linda McCargar, PhD

I understand that as a participant in the study, I will be required to:

1. have body weight measured during treatment appointments at the British Columbia Cancer Agency
2. keep a record of all food and fluid consumed for three days during each of the two test periods, which will require approximately 30 minutes of recording time on each of the two occasions
3. have resting energy expenditure measured at St. Paul's Hospital laboratory after an 12 hour overnight fast, which will require collection of breath samples over a period of 15 minutes for an estimated total testing time of 1 hour during each test period
4. have body composition measured twice during the study at St. Paul's Hospital using x-ray technology, which will require approximately 30 minutes on both occasions
5. keep a record of physical activity in a 3-day diary during both of the test periods, which will require approximately 30 minutes on each of the two occasions.

The estimated total time commitment for participation in the study is approximately 6 hours, a large part of which will be spent lying or resting comfortably during measurements or recording information.

Exclusions:

I understand that the following women will be excluded from participation: (1) women with advanced stage breast cancer; (2) women who are not within 2.0 kg (approximately 4.5 lbs.) of their usual weight at the time of the study; and (3) women who are not a candidate for radiation or chemotherapy.

Risks:

There are no risks involved in participation of this study. All measurements are non-invasive, and will allow you to continue with your normal routine. The measurement of body composition using x-ray has a low radiation dose, approximately one-tenth of a typical chest x-ray.