Thomas Jefferson University

THOMAS JEFFERSON UNIVERSITY
Kimmel Cancer Center

CAREFOR Study: A Feasibility Pilot Trial Evaluating Caloric Restriction for Oncology Research in Early Stage breast cancer patients

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Funding Sponsor:	Ladies of Port Richmond Pilot Award

Version:	Date:
Initial, 1	11/7/12
AMDT. 2	4/3/13
3.0	12/3/2013
4.0	5/21/2014
4.1	1/9/2015
4.2	1/4/2016

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Table of Contents

List of Abbreviations

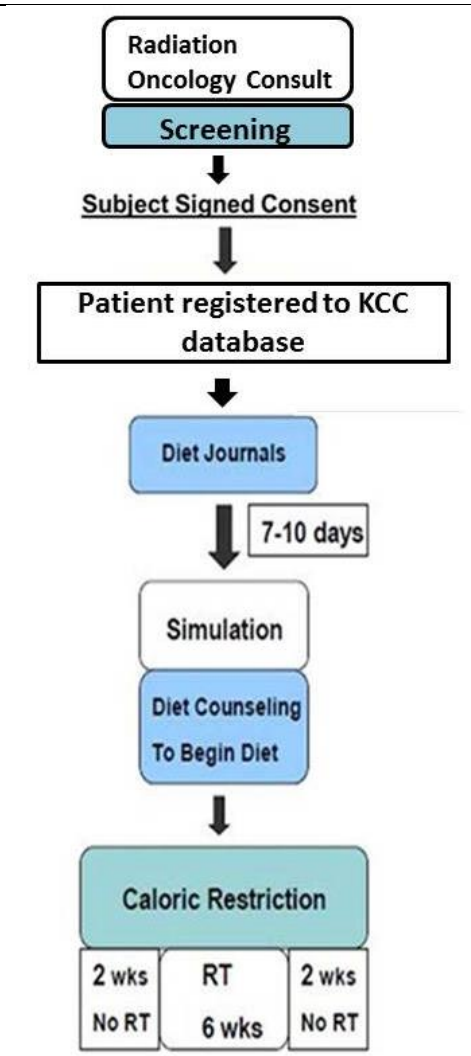
BrCa: breast cancer
CR: caloric restriction
RT: radiation
IGF: insulin-like growth factor
NCI: National Cancer Institute
BCT: Breast conserving therapy
TJUH: Thomas Jefferson University Hospital

Study Summary

Title	CAREFOR study: A feasibility pilot trial evaluating caloric restriction for oncology research in early stage breast cancer patients
Short Title	CAREFOR Study: Caloric Restriction for Oncology Research
Phase	Pilot Trial
Methodology/ Study Design	Single site (early stage breast cancer), Pilot study with one arm
Study Duration	5 years
Study Center(s)	Thomas Jefferson University Hospital

Objectives	The primary objectives are as follows:
	
	The study will be conducted in two phases. The first phase will enroll 40 patients. At the end of it, we will determine adherence to CR. We will then proceed to the second phase which will enroll an additional 50 patients, for a total study sample size of 90, and at its end we will assess toxicity, as well as potential predictors of it.
	
	Phase 1: Investigate the feasibility of a clinical trial administering ionizing radiation with concurrent CR for the treatment of breast cancer. True adherence will be defined as a successful reduction of 25% of total calories based on diet journals in at least 80% of the logged events.
	
	Phase 2: Acute skin toxicity as defined by the National Cancer Institute Common Toxicity Criteria (NCI CTCv.4 for skin reaction, pain and the occurrence of moist desquamation) will be followed to ensure noninferiority as compared with historical controls.
	
	The secondary objectives are as follows:
	
	Investigate measurable changes of patient characteristics and tissue and serum from fasting/CR conditions to determine a metric for evaluating this treatment in future studies.
	• Weight: Weight will be monitored by body mass index, at baseline, week 1, 3, 5 and 7, conclusion and 4 weeks after diet is complete. Body fat measurements via calipers and bioimpedance which will be done at baseline, conclusion and 4 weeks after diet is completed. Vital signs will be monitored weekly.
	• Serum:
	  • At initiation of diet, conclusion of diet and 4 weeks after diet is complete, fasting labs will be drawn:
	  • Clinical Lab: CBC, basic metabolic panel, hemoglobin A1C, triglycerides, insulin, IGF-1, erythrocyte sedimentation rate (ESR), adiponectin, leptin and estradiol
	  • Other Serum Markers: IGF-1R, IRS-1, proteomic and/or genomic analysis
	  • At week 5: a fasting insulin level will be evaluated.
	• Psycho-social evaluation: Patients will have psycho-social evaluation using the FACT-B test and the PROMIS cancer fatigue short form at baseline, week 5, conclusion and 4 weeks after conclusion.
	• Outcomes: Local recurrence, progression free survival, distant metastases and overall survival will be assessed through patient records after study has been completed.
	• Toxicity: acute skin reaction or pain using the National Cancer Institute Common Toxicity Criteria (NCI CTC) version 4.0 scale22 will be assessed. Number of patients experiencing toxicity and time to occurrence of toxicity will be recorded. This toxicity will be compared to historical controls from TJUH who have also been treated for a 6 – 6.5 week course of radiation.

Number of Subjects	90
Diagnosis and Main Inclusion Criteria	Patients with DCIS or invasive breast cancer who will receive radiation and are appropriate candidates for breast conservation to be treated to the whole breast
Study Therapy, Dose, Route, Regimen	Radiation and Caloric Restriction: a 25% reduction in total caloric intake
Duration of administration and follow-up	Caloric Restriction for 10weeks (2weeks minimum prior to radiation, during 6-6.5 weeks of radiation and 2 weeks minimum after for a total of at least 10weeks) with a follow up visit 4 weeks after treatment completion.
Reference therapy	Patients acute toxicity on this trial will be compared with historic controls of other patients who received 6-6.5 weeks of radiation at Bodine Cancer Center
Statistical Methodology	The study will enroll a total of 90 patients. Phase 1: With a sample size of 40, the study has 83% power to establish that adherence is higher than 60%, assuming that true adherence will be 80% or greater (one-sided exact binomial test with alpha 0.05). Phase 2: We will compute the proportion of patients with toxicity, along with a 95% exact confidence interval. Our institution's historical toxicity rate among similar patients is about 80% and we aim to prove that the dietary intervention is non-inferior with an absolute margin of 10%, using an exact binomial test. With a total sample size of 90 and assuming that true toxicity will be 80% or lower, we have 82% power (with one-sided alpha of 0.05).

Schema	 Radiation Oncology Consult Screening Subject Signed Consent Patient registered to KCC database Diet Journals 7-10 days Simulation Diet Counseling To Begin Diet Caloric Restriction 2 wks No RT RT 6 wks 2 wks No RT

1 INTRODUCTION

This document is a protocol for a human research study. This study is to be conducted according to US and international standards of Good Clinical Practice (FDA Title 21 part 312 and International Conference on Harmonization guidelines), applicable government regulations and Institutional research policies and procedures.

1.1 Specific Aims and Hypothesis

We hypothesize that a dietary change such as fasting may alter tumor biology. Further we hypothesize that a 25% reduction in caloric intake is a feasible intervention for early stage breast cancer patients to adhere to during radiation therapy.

To this end, in this feasibility trial we will (1) investigate the feasibility of a clinical trial administering ionizing radiation with concurrent CR for the treatment of breast cancer (2) Acute skin toxicity as defined by the National Cancer Institute Common Toxicity Criteria (NCI CTCv.4 for skin reaction, pain and the occurrence of moist desquamation) will be followed to ensure noninferiority as compared with historical controls. (3) investigate measurable changes of patient characteristics along with serum markers from CR to determine a metric for evaluating this treatment in future studies.

The use of caloric restriction as a novel intervention has the potential to change the biology of tumors and enhance the clinical benefit of standard cancer therapies. If this trial is successful and it is determined that patients can achieve successful caloric restriction during breast cancer treatment, the long term goal will be to open a larger study to determine if this treatment is more efficacious than using radiation alone.

1.2 Background and Rationale

CR, or a diet modification aiming to reduce the total intake of calories by 20-30%, has been shown to increase longevity across multiple species. Recently, there has been growing interest in the potential role of CR as a treatment modality for age-related diseases such as cancer because an increasing body of literature has demonstrated that there is a metabolic component to both carcinogenesis and tumor progression. In fact, many of the molecular pathways that are induced by CR, such as IGF1-R, Akt and mTOR pathways, are also known to be perturbed in cancer and are currently targets of novel cancer therapies. Therefore, alteration of multiple steps in these pathways by CR may render cancer cells more susceptible to standard cytotoxic treatment with radiation therapy.

CR has been shown to decrease the incidence and progression of spontaneous breast cancers in murine models, and to protect normal tissue during chemotherapy. Our preliminary results show that CR represses tumor growth in an additive manner when combined with radiation in 2 different aggressive murine models (4T1 and 67NR) of breast cancer (Fig 1). Our results at the molecular level demonstrate that various components of the IGF-1R pathway are downregulated with CR and RT used separately, and are further decreased by the combination of treatments, suggesting a role for CR in the observed repression of tumor growth (Fig 2).

Figure 1: Tumor re-growth-delay curves for tumors created from 4T1 breast cancer cell line: Ten mice were treated with either: ad libitum (AL) diet, radiation (RT), a 30% reduction in their calories (CR), or CR + RT. Compared to the AL cohort, for 4T1 tumors at 1000mm3 RT produced a 23% growth delay, CR 56%, and CR+RT 82%.

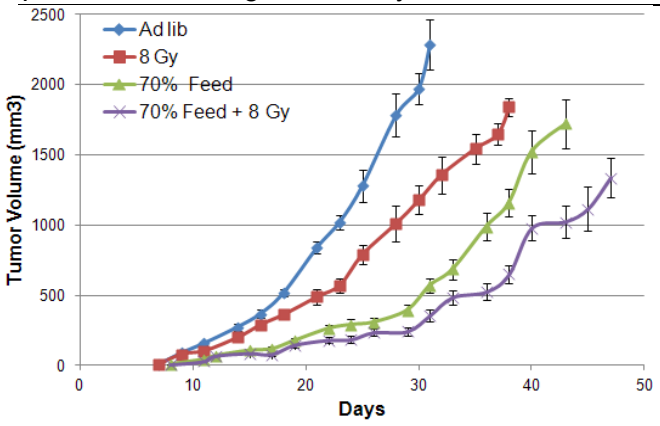
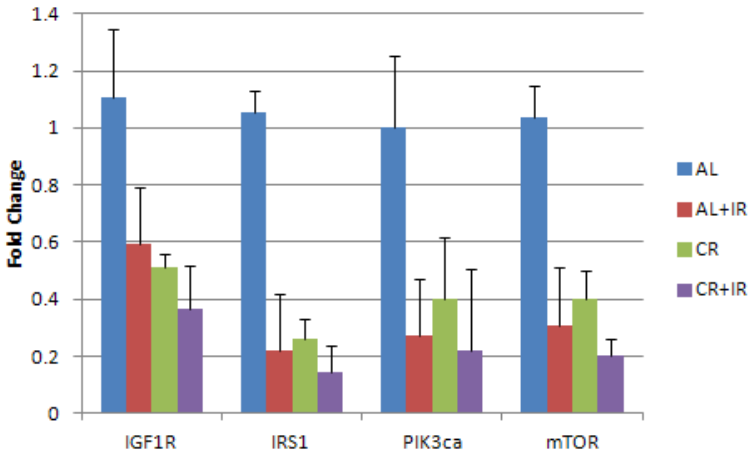


Figure 2. Expression of members of the IGF-1R pathway. RT-PCR was performed for molecules in the IGF-1R pathway(IGF-1R, IRS, PIk3ca, and mTOR). For all of these molecules, CR, radiation, and the combination of both treatments resulted in downregulation which implicates this pathway in mediating the tumor regression noted.



Although the preclinical data appears promising, it is unknown if patients will want to or be able to adhere to a reduction in calories during radiation therapy. In the radiation clinic, many patients inquire about potentially beneficial dietary alterations. Although CR requires a significant commitment, we have shown through a TJUH IRB approved questionnaire that 75% of breast cancer patients queried at our institution would be interested in enrolling on such a diet related intervention trial (manuscript under review). Because CR may act as a complementary therapeutic modality in the treatment of women with breast cancer, its full capacity as a therapeutic intervention needs to be assessed.

It seems logical to propose that combining CR with genotoxic therapies such as radiation, in the treatment of breast cancer, could both retard tumor progression as well as confer significant therapeutic advantage by increasing the response of tumors

to the cytotoxicity of standard therapies. Therefore, in this proposal, we intend to investigate the feasibility of administering CR in combination with radiation therapy for early stage breast cancer, employing a clinical trial and evaluating biomarkers to monitor the progress of the trial. In addition, we lay the groundwork for identifying tools that will assist patients with compliance, and we determine which may be most beneficial for women to use in a larger randomized trial based on the results obtained here.

Specific Aim 1: In a clinical trial, will investigate the ability of CR to modulate the effects of radiation in the treatment of early breast cancer. Aim 1a. Adherence will be assessed and is defined for each patient as achieving 25% reduction of her normal caloric intake (weekly average of diet journals), during at least 80% of the days during the intervention. Aim 1b. Acute skin toxicity as defined by the National Cancer Institute Common Toxicity Criteria (NCI CTCv.4 for skin reaction, pain and the occurrence of moist desquamation) will be followed to ensure noninferiority as compared with historical controls. **Specific Aim 2: Investigate measurable changes of patient characteristics along with serum markers from CR to determine a metric for evaluating this treatment in future studies.** Patient characteristics such as weight, vital signs, body fat measurements, psychosocial evaluation and outcomes will be monitored. Additionally, members of the IGF-1R-AKT pathway, and glucose and insulin in the serum, will be assessed to create a molecular signature of response to this therapy.

The innovative use of caloric restriction as a novel therapeutic option has the potential to change the biology of tumors and enhance the clinical benefit of current treatments for breast cancer. If patients are noted to be compliant, we will be able to open a larger study to determine if the combination of radiation and caloric restriction is more efficacious than radiation alone.

1.3 Study Therapy

Baseline caloric intake will be assessed by food diaries for 7-10 days prior to radiation treatment planning. Recommendations by nutritional counseling will be made to decrease total caloric intake by 25% and the patient will begin this diet immediately after the planning session and for 2 weeks before starting radiation. The patient will then remain on this calorically restricted diet as measured by food diaries until completion of radiation treatment and for an additional 2 weeks for a total of 10 weeks.

Restriction of calories is the primary objective of dietary modification and will be tailored to each patient by the discretion of the recommending physician in Integrative Medicine to ensure overall nutrition. Diet guidelines and compliance will be reviewed at weekly on-treatment visits by study staff including physicians and diet counselors.

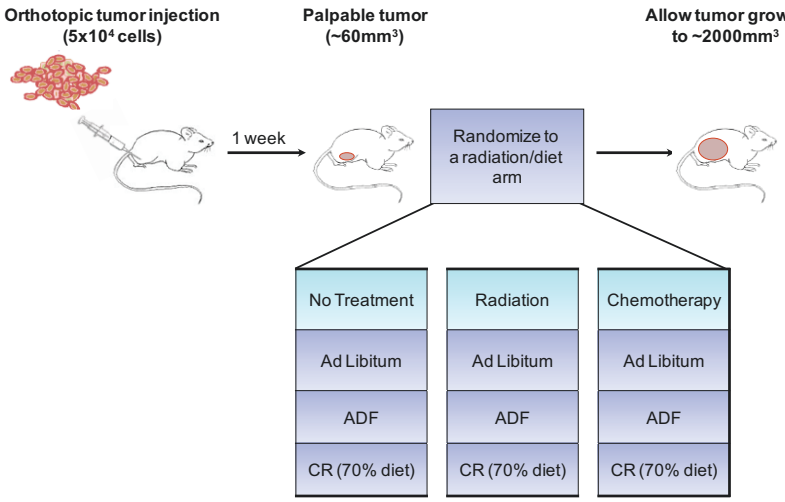
1.4 Preclinical Data

Delaying Tumor Regrowth using Caloric Restriction and Radiation

An early focus of our laboratory was the use of CR to reduce tumor proliferation and progression in breast cancer. We first generated a reproducible mouse model to assess various modalities of treatment. Specifically, we tested the syngeneic and

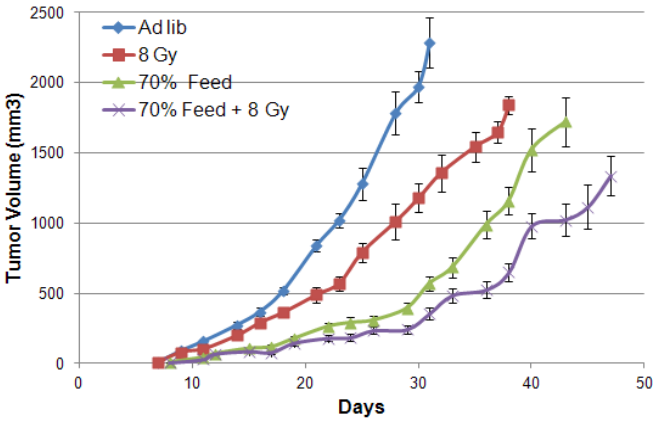
highly metastatic 4T1 cell lines in our model. Female Balb/c mice at postnatal week 14, were implanted with 5 x 104 4T1 tumor cells into the mammary fat pad, and tumors were measured 3 times per week using manual calipers. Mice were euthanized when tumors reached 2cm.

Figure 3: Trial Design. The food intake of mice monitored for 2 weeks before tumors were implanted into the mammary fat pad of mice.



Intervention: Cohorts consisting of 10 mice each were treated as shown (Fig. 3) with either radiation, dietary intervention alone or in combination with radiation after the tumors were palpable to an average size of 60 mm3. The diets were either ad libitum (AL) feeding or a 30% reduction in caloric intake (over an 18-day period, animals were stepped down in 10% increments to ensure animal tolerability). Average food intake per animal was determined for all groups by weighing food 2-3 times/week after the animals were singly housed for at least two weeks prior to implantation. When the tumor became palpable (~5-7mm), approximately 1 week after implant, animals received either a diet modification, were radiated to the primary tumor, or received both treatments. To establish the dose of radiation to treat mice implanted with 4T1 cells, clonogenic assays were performed and a dose of radiation was chosen to achieve a 90% cell kill in vitro. After the animals had palpable tumors, they were placed in a custom jig and a dose of 8 Gy was administered to the primary tumors with the rest of their bodies shielded. Primary tumor volume was measured 3 times per week and is represented in Fig 4.

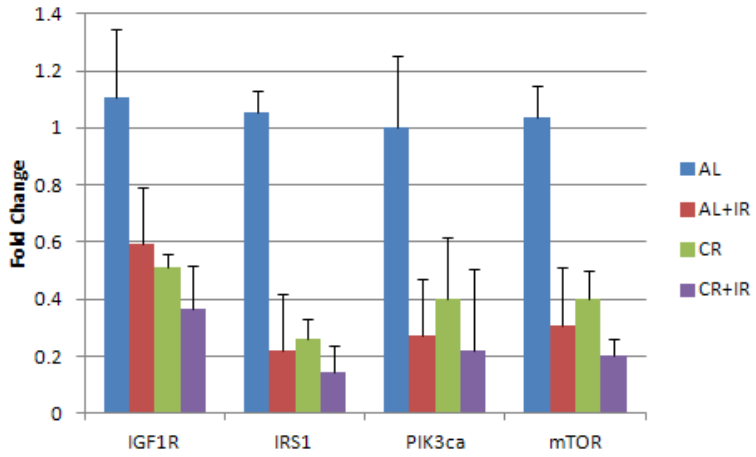
Figure 4: Tumor re-growth-delay curves for tumors created from 4T1 breast cancer cell line. Ten mice were treated with either: ad libitum (AL) diet, radiation (RT), a 30% reduction in their calories (CR), or CR + RT. Compared to the AL cohort, for 4T1 tumors at 1000mm3 RT produced a 23% growth delay, CR 56%, and CR+RT 82%.



CR alters the IGF-1R survival-signaling pathway

To determine if altering the IGF-1R pro-survival pathway might be responsible for the additive tumor regression noted between CR and irradiation, qRT-PCR was performed on grossly dissected 4T1 tumors from the previous experiment using primers for IGF-1R, IRS, PIk3ca, and mTOR.

Figure 5: Expression of members of the IGF-1R pathway. RT-PCR was performed for molecules in the IGF-1R pathway(IGF-1R, IRS, PIk3ca, and mTOR). For all of these molecules, CR, radiation, and the combination of both treatments resulted in downregulation which implicates this pathway in mediating the tumor regression noted.



These results (Fig. 5) demonstrated that multiple molecules in the IGF-1R/AKT pathway are downregulated with CR alone or in combination with radiation. Since the

IGF-1R/AKT is involved in apoptosis and based on these results we propose that this work warrants further investigation of this pathway is warranted in order to determine whether pathway components contribute to the beneficial effects of CR in breast cancer.

1.5 Clinical Data to Date

Although there have been no published trials assessing radiation therapy with a diet modification to date, there are now a number of registered trials (www.clinicaltrials.gov) assessing a ketogenic diet with cancer therapy for lung cancer, pancreatic cancer, primary brain tumors and metastatic cancer.

There are published trials in the non-oncologic realm however; showing that caloric restriction is feasible and patients are able to be compliant in other diseases or in healthy volunteers. For example, the Comprehensive Assessment of Long-term Effects of Reducing Intake of Energy (CALERIE) is a multi-center randomized controlled trial that placed patients on a 25% caloric reduction for 2 years. A number of early assessments from this trial have now been published, revealing that this regimen is feasible and that the fasting insulin level was decreased with diet modification. Cognitive function was not significantly altered in individuals undergoing CR. Other data exists from the Biosphere 2 project in Arizona, where patients were kept on a CR diet of1,780 kcal/day for 2 years. This regimen would be more similar to those likely used in human cancer CR clinical trials. One-year CR studies have shown feasibility and adherence metrics have been developed as well.

Determining Interest in a CR Clinical Trial: Many patients express an interest in dietary changes they can make to improve their cancer survival but the data supporting such interventions is scarce. To begin to develop a protocol for using CR to treat patients, we set out to assess the feasibility of using CR in a clinical setting. Specifically, we distributed an IRB-approved questionnaire to our oncology patients querying patient interest in participating in a CR study. We found that 75% would participate in a CR trial. The patients identified several tools they believed would help them with dietary trial adherence including speaking with a dietician weekly and weekly phone conversations with the physician. This demonstrates that there is patient interest in dietary interventions and that a trial using CR could successfully accrue patients. We have since worked with the Integrative Medicine Department to develop a strategy to implement a CR diet and to monitor and ensure adherence.

1.6 Dose Rationale and Risk/Benefits

The patients will undergo a 25% reduction in total caloric intake since this is a) the reduction used in other clinical trials that employ caloric restriction and, b) the definition of caloric restriction and the percent reduction noted to effect molecular targets in the IGF pathway.

The patients will undergo CR for a total of 10 weeks because previous studies have noted that the maximum effect of CR seems to be reached at 5 weeks. It is then important to incorporate at least 5 weeks for stabilization of physiologic processes

under caloric restriction [1].

The diet modification proposed should not induce many risks, and every effort will be made to insure that patients are receiving adequate overall nutrition. Although some patients may experience weight loss and fatigue, other risks should be minimal. These risks may include: decreased bone mineral density, decreased muscle mass and strength, depression, decreased sex drive, fatigue, irritability, fainting, rashes, acidosis, malnutrition, constipation, dehydration, cholelithiasis and reversible amenorrhea.

Because obesity has been proven a poor prognostic factor in those patients with breast cancer, dietary intervention may be ideal for improving outcomes for these patients who decrease their caloric intake.

2 STUDY OBJECTIVES

2.1 Primary Objective

Aim 1a. Investigate the feasibility of a clinical trial administering ionizing radiation with concurrent CR for the treatment of breast cancer. True adherence will be defined as a successful reduction of 25% of total calories based on diet journals in at least 80% of the logged events.

Aim 1b. Acute skin toxicity as defined by the National Cancer Institute Common Toxicity Criteria (NCI CTCv.4 for skin reaction, pain and the occurrence of moist desquamation) will be followed to ensure noninferiority as compared with historical controls.

2.2 Secondary Objective

Investigate measurable changes of patient characteristics and tissue and serum from fasting/CR conditions to determine a metric for evaluating this treatment in future studies.

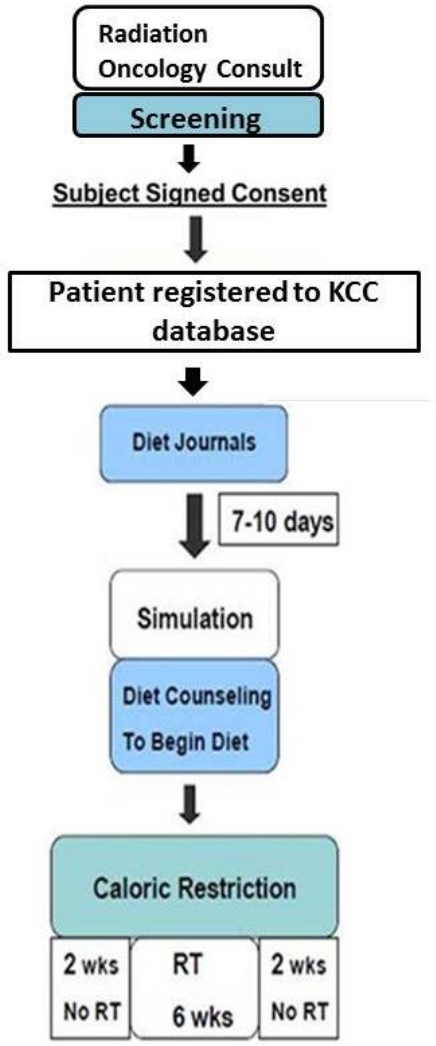
- Weight: Weight will be monitored by body mass index, at baseline, week 1, 3, 5 and 7, conclusion and 4 weeks after diet is complete. Body fat measurements via calipers and bioimpedance which will be done at baseline, conclusion and 4 weeks after diet is completed. Vital signs will be monitored weekly.
- Serum:
    - At initiation of diet, conclusion of diet and 4 weeks after diet is complete, fasting labs will be drawn:
        - Clinical Lab: CBC, basic metabolic panel, hemoglobin A1C, triglycerides, insulin, IGF-1, erythrocyte sedimentation rate (ESR), adiponectin, leptin and estradiol
        - Other Serum Markers: IGF-1R, IRS-1, genomic and or proteomic analysis
    - At week 5: a fasting insulin level will be evaluated.

- Psycho-social evaluation: Patients will have psycho-social evaluation using the FACT-B test and the PROMIS cancer fatigue short form at baseline, week 5, conclusion and 4 weeks after conclusion.
- Outcomes: Local recurrence, progression free survival, distant metastases and overall survival will be assessed through patient records after study has been completed.
- Toxicity: acute skin reaction or pain using the National Cancer Institute Common Toxicity Criteria (NCI CTC) version 4.0 scale22 will be assessed. Number of patients experiencing toxicity and time to occurrence of toxicity will be recorded. This toxicity will be compared to historical controls from TJUH who have also been treated for a 6 week course of radiation.

3 Study Design

3.1 General Design

- This is a pilot trial to assess feasibility and toxicity of the dietary intervention during radiation.
- Expected duration of subject participation: approximately 20 weeks, with 10 weeks of diet and follow up
- Section 6.1 outlines the specific trial periods.



3.2 Primary Study Endpoints

Objective: Investigate the feasibility of a clinical trial administering ionizing radiation with concurrent CR for the treatment of breast cancer. True adherence will be defined as a successful reduction of 25% of total calories based on diet journals in at least 80% of the logged events. Acute skin toxicity as defined by the National Cancer Institute Common Toxicity Criteria (NCI CTCv.4 for skin reaction, pain and the occurrence of moist desquamation) will be followed to ensure noninferiority as compared with historical controls.

To obtain baseline caloric intake, patients will keep food diaries for 7 to 10 days. On the basis of these diaries, a caloric intake will be computed for each day. Each patient's baseline (pre-diet) caloric intake will then be the average caloric intake in this pre-diet phase. The target caloric intake during the diet phase will be set to 75% of this baseline average (25% restriction).

The diet phase will be defined as the entire length that a patient is on the calorically restricted diet. This includes a minimum of 2 weeks before the patient starts radiation therapy and a minimum of 2 weeks after completion of radiation therapy. This will guarantee that patients have been on the diet for a minimum of 10 weeks, regardless of whether or not the patients have exceeded the 10 weeks. In the diet phase, patients will also keep daily food diaries. An average daily caloric intake will be computed for each week. If that daily average is more than the restricted target or if there are fewer than 4 diaries during any given week, that week will be considered as non-adherent. Overall adherence with the diet intervention over the entire study will be defined as at least 80% of all logged events meeting the diet restriction target.

3.3 Secondary Study Endpoints

Investigate measurable changes of patient characteristics and tissue and serum from fasting/CR conditions to determine a metric for evaluating this treatment in future studies.

- Weight: Weight will be monitored as a percent change and by body mass index as weight in kg divided by height in meters squared, at baseline, week 1, 3, 5 and 7, conclusion and 4 weeks after diet is complete.
- Body Fat Measurement: Body fat percentage will be done at baseline, conclusion and 4 weeks after diet is complete and will be determined by the Durnin-Womersley 4-fold technique. All skinfold measurements should be made on the right side of the body in mm using a body fat caliper. Body fat caliper will be placed 1 cm away from thumb and finger, perpendicular to the skinfold, and halfway between the crest and base of fold. A pinch will be maintained with the body fat caliper for 1 to 2 seconds before reading the caliper. Duplicate measurements will be taken at each site, allowing time for skin to regain normal texture and thickness. Measurements will be taken at the:
    - Biceps: Measured on a vertical fold at the upper arms frontside, half way between shoulder and elbow.
    - Triceps: Measured on a vertical fold at mid of the upper arms backside.
    - Scapula: Measured on a diagonal fold on the back, at the lower edge of the scapula. Angle of inclination should be 45°, clockwise.
    - Hip: Measured on a diagonal fold straight over the pelvis, close to the navel. Angle of inclination should be 30°, clockwise.
- Bioimpedance: Bioimpedance will be taken at baseline, conclusion and 4 weeks after diet is completed and will be measured in Ω/m^2.
- Vitals: Vital signs including temperature, blood pressure, heart rate and respiratory rate will be monitored weekly.
- Serum (collection procedures detailed in Appendix VI):
    - At initiation of diet, conclusion of diet and 4 weeks after diet is complete, fasting labs will be drawn:
        - Clinical Lab: CBC, basic metabolic panel, hemoglobin A1C, triglycerides, insulin, IGF-1, erythrocyte sedimentation rate (ESR), adiponectin, leptin and estradiol
        - Other Serum Markers: IGF-1R, IRS-1, genomic and/or proteomic analysis
    - At week 5: a fasting insulin level will be evaluated.

- Psycho-social evaluation: Patients will have psycho-social evaluation using the FACT-B test and the PROMIS cancer fatigue short form at baseline, week 5, conclusion and 4 weeks after conclusion. (Forms detailed in CRFs in Appendix VII)
- Outcomes: Local recurrence, progression free survival, distant metastases and overall survival will be assessed through patient records after study has been completed.
- Toxicity: acute skin reaction or pain using the National Cancer Institute Common Toxicity Criteria (NCI CTC) version 4.0 scale22 will be assessed. Number of patients experiencing toxicity and time to occurrence of toxicity will be recorded (see Appendix III for toxicity scale). This toxicity will be compared to historical controls from TJUH who have also been treated for a 6-6.5 week course of radiation.

3.4 Primary Safety Endpoints

Acute toxicities will be evaluated by the CTCAE, Version 4.0. (*http://ctep.info.nih.gov*). If a patient has a serious adverse event such as all unexpected hospitalizations and all grade 4 and 5 SAEs, the patient will be removed from the trial. See Appendix III for scale.

4 Subject Selection and Withdrawal

Patients must have baseline evaluations performed prior to the first dose of study drug and must meet all inclusion and exclusion criteria. Results of all baseline evaluations will be reviewed by the Principal Investigator prior to enrollment, to verify that all inclusion and exclusion criteria have been satisfied. In addition, the patient must be thoroughly informed about all aspects of the study, including the study visit schedule and required evaluations and all regulatory requirements for informed consent. The written informed consent must be obtained from the patient prior to screening procedures being performed. The following criteria apply to all patients enrolled onto the study unless otherwise specified.

4.1 Inclusion Criteria

1. Pathologically proven diagnosis of DCIS or invasive breast cancer
2. Ability to have breast conservation as determined by the judgment of the radiation oncologist, for which the radiation oncologist has determined that he or she will only treat the whole breast and not regional lymph nodes
3. The patient must be female
4. Age ≥ 18
5. If multifocal breast cancer, then it must be able to be resected through a single lumpectomy incision
6. Appropriate stage for protocol entry, including no clinical evidence for distant metastases, based upon the following minimum diagnostic workup:
    - History/physical examination, including breast exam and documentation of weight and Karnofsky Performance Status of 80-100% at study entry.
7. Women of childbearing potential must be non-pregnant and non-lactating and willing to use medically acceptable form of contraception during radiation therapy
8. Patient must capable of and provide study specific informed consent prior to study entry
9. BMI ≥21

10. Weight ≥100lbs
11. No prior history of non-breast invasive malignancies in the past 1 years
12. Patient must not have any of the following severe, active co-morbidity, defined as follows:
    - Unstable angina and/or congestive heart failure requiring hospitalization within the last 6 months
    - Transmural myocardial infarction within the last 6 months
    - Acute bacterial or fungal infection requiring intravenous antibiotics at the time of registration;
    - Chronic Obstructive Pulmonary Disease exacerbation or other respiratory illness requiring hospitalization or precluding study therapy within 30 days before registration;
    - Hepatic insufficiency resulting in clinical jaundice and/or coagulation defects; note, however, that laboratory tests for liver function and coagulation parameters are not required for entry into this protocol
    - Acquired Immune Deficiency Syndrome (AIDS) or HIV positive based upon current CDC definition; note, however, that HIV testing is not required for entry into this protocol. The need to exclude patients with AIDS or HIV from this protocol is necessary because anti-retrivirals may alter patient metabolism.
    - Gastrointestinal/Malabsorption disorder at the discretion of the Principal Investigator
    - Inflammatory Bowel Disease
    - Celiac Disease
    - Chronic Pancreatitis
    - Chronic Diarrhea or Vomiting
    - Active Eating Disorder
    -
13. Patient must not have active systemic lupus erythematosus, or any history of active scleroderma, or dermatomyositis with active rash
14. No prior radiotherapy to the ipsilateral breast or prior radiation to the region of the breast that would result in overlap of radiation therapy fields
15. Not currently taking steroids
16. No history of or current active drug/alcohol dependence.
17. No patients being decisionally impaired.

4.2 Exclusion Criteria

1. Patient is not a candidate for breast conservation.
2. Patient is male.
3. Age <18 years
4. Patient requires regional lymph node irradiation therapy
5. Patient has evidence of distant metastases
6. Karnofsky Performance Status less than 80% within 60 days prior to study.
7. Ipsilateral mammogram done greater than 6 months prior to study.
8. Women of childbearing potential with a positive serum beta hCG.
9. Patient unable to consent or comply with study guidelines.
10. BMI < 21
11. Weight < 100lbs
12. Unintentional weight loss ≥10% in the last 3 mos

13. Prior invasive non-breast malignancy unless disease free for a minimum of 1 year prior to registration
14. Two or more breast cancers not resectable through a single lumpectomy incision
15. Non-epithelial breast malignancies such as sarcoma or lymphoma
16. Prior radiotherapy to the ipsilateral breast or prior radiation to the region of the breast that would result in overlap of radiation therapy fields
17. Severe, active co-morbidity, defined as follows:
    - Unstable angina and/or congestive heart failure requiring hospitalization within the last 6 months
    - Transmural myocardial infarction within the last 6 months
    - Acute bacterial or fungal infection requiring intravenous antibiotics at the time of registration;
    - Chronic Obstructive Pulmonary Disease exacerbation or other respiratory illness requiring hospitalization or precluding study therapy within 30 days before registration;
    - Hepatic insufficiency resulting in clinical jaundice and/or coagulation defects; note, however,that laboratory tests for liver function and coagulation parameters are not required for entry into this protocol
    - Acquired Immune Deficiency Syndrome (AIDS) or HIV positive based upon current CDC definition; note,however, that HIV testing is not required for entry into this protocol. The need to exclude patients with AIDS or HIV from this protocol is necessary because anti-retrivirals may alter patient metabolism.
18. Active systemic lupus erythematosus, or any history of active scleroderma, dermatomyositis with active rash
19. Active Gastrointestinal/Malabsorption disorder at the discretion of the Principal Investigator
    - Inflammatory Bowel Disease
    - Celiac Disease
    - Chronic Pancreatitis
    - Chronic Diarrhea or Vomiting
    - Active Eating Disorder
20. Current use of steroids
21. Active drug/alcohol dependence or abuse history.
22. Decisionally impaired patients.

4.3 Gender/Minority/Pediatric Inclusion for Research

This protocol will enroll all women with breast cancer and will include minorities in the research protocol. Pediatric patients are excluded.

4.4 Subject Recruitment and Screening

Patients who are 18 year of age or older and are candidates for breast conservation for their breast cancer are eligible for the study. Patients can be recruited from the PI, co-investigators' or referring physician's clinical practices. We have designed a brochure to try and help with patient recruitment. This brochure is attached in the Appendix VIII Section. Potential study subject should be referred to PI or study designated research nurse/research associate. Appropriate laboratory or diagnostic testing necessary to meet any noted inclusion or exclusion criteria will be ordered

through the recruiting physician. PI of the study or study designated research nurse/research associate will screen and determine the final eligibility of the subject for enrollment.

4.5 Early Withdrawal of Subjects

4.5.1 When and How to Withdraw Subjects

Patients will be informed that they have the right to withdraw from the study at any time for any reason, without prejudice to their medical care. The investigator also has the right to withdraw patients from the study for any of the following reasons:

1. Intercurrent illness
2. Occurrence of an unacceptable adverse event such as a Grade ≥ 4 toxicity or ≥ 20% weight
3. Missing more than 3 consecutive days of planned radiation
4. Patient request
5. Protocol violations based on the judgment of PI
6. Non-compliance
7. Administrative reasons
8. Failure to return for follow-up
9. General or specific changes in the patient's condition unacceptable for further treatment in the judgment of the investigator
10. Patients may withdraw from the study voluntarily at any time; however, the Principal Investigator reserves the right to remove patients from the study for any of the following reasons.
11. Radiation toxicity becomes too severe and the patient can no longer tolerate consecutive radiation treatments as determined by treating radiation oncologist.
12. Patients are hospitalized for another condition that is unrelated to breast cancer. Particularly admissions lasting longer than 4 days.
13. Patients develop any of the exclusionary conditions during treatments including: hepatic insufficiency, diabetes, disorders requiring corticosteroid treatment, renal failure or pregnancy.
14. Patients become sexually active and do not wish to use contraception or patients discontinue previous method of contraception and remain sexually active.

At the time of withdrawal, all study procedures outlined for the End of Study visit should be completed. The primary reason for a patient's withdrawal from the study is to be recorded in the source documents.

4.5.2 Data Collection and Follow-up for Withdrawn Subjects

According to FDA regulations, when a subject withdraws from the study, the data collected on the subject to the point of withdrawal remains part of the study database and may not be removed.

A subject who is withdrawing needs to state whether he/she wishes to provide continued follow-up and further data collection subsequent to withdrawal from the interventional portion of the study.

If a subject withdraws from the interventional portion of the study, but agrees to continued follow-up of associated clinical outcome information as described in the previous bullet, the subject will continue follow up visit and evaluation per the protocol.

If a subject withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, study data related to the subject collected prior to the subject's withdrawal from the study will included in the study analysis. However, the subject's clinical data will not be used for dose escalation determination.

5 Study Drug/Therapy

5.1 Description

Baseline caloric intake will be assessed by food diaries for 7 to 10 days prior to radiation treatment planning. Recommendations by nutritional counseling will be made to decrease total caloric intake by 25% and the patient will begin this diet immediately after the planning session and for a minimum of 2 weeks before starting radiation. The patient will then remain on this calorically restricted diet as measured by food diaries until completion of radiation treatment and for a minimum of 2 weeks after the completion of the radiation course. This is done to ensure that he patients undergo caloric restriction for a minimum of 10 weeks +/-1-2 weeks.

Restriction of calories is the primary objective of dietary modification and will be tailored to each patient by the discretion of the recommending physician in Integrative Medicine to ensure overall nutrition. Diet guidelines and compliance will be reviewed at weekly on-treatment visits by study staff including physicians and diet counselors.

5.2 Treatment Regimen

5.2.1 Prior to Radiation:

Caloric restriction to 75% of normal calorie intake will begin when patients present for radiation treatment planning. Prior to this, patients will have recorded their daily intake in food journals for 2 weeks. Patients will remain on this calorically restricted diet until completion of radiation treatment for a total of 10 weeks.

Restriction of calories is the primary objective of dietary modification; however, to patients will be encouraged to maintain adequate nutrient intake. Diet guidelines and adherence will be enforced at weekly on-treatment visits by study staff including physicians and diet counselors.

5.3 Risks of Caloric Restriction

Likely (>10%)

- Weight loss
- Fatigue
- Irritability

Possible

- Decreased bone mineral density
- Decreased muscle mass and strength
- Dehydration
- Constipation
- Depression
- Fainting

Rare (<2%)

- Cholelithiasis
- Reversible amenorrhea
- Malnutrition
- Reduced sex drive
- Acidosis

5.4 Method for Assigning Subjects to Treatment Groups

As a feasibility trial, all patients will be expected to be on treatment as defined by caloric restriction, radiation therapy and nutritional counseling.

5.5 Preparation and Administration of Study Drug/Therapy

Patients will be expected to keep food diaries for 7 to 10 days prior to radiation treatment planning in order to calculate each patients appropriate calorie intake during the treatment period. Initially, patients will have a consultation with integrative medicine and they will meet weekly with research staff for nutritional guidance and behavioral counseling to maintain their dietary modification. Patients will be expected to record their dietary intake on a daily basis while on treatment and these food journals will be collected weekly and modifications will be suggested accordingly. Patients will ultimately be responsible for modifying their diet as recommended to them.

5.6 Compliance Monitoring

Adherence to dietary modification will be monitored by self-reported calorie intake in food journals that will be collected on a weekly basis. Patients will be expected to complete food diaries accurately to represent the type and quantity of food they consumed. Patients who have internet access at home and are comfortable with computers will be given the option of using an online food diary that is password protected, but viewable by the study staff. Should patients select this option, they will be assigned a username and create their own password.

The mean weekly caloric intake will be measured and adherence will compared with their baseline evaluation. Patients will have to maintain a weekly 25% reduction of caloric intake for 80% of the logged events in order to be considered compliant for this trial.

See Appendix IX for printed food diary and access to online food diary.

5.7 Prior and Concomitant Therapy

Patients should continue taking their daily medications on a regular basis. Patients should not be taking corticosteroids, anti-retrovirals that would exclude them from participation.

6 Study Procedures

6.1 Treatment Overview

		Wk 1	Wk 2	Wk 3-4	Wk 5-10.5	Wk 11-12
Patients post-lumpectomy	Day	All	All	All	1 2 3 4 5 6 7	All
	Diet	Normal	Normal	CR Diet	Continue CR Diet	CR Diet
	Radiation	None	Simulation	None		None

6.2 Study Visit Schedule

6.2.1 Screening

Eligibility of patients will be verified based on clinical staging and any need for adjuvant chemotherapy as well as previously stated eligibility criteria. Those eligible patients will receive detailed information about the study including a step-by-step outline of proposed treatment including radiation therapy and diet modification. Patients will be informed of possible risks and benefits. Informed consent will be obtained from patients. A full history and physical examination will be performed on consented patients. Baseline weight and BMI will be taken. In addition, blood will be drawn for eligibility measurements of beta-hCG if appropriate.

6.2.2 Phase I—Pre-treatment

Visit 1: Patients will report to the Radiation Oncology Department for radiation treatment planning to include CT simulation. Food diaries from the previous 7-10 days will be collected and analyzed to create a diet plan for each patient. Integrative medicine will meet with patients to counsel them on lifestyle changes and behavioral aspects of dietary modification. Dietary counselors will give patients guidelines for dietary modification including the appropriate amount of calories that each patient should be receiving and what kinds of foods they should avoid or eat more of. Nutritional counseling will be done using behavioral cues to encourage adherence (see Appendix V for worksheets). Patients will be instructed to begin their new diet starting at this visit and to continue logging foods into their journals. They will complete the journal daily. Patients will undergo a focused examination to assess initial breast appearance and texture for comparison as patients receive radiation therapy. Fasting blood will be drawn for baseline laboratories at this visit. Clinical measurements will include CBC w/diff, CMP, HbA1c, IGF-1, adiponectin, leptin, estradiol, triglycerides, insulin, ESR. Separately, blood samples will also be

analyzed for the following: IGF-1R, IRS-1 and other experimental endpoints such as genomic or proteomic alterations. Baseline psychosocial evaluation will be done using the FACT-B form as well as a baseline fatigue assessment using the PROMIS cancer fatigue short form (see appendix XI). Weight, height, vital signs, bioimpedance and caliper measurements will be done.

Phone Intervention: Patients will be contacted at least once a week during the time they are keeping the food journal to determine if help is needed.

Visit 2: Week 1 or day 7 (±2 day) of diet. Weight will be measured and vital signs will be taken. Food diary from previous week to be collected, as well as 24hr recall of diet.

Visit 3: Week 2 of diet. Weight will be measured and vital signs will be taken. Food diary from previous week to be collected, as well as 24hr recall of diet.

6.2.3 Phase II—Visits During Radiation Treatment

Visit 4-9: Patients will be monitored for acute radiation toxicity including skin changes and desquamation. Patients will be questioned and examined to ensure general health and will be reassured about radiation-related side effects. Patients will turn in their food diary from the previous week and dietary counselors will review these with the patients to determine how they can continue to comply with dietary modification. At each visit, a 24hr recall of diet will be asked of the patient and compared with the diet journal to determine the self reporting accuracy. Each week during this period, patients will be counseled on their diet and given behavioral modification lessons corresponding to specific weeks in the diet (see Appendix V for worksheets). Weight will be taken at weeks 3, 5 and 7 of the diet, corresponding to weeks 1, 3 and 5 of radiation and vital signs will be performed weekly. FACT-B psychosocial assessment will be given at visit 7along with the PROMIS cancer fatigue short form. In addition, at visit 7 (week 5 of diet) patients will have a fasting blood draw done for insulin level.

Radiation will be planned to be administered 5 days a week, Monday through Friday. Radiation is given for approximately 6-6.5 weeks or 30-33 treatments.

6.2.4 Phase III—Post Radiation Treatment

Visit 10: Week 9 of diet,for scheduling purposes. Weight and vital signs will be measured. Patients will be monitored for acute radiation toxicity including skin changes and desquamation. Patients will turn in their food diary from the previous week and dietary counselors will review these with the patients to determine how they can continue to comply with dietary modification. A 24hr recall of diet will be asked of the patient and compared with the diet journal to determine the self-reporting accuracy. Patients will be counseled on behavioral modification for the final week of their diet (see Appendix V for worksheet). Weight and vital signs will be measured.

Visit 11: Week 10 of diet, +/- 3-5 days for scheduling purposes, last day of diet; Fasting blood draw to be done for CBC, basic metabolic panel, hemoglobin A1C, triglycerides, insulin, IGF-1, erythrocyte sedimentation rate (ESR), adiponectin, leptin and estradiol. Separately, blood will be analyzed for IRS-1, IGF-1R. Weight and vital signs will be measured. Conclusion bioimpedance and caliper measurements will be taken. Patients will be monitored for acute radiation toxicity including skin changes and desquamation. Patients will turn in their food diary from the previous week and dietary counselors will review these with the patients to determine how they can continue to comply with dietary modification. A 24hr recall of diet will be asked of the patient and compared with the diet journal to determine self-reporting accuracy. Patients will complete the FACT-B psychosocial evaluation as well as the PROMIS cancer fatigue short form.

Visit 12: 4 weeks after completion of diet. Fasting blood draw to be done for CBC, basic metabolic panel, hemoglobin A1C, triglycerides, insulin, IGF-1, erythrocyte sedimentation rate (ESR), adiponectin, leptin and estradiol. Separately, blood will be analyzed for IRS-1, IGF-1R. Weight, bioimpedence, caliper measurements and vital signs will be measured. Patients will be monitored for acute radiation toxicity including skin changes and desquamation. Patients will turn in their food diary from the last diet week. FACT-B and PROMIS cancer fatigue short form will be administered.

6.3 Study Flowchart

Examination	Pre-Treatment			Radiation Treatment								Post RT		Follow-up
	Screening	Surgery	Sim	Week of Caloric Restriction Diet										
				1	2	3	4	5	6	7	8	9	10	
Visit Number	0	1	2	3 D7	4 D14	5	6	7	8	9	10	11	12 Last	13
Informed Consent	X													
Background Info (demographics, meds, medical history)	X													
Inclusion/Exclusion Criteria	X													
Vital Signs			X	X	X	X	X	X	X	X	X	X	X	X
H&P; Performance Status	X													
Focused Physical			X			X	X	X	X	X	X			X
Weight, BMI	X		X	X		X		X		X			X	X
Caliper Measurements, Bioimpedance			X										X	X

Clinical Labs: CBC w/diff, CMP, HbA1c Serum: IGF-1, adiponectin, leptin, estradiol, triglycerides, fasting insulin, ESR			X										X	X
Fasting insulin level								X						
Other Labs: IGF-1R, IRS-1,			X										X	X
FACT-B Psychosocial Evaluation			X					X					X	X
PROMIS cancer fatigue short form			X					X					X	X
Specimen sent to Pathology for histologic exam andER, PR, HER2		X												
Dietary Counseling	X		X			X	X	X	X	X	X			
Behavioral Counseling				X		X	X	X	X	X	X	X		
Food Diary Collected			X	X	X	X	X	X	X	X	X	X	X	
Acute Toxicity Assessment			X			X	X	X	X	X	X	X	X	X

Key: H&P=Full history and physical exam
Sim=Radiation simulation planning session
RT=Radiation Therapy
D7=Day 7 of caloric restriction diet; D14=Day 14 of caloric restriction diet
Last=Final day of caloric restriction diet

6.4 Radiation Treatment

6.4.1 Dose Specifications

6.4.1.1 Breast: 50 Gy in 25 fractions of 2 Gy.

6.4.1.2 Lumpectomy PTV Cavity: Total dose will be 10-16 Gy in 5-8 fractions

6.4.1.3 Total radiation dose 60-66Gy

6.4.2 Technical Factors

6.4.2.1 The patient may be treated by photon or electron radiation therapy. Fields and treatment type will be up to the discretion of the treating radiation oncologist and may include but is not limited to 3D-RT, IMRT and en face.

6.4.2.2 The guidelines for IMRT in this trial will conform to the policies set by the Advanced Technology Consortium (ATC) and the National Cancer Institute (NCI) http://atc.wustl.edu/home/NCI/NCI_IMRT_Guidelines.html

6.4.2.3 Megavoltage photon beams with energies ≥6 MV and megavoltage electron beams are required.

6.4.3 Localization, Simulation, and Immobilization

6.4.3.1 Simulation and treatment may be performed with the patient in the supine or prone position.

6.4.3.2 Patients should be optimally positioned with immobilization devices at the discretion of the treating physician such as alpha cradle casts, breast boards, wing boards.

6.4.3.3 Methods to minimize the cardiac exposure to RT like heart block, gating or breathhold are allowed at the discretion of the treating physician

6.4.3.4 For large-breasted patients, including those with a large inframammary skin fold, devices to improve positioning of the breast are permissible.

6.4.3.5 A treatment planning CT scan in the treatment position will be required to define the tumor bed for boost.

6.4.3.5.1 The CT required for generation of a virtual plan with 3DCRT or IMRT must be post-lumpectomy

6.4.3.5.2 Radio-opaque markers must be placed on external landmarks at the acquisition of the CT scan to facilitate contouring segmentation of the CT data-set. These markers should identify: 1) The lumpectomy incision 2) Additional markers to define the clinical borders of tangent fields (e.g. based on the palpable breast tissue and boney landmarks).

6.4.3.5.3 The CT should extend cephalad to start at or above the mandible and extend sufficiently caudally (or inferiorly) to the inframammary fold to encompass the entire lung volume. A CT scan image thickness of ≤0.5 cm should be employed.

6.4.3.5.4 External skin localizing marks, which may include permanent tattoos, are recommended for radiation daily localization and set-up accuracy.

6.4.4 Treatment Planning/Target Volumes

6.4.4.1 Planning isodose lines will be chosen by treating physician.

6.4.4.2 Target Volumes and Normal Structures

6.4.4.3 Lumpectomy CTV: Contour using all available clinical and radiographic information including the excision cavity volume, architectural distortion, lumpectomy scar, seroma and/or extent of surgical clips (clips are strongly recommended). Patients without a clearly identifiable lumpectomy bed do not need a boost. Lumpectomy CTV volume will be expanded by 1.5 to 2cm at the physicians discretion and the expanded volume (Lumpectomy PTV) will be treated.

6.4.4.4 Ipsilateral lung. This may be contoured with auto-segmentation with manual

verification.

6.4.4.5 Contralateral lung. This may be contoured with auto-segmentation with manual verification

6.4.4.6 Heart: The heart should be contoured beginning just inferior to the level in which the pulmonary trunk branches into the left and right pulmonary arteries (PA). Above the PA, none of the hearts 4 chambers are present. All the mediastinal tissue below this level should be contoured, including the great vessels (ascending and descending aorta, inferior vena cava). The heart should be contoured on every contiguous slice thereafter to its inferiormost extent near the diaphragm. If one can identify the esophagus, this structure should be excluded from the heart. One need not include pericardial fat, if present. Contouring along the pericardium itself, when visible, is appropriate.

6.5 Treatment Verification

6.5.1 Before first treatment:

Portal films or images of each 3DCRT beam and an orthogonal pair for all patients must be obtained and approved by a physician prior to initiation of treatment.

6.5.2 Subsequent images or films:

Subsequent treatment images may be obtained every fraction. At the minimum, orthogonal pair films or treatment images must be obtained prior to fraction number 5 and every 5 fractions subsequently. The imaging modality and process should be performed based on the institutional guidelines.

6.6 Radiation Therapy Adverse Events

All Radiation Therapy AEs will be scored according to the NCI Common Terminology Criteria for Adverse Events (CTCAE) version 4

Short Term: Fatigue is an anticipated systemic reaction to radiation treatment. Skin erythema, desquamation, breast edema, breast tenderness and myositis are potential local reactions.

Long Term: Long term effects possibly include radiation pneumonitis, rib fractures, second malignancy and for left-sided lesions cardiac complications

7 STATISTICAL PLAN

7.1 Sample Size Determination

The study will enroll a total of 90 patients. For Phase 1, with a sample size of 40, the study has 83% power to establish that adherence is higher than 60%, assuming that true adherence will be 80% or greater (one-sided exact binomial test with alpha 0.05).

7.2 Statistical Methods

Primary endpoint (adherence). We will compute the proportion of patients who are adherent to the diet restriction (as defined in section 3.2), along with a 95% exact confidence interval. We will also use an exact binomial test (with a one-sided alpha of 0.05) to test whether adherence is greater than 60%.

Aim 1b. We will compute the proportion of patients with toxicity, along with a 95% exact confidence interval. Our institution's historical toxicity rate among similar patients is about 80% and we aim to prove that the dietary intervention is non-inferior with an absolute margin of 10%, using an exact binomial test. With a total sample size of 90 and assuming that true toxicity will be 80% or lower, we have 82% power (with one-sided alpha of 0.05).

Secondary endpoints. The change in body fat measurement between baseline and the end of the study will be analyzed via a paired t-test. Weight changes over time will be assessed by modeling BMI as a function of time (baseline, diet weeks 1, 3, 5, 7, and 10) via mixed-effects regression. The patterns of change over time in vital signs, insulin and other clinical labs, serum markers, and psycho-social outcomes (FACT-B) will also be analyzed similarly. If some of these measures are skewed, we will transform them (e.g., log) before the analyses. Finally, local recurrence, distant metastases, progression free survival, and overall survival will be analyzed via survival methods, specifically the Kaplan-Meier method and the logrank test. If sufficient events occur, we may assess the impact of various patient and clinical/treatment variables on these outcomes via Cox proportional hazards regression.

Local recurrence, progression free survival, distant metastases and overall survival will be assessed and compared with historic controls using the Kaplan Meier method. Local recurrence, progression free survival, distant metastases and overall survival will be measured from the date of study enrollment to time of event.

7.3 Subject Population(s) for Analysis

All subjects enrolled in the study who completed at least 4 food diaries per week during the diet modification phase will be used for analysis.

8 Safety and Adverse Events

8.1 Definitions

8.1.1 Adverse Event

An ***adverse event*** (AE) is any symptom, sign, illness or experience that develops or worsens in severity during the course of the study. Intercurrent illnesses or injuries should be regarded as adverse events. Abnormal results of diagnostic procedures are considered to be adverse events if the abnormality:

- results in study withdrawal
- is associated with a serious adverse event

- is associated with clinical signs or symptoms
- leads to additional treatment or to further diagnostic tests
- is considered by the investigator to be of clinical significance

8.1.2 Serious Adverse Event

Adverse events are classified as serious or non-serious.

A ***serious adverse event*** is any AE that is:

- fatal
- life-threatening
- requires or prolongs hospital stay
- results in persistent or significant disability or incapacity
- a congenital anomaly or birth defect
- an important medical event

Important medical events are those that may not be immediately life threatening, but are clearly of major clinical significance. They may jeopardize the subject, and may require intervention to prevent one of the other serious outcomes noted above. For example, drug overdose or abuse, a seizure that did not result in in-patient hospitalization, or intensive treatment of bronchospasm in an emergency department would typically be considered serious.

All adverse events that do not meet any of the criteria for serious should be regarded as non-serious adverse events.

8.1.3 Adverse Event Reporting Period

The study period during which adverse events must be reported is normally defined as the period from the initiation of any study procedures to the end of the study treatment follow-up. For this study, the study treatment follow-up is defined as 30 days following the last administration of study treatment.

8.1.4 Preexisting Condition

A preexisting condition is one that is present at the start of the study. A preexisting condition should be recorded as an adverse event if the frequency, intensity, or the character of the condition worsens during the study period.

8.1.5 General Physical Examination Findings

At screening, any clinically significant abnormality should be recorded as a preexisting condition. At the end of the study, any new clinically significant findings/abnormalities that meet the definition of an adverse event must also be recorded and documented as an adverse event.

8.1.6 Post-study Adverse Event

All unresolved adverse events should be followed by the investigator until the events are resolved, the subject is lost to follow-up, or the adverse event is

otherwise explained. At the last scheduled visit, the investigator should instruct each subject to report any subsequent event(s) that the subject, or the subject's personal physician, believes might reasonably be related to participation in this study. The investigator should notify the study sponsor of any death or adverse event occurring at any time after a subject has discontinued or terminated study participation that may reasonably be related to this study. The sponsor should also be notified if the investigator should become aware of the development of cancer or of a congenital anomaly in a subsequently conceived offspring of a subject that has participated in this study.

8.1.7 Abnormal Laboratory Values

A clinical laboratory abnormality should be documented as an adverse event if any one of the following conditions is met:

- The laboratory abnormality is not otherwise refuted by a repeat test to confirm the abnormality
- The abnormality suggests a disease and/or organ toxicity
- The abnormality is of a degree that requires active management; e.g. change of dose, discontinuation of the drug, more frequent follow-up assessments, further diagnostic investigation, etc.

8.1.8 Hospitalization, Prolonged Hospitalization or Surgery

Any adverse event that results in hospitalization or prolonged hospitalization should be documented and reported as a serious adverse event unless specifically instructed otherwise in this protocol. Any condition responsible for surgery should be documented as an adverse event if the condition meets the criteria for and adverse event.

Neither the condition, hospitalization, prolonged hospitalization, nor surgery are reported as an adverse event in the following circumstances:

- Hospitalization or prolonged hospitalization for diagnostic or elective surgical procedures for a preexisting condition. Surgery should not be reported as an outcome of an adverse event if the purpose of the surgery was elective or diagnostic and the outcome was uneventful.
- Hospitalization or prolonged hospitalization required to allow efficacy measurement for the study.
- Hospitalization or prolonged hospitalization for therapy of the target disease of the study, unless it is a worsening or increase in frequency of hospital admissions as judged by the clinical investigator.

8.2 Recording of Adverse Events

At each contact with the subject, the investigator must seek information on adverse events by specific questioning and, as appropriate, by examination. Information on all adverse events should be recorded immediately in the source document, and also in the appropriate adverse event module of the case report form (CRF). All clearly related signs, symptoms, and abnormal diagnostic procedures results should be

recorded in the source document, though should be grouped under one diagnosis.

All adverse events occurring during the study period must be recorded. The clinical course of each event should be followed until resolution, stabilization, or until it has been determined that the study treatment or participation is not the cause. Serious adverse events that are still ongoing at the end of the study period must be followed up to determine the final outcome. Any serious adverse event that occurs after the study period and is considered to be possibly related to the study treatment or study participation should be recorded and reported immediately.

8.3 Unblinding Procedures

This is single arm study. There is no unblinding procedure.

8.4 Stopping Rules

There will be no formal interim analyses for purposes of stopping the study early. However, descriptive analyses for monitoring accrual and study implementation will be carried out throughout the study.

8.5 Data and Safety Monitoring Plan

It is the responsibility of the Principal Investigator to oversee the safety of the study at his/her site. This safety monitoring will include careful assessment and appropriate reporting of adverse events as noted above, as well as the compliance and implementation of the KCC data and safety-monitoring plan. Medical monitoring will include a regular assessment of the number and type of serious adverse events by both the assigned Medical Monitor and the KCC DSMC.

8.5.1 Medical Monitoring and AE/SAE Reporting

A Medical Monitor is assigned to this study at the Thomas Jefferson University. This is a physician/pharmacist who is not directly involved in the trial, and is not currently collaborating with the sponsor/investigator on any other trial. The role of the Medical Monitor is to review all reportable AEs/SAEs (in real-time) including grading, toxicity assignments, non-reportable AEs (quarterly), protocol violations/deviations, as well as all other safety data and activity data observed in the ongoing clinical trial occurring at Thomas Jefferson University. The Medical Monitor may recommend reporting of adverse events and relevant safety data, and may also recommend suspension or termination of the study to the DSMC and TJU IRB.

Every KCC investigator initiated protocol includes requirements for reporting of adverse events based on CTC 4.0. All events are reported to the IRB and Medical Monitor using a password protected web-site. In addition all unexpected and serious adverse events (SAEs) are reported to the TJU IRB and to the Food and Drug Administration (FDA) if applicable. The investigator is required to submit all unexpected and serious adverse events to the TJU IRB and the Medical Monitor within the timeframes outlined in the below table. All AE/SAEs will be reported to

the DSMC at the quarterly DSMC review meetings; however, if the Medical Monitor determines corrective action is necessary, an "ad hoc" DSMC meeting will be called. ***Fatal adverse events related to treatment which are unexpected must be reported within 24 hours to the TJU IRB and the DSMC. Fatalities not related to the study drug/device must be reported within 5 days.*** A summary of the reporting requirements for KCC investigator initiated Phase I and Phase II studies are presented below.

	Grade 1	Grade 2	Grade 2	Grade 3		Grade 3		Grades 4 and 5
	Unexpected and Expected	Unexpected	Expected	Unexpected with Hospitalization	Unexpected without Hospitalization	Expected with Hospitalization	Expected without Hospitalization	Unexpected and Expected
Unrelated Unlikely	Reviewed at Quarterly DSMC Meeting and IRB Annual Review	Reviewed at Quarterly DSMC Meeting and IRB Annual Review	Reviewed at Quarterly DSMC Meeting and IRB Annual Review	5 Working Days	Reviewed at Quarterly DSMC Meeting and IRB Annual Review	5 Working Days	Reviewed at Quarterly DSMC Meeting and IRB Annual Review	Phase 1 - 48 Hours (Death: 24 Hours) Phase 2 - 5 Working Days
Possible Probable Definite	Reviewed at Quarterly DSMC Meeting and IRB Annual Review	5 working days	Reviewed at Quarterly DSMC Meeting and IRB Annual Review	48 Hours (Death: 24 Hours)	Phase 1 - 48 Hours Phase 2 - 5 Working Days	48 Hours (Death: 24 Hours)	Reviewed at Quarterly DSMC Meeting and IRB Annual Review	Phase 1 and Phase 2 - 48 Hours (Death: 24 Hours)

**NOTE: This table is based on the NCI AE/SAE reporting Guidelines and the TJU IRB Policy and Procedures. Please follow the individual protocol AE/SAE reporting guidelines if more stringent reporting procedures are specified.

8.5.2 Data and Safety Monitoring Committee

Data and Safety Monitoring Committee (DSMC) is the Data and Safety Monitoring Board (DSMB) for the KCC. The DSMC is a multidisciplinary committee charged with overseeing the monitoring of safety of participants in clinical trials, and the conduct, progress, validity, and integrity of the data for all clinical trials at the Thomas Jefferson University KCC. The committee meets quarterly to review the progress and safety of all active research protocols that are not monitored by another safety and data monitoring committee or board.

- The DSMC meets quarterly. Additional DSMC meetings are scheduled based on the nature and number of trials being monitored over a specified time period. The DSMC meets (by conference call) within 24 hours following the notification of an unexpected adverse event felt to be related to the study drug.
- Prior to each DSMC meeting, each board member, is provided a printout of all reported AEs and SAEs occurring during the reporting period for this clinical trial.

The principal investigator provides a detailed and comprehensive narrative assessment of current adverse events to date, indicating their possible significance and whether these toxicities have affected the conduct of the trial. DSMC members are provided with the principal investigator's assessment, a written report summarizing adverse events, safety data, and activity data observed during the specified time period described in each protocol, as well as recommendations from the Medical Monitor. A review of outcome results (response, toxicity and adverse events) and factors external to the study (such as scientific or therapeutic developments) is discussed, and the Committee votes on the status of each study.

- A summary of the board's action is sent to each investigator, the CCRRC and TJU IRBs. The DSMC actions may include recommendations/requirements that will lead to improved patient safety and/or efficacy, significant benefits or risks that have developed, or other changes determined to be necessary. The DSMC may also take note of slow accrual or lack of scientific progress, and refer such issues to the CCRRC. The DSMC provides the investigator with the rationale for any decision made.

9 Data Handling and Record Keeping

9.1 Confidentiality

Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Those regulations require a signed subject authorization informing the subject of the following:

- What protected health information (PHI) will be collected from subjects in this study
- Who will have access to that information and why
- Who will use or disclose that information
- The rights of a research subject to revoke their authorization for use of their PHI.

In the event that a subject revokes authorization to collect or use PHI, the investigator, by regulation, retains the ability to use all information collected prior to the revocation of subject authorization. For subjects that have revoked authorization to collect or use PHI, attempts should be made to obtain permission to collect at least vital status (i.e. that the subject is alive) at the end of their scheduled study period.

9.2 Source Documents

Source data is all information, original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents. Examples of these original documents, and data records include: hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories, and at medico-technical departments involved in the clinical trial.

9.3 Case Report Forms

The study case report form (CRF) is the primary data collection instrument for the study. All data requested on the CRF must be recorded. All missing data must be explained. If a space on the CRF is left blank because the procedure was not done or the question was not asked, write “N/D”. If the item is not applicable to the individual case, write “N/A”. All entries should be printed legibly in black ink. If any entry error has been made, to correct such an error, draw a single straight line through the incorrect entry and enter the correct data above it. All such changes must be initialed and dated. DO NOT ERASE OR WHITE OUT ERRORS. For clarification of illegible or uncertain entries, print the clarification above the item, then initial and date it.

CRFs are found in the Appendix VII.

9.4 Records Retention

It is the investigator’s responsibility to retain study essential documents for at least 2 years after the last approval of a marketing application in their country and until there are no pending or contemplated marketing applications in their country or at least 2 years have elapsed since the trial began.

10 STUDY MONITORING, AUDITING, AND INSPECTING

10.1 Study Monitoring Plan

The investigator will allocate adequate time for monitoring activities. The Investigator will also ensure that the medical monitor or other compliance or quality assurance reviewer is given access to all the above noted study-related documents and study related facilities (e.g. pharmacy, diagnostic laboratory, etc.), and has adequate space to conduct the monitoring visit.

10.2 Auditing and Inspecting

The investigator will permit study-related monitoring, audits, and inspections by the IRB, the funding sponsor, government regulatory bodies, and University compliance and quality assurance groups of all study related documents (e.g. source documents, regulatory documents, data collection instruments, study data etc.). The investigator will ensure the capability for inspections of applicable study-related facilities (e.g. pharmacy, diagnostic laboratory, etc.).

Participation as an investigator in this study implies acceptance of potential inspection by government regulatory authorities and applicable University compliance and quality assurance offices.

10.2.1 Independent External and Internal Audits

In addition to review by the DSMC, all studies initiated by KCC investigators are audited by an independent auditor once they have achieved 10% of target accrual. However, a study can be audited at any time based on recommendations by the

IRB, DSMC, CCRRC and/or the Director of Clinical Investigations, KCC. Studies are re-audited once they have achieved 50% of target accrual. Special audits may be recommended by the IRB, DSMC or CCRRC based on prior findings, allegations of scientific misconduct and where significant irregularities are found through quality control procedures. Any irregularities identified as part of this process would result in a full audit of that study.

In addition to the audits at 10 and 50%, the CRMO randomly audits at least 10 percent of all patients entered into therapeutic KCC trials and other trials as necessary, on at least a bi-annual basis, to verify that there is a signed and dated patient consent form, the patient has met the eligibility criteria, and that SAEs are documented and reported to the TJU IRB.

All audit reports are submitted to the DSMC for review and action (when appropriate). A copy of this report and recommended DSMC action is sent to the CCRRC and TJU IRB. The committee regards the scientific review process as dynamic and constructive rather than punitive. The review process is designed to assist Principal Investigators in ensuring the safety of study subjects and the adequacy and accuracy of any data generated. The TJU IRB may, based on the DSMC and auditor's recommendation, suspend or terminate the trial.

11 Ethical Considerations

This study is to be conducted according to US and international standards of Good Clinical Practice (FDA Title 21 part 312 and International Conference on Harmonization guidelines), applicable government regulations and Institutional research policies and procedures.

This protocol and any amendments will be submitted to a properly constituted independent Institutional Review Board (IRB), in agreement with local legal prescriptions, for formal approval of the study conduct. The decision of the IRB concerning the conduct of the study will be made in writing to the investigator before commencement of this study.

All subjects for this study will be provided a consent form that is compliant with local and federal regulations, describing this study and providing sufficient information for subjects to make an informed decision about their participation in this study. See Attachment for a copy of the Subject Informed Consent Form. This consent form will be submitted with the protocol for review and approval by the IRB for the study. The formal consent of a subject, using the IRB-approved consent form, must be obtained before that subject is submitted to any study procedure. This consent form must be signed by the subject or legally acceptable surrogate, and the investigator-designated research professional obtaining the consent.

12 Study Finances

12.1 Funding Source

This study is financed through a generous pilot grant from the Ladies of Port

Richmond. It is also financed in part by the Kimmel Cancer Center's NCI Cancer Center Support Grant P30 CA56036.

12.2 Conflict of Interest

Any investigator who has a conflict of interest with this study (patent ownership, royalties, or financial gain greater than the minimum allowable by their institution, etc.) must have the conflict reviewed by a properly constituted Conflict of Interest Committee with a Committee-sanctioned conflict management plan that has been reviewed and approved by the study sponsor prior to participation in this study. All Jefferson University Investigators will follow the TJU Conflicts of Interest Policy for Employees (107.03).

13 Publication Plan

All investigators involved in the portion of the trial being published will review manuscripts prior to publication. The Principal Investigator will be ultimately responsible for the content of all manuscripts.

14 Specimen Banking

Tissue and blood specimen banking is included in this protocol. Tissue and blood specimens will be stored in a secure -70° freezer in the Bodine Cancer Center.

Specimen collections will be performed on consented patients. Please see Appendix VI for detailed information on schedule, amount, storage and shipping requirement.

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16 APPENDICES

Appendix I: Patient Thank You Letter

This is a template to prepare a letter thanking the patient for enrolling in this trial. The template is intended as a guide and can be tailored to each patient's situation. This is to increase the awareness of the importance of clinical trials and improve accrual and follow-through.

[PATIENT NAME] [DATE]
[PATIENT ADDRESS]

Dear [PATIENT SALUTATION],

Thank you for agreeing to take part in this important research study. Many questions remain unanswered in cancer. With the help of people like you who participate in clinical trials, we will achieve our goal of effectively treating and ultimately curing cancer.

We believe you will receive high quality, complete care. I and my research staff will maintain very close contact with you. This will allow me to provide you with the best care while learning as much as possible to help you and other patients.

On behalf of *Thomas Jefferson University*, we thank you again and look forward to helping you.

Sincerely,
[PHYSICIAN NAME]

Appendix II: Karnofsky Performance Scale

Able to carry on normal activity and to work; no special care needed.	100	Normal no complaints; no evidence of disease.
	90	Able to carry on normal activity; minor signs or symptoms of disease.
	80	Normal activity with effort; some signs or symptoms of disease.
Unable to work; able to live at home and care for most personal needs; varying amount of assistance needed.	70	Cares for self; unable to carry on normal activity or to do active work.
	60	Requires occasional assistance, but is able to care for most of his personal needs.
	50	Requires considerable assistance and frequent medical care.
Unable to care for self; requires equivalent of institutional or hospital care; disease may be progressing rapidly.	40	Disabled; requires special care and assistance.
	30	Severely disabled; hospital admission is indicated although death not imminent.
	20	Very sick; hospital admission necessary; active supportive treatment necessary.
	10	Moribund; fatal processes progressing rapidly.
	0	Dead

Appendix III: Common Toxicity Criteria Version 4.0

http://ctep.cancer.gov/reporting/ctc.html

Appendix IV: Visit Schedule

(please refer to appendix VI for blood specimen banking schedule)

Appendix V. Behavioral Modification Worksheets

Initially patients will be counseled on eating healthy and dietary modification before beginning their diet. They will complete the worksheets labeled "Be a Fat Detective", "Eating Less Fat" and "Healthy Eating" during this first week.

Be a Fat Detective.

We'll begin today to keep track of your weight.

Your starting weight was _____ pounds.

Your weight goal is _____ pounds.

To keep track of your weight:

- At every session, mark it on the How Am I Doing? graph.
- Weigh yourself at home every_____

on the same scale, and

at this time of day _____ .

Write your weight on the back of your Keeping Track book.

\PTCORE\01DIETICT.PT

Lifestyle Balance
Be a Fat Detective, Page 1

To help you lose weight, we'll help you **eat healthy.**

Healthy eating involves **eating less fat.**

- **Eating too much fat is "fattening" (makes us fat). By eating less fat, you can lose weight.**

> In fact, fat is the most fattening of all the things we eat.
>
> Fat contains **more than twice the calories** as the same amount of sugar, starch, or protein.

Even small amounts of high fat foods are high in calories. Compare:

		Grams of fat	*Calories*
	¼ cup peanuts	18	212
	3 cups plain, air-popped pocorn (12 times as much food!)	1	92

- **Fat is related to heart disease and diabetes.**

> Research has shown that eating a lot of fat can increase your cholesterol level. Cholesterol is one type of fat in your blood. The higher your cholesterol, the greater your chance of having a heart attack. Research has also shown that eating a lot of fat may increase your chances of getting diabetes.

What kinds of foods do you eat that are high in fat?

1. _____
2. _____
3. _____
4. _____
5. _____
6. _____
7. _____
8. _____
9. _____
10. _____

Most of the fat we eat (70% of it) is hidden in foods.

Let's uncover it! Here's a lunch menu:

Fried fish sandwich	5 teaspoons of fat
Large French fries	6 teaspoons of fat
Apple turnover, fried	4 teaspoons of fat
Milkshake, with ice cream	5 teaspoons of fat
Total:	20 teaspoons of fat (That's about 1 entire stick of butter or margarine!)

\\PTCORE\01\DIETECT.PT

Lifestyle Balance
Be a Fat Detective, Page 3

Keep track of the fat you eat every day.

1. **Write down everything you eat and drink.**

   It's the **most important** part of changing your behavior.

   Spelling is NOT important. What IS important is to:
   - Be honest (write down what you really eat).
   - Be accurate (measure portions, read labels).
   - Be complete (include everything).

2. **Figure out how much fat is in every food. Write it down.**

   - Figure out the amount of each food you ate.
   - Look up each food in the Fat Counter.
   - Compare the amount of food YOU ate with the amount in the Fat Counter to see how much fat you ate.

3. **Add up the fat you eat during the day.**

Your fat gram goal or "budget" is to

stay under _____ grams of fat each day.

A gram is the way fat in food is measured. A gram is a unit of weight.
A paper clip weighs about 1 gram.

It may be hard to reach your fat gram goal at first.
Just try to **get as close to your goal as you can.**

Keeping Track (practice page)

For each food below:

- Look up the food in the Fat Counter,
- Figure out the grams of fat in the amount you ate.

Time	Amount	Food: Name/Description	Grams of Fat	Calories

Practice Page

Total: _____ _____

When you use the Fat Counter:

Can't find a food?

- Use the fat gram value for a food that's the most like it. (For example, use nut bread for zucchini bread.)
- Write the name of the food in the back of your Fat Counter. Ask your Lifestyle Coach about it next week.

Have trouble figuring the grams of fat?

- Just write down the food and amount.
- Your Lifestyle Coach will help you next week.

Make a recipe?

- For many recipes, you can simply write down how much of each ingredient you ate. For example, in a stew, how much meat did you eat? Carrots? And so on.
- If you cook from recipes often, bring in some favorite recipes next week. Your Lifestyle Coach will help you count the grams of fat in them.

✣ *Eat a packaged food?* Look on the label for the fat grams.

Nutrition Facts

Serving Size 1 oz. (28g/about 21 pieces)
Servings Per Container 10

Amount Per Serving
Calories 150 Calories from Fat 80

	% Daily Value*
Total Fat 9 g	**14%**
Saturated Fat 2g	**10%**
Cholesterol 0mg	**0%**
Sodium 300mg	**12%**
Total Carbohydrate 16 g	**5%**
Dietary Fiber less than 1g	**1%**
Sugars less than 1 g	
Protein 2g	

Vitamin A	0%	Vitamin C	0%
Calcium	0%	Iron	2%

* Percent Daily Values are based on a 2,000 calorie diet. Your daily values may be higher or lower depending on your calorie needs:

	Calories	2,000	2,500	
Total Fat	Less than		65g	80g
Sat Fat	Less than	20g	25g	
Cholesterol	Less than	300mg	300mg	
Sodium	Less than	2,400mg	2,400mg	
Total Carbohydrate		300g	375g	
Dietary Fiber		25g	30g	

Calories per gram:
Fat 9 Carbohydrate 4 Protein 4

❖ Look at the **Serving Size**. (Is this the amount you ate?)

❖ Look at the **Total Fat grams per serving.**

What if you eat a larger serving than is listed on the label?

You will be eating more fat grams than are listed on the label.

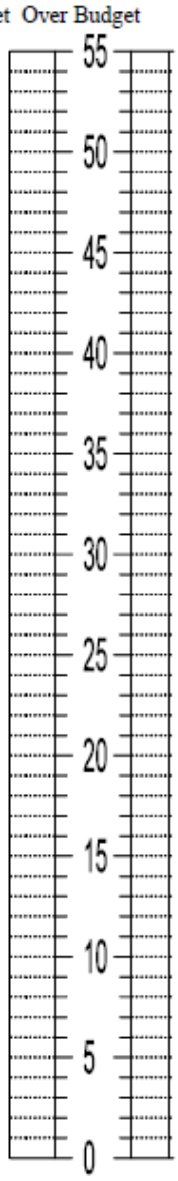
\PTCORE\01DETECT.PT

Lifestyle Balance
Be a Fat Detective, Page 7

Adding up the fat grams.

Amount	Food: Name/Description	Grams of Fat/ *Running Total*

Practice Page



To do next week:

I will:

Keep track of my weight.

- Weigh myself at home every_____

  at this time of day _____ .
- Record my weight on the back of the Keeping Track book.

Keep track of what I eat and drink.

- Write down everything I eat and drink in the Keeping Track book.
- Use the Fat Counter to figure out how much fat is in what I ate.

  Write the fat grams down in the Keeping Track book.
- Keep a running fat gram total throughout the day. Try using the Fat Bank, too.
- Come as close to my fat gram goal as I can.

Keep track of my physical activity.

- Be active for_____ .

Three Ways to Eat Less Fat.

Weighing and measuring foods is important.

Metal or plastic measuring cups and spoons (for solid foods)
- Fill. Level off before you record.

Glass measuring cup (for liquids)
- Read the line at eye level.

Scale (for meats, cheese, etc.)
- Weigh meats **after** they are cooked.
  4 oz. raw = 3 oz. cooked (about the size of a deck of cards)

Most people are surprised when they weigh and measure foods.

Our eyes can play tricks on us.
- Write down the name of each food on display.
- Guess the amount.
- Weigh or measure the food. Or look at the bottom of the food model. Write down the actual amount.
- Figure the fat grams for the actual amount.

Food	Guessed amount	Actual amount	Grams of Fat	Teaspoons of Fat*

* Your Lifestyle Coach will fill in this column to show you the hidden fat.

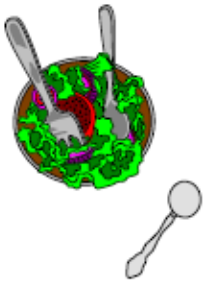
The three ways to eat less fat:

1. Eat high-fat foods *less often.*

Example: Don't eat French fries every day.

Have them only once a week.
(That's about 132 fewer grams of fat per week!)

2. Eat *smaller amounts* of high-fat foods.



Cutting back even a little on the amount you eat can make a big difference.

Example: At the salad bar, don't use the ladle to pour on salad dressing. Most salad dressing ladles hold 4 tablespoons
(32 grams of fat for regular dressing!).

Instead, use a regular spoon from your place setting. Most hold 1 tablespoon or less.
(That's 24 fewer grams of fat!)

3. Eat *lower-fat foods instead.*

In the coming months, you'll discover a number of ways to "eat lower-fat foods instead."

Ways to Eat Lower-Fat Foods Instead	For example, instead of this food:	Fat (g)	Choose this food:	Fat (g)
Instead of high-fat foods, pick low-fat foods.	Potato chips, 1-ounce bag	11	Pretzels, 1-ounce bag 	1
Instead of high-fat foods, use low-fat substitutes.*	Regular margarine, 1 teaspoon	4	Low-fat margarine, 1 teaspoon 	2
Find ways to lower the amount of fat in meats you eat.	Roast beef (chuck), untrimmed, 3 oz.	22	Roast beef (top round), trimmed, 3 oz. 	4
Instead of flavoring foods with fat, use low-fat flavorings.	Baked potato with 2 tablespoons sour cream	6	Baked potato with salsa 	0
Avoid frying foods; use other healthier ways to cook.	Chicken breast, with skin, breaded, fried	24	Chicken breast with skin, grilled 	9

*** Warning:** Low-fat or fat-free products still contain calories. Be careful about how much you eat. In fact, some low-fat or fat-free products are *very* high in calories because they're loaded with sugar. Check the label. For example:

½ cup nonfat frozen yogurt 100 calories
½ cup regular ice cream (10-12% fat) 143 calories

Menu Make-Over

The menus below show examples of small changes that make a big difference in fat grams saved.

High-fat Breakfast	Ways to lower the fat	Make-Over	Grams of fat saved
Fried egg	Pick low-fat foods.	Cold cereal (1 cup)	6
Milk, whole, 1 cup	Use low-fat substitutes.	Milk, skim, 1 cup	8
Toast, 1 slice, with 1 tsp. margarine	Use low-fat flavorings.	Toast, 1 slice, with 1 tsp. jam	4
Coffee, 1 cup, w/2 Tbsp. half + half	Use low-fat substitutes.	Coffee, 1 c., w/2 Tbsp. nonfat creamer	6
High-fat Snack			
Doughnut, glazed, yeast, 1 (4" diameter)	Pick low-fat foods.	Apple, 1 (2-3/4" diameter)	21
High-fat Lunch			
Bread, 2 sl., with 1 Tbsp. mayonnaise	Eat smaller amounts.	Bread, 2 sl., with 1 tsp.	7
Bologna, beef or pork, 1 ounce	Lower the fat in meats.	mayonnaise	7
American cheese, 1 ounce	Use low-fat substitutes.	Turkey breast, 1 ounce	6
Potato chips, 1-ounce bag	Eat smaller amounts.	American cheese, low-fat, 1 ounce	3
		Potato chips, ½ of a 1-ounce bag	
High-fat Dinner			
Fish, flounder, deep fried, 3 oz.	Cook in healthy ways.	Fish, flounder, baked without fat, 3 oz.	14
Mashed potatoes, ½ cup	Use low-fat flavorings.	Mashed potatoes, ½ c., no butter added	6
Gravy, ¼ cup	Use low-fat substitutes.	Gravy, from mix, with water, ¼ cup	5
Green beans, w/bacon, ½ cup	Use low-fat flavorings.	Green beans, with nonfat broth, ½ cup	2
Tossed salad w/2 Tbsp. French drsg.	Use low-fat substitutes.	Tossed salad w/2 Tbsp. fat-free drsg.	16
Ice cream, premium, ½ cup	Eat less often.	Orange, 1 [Save ice cream for a rare treat.]	12

\PTCORE\05THREE.PT

Lifestyle Balance
Three Ways to Eat Less Fat, Page 4

To do next week:

I will:

Keep track of my weight, what I eat, and my activity.

Keep a running fat gram total.

Try to stay under your fat gram goal (budget).

Be active for _____ .

Make a plan to eat less fat and follow it.

- Write down 5 foods you eat that are high in fat. Circle one.
- Pick one of the 3 ways to eat less fat from that food. Write down what you will do next week. Be sure it is **something you can do.**

My top 5 high-fat foods	The 3 Ways to Eat Less Fat		
	I will eat it only this (less) often:	I will eat only this (smaller) amount:	I will eat this (lower-fat) food instead:

What I will need to do to reach this goal:

_____

Problems I might have and what I will do to solve them:

_____

Before the next session, answer these questions:

- Did you follow your plan? ___Yes ___No ___ Almost
- What problems did you have following your plan?

  _____
- What could you do differently next week?

  _____

Thomas Jefferson University

Menu Make-Over

Use this work sheet to practice cutting the fat from high-fat meals and snacks.

Breakfast	Makeover	Grams of fat saved

Lunch		

Dinner		

Snacks		

\PTCORE\05THREE.PT

Lifestyle Balance
Menu Make-Over

Healthy Eating.

Eating less fat is essential to losing weight.
It's also one important part of healthy eating.

Some of the other parts of healthy eating include:

... the way you eat.

A regular pattern of meals is important.

A regular pattern will keep you from getting too hungry and losing control.

Eat slowly.

If you eat slowly, you will:

- Digest your food better.
- Be more aware of what you're eating.
- Be more aware of when you're full.

Try pausing between bites. Put down your utensils.
Enjoy the taste of your food.

Don't worry about cleaning your plate.

Serve yourself smaller portions to begin with.

... what you eat overall.

The Food Pyramid: *Low-Fat Choices*


Breads, cereals, rice, pasta (6-11 servings)

_____

_____


Vegetables (3-5 servings)

_____

_____


Fruit (2-4 servings)

_____

_____


Milk, yogurt, cheese (2-3 servings)

_____

_____


Meat, poultry, fish, dry beans, eggs
(2-3 servings)

_____

_____


Fats, sweets, alcohol (use only in small amounts)
Choices that are lower in fat:

_____

_____

The Food Pyramid

Group	Example low-fat foods, serving	High-fat (or high-sugar) foods
 Breads, cereals, rice, pastas (6-11 svg.)	- 1 slice bread or tortilla - ½ bagel, English muffin, pita bread - 4-6 crackers - ½ cup cooked cereal, pasta, bulgur, rice - 3/4 cup dry cereal	- Croissants, sweet rolls, doughnuts, muffins, Danish pastry, biscuits, high-fat crackers, regular tortilla chips, fried tortillas - Granola-type cereals
Vegetables (3-5 servings) 	- 1 cup raw vegetables - ½ cup cooked vegetables or vegetable juice	- Vegetables with butter/margarine, cream, or cheese sauces - Fried vegetables, olives, avocadoes
Fruits (2-4 svg.) 	- 1 small fresh fruit - ½ cup canned fruit or fruit juice	- Fruits in pastry (as in pies), coconut - High in sugar: dried fruit, juices or drinks sweetened with sugar, fruit canned in syrup, large amounts of fruit juice
Milk, yogurt, cheese (2-3 svg.) 	- 1 cup skim or 1% milk - 1 cup low- or nonfat yogurt - 2-3 ounces low- or nonfat cheese (< 2 grams fat/ounce)	- 2% or whole milk - Regular cheese (>2 grams fat/ounce) - High in sugar: yogurt with added sugar
Meat, poultry, fish, dry beans, eggs (2-3 svg.) 	- 2-3 ounces cooked lean meat, poultry (without skin), or fish - ½ cup tuna, canned in water - ½ cup cooked dry beans, lentils, split peas - 1 egg or ¼ cup egg substitute	- Peanuts, peanut butter, all nuts - Bacon, sausage, hot dogs, hamburgers, luncheon meats, most red meats (except lean, trimmed cuts) - Chicken or turkey with skin - Tuna canned in oil - Beans cooked in lard or salt pork
Fats, sweets, alcohol (limit) 	Low-fat substitutes: - Low-fat or fat-free margarine, mayonnaise, salad dressings, cream cheese, or sour cream - Low-fat whipped topping - Fat-free frozen yogurt Foods lower in sugar: - All fruit jams - Diet soft drinks - Lite syrup	- Regular margarine, shortening, lard, oil, butter, mayonnaise, salad dressing, cream cheese, sour cream - Half and half, whipped cream - Cakes, cookies, ice cream, candy, cupcakes - Honey, jelly, syrup, sugar - Soft drinks

Rate Your Plate

1. Pick two days from last week's Keeping Track. Fill in the dates.

2. Check one box for every serving that you ate from the Food Pyramid groups. The shaded boxes show you the minumum number of servings recommended.

Date: _____

Bread, cereal, rice, pasta											
Vegetables											
Fruit											
Milk, yogurt, cheese											
Meat, poultry, fish, dry beans, eggs											
Fats, sweets, alcohol											

Date: _____

Bread, cereal, rice, pasta											
Vegetables											
Fruit											
Milk, yogurt, cheese											
Meat, poultry, fish, dry beans, eggs											
Fats, sweets, alcohol											

\PTCORE\06HEALT.PT

Lifestyle Balance
Healthy Eating, Page 4

What could *you* do to better match the Food Pyramid?

Pyramid Group	Breakfast	Lunch	Dinner	Snacks	Total Servings	Goal
Bread, cereal, rice, pasta						6-11 servings
Vegetables						3-5 servings
Fruit						2-4 servings
Milk, yogurt, cheese						2-3 servings
Meat, poultry, fish, dry beans, eggs						2-3 servings
Fats, sweets, alcohol						Only small amounts

The Food Pyramid and "eating lower-fat foods instead" work together.

Instead of high-fat foods, pick low-fat foods.

Choose fresh fruit and vegetables for snacks.
Serve vegetarian dinners several times a week.
Eat fruit for dessert.
Other:

Instead of high-fat foods, use lower-fat substitutes.

Use low-fat or fat-free:		
Margarine	Cheese, cream cheese	Frozen yogurt
Mayonnaise	Salad dressing	Sour cream
Skim or 1% milk.		
Other:		

Instead of flavoring foods with fat, use low-fat flavorings.

To flavor these foods:	Use these low-fat flavorings:
Potatoes, vegetables	- Low-fat margarine (small amount), nonfat sour cream, defatted broth, low-fat or fat-free plain yogurt, salsa. - Herbs,mustard, lemon juice.
Bread	Nonfat cream cheese, low-fat margarine (small amount), all fruit jams.
Pancakes	Fruit, low-calorie syrup, unsweetened applesauce, crushed berries.
Salads	Nonfat or low-fat salad dressing, lemon juice, vinegar
Pasta, rice	Spaghetti sauce without meat or added fat, chopped vegetables, white sauce made with skim or 1% milk and no fat.
Other:	

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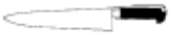
Lifestyle Balance
Healthy Eating, Page 6

Find ways to lower the fat in meats you eat.

Buy lean cuts (round, loin, sirloin, leg).
Trim all the fat you can see. 
Bake, roast, broil, barbecue, grill instead of fry. Or stir-fry: Heat pan to high heat. Add no more than 1 teaspoon oil or use vegetable cooking spray or defatted broth. Add thinly sliced meat. Stir until cooked well.
Remove the skin from chicken and turkey. (This can be done before or after cooking.)  Choose white meat.
Drain off fat after cooking. Blot with a paper towel. For ground beef, put in a colander after cooking, and rinse with hot water.
Flavor meats with low-fat flavorings, such as BBQ, Tabasco, catsup, lemon juice, or Worcestershire.
Other:

Avoid frying foods. Use other, healthier ways to cook.

Poach, boil, or scramble eggs (or egg whites) with vegetable cooking spray. Use two egg whites instead of a whole egg.
Microwave, steam, or boil vegetables in a small amount of water.    Or stir-fry (see directions above).
Cook meats without adding fat (see ideas above).
Other:

To do next week:

I will:

- Keep track of my weight, eating and activity.
- Fill out the Rate Your Plate form every day.

Use the next two pages.

Answer these questions before our next session:

Did you make any changes during the week to better match the Food Pyramid? If yes, what were they?

_____

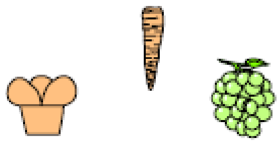
_____

What problems did you have? How did you solve them?

_____

_____

_____



Rate Your Plate

Check one box for every serving that you eat from the Food Pyramid groups.
The shaded boxes show you the minimum number of servings recommended.

Date: ________________

Bread, cereal, rice, pasta											
Vegetables											
Fruit											
Milk, yogurt, cheese											
Meat, poultry, fish, dry beans, eggs											
Fats, sweets, alcohol											

Date: ________________

Bread, cereal, rice, pasta											
Vegetables											
Fruit											
Milk, yogurt, cheese											
Meat, poultry, fish, dry beans, eggs											
Fats, sweets, alcohol											

Date: ________________

Bread, cereal, rice, pasta											
Vegetables											
Fruit											
Milk, yogurt, cheese											
Meat, poultry, fish, dry beans, eggs											
Fats, sweets, alcohol											

Date: ________________

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Lifestyle Balance
Healthy Eating, Page 9

Bread, cereal, rice, pasta											
Vegetables											
Fruit											
Milk, yogurt, cheese											
Meat, poultry, fish, dry beans, eggs											
Fats, sweets, alcohol											

Date: ________________

Bread, cereal, rice, pasta											
Vegetables											
Fruit											
Milk, yogurt, cheese											
Meat, poultry, fish, dry beans, eggs											
Fats, sweets, alcohol											

Date: ________________

Bread, cereal, rice, pasta											
Vegetables											
Fruit											
Milk, yogurt, cheese											
Meat, poultry, fish, dry beans, eggs											
Fats, sweets, alcohol											

Date: ________________

Bread, cereal, rice, pasta											
Vegetables											
Fruit											
Milk, yogurt, cheese											
Meat, poultry, fish, dry beans, eggs											
Fats, sweets, alcohol											

Patients will complete this worksheet on environmental cues during week 1 of radiation/week 3 of diet.

Take Charge of What's Around You.

What "cues" you (or makes you want) to eat?

- Hunger.
- What you're thinking or feeling.
- What other people say and do.
- Sight and smell of food.
- Certain activities that make you think about food, like watching TV or reading magazines.

Examples:

"Cue"	Makes you want to eat:
You see a carton of ice cream.	Ice cream.
You turn on the TV. 	Potato chips. 
You go to the movies.	Popcorn.

When you respond to a food cue in the same way, over and over again, you build a **habit.**

How can you change problem food cues and habits?

1. **Stay away from the cue.** Or keep it out of sight.

2. **Build a new, healthier habit.**
   Practice responding to the cue in a healthier way.
   Add a new cue that helps you lead a healthier life.

Remember, it takes time to break an old habit or build a new one.

Common problem food cues

At home:	Living room:	TV, computer, telephone, candy dishes.
	Kitchen:	Ready-to-eat foods (ice cream, cheese, cookies), foods being cooked, leftovers.
	Dining room:	Serving dishes on table, large dinner plates, leftovers on plates.
At work:		Bakery on the way to work, high-fat/calorie foods in public areas (doughnuts, high-fat coffee creamers, candy), or in desk, vending machines.

Remember:

1. **Keep high-fat/calorie foods out of your house and work place.**
   Or keep them out of sight. *Out of sight is out of mind.*

   Keep lower-fat/calorie choices easy to reach, in sight, and ready to eat.
   Examples: Fresh fruits, raw vegetables (already washed and prepared), nonfat dips, pretzels, low-fat popcorn, diet drinks, sugar-free Jell-O, sugar-free popsicles.

2. **Limit your eating to one place.**

3. **When you eat, limit other activities.**

Where you shop: _____

Shopping tips

- Make a shopping list ahead of time. Stick to the list!
- Don't go shopping when you're hungry.
- Avoid sections in the store that are tempting to you, if possible.
- Ask the grocery store manager to order low-fat/calorie foods you want.
- Only use food coupons for low-fat/calorie foods, not for high-fat foods.

Activity Cues

1. Add positive activity cues to your life.

- Keep these in sight: Shoes, bag, mat, bike.
  Calendar or graph.
  Video and magazines.
  Photos, posters.
  Reminders.

- Set up a regular "activity date" with a friend or family member.
- Set a timer or alarm on your watch to remind you to be active.
- Others: _____

2. Get rid of cues for being inactive.

- **Limit TV watching.** Or be active while you watch TV.
- Don't pile things at the bottom of the stairs. Climb the stairs each time something needs to be taken upstairs.
- Others: _____

You can make food and activity cues
work ***FOR*** you,
not against you.

To do next week:

I will:
Get rid of one problem *food* cue.

What problem food cue will you get rid of? _____
What will you need to do to get rid of it?
_____

What problems might you have? What will you do to solve them?

_____

Add one positive cue for *being more active*.

What activity cue will you add? _____

What will you need to do to add it?
_____

What problems might you have? What will you do to solve them?

_____

Keep track of my weight, eating, and activity.
Do my best to reach my goals.

Before the next meeting, answer these questions:

Did you follow your plan? ___Yes ___No ___ Almost
What problems did you have?
_____
What could you do differently next week?

_____

Patients will complete this worksheet on problem solving during week 2 of radiation/week 4 of their diet.

Problem Solving.

Many things can get in the way
of being more active and eating less fat and calories.
But problems **can** be solved.

The five steps to solving a problem:

1. Describe the problem in detail.

Be specific.

Look at what led up to the problem.
Find the **action (or behavior) chain.**

Try to see the steps (links) in the action chain. Look for:
- Things that "cue" you (or make you want) to eat or be inactive.
- People who don't support you.
- Thoughts or feelings that get in your way.

Sarah's Action Chain

- Didn't eat lunch.
- Boss was critical.
- Sarah felt stressed and anxious.
- Came home tired, upset, and hungry.
- Went right to the kitchen.
- Saw cookies on counter.
- Ate cookies.

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2. Brainstorm your options.

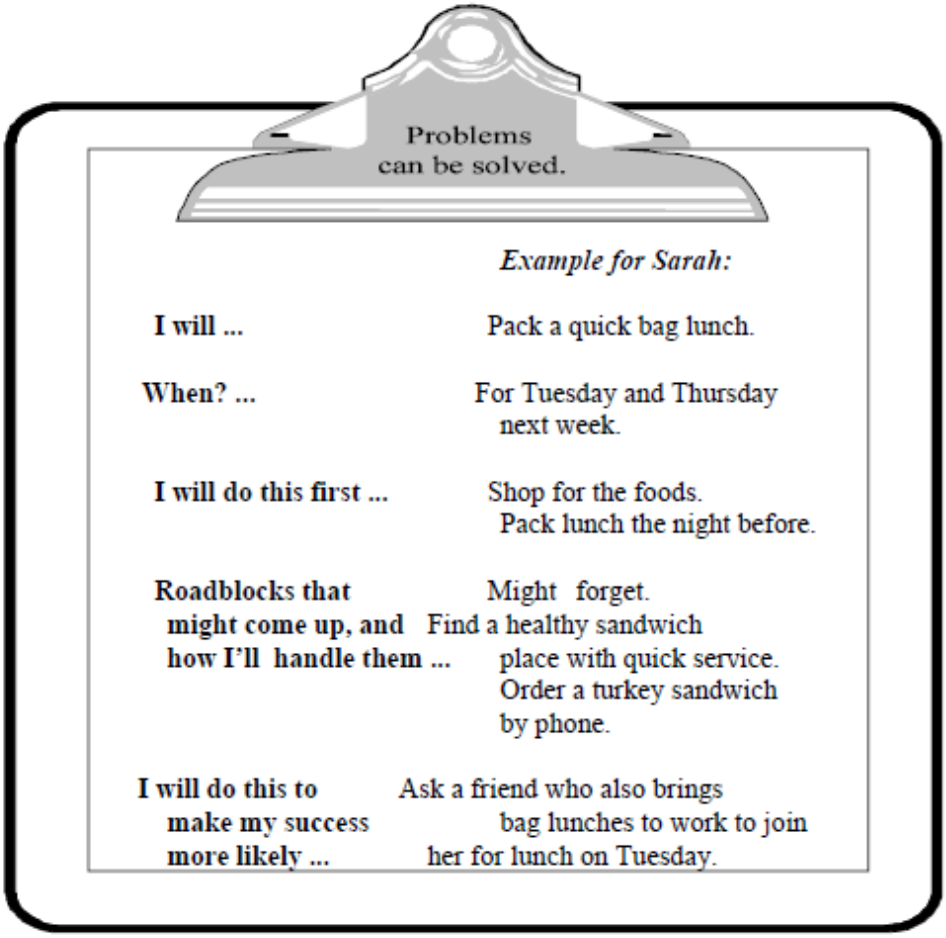
Links	*Some of Sarah's Options*
Didn't eat lunch.	✣ Quit her job. (Just kidding.) ✣ Pack a quick bag lunch.
Boss was critical. Sarah felt stressed and anxious.	✣ Talk with her boss about solving the problems at work. ✣ Take a break. ✣ Get support from a co-worker.
Came home tired, upset, and hungry.	✣ Go for a walk after work to unwind.
Went right to the kitchen.	✣ Enter house through different door. ✣ Plan something to do the minute she gets home (like getting out in the yard, straightening a closet or room in the house).
Saw cookies on counter.	✣ Don't buy cookies. ✣ Keep cookies out of sight. ✣ Keep fruit in sight.

3. Pick one option to try.

Weigh the pros and cons.
Choose one that is **very likely to work** and that **you can do**.

Try to break as many links as you can,
as early as you can.

4. Make a positive action plan.



Example for Sarah:

I will ...	Pack a quick bag lunch.
When? ...	For Tuesday and Thursday next week.
I will do this first ...	Shop for the foods. Pack lunch the night before.
Roadblocks that might come up, and how I'll handle them ...	Might forget. Find a healthy sandwich place with quick service. Order a turkey sandwich by phone.
I will do this to make my success more likely ...	Ask a friend who also brings bag lunches to work to join her for lunch on Tuesday.

5. Try it. See how it goes.

Did it work? If not, what went wrong? Problem solve again.

Problem solving is a *process*. Don't give up!

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The Lifestyle Balance *Problem Solver*

Describe the problem in detail. Be specific.

Find the action chain. Links	Brainstorm your options. Options
	

Pick one option. Is it very likely to work? Can you do it?

Make a positive action plan.

Problems can be solved.

I will: _____

When? _____

I will do this first: _____

Roadblocks that might come up:	I will handle them by:
_____	_____
_____	_____
_____	_____

I will do this to make my success more likely:

_____

How can we help you?

To do next week:

I will:

Keep Track of my weight, eating and physical activity.

Try my action plan. Did it work? If not, what went wrong?

_____

Patients will complete this worksheet on dining out during week 3 of radiation/week 5 of diet.

Four Keys to Healthy Eating Out.

1. Plan ahead.

- Call ahead to ask about low-fat choices.
- Pick where you eat out carefully. Go somewhere that offers low-fat choices.
- Eat less fat and fewer calories during other meals that day.
- Eat a little something before you go out. Or drink a large, low-calorie beverage.
- Plan what to order without looking at the menu.
- Don't drink alcohol before eating.
- For parties or dinner parties: Bring something from home to share with others.

2. Ask for what you want. Be firm and friendly.

Ask for the foods you want:

- Ask for lower-fat foods.
- Can foods be cooked in a different way?
- Don't be afraid to ask for foods that aren't on the menu.

Ask for the amounts you want:

- Ask how much is usually served.
- Order salad dressing, gravy, sauces, or spreads "on the side."
- Ask for less cheese or no cheese.
- Split a main dish or dessert with someone.
- Order a small size (appetizer, senior citizen's, children's size).
- Before or after the meal, have the amount you don't want to eat put in a container to take home.

How to ask for what you want.

- Begin with "I", not "You."
- Use a firm and friendly tone of voice that can be heard.
- Look the person in the eye.
- Repeat your needs until you are heard. Keep your voice calm.

Wishy-washy	"Oh, well. I guess they couldn't broil the fish."
Threatening	"You said you would broil my fish!"
Firm and friendly	"This looks very nice. But I asked for my fish to be broiled, not fried. Would you have some broiled for me, please?"

3. Take charge of what's around you.

- Be the first to order.
- Keep foods off the table that you don't want to eat.
- Ask that your plate be removed as soon as you finish.

4. Choose foods carefully.

Watch out for these high-fat words on menus.

Au gratin	Hollandaise
Breaded	Parmesan
Buttered or buttery	Pastry
Cheese sauce	Rich
Creamed, creamy, in cream sauce	Sauteed
Fried, deep fried, french fried, batter fried, pan fried	Escalloped
Gravy	Scalloped
	Seasoned
	Southern style

Look for these low-fat words, instead.

Baked	Poached
Broiled	Roasted
Boiled	Steamed
Grilled	Stir-fried

Watch out for sauces.
Think about what you really *need* to eat.
Trim visible fat off meat.
Take skin off chicken.

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What's on the menu?

You can make lower-fat choices, no matter what kind of restaurant you go to. Be sure to ask the waiter how the food is prepared.

Note: Most restaurants serve a tossed salad--a low-fat choice if topped with lemon juice, vinegar, or a low-fat dressing.

GO! Lower-fat choices	CAUTION! High-fat choices
Pizza - Plain cheese pizza (ask for half the cheese or low-fat cheese). - Onions, green peppers, mushrooms.	- Meat toppings (sausage/pepperoni) - Olives .
Burger Place (fast food) - Grilled, broiled, or roasted chicken, without sauce. - Broiled, extra lean burger.	- Regular hamburger, cheeseburger. - French fries. - Fried fish or chicken. - Mayonnaise-based sauces.
Mexican - Heated (not fried) tortillas. - Grilled chicken or beef fajitas. - Soft tacos (corn or flour tortillas). - Salsa.	- Enchiladas. - Chili con queso. - Fried tortillas, tortilla chips. - Sour cream, guacamole. - Crisp tacos.
Chinese and Japanese - Stir-fried chicken. - Stir-fried vegetables. - Steamed rice. - Soup. - Teriyaki.	- Egg foo yung. - Fried chicken, beef, or fish. - Fried rice or noodles. - Egg rolls. - Fried won ton. - Tempura.
Italian - Spaghetti with meatless tomato sauce. - Minestrone soup.	- Sausage. - Lasagna, manicotti, other pasta dishes with cheese or cream. - Fried or breaded dishes (like veal or eggplan parmesan).
Seafood - Broiled, baked, or boiled seafood with lemon. - Plain baked potato.	- Fried fish. - Fried vegetables. - French fries
Steakhouses - Shrimp cocktail. - Broiled chicken or fish. - Plain baked potato.	Steak (except trim med lean cuts). - Fried fish or chicken. - Onion rings, other fried vegetables. - French fries.

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Fast food *can* be lower in fat.

The following fast foods contain from 0 to 12 grams of fat per serving. Most fast foods contain 20 to 50 grams of fat.

Food Items	Fat (g)	Calories
ARBY'S		
Junior Roast Beef	11	233
Light Roast Beef Deluxe	10	294
Light Roast Chicken Deluxe	7	276
Light Roast Turkey Deluxe	6	260
Garden Salad (no drsg.)	5	117
Roast Chicken Salad	7	204
BOSTON MARKET		
1/4 White Meat Chicken without wing or skin	4	160
Plain Chicken Breast Sandwich	4	430
Chicken Soup	3	80
BBQ Baked Beans	9	330
Corn Bread	6	200
New Potatoes	3	140
Homestyle Mashed Potatoes	8	180
Rice Pilaf	5	180
Steamed Vegetables	0	35
Zucchini Marinara	4	80
Fruit Salad	0	70
Cranberry Relish	5	370
Butter Nut Squash	6	160
Buttered Corn	4	190

Food Items	Fat (g)	Calories
BURGER KING		
Broiled Chicken Salad (no drsg.)	10	200
Chicken Tenders (6 pieces)	12	250
Garden Salad (no drsg.)	5	90
Side Salad (no drsg.)	3	50
CHICK-FIL-A		
Chicken Sandwich	9	290
Chicken Salad on Whole Wheat	5	320
Chargrilled Chicken Sandwich	3	280
Grilled 'N Lites	2	100
Chicken Soup	1	110
Chargrilled Chicken Garden Salad	3	170
Tossed Salad (no drsg.)	0	70
Carrot-Raisin Salad	2	150
DOMINOS PIZZA (12-inch Hand-tossed)		
Cheese (2 slices)	10	344
Ham (2 slices)	10	362
Veggie (2 slices)	10	360

Fat and calorie values are from **Nutrition in the Fast Lane**, © 1995, Franklin Publishing, Inc.

Food Items	Fat (g)	Calories
HARDEE'S		
Grilled Chicken Sandwich	9	290
Hot Ham N'Cheese Sandwich	11	300
Mashed Potatoes	0	70
Grilled Chicken Salad	3	150
Side Salad (no dressing)	0	25
KFC		
Drumstick (Original Rec.)	7	130
1/4 Breast (w/o skin/wing, Rotisserie)	6	199
Value BBQ Flavored Chicken Sandwich	8	256
Green Beans	1	36
Red Beans and Rice	3	114
BBQ Baked Beans	2	132
Garden Rice	1	75
Potatoes with gravy	5	109
Coleslaw	6	114
LONG JOHN SILVER'S		
Flavorbaked Chicken Sandwich	10	290
Flavorbaked Chicken (1 piece)	4	150
Flavorbaked Fish (1 piece)	4	120
Ocean Chef Salad	2	100
Chicken - Light Herb	4	120
Side Salad	0	25
Rice Pilaf	3	140
Roll (no butter)	0	110
Cole Slaw	6	140
Green Beans	4	30
Hush Puppies (1 serving)	3	60
Baked Potato (1, no topping)	0	210
Corn Cobbette (no butter)	0	80

Food Items	Fat (g)	Calories
MCDONALD'S		
Hamburger (single)	9	270
McGrilled Chicken Sandwich	3	250
Chicken Fajita	8	190
McLean Deluxe	12	340
Chef Salad (no drsg.)	11	210
Chunky Chicken Salad (no drsg.)	5	160
Garden Salad (no drsg.)	4	80
Side Salad (no drsg.)	2	45
Lite Vinaigrette Drsg.	2	50
TACO BELL		
Light Taco	5	140
Light Soft Taco	5	180
Light Chicken Soft Taco	5	180
Light Bean Burito	6	330
Seasoned Rice	3	110
Pintos N' Cheese	9	190
Light Chicken Burrito	6	290
WENDY'S		
Small Chili	7	210
Grilled Chicken Sandwich	7	290
Jr. Hamburger	10	270
Plain Baked Potato	0	310
Side Salad	3	60
Grilled Chicken Salad	8	200
Caesar Side Salad	5	110
Deluxe Garden Salad	6	110
Frosty Dairy Dessert (small)	10	340

Fat and calorie values are from **Nutrition in the Fast Lane**, © 1995, Franklin Publishing, Inc.

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Lifestyle Balance
The Four Keys to Healthy Eating Out, Page 6

Describe a problem you have when you eat out:

_____

Choose one of the four keys to healthy eating out. Make a positive action plan.

Problems can be solved.

I will: _____

When? _____

I will do this first: _____

Roadblocks that might come up: I will handle them by:

_____ _____

_____ _____

I will do this to make my success more likely:

_____

How can we help you?

To do next week:

Keeping Track

I will:

Keep track of my weight, eating and activity.
Try my action plan. Did it work? If not, what went wrong?

_____

Patients will complete this worksheet on negative thoughts during week 4 of radiation/week 6 of diet.

Talk Back to Negative Thoughts.

Everyone has negative thoughts at times.
Negative thoughts can lead you to overeat or be inactive.
A vicious cycle of self-defeat can result.

Example: *Thought:* "I'm tired of working so hard.

I can never eat what I want."
Result: You eat potato chips.
Thought: "I did it again. I'll never lose weight."
Result: You feel discouraged and eat more.

Some common negative thoughts:		Example(s)
Good or Bad	Divide the world into: ✣ Good or bad foods; ✣ Seeing yourself as a success or failure; ✣ Being on or off the program.	"Look at what I did. I ate that cake. I'll never be able to succeed
Excuses	Blame something or someone else for our problems. We don't mean to go off the program, but we "can't help it."	"I don't have the willpower." "I have to buy these cookies just in case company drops in."
Should	Expect perfection. A set-up for disappointment. Lead to anger and resentment.	"I should have eaten less of that dessert."
Not As Good As	Compare ourselves to someone else. Blame ourselves for not measuring up.	"Mary lost two pounds this week, and I only lost one."
Give Up	Defeat ourselves. Often follow the other kinds of negative thoughts.	"This program is too hard. I might as well forget it."

How to talk back to a negative thought:

1. Catch yourself. Think, "I'm doing it to myself."
2. Imagine shouting, "STOP!" to yourself. Picture a huge, red stop sign.
3. Talk back with a positive thought.

Negative thought:	Talk back with a positive thought:
Good or Bad	**Work toward Balance**
• "I can never eat dessert again." • "Look at what I did. I ate that cake. I'll never succeed."	• "I can eat that dessert and then cut back on something else." • "One slip-up isn't the end of the world. I can get back on track."
Excuses	**It's Worth a Try**
• "It's too cold to take a walk." • "I don't have the willpower."	• "I can try going for a walk and stop if it gets too cold." • "It's hard to change old habits, but I'll give it a try and see how it works."
Should	**It's My Choice**
• "I should have eaten less dessert." • "I have to write down everything I eat."	• "It was my choice. Next time I can decide not to eat so much." • "I'm writing down everything I eat because it helps me eat better."
Not As Good As	**Everyone's Different**
• "Mary lost two pounds this week, and I only lost one."	• "It's not a race. Mary and I can lose weight at different rates and both succeed."
Give Up	**One Step at a Time**
• "This program is too hard. I might as well forget it." • "I'll never get it right."	• "I've learned something about what's hard for me." • "I'll try something different next time."

Practice:

1. Write examples of negative thoughts below.
2. Say each thought out loud, then say, "Stop!"
3. Talk back, again out loud, with a positive thought. Write it down.

Negative thought	STOP!	Positive thought
		
		
		
		
		

To do next week:

I will:

- Keep track of my weight, eating and activity.
- Catch myself thinking negative thoughts.
  Write them in my Keeping Track books.
- Practice STOP -ping them and talking back with positive thoughts.

Patients will complete this worksheet on social cues during week 5 of radiation/week 7 of diet.

Make Social Cues Work *for* You.

Social cues: What other people say or do that affects your eating and activity.

Problem social cues:	**Examples:**
The sight of other people eating problem foods or being inactive.	
Being offered (or pressured to eat) problem foods or invited to do something inactive.	
Being nagged.	
Hearing complaints.	

Helpful social cues:	**Examples:**
The sight of other people eating healthy foods or being active.	
Being offered healthy foods or invited to do something active.	
Being praised. 	
Hearing compliments.	

When you respond to a social cue in the same way, you build a **habit.**
The other person has *also* learned a habit.

This makes social cues even harder to change than other cues.

To change problem social cues:

1. **Stay away from the cue, if you can.**

   Example: Move to a different room.

2. **Change the cue, if you can.**

   Discuss the problem with the other person.
   Brainstorm options.

Ask others to:

- **Praise you for your efforts and**
- **Ignore your slips.**

This is KEY to your success.

3. **Practice responding in a more healthy way.**

   Say "No" to food offers.
   Show others you know they mean well.
   Suggest something they can do to help you.

   Example: "No, thanks. But I'd love a glass of ice water."

Remember, it takes time to change habits.

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To add helpful social cues:

- Spend time with people who are active and make healthy food choices.
- Put yourself in places where people are active.
- Set up a regular "date" with others to be active.

- Ask your friends to call you to remind you to be active or to set up dates to be active.
- Bring a low-fat/calorie food to share when you go to a dinner party.
- Be the first to order when you eat out at a restaurant.
- Be social by doing something active. Take a walk and talk.
- Others:

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Lifestyle Balance
Make Social Cues Work *for* You, Page 3

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Who could provide support for you?

For healthy eating: _____

For being more active: _____

What could they do to help you? Here are some ideas.

Ways to help me eat healthy:

- ❖ Serve low-fat/calorie foods for meals.
- ❖ Eat low-fat/calorie foods when I'm nearby.
- ❖ Don't tempt me with problem foods as a reward or gift.
- ❖ Clear the table and put food away as soon as the meal is over.
- ❖ Help with cooking, shopping, or cleaning up after meals.
- ❖ Don't offer me second helpings.
- ❖ Encourage me to cook new foods.
- ❖ Praise my efforts to eat healthier foods.
- ❖ Other: _____ _____

Ways to help me be more active:

- ❖ Go for a walk with me. Or do other physical activities with me.
- ❖ Plan social events around being active.
- ❖ Compromise when my being active conflicts with your schedule.
- ❖ Praise me when I do my scheduled activity. Don't remind me when I don't.
- ❖ Babysit for me so I can take a walk.
- ❖ Set up a regular date with me to be active.
- ❖ Encourage me to go out for a walk when I'm debating whether or not to go.
- ❖ Try to achieve and maintain the DPP goals with me.
- ❖ Other: _____ _____

Social cues are powerful at social events.

Social events:

- Upset our routine.
- Challenge us with unique food and social cues.
- May involve habits that have developed over many years and so can be very powerful.

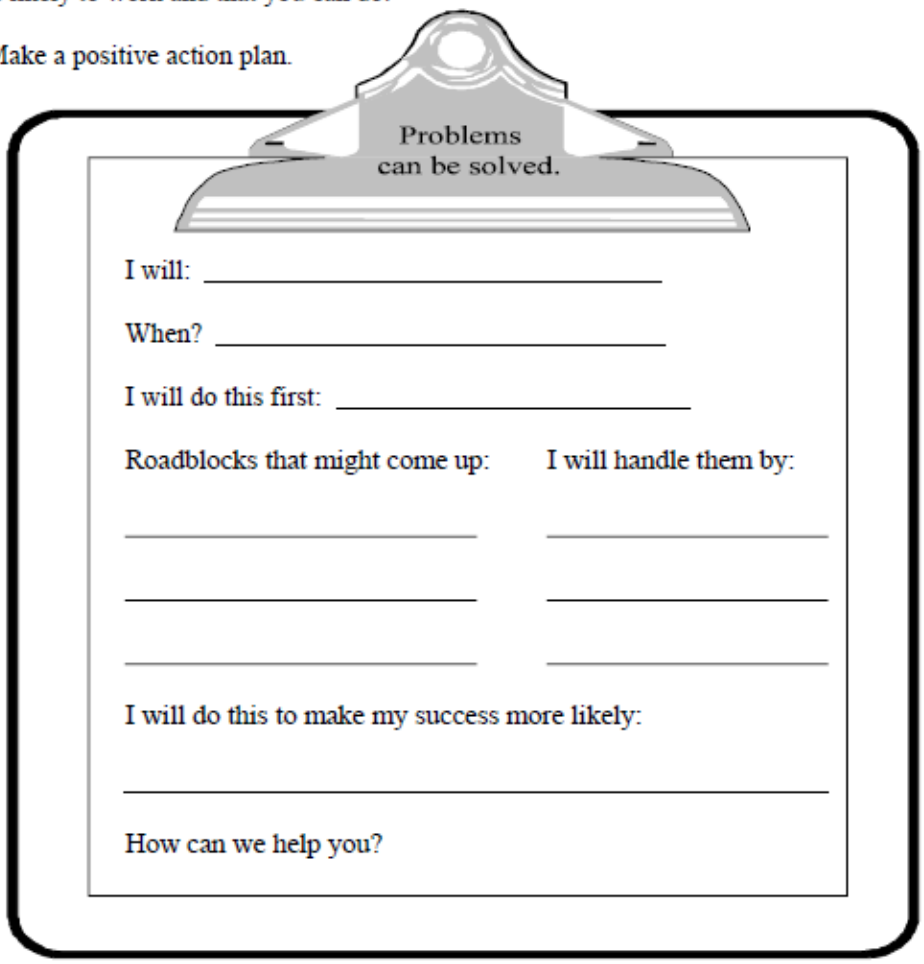
To handle social events, problem solve. Brainstorm your options. Some ideas:

Options:	Examples:
Plan ahead.	✣ Eat something before the event. ✣ Plan your meal in advance. ✣ Budget your fat grams ahead of time. Plan to eat the best (in small portions) and leave the rest. ✣ Bring a tasty, low-fat dish to share.
Stay away from problem cues.	✣ Stand as far away as you can from the table with the food. Keep your hands busy with a glass of water, coffee, tea, or diet soda. ✣ Watch the alcohol. It lowers your will power and increases appetite. ✣ Clear the table as soon as possible. Put the food away.
Change problem cues.	✣ Discuss your goals with your family, friends, guests, host or hostess. ✣ Ask others to praise your efforts and ignore your slips.
Respond to problem cues in a more healthy way.	✣ Practice a polite, but firm, "No, thank you." ✣ Suggest something else they can do to help you. "No thanks, but I'd love a glass of ice water."
Add helpful cues.	✣ Serve healthy foods or bring some to share. Use low-fat products to lower the fat in favorite recipes. Try some new, low-fat recipes. ✣ Ask a friend or family member for support (split dessert with you, take a walk together, offer you healthy food choices). ✣ Plan things to do that are active and don't involve food.

Describe a social cue that's a *problem* for you. _____

Pick one idea from this session for changing that social cue. Choose one that is likely to work and that you can do.

Make a positive action plan.



I will: _____

When? _____

I will do this first: _____

Roadblocks that might come up:	I will handle them by:
_____	_____
_____	_____
_____	_____

I will do this to make my success more likely:

_____

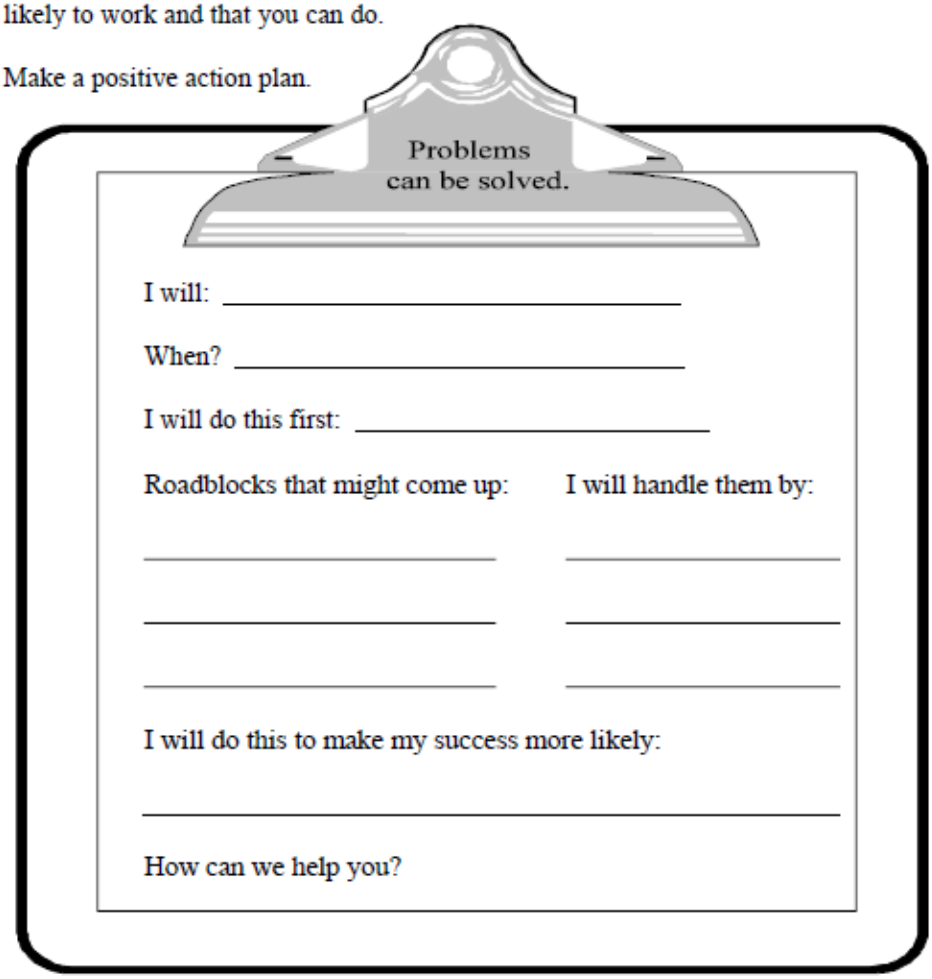
How can we help you?

Describe a *positive* social cue you'd like to add to your life.

_____

Pick one idea from this session for adding that social cue. Choose one that is likely to work and that you can do.

Make a positive action plan.



To do next week:

I will:

Keep track of my weight, eating and activity.

Try my two action plans for making social cues work for me.

Answer these questions:

Did my action plans work? _____

If not, what went wrong? _____

_____

What could I do differently next time? _____

_____

Patients will go through the following worksheet during week 6 of radiation/week 8 of diet.

You Can Manage Stress.

Stress is tension or pressure.
Many people react to stress by overeating or being inactive.

What kinds of things make you feel stressed?

What is it like for you when you get stressed?

Ways to prevent stress:

Practice saying, "No."
Try to say "Yes" only when it is important to you.

Share some of your work with others.

Set goals you can reach.

Take charge of your time.
- Make schedules with the real world in mind.
- Get organized.

Use problem solving:
- Describe the problem in detail.
- Brainstorm your options.
- Pick one option to try.
- Make an action plan.
- Try it. See how it goes.

Plan ahead.
- Think about the kind of situations that are stressful for you.
- Plan for how to handle them or work around them.

Keep things in perspective.
Remember your purpose.
- Think of all the good things in your life.

Reach out to people.

Be physically active.

When you can't avoid stress:

Catch yourself feeling stressed as early as you can.
Take a 10-minute "time out."

- Move those muscles.
- Pamper yourself. Just take 10 minutes for YOURSELF.
- Breathe. Try this: Take a full, deep breath. Count to five. Then let go of your breath slowly. Let the muscles in your face, arms, legs, and body go completely loose.

The DPP may cause stress.

Possible source of stress	Way(s) to manage stress	Examples
Extra time spent in food preparation, shopping.	- Share some of your work. - Take charge of your time.	- Ask spouse to help shop. - Make double recipes. Freeze part for later.
Feel deprived when can't eat favorite foods.	- Set goals you can reach. - Keep things in perspective.	- Allow yourself to have favorite foods in small amounts now and then. - Remind yourself how important preventing diabetes is to you.
Upset if your family doesn't like low-fat foods.	- Reach out to people. - Use the steps for solving problems.	- Ask your family to support your efforts to try new foods. - Discuss your feelings and your commitment to weight loss with your family. Brainstorm options with them. Try one.
Feel uncomfortable participating in social activities where high-fat foods are available.	- Practice saying, "No." - Reach out to people. - Plan ahead.	- Turn down invitations that aren't important to you. - Call the host or hostess ahead and ask what will be served and if you can bring a low-fat dish. - Before you go to a party, plan what foods you will choose.
Feel stressed by trying to fit activity into an already busy schedule.	- Plan ahead. - Problem solve.	- Make an appointment to be active. - Combine activity with other events you plan to do anyhow. (Take a walking meeting. Go hiking with the family.)

_____

Other major sources of stress for you:

_____

Choose one source of stress. Make a positive action plan:

To do next week:

I will:

Keep track of my weight, eating and activity.

Try my action plan for managing stress.

Did it work? If not, what went wrong?

_____

_____

Prior to the final week of their diet, patients will go through this worksheet on staying motivated.

Ways to Stay Motivated.

Progress Review

Changes you've made to be more active:

_____

_____

_____

Changes you've made to eat less fat (and fewer calories):

_____

_____

_____

Have you reached your weight goal? Yes No

Have you reached your activity goal? Yes No

If not, what will you do to improve your progress?

_____

_____

_____

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Ways to stay motivated:

1. Stay aware of the benefits you've achieved and hope to achieve.

What did you hope to achieve when you first joined ?
Have you reached these goals?

_____

_____

What would you like to achieve in the next six months ?

_____

_____

2. Recognize your successes.

What changes in your eating and activity do you feel proudest of?

_____

_____

_____

_____

3. Keep visible signs of your progress.

Post weight and activity graphs on your refrigerator door.

Mark your activity milestones on a map toward a particular goal.

Measure yourself (waist, belt size) once a month.

4. Keep track of your weight, eating and activity.

Record your activity daily.

Record what you eat this often: _____

Record your weight on: _____

5. Add variety to your routine.

How have you varied your activity?

_____

What meals, snacks, or foods are you most bored with?

_____

Can you think of some ways to vary this part of your eating?

_____

_____

6. Set new goals for yourself. Develop ways to reward yourself when you meet each goal.

Goals: Specific, short-term, just enough of a challenge.

Rewards: Something you will do or buy **if and only if** you reach your goal.

What are some non-food ways you can reward yourself for reaching a goal?

_____

_____

_____

_____

7. Create some friendly competition.

Set up the kind of competition in which you both win.

8. Use the Lifestyle Balance staff and others to help you stay motivated.

Call a Lifestyle Balance staff member, participant, or friend for encouragement and support.

Choose one way to stay motivated that would be helpful to you now.

_____

Make a positive action plan:

To do next week:

I will:

Keep track of my weight, eating and activity.

Try my action plan for staying motivated.

Did it work? If not, what went wrong?

_____

Appendix VI. Blood/Tissue Specimen Collection and Banking

Blood

1. Blood specimen collections will be performed on each patient.
2. Timing: baseline at radiation simulation visit, conclusion of diet and 4 weeks after radiation.
3. Collection: Each time, 20-30 cc blood will be collected using two sodium heparin vacutainer tubes.
4. Sample preparation: Blood specimens collected from Thomas Jefferson University should be processed locally the same day of collection. Processed samples (serum and plasma) should be given to Dr. Simone or member of her laboratory.
5. Process: All blood specimens collected will be processed locally within 24 hr of collection. The blood specimens will be processed for plasma and serum.
6. Storage: Plasma specimens and serum will be stored in liquid nitrogen or a -70-80°C freezer

Appendix VII. Case Report Forms

THOMAS JEFFERSON UNIVERSITY HOSPITAL
DEPARTMENT OF RADIATION ONCOLOGY

CAREFOR Study: A Feasibility Pilot Trial Evaluating Caloric Restriction for Oncology Research in Early Stage Breast Cancer Patients

REGISTRATION FORM

Patient's Initials_____ Case#_____ Dose Level_____

MR#_____ Date of birth_____

Address_____

_____

Telephone_____

Sex_____ Race_____ Ethnicity _____

Insurance_____

Radiation Oncologist:_____

Medical Oncologist:_____

Resident:_____

Signature_____ Date_____

CAREFOR Study Case Report Form (CRF)—Screening Visit

Date of Screening:_____

Patient Demographics

Age:_____ Race:_____

Current Address (for mailing purposes):

_____

_____

Emergency Contact:_____

Marital Status:_____

Highest Education Level Completed:_____

Past Medical History and Relevant Clinical Information

Date of Diagnosis:_____

How was the mass found?

- ☐ MMG
- ☐ SBE
- ☐ Physician Exam
- ☐ Other:_____

Date of most recent mammogram:_____

Side of Breast Mass (L v. R):_____

Previous History of Breast Cancer:_____

_____

Family History of Breast Cancer:_____

_____

If applicable, what treatment was received for previous breast cancer:_____

_____ Previous History of any other malignancy (include dates of diagnosis and NED date):_____

_____

_____

Is this patient a candidate for breast conservation?_____

_____ Oral Contraceptive Use (current or past): Y or N

Hormone Replacement Use: Y or N

Date of last period_____ Age at menarche:_____

Gravida/Para:_____

Previous diagnosis of any of the following:

Unstable Angina

Coronary Artery Disease

Myocardial Infarct, if yes please indicate date of event:_____
CHF
Valvular Disease
Arrythmias/Pacemaker Placement
Diabetes
Severe Asthma
Autoimmune Disorder (specifically SLE, scleroderma, dermatomyositis)
Any Disease Requiring Chronic Steroid Use
Inflammatory Bowel Disease
Celiac Disease
Chronic Pancreatitis
Chronic Diarrhea or Vomiting
Active Eating Disorder
Renal Failure or CKD
Pituitary Secreting Tumor
HIV Positive Status or AIDS including any AIDS defining illness
Hepatic Insufficiency

Recent hospitalization (within the last 6 months, include diagnosis and length of stay):_____
_____
_____

Recent Weight Loss (include baseline weight and pounds lost):_____
_____

Surgical History
Please indicate any major surgeries, the date or at least the year of the surgery and whether or not there were any post-op complications:

Surgery	Date	Pre-op Diagnosis	Post-Op Complications

Pertinent Social History
Current Occupation:_____
Habitation Status (alone or with family):_____
Alcohol Use:_____
Previous of Current Use of Illicit Drugs:_____
Smoker (indicate pack/year for current or past and year of cessation):_____
_____
_____

Currently Sexually Active: Y or N

If yes, what type of contraception is being used?_____
If no contraception, is the patient willing to use contraception for the duration of the study/treatment period?_____

Allergies:

_____
_____
_____

Current Medications (indicate dose, route, frequency and start date):

Medication	Dose	Route	Frequency	Start Date

Physical Examination

Height:_____ Weight:_____ BMI:_____

Karnofsky Performance Status:

Please assess the patient's performance status based on the table provided. Circle the most appropriate functional capacity.

Able to carry on normal activity and to work; no special care needed.	100	Normal no complaints; no evidence of disease.
	90	Able to carry on normal activity; minor signs or symptoms of disease.
	80	Normal activity with effort; some signs or symptoms of disease.
Unable to work; able to live at home and care for most personal needs; varying amount of assistance needed.	70	Cares for self; unable to carry on normal activity or to do active work.
	60	Requires occasional assistance, but is able to care for most of his personal needs.
	50	Requires considerable assistance and frequent medical care.
Unable to care for self; requires equivalent of institutional or hospital care; disease may be progressing rapidly.	40	Disabled; requires special care and assistance.
	30	Severely disabled; hospital admission is indicated although death not imminent.
	20	Very sick; hospital admission necessary; active supportive treatment necessary.
	10	Moribund; fatal processes progressing rapidly.
	0	Dead

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We will work together as a TEAM.

I will count on you to:

- Come to sessions and bring your Lifestyle Balance notebook.
  Call 24 hours ahead if you must miss a session.

- Do your best to reach your eating and activity goals.
  That includes doing home activities to practice what you learn.
- Keep track of your eating and activity 7 days a week.
  Be honest. (Don't try to "please me.")

- Keep track of your weight at home.
- Let me know if you have any problems.
- Stay willing and open to change. Always "hang in there."

You can count on me to:

- Go over your records of what you eat and your activity.
  Notice what you are doing well and what can be improved.

- Answer your questions.
- Be honest.
- Stand by you during hard times.
- Believe you can reach your eating and activity goals.
  Always "hang in there" for you. Support and help you.

We agree to work together in the ways described above.

Signed: _____

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Kimmel Cancer Center

CAREFOR Inclusion/Exclusion Criteria Checklist

Inclusion Criteria:

Patients must meet all of the following criteria in order to be considered for entry into the CAREFOR trial.

- ☐ Pathologically confirmed diagnosis of DCIS or invasive breast cancer
- ☐ Female patient, 18 years or older
- ☐ Candidate for breast conservation
- ☐ Karnofsky performance status at least 80%
- ☐ Negative serum beta-hCG if appropriate
- ☐ Willing to use contraception, not sexually active or post-menopausal
- ☐ BMI > 21
- ☐ Weight > 100lbs

Exclusion Criteria:

In addition to meeting inclusion criteria, patients are ineligible for enrollment if any of the following exclusion criteria are met.

- ☐ Intentional weight loss > 10% of total body weight within the last 3 months prior to trial enrollment.
- ☐ Prior non-breast invasive malignancy, unless free of disease for at least 1 year prior to trial enrollment.
- ☐ Two or more breast cancers not resectable through a single lumpectomy site.
- ☐ Non-epithelial breast malignancies such as sarcoma or lymphoma.
- ☐ Prior radiotherapy to ipsilateral breast that would result in overlapping radiation fields.
- ☐ Severe, active comorbidities to include any one of the following:
    - Unstable angina or CHF requiring hospitalization in the last 6 months
    - COPD exacerbation requiring hospitalization within 30 days of registration
    - Transmural myocardial infarct in the past 6 months
    - Acute bacterial or fungal infection requiring IV antibiotics at the time of registration

- Hepatic insufficiency resulting in clinical jaundice
- AIDS or HIV positive according to CDC guidelines

- Active systemic lupus erythematosus, scleroderma or dermatomyositis with rash.
- Medical or psychiatric condition preventing the patient from providing informed consent or from adhering to diet guidelines.
- Currently taking diet supplements
- Active gastrointestinal/malabsorption syndrome to include:
  - Inflammatory Bowel Disease
  - Celiac Disease
  - Chronic Pancreatitis
  - Chronic Diarrhea or Vomiting
  - Active Eating Disorder
- Currently using steroids
-
- Active/history of substance abuse or dependency to include prescription or illicit drugs as well as alcohol.
- Decisionally impaired patients.

Checklist for Screening Visit:

Informed Consent for Trial Obtained	
All Sections of CRF Completed	
Inclusion/Exclusion Criteria Evaluated	
Blood draw: Beta-HCG	
H&P; Performance Status	
Weight, BMI	
Based on screening patient appears eligible	

CAREFOR Study Case Report Form (CRF)—Radiation Treatment Planning Visit

Date of Sim Visit:_____

Lumpectomy Details

Please indicate the actual date of the lumpectomy, whether or not there were any post-op complications and the status of the Path report:

Surgery Date	Pre-op Diagnosis	Post-Op Complications

Path Report Received? Y or N

Attach a copy of the Path Report to this visit.

Verify Allergies:

Changes to Current Medications (indicate dose, route, frequency and start date):

Medication	Dose	Route	Frequency	Start Date

Physical Examination

Height:_____ Weight:_____ BMI:_____

Vital Signs: BP:_____ HR:_____ Temp:_____ RR:_____

Caliper Measurements:_____

Bioimpedance Measurement:_____

Please indicate the status (normal or abnormal) of each system listed below. If abnormal, please make notes. Give detailed description of breast exam in the notes section.

Organ System	Status	Notes
CVS	Normal Abnormal	_____
Pulm	Normal Abnormal	_____
GI	Normal Abnormal	_____
Neuro	Normal Abnormal	_____
Breast	Normal Abnormal	_____

CTCAE v4.0 Evaluation

Please evaluate the patient at baseline for comparison during and post-radiation.

	Grade				
Adverse Event	1	2	3	4	5
Dermatitis radiation	Faint erythema or dry desquamation	Moderate to brisk erythema; patchy moist desquamation, mostly confined to skin folds and creases; moderate edema	Moist desquamation in areas other than skin folds and creases; bleeding induced by minor trauma or abrasion	Life-threatening consequences; skin necrosis or ulceration of full thickness dermis; spontaneous bleeding from involved site; skin graft indicated	Death
Definition: A finding of cutaneous inflammatory reaction occurring as a result of exposure to biologically effective levels of ionizing radiation.					
Skin hyperpigmentation	Hyperpigmentation covering <10% BSA; no psychosocial impact	Hyperpigmentation covering >10% BSA; associated psychosocial impact	-	-	-
Definition: A disorder characterized by darkening of the skin due to excessive melanin deposition.					
Fatigue	Fatigue relieved by rest	Fatigue not relieved by rest; limiting instrumental ADL	Fatigue not relieved by rest, limiting self care ADL	-	-
Definition: A disorder characterized by a state of generalized weakness with a pronounced inability to summon sufficient energy to accomplish daily activities.					

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FACT-B (Version 4)

Below is a list of statements that other people with your illness have said are important. **Please circle or mark one number per line to indicate your response as it applies to the past 7 days.**

	PHYSICAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GP1	I have a lack of energy	0	1	2	3	4
GP2	I have nausea	0	1	2	3	4
GP3	Because of my physical condition, I have trouble meeting the needs of my family	0	1	2	3	4
GP4	I have pain	0	1	2	3	4
GP5	I am bothered by side effects of treatment	0	1	2	3	4
GP6	I feel ill	0	1	2	3	4
GP7	I am forced to spend time in bed	0	1	2	3	4

	SOCIAL/FAMILY WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GS1	I feel close to my friends	0	1	2	3	4
GS2	I get emotional support from my family	0	1	2	3	4
GS3	I get support from my friends	0	1	2	3	4
GS4	My family has accepted my illness	0	1	2	3	4
GS5	I am satisfied with family communication about my illness	0	1	2	3	4
GS6	I feel close to my partner (or the person who is my main support)	0	1	2	3	4
Q1	*Regardless of your current level of sexual activity, please answer the following question. If you prefer not to answer it, please mark this box* ☐ *and go to the next section.*					
GS7	I am satisfied with my sex life	0	1	2	3	4

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FACT-B (Version 4)

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

	EMOTIONAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GE1	I feel sad	0	1	2	3	4
GE2	I am satisfied with how I am coping with my illness	0	1	2	3	4
GE3	I am losing hope in the fight against my illness	0	1	2	3	4
GE4	I feel nervous	0	1	2	3	4
GE5	I worry about dying	0	1	2	3	4
GE6	I worry that my condition will get worse	0	1	2	3	4

	FUNCTIONAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GF1	I am able to work (include work at home)	0	1	2	3	4
GF2	My work (include work at home) is fulfilling	0	1	2	3	4
GF3	I am able to enjoy life	0	1	2	3	4
GF4	I have accepted my illness	0	1	2	3	4
GF5	I am sleeping well	0	1	2	3	4
GF6	I am enjoying the things I usually do for fun	0	1	2	3	4
GF7	I am content with the quality of my life right now	0	1	2	3	4

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Thomas Jefferson University

FACT-B (Version 4)

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

	ADDITIONAL CONCERNS	Not at all	A little bit	Some-what	Quite a bit	Very much
B1	I have been short of breath	0	1	2	3	4
B2	I am self-conscious about the way I dress	0	1	2	3	4
B3	One or both of my arms are swollen or tender	0	1	2	3	4
B4	I feel sexually attractive	0	1	2	3	4
B5	I am bothered by hair loss	0	1	2	3	4
B6	I worry that other members of my family might someday get the same illness I have	0	1	2	3	4
B7	I worry about the effect of stress on my illness	0	1	2	3	4
B8	I am bothered by a change in weight	0	1	2	3	4
B9	I am able to feel like a woman	0	1	2	3	4
P2	I have certain parts of my body where I experience pain	0	1	2	3	4

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Table 2. Preliminary PROMIS Cancer Fatigue Short Form

Please respond to each question by checking one box

Item	In the Past 7 Days ...	Never	Rarely	Sometimes	Often	Always
FATEXP 20	How often did you feel tired?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
FATEXP 5	How often did you experience extreme exhaustion?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
FATEXP 18	How often did you run out of energy?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
FATIMP 33	How often did your fatigue limit you at work (include work at home)?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
FATIMP 30	How often were you too tired to think clearly?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
FATIMP 21	How often were you too tired to take a bath or shower?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
FATIMP 40	How often did you have enough energy to exercise strenuously?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Abbreviations: PROMIS, Patient-Reported Outcomes Measurement Information System; FATEXP, Fatigue Experience; FATIMP, Fatigue Impact.
Reprinted with permission of the PROMIS Health Organization and the PROMIS Cooperative Group.

Checklist for Sim Visit:

Pathology Report Obtained and Attached	
Baseline Labs: CBC w/diff, CMP, HbA1c Serum: IGF-1, adiponectin, leptin, estradiol, triglycerides, ESR, insulin, glucose	
Blood Sample sent to Dr. Simone's lab for further analysis	
All Sections of CRF Completed	
FACT-B Completed by patient	
Weight, BMI, Body fat persent, bioimpedance	
Food diaries collected at this visit	
Dietary Counseling for caloric restriction diet alterations	

Please attach a copy of patient's labs when available.
Please attach a copy of food diary.

CAREFOR Study Case Report Form (CRF)—Diet Support Visit: Day 7 of CR Diet

Date of Visit:_____

Changes to Current Medications (indicate dose, route, frequency and start date):

Medication	Dose	Route	Frequency	Start Date

Height:_____ Weight:_____ BMI:_____

Vital Signs: BP:_____ HR:_____ Temp:_____ RR:_____

Food Diary Received and Completed: Y or N

If no, must collect at next visit.

Checklist for D7 Visit:

All Sections of CRF Completed	
Weight, BMI	
Food diary collected at this visit	

Please attach a copy of food diary.

24 hour recall of food intake:

Meal	**Food Type**	**Amount**

CAREFOR Study Case Report Form (CRF)—Diet Support Visit: Day 14 of CR Diet

Date of Visit:_____

Changes to Current Medications (indicate dose, route, frequency and start date):

Medication	Dose	Route	Frequency	Start Date

Height:_____ Weight:_____ BMI:_____

Vital Signs: BP:_____ HR:_____ Temp:_____ RR:_____

Food Diary Received and Completed: Y or N

If no, must collect at next visit.

Checklist for D14 Visit:

All Sections of CRF Completed	
Weight, BMI	
Food diary collected at this visit	

Please attach a copy of food diary.

24 hour recall of food intake:

Meal	**Food Type**	**Amount**

CAREFOR Study Case Report Form (CRF)—Radiation Treatment

Date of Visit:_____ **Weeks of Radiation Completed:**_____

Changes to Current Medications (indicate dose, route, frequency and start date):

Medication	Dose	Route	Frequency	Start Date

Food Diary Received and Completed: Y or N If no, must collect at next visit.

Physical Examination

Height:_____ Weight:_____ BMI:_____

Vital Signs: BP:_____ HR:_____ Temp:_____ RR:_____

Please indicate the status (normal or abnormal) of each system listed below. If abnormal, please make notes. Give detailed description of breast exam in the notes section.

Breast	Normal	Abnormal	_____
			_____
			_____
Erythema	Mild	Moderate	Severe
Hyperpigmentation	Mild	Moderate	Severe
Desquamation	Yes	No	
Dermatitis	Yes	No	
Edema	Yes	No	

CTCAE v4.0 Evaluation

	Grade				
Adverse Event	1	2	3	4	5
Dermatitis radiation	Faint erythema or dry desquamation	Moderate to brisk erythema; patchy moist desquamation, mostly confined to skin folds and creases; moderate edema	Moist desquamation in areas other than skin folds and creases; bleeding induced by minor trauma or abrasion	Life-threatening consequences; skin necrosis or ulceration of full thickness dermis; spontaneous bleeding from involved site; skin graft indicated	Death
Definition: A finding of cutaneous inflammatory reaction occurring as a result of exposure to biologically effective levels of ionizing radiation.					
Skin hyperpigmentation	Hyperpigmentation covering <10% BSA; no psychosocial impact	Hyperpigmentation covering >10% BSA; associated psychosocial impact	-	-	-
Definition: A disorder characterized by darkening of the skin due to excessive melanin deposition.					
Fatigue	Fatigue relieved by rest	Fatigue not relieved by rest; limiting instrumental ADL	Fatigue not relieved by rest, limiting self care ADL	-	-
Definition: A disorder characterized by a state of generalized weakness with a pronounced inability to summon sufficient energy to accomplish daily activities.					

Checklist for Visit:

All Sections of CRF Completed	

Weight, BMI	
Food diary collected at this visit	
Dietary Counseling for caloric restriction diet alterations	

Please attach a copy of patient's labs when available.
Please attach a copy of food diary.

24 hour recall of food intake:

Meal Food Type Amount

CAREFOR Study Case Report Form (CRF)—Post RT Visit 1

Date of Visit:_____ **Date Radiation Completed:**_____

Height:_____ Weight:_____ BMI:_____
Vital Signs: BP:_____ HR:_____ Temp:_____ RR:_____

Changes to Current Medications (indicate dose, route, frequency and start date):

Medication	Dose	Route	Frequency	Start Date

Food Diary Received and Completed: Y or N If no, must collect at next visit.

Breast Exam Normal Abnormal Notes:_____

Erythema	Mild	Moderate	Severe
Hyperpigmentation	Mild	Moderate	Severe
Desquamation	Yes	No	
Dermatitis	Yes	No	
Edema	Yes	No	

CTCAE v4.0 Evaluation

	Grade				
Adverse Event	1	2	3	4	5
Dermatitis radiation	Faint erythema or dry desquamation	Moderate to brisk erythema; patchy moist desquamation, mostly confined to skin folds and creases; moderate edema	Moist desquamation in areas other than skin folds and creases; bleeding induced by minor trauma or abrasion	Life-threatening consequences; skin necrosis or ulceration of full thickness dermis; spontaneous bleeding from involved site; skin graft indicated	Death
Definition: A finding of cutaneous inflammatory reaction occurring as a result of exposure to biologically effective levels of ionizing radiation.					
Skin hyperpigmentation	Hyperpigmentation covering <10% BSA; no psychosocial impact	Hyperpigmentation covering >10% BSA; associated psychosocial impact	-	-	-
Definition: A disorder characterized by darkening of the skin due to excessive melanin deposition.					
Fatigue	Fatigue relieved by rest	Fatigue not relieved by rest; limiting instrumental ADL	Fatigue not relieved by rest, limiting self care ADL	-	-
Definition: A disorder characterized by a state of generalized weakness with a pronounced inability to summon sufficient energy to accomplish daily activities.					

Checklist for Visit:

All Sections of CRF Completed	
Weight, BMI	
Food diary collected at this visit	

Please attach a copy of patient's labs when available.
Please attach a copy of food diary.

24 hour recall of food intake:

Meal	**Food Type**	**Amount**

CAREFOR Study Case Report Form (CRF)—Post RT Visit 2

Date of Visit:_____ **Date Radiation Completed:**_____

Height:_____ Weight:_____ BMI:_____
Vital Signs: BP:_____ HR:_____ Temp:_____ RR:_____
Caliper Measurements:_____

Bioimpedance Measurement:_____

Changes to Current Medications (indicate dose, route, frequency and start date):

Medication	Dose	Route	Frequency	Start Date

Food Diary Received and Completed: Y or N
If no, must collect at next visit.

Breast Exam Normal Abnormal Notes:_____

Erythema	Mild	Moderate	Severe
Hyperpigmentation	Mild	Moderate	Severe
Desquamation	Yes	No	
Dermatitis	Yes	No	
Edema	Yes	No	

CTCAE v4.0 Evaluation

	Grade				
Adverse Event	1	2	3	4	5
Dermatitis radiation	Faint erythema or dry desquamation	Moderate to brisk erythema; patchy moist desquamation, mostly confined to skin folds and creases; moderate edema	Moist desquamation in areas other than skin folds and creases; bleeding induced by minor trauma or abrasion	Life-threatening consequences; skin necrosis or ulceration of full thickness dermis; spontaneous bleeding from involved site; skin graft indicated	Death
Definition: A finding of cutaneous inflammatory reaction occurring as a result of exposure to biologically effective levels of ionizing radiation.					
Skin hyperpigmentation	Hyperpigmentation covering <10% BSA; no psychosocial impact	Hyperpigmentation covering >10% BSA; associated psychosocial impact	-	-	-
Definition: A disorder characterized by darkening of the skin due to excessive melanin deposition.					
Fatigue	Fatigue relieved by rest	Fatigue not relieved by rest; limiting instrumental ADL	Fatigue not relieved by rest, limiting self care ADL	-	-
Definition: A disorder characterized by a state of generalized weakness with a pronounced inability to summon sufficient energy to accomplish daily activities.					

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FACT-B (Version 4)

Below is a list of statements that other people with your illness have said are important. **Please circle or mark one number per line to indicate your response as it applies to the past 7 days.**

	PHYSICAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GP1	I have a lack of energy	0	1	2	3	4
GP2	I have nausea	0	1	2	3	4
GP3	Because of my physical condition, I have trouble meeting the needs of my family	0	1	2	3	4
GP4	I have pain	0	1	2	3	4
GP5	I am bothered by side effects of treatment	0	1	2	3	4
GP6	I feel ill	0	1	2	3	4
GP7	I am forced to spend time in bed	0	1	2	3	4

	SOCIAL/FAMILY WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GS1	I feel close to my friends	0	1	2	3	4
GS2	I get emotional support from my family	0	1	2	3	4
GS3	I get support from my friends	0	1	2	3	4
GS4	My family has accepted my illness	0	1	2	3	4
GS5	I am satisfied with family communication about my illness	0	1	2	3	4
GS6	I feel close to my partner (or the person who is my main support)	0	1	2	3	4
Q1	*Regardless of your current level of sexual activity, please answer the following question. If you prefer not to answer it, please mark this box* ☐ *and go to the next section.*					
GS7	I am satisfied with my sex life	0	1	2	3	4

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FACT-B (Version 4)

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

	EMOTIONAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GE1	I feel sad	0	1	2	3	4
GE2	I am satisfied with how I am coping with my illness	0	1	2	3	4
GE3	I am losing hope in the fight against my illness	0	1	2	3	4
GE4	I feel nervous	0	1	2	3	4
GE5	I worry about dying	0	1	2	3	4
GE6	I worry that my condition will get worse	0	1	2	3	4

	FUNCTIONAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GF1	I am able to work (include work at home)	0	1	2	3	4
GF2	My work (include work at home) is fulfilling	0	1	2	3	4
GF3	I am able to enjoy life	0	1	2	3	4
GF4	I have accepted my illness	0	1	2	3	4
GF5	I am sleeping well	0	1	2	3	4
GF6	I am enjoying the things I usually do for fun	0	1	2	3	4
GF7	I am content with the quality of my life right now	0	1	2	3	4

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FACT-B (Version 4)

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

	ADDITIONAL CONCERNS	Not at all	A little bit	Some-what	Quite a bit	Very much
B1	I have been short of breath	0	1	2	3	4
B2	I am self-conscious about the way I dress	0	1	2	3	4
B3	One or both of my arms are swollen or tender	0	1	2	3	4
B4	I feel sexually attractive	0	1	2	3	4
B5	I am bothered by hair loss	0	1	2	3	4
B6	I worry that other members of my family might someday get the same illness I have	0	1	2	3	4
B7	I worry about the effect of stress on my illness	0	1	2	3	4
B8	I am bothered by a change in weight	0	1	2	3	4
B9	I am able to feel like a woman	0	1	2	3	4
P2	I have certain parts of my body where I experience pain	0	1	2	3	4

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Table 2. Preliminary PROMIS Cancer Fatigue Short Form

Please respond to each question by checking one box

Item	In the Past 7 Days ...	Never	Rarely	Sometimes	Often	Always
FATEXP 20	How often did you feel tired?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
FATEXP 5	How often did you experience extreme exhaustion?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
FATEXP 18	How often did you run out of energy?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
FATIMP 33	How often did your fatigue limit you at work (include work at home)?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
FATIMP 30	How often were you too tired to think clearly?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
FATIMP 21	How often were you too tired to take a bath or shower?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
FATIMP 40	How often did you have enough energy to exercise strenuously?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Abbreviations: PROMIS, Patient-Reported Outcomes Measurement Information System; FATEXP, Fatigue Experience; FATIMP, Fatigue Impact.
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Checklist for Visit:

Completion Labs: CBC w/diff, CMP, HbA1c Serum: IGF-1, adiponectin, leptin, estradiol, triglycerides, ESR, insulin, glucose	
Blood Sample sent to Dr. Simone's lab for further analysis	
All Sections of CRF Completed	
FACT-B Completed by patient	
Weight, BMI, Body fat percent, bioimpedance	
Food diary collected at this visit	

Please attach a copy of patient's labs when available.
Please attach a copy of food diary.

24 hour recall of food intake:

Meal	**Food Type**	**Amount**

CAREFOR Study Case Report Form (CRF)—Follow-up Visit

Date of Visit:_____

Physical Examination

Height:_____ Weight:_____ BMI:_____

Vital Signs: BP:_____ HR:_____ Temp:_____ RR:_____

Caliper Measurements:_____

Bioimpedance Measurement:_____

Changes to Current Medications (indicate dose, route, frequency and start date):

Medication	Dose	Route	Frequency	Start Date

Please indicate the status (normal or abnormal) of each system listed below. If abnormal, please make notes. Give detailed description of breast exam in the notes section.

Breast Exam Normal Abnormal Notes:_____

Erythema	Mild	Moderate	Severe
Hyperpigmentation	Mild	Moderate	Severe
Desquamation	Yes	No	
Dermatitis	Yes	No	
Edema	Yes	No	

CTCAE v4.0 Evaluation

	Grade				
Adverse Event	1	2	3	4	5
Dermatitis radiation	Faint erythema or dry desquamation	Moderate to brisk erythema; patchy moist desquamation, mostly confined to skin folds and creases; moderate edema	Moist desquamation in areas other than skin folds and creases; bleeding induced by minor trauma or abrasion	Life-threatening consequences; skin necrosis or ulceration of full thickness dermis; spontaneous bleeding from involved site; skin graft indicated	Death
Definition: A finding of cutaneous inflammatory reaction occurring as a result of exposure to biologically effective levels of ionizing radiation.					
Skin hyperpigmentation	Hyperpigmentation covering <10% BSA; no psychosocial impact	Hyperpigmentation covering >10% BSA; associated psychosocial impact	-	-	-
Definition: A disorder characterized by darkening of the skin due to excessive melanin deposition.					
Fatigue	Fatigue relieved by rest	Fatigue not relieved by rest; limiting instrumental ADL	Fatigue not relieved by rest, limiting self care ADL	-	-
Definition: A disorder characterized by a state of generalized weakness with a pronounced inability to summon sufficient energy to accomplish daily activities.					

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FACT-B (Version 4)

Below is a list of statements that other people with your illness have said are important. **Please circle or mark one number per line to indicate your response as it applies to the past 7 days.**

	PHYSICAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GP1	I have a lack of energy	0	1	2	3	4
GP2	I have nausea	0	1	2	3	4
GP3	Because of my physical condition, I have trouble meeting the needs of my family	0	1	2	3	4
GP4	I have pain	0	1	2	3	4
GP5	I am bothered by side effects of treatment	0	1	2	3	4
GP6	I feel ill	0	1	2	3	4
GP7	I am forced to spend time in bed	0	1	2	3	4

	SOCIAL/FAMILY WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GS1	I feel close to my friends	0	1	2	3	4
GS2	I get emotional support from my family	0	1	2	3	4
GS3	I get support from my friends	0	1	2	3	4
GS4	My family has accepted my illness	0	1	2	3	4
GS5	I am satisfied with family communication about my illness	0	1	2	3	4
GS6	I feel close to my partner (or the person who is my main support)	0	1	2	3	4
Q1	*Regardless of your current level of sexual activity, please answer the following question. If you prefer not to answer it, please mark this box* ☐ *and go to the next section.*					
GS7	I am satisfied with my sex life	0	1	2	3	4

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FACT-B (Version 4)

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

	EMOTIONAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GE1	I feel sad	0	1	2	3	4
GE2	I am satisfied with how I am coping with my illness	0	1	2	3	4
GE3	I am losing hope in the fight against my illness	0	1	2	3	4
GE4	I feel nervous	0	1	2	3	4
GE5	I worry about dying	0	1	2	3	4
GE6	I worry that my condition will get worse	0	1	2	3	4

	FUNCTIONAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GF1	I am able to work (include work at home)	0	1	2	3	4
GF2	My work (include work at home) is fulfilling	0	1	2	3	4
GF3	I am able to enjoy life	0	1	2	3	4
GF4	I have accepted my illness	0	1	2	3	4
GF5	I am sleeping well	0	1	2	3	4
GF6	I am enjoying the things I usually do for fun	0	1	2	3	4
GF7	I am content with the quality of my life right now	0	1	2	3	4

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FACT-B (Version 4)

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

	ADDITIONAL CONCERNS	Not at all	A little bit	Some-what	Quite a bit	Very much
B1	I have been short of breath	0	1	2	3	4
B2	I am self-conscious about the way I dress	0	1	2	3	4
B3	One or both of my arms are swollen or tender	0	1	2	3	4
B4	I feel sexually attractive	0	1	2	3	4
B5	I am bothered by hair loss	0	1	2	3	4
B6	I worry that other members of my family might someday get the same illness I have	0	1	2	3	4
B7	I worry about the effect of stress on my illness	0	1	2	3	4
B8	I am bothered by a change in weight	0	1	2	3	4
B9	I am able to feel like a woman	0	1	2	3	4
P2	I have certain parts of my body where I experience pain	0	1	2	3	4

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Table 2. Preliminary PROMIS Cancer Fatigue Short Form

Please respond to each question by checking one box

Item	In the Past 7 Days …	Never	Rarely	Sometimes	Often	Always
FATEXP 20	How often did you feel tired?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
FATEXP 5	How often did you experience extreme exhaustion?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
FATEXP 18	How often did you run out of energy?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
FATIMP 33	How often did your fatigue limit you at work (include work at home)?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
FATIMP 30	How often were you too tired to think clearly?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
FATIMP 21	How often were you too tired to take a bath or shower?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
FATIMP 40	How often did you have enough energy to exercise strenuously?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Abbreviations: PROMIS, Patient-Reported Outcomes Measurement Information System; FATEXP, Fatigue Experience; FATIMP, Fatigue Impact.
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Checklist for Follow-up Visit:

Follow-up Labs: CBC w/diff, CMP, HbA1c Serum: IGF-1, adiponectin, leptin, estradiol, triglycerides, ESR, insulin, glucose	
Blood Sample sent to Dr. Simone's lab for further analysis	
All Sections of CRF Completed	
FACT-B Completed by patient	
Weight, BMI, Body fat percent, bioimpedance	
Food diaries collected at this visit	

Please attach a copy of patient's labs when available.

THOMAS JEFFERSON UNIVERSITY HOSPITAL
DEPARTMENT OF RADIATION ONCOLOGY

CAREFOR Study: A Feasibility Pilot Trial Evaluating Caloric Restriction for Oncology Research in Early Stage Breast Cancer Patients

WITHDRAWAL FORM

Patient Initials _____ MR# _____

Patient ID # _____

Please initial below:

_____ *I no longer wish to participate in this research study.*

_____ *I am withdrawing from the study treatment, but I agree to the research coordinator following up with me periodically to see how I am doing.*

Please sign below:

Patient: _____ Date: _____

Witnessed By: _____ Date: _____

Thomas Jefferson University

SUBJECT ENROLLMENT

Enrollment Through: (MM/DD/YY):_____

Protocol Title:	Principal Investigator:	Institution:
CAREF0R Study: A Feasibility Pilot Trial Evaluating Caloric Restriction for Oncology Research in Early Stage Breast Cancer Patients	Nicole Simone, MD	Thomas Jefferscn University Hospital
Study Coordinator Information: Name: Kelly J. Shipman, BA, CCRP Email: Kelly.shipman@jeffersonhospital.org Phone #: 215-955-8619		

Patient Study #	Patient Initials	Date On Study	Date of First Dose	Date Off Study	Comments

Protocol Title:	Principal Investigator:	Institution:
CAREFOR Study: A Feasibility Pilot Trial Evaluating Caloric Restriction for Oncology Research in Early Stage Breast Cancer Patients		Thomas Jefferson University Hospital

Patient Study #	Patient Initials	Date On Study	Date of First Dose	Date Off Study	Comments

Thomas Jefferson University Hospital
Department of Radiation Oncology
CAREFOR Study

Current Medication Flowsheet

Date Started	Medication	Indication	Route	Frequency	Dose	Date Stopped

Allergies:

Physician Signature: _____ Date:_____

Study : _____Patient Case No. _____Time Frame/Cycle #

Intermittent RT

(circle one): Y or N, N/A

Thomas Jefferson University

Protocol Office AE Toxicity Flowsheet

Date AE Started	Brief Description of Event◆	Numeric Grade *CTC 3.0*	AEs	Attribution *(Related to therapy)*	AE Attribution (Potential cause)	Action *(Check all that apply)*	Outcome
Date: ☐New ☐F-U		☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4	☐ AE ☐ SAE	☐ Unrelated ☐ Unlikely ☐ Possible ☐ Probable ☐ Definite	☐ Chemotherapy ☐ Radiation ☐ Hormone-specify _____ ☐ Other_	☐ none required ☐ dose reduced* ☐ dose held* ☐ Adeers ☐ IRB notified ☐ MedWatch 3500A ☐ Other_____	☐ Resolved End Date _____ ☐Ongoing
Date: ☐New ☐F-U		☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4	☐ AE ☐ SAE	☐ Unrelated ☐ Unlikely ☐ Possible ☐ Probable ☐ Definite	☐ Chemotherapy ☐ Radiation ☐ Hormone-specify _____ ☐ Other	☐ none required ☐ dose reduced* ☐ dose held* ☐ Adeers ☐ IRB notified ☐ MedWatch 3500A ☐ Other_____	☐ Resolved End Date: _____ ☐Ongoing
Date: ☐New ☐F-U		☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4	☐ AE ☐ SAE	☐ Unrelated ☐ Unlikely ☐ Possible ☐ Probable ☐ Definite	☐ Chemotherapy ☐ Radiation ☐ Hormone-specify _____ ☐ Other_____ _____	☐ none required ☐ dose reduced* ☐ dose held* ☐ Adeers ☐ IRB notified ☐ MedWatch 3500A ☐ Other_____	☐ Resolved End Date: _____ ☐Ongoing
Date: ☐New ☐F-U		☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4	☐ AE ☐ SAE	☐ Unrelated ☐ Unlikely ☐ Possible ☐ Probable ☐ Definite	☐ Chemotherapy ☐ Radiation ☐ Hormone-specify _____ ☐ Other_____ _____	☐ none required ☐ dose reduced* ☐ dose held* ☐ Adeers ☐ IRB notified ☐ MedWatch 3500A ☐ Other_____	☐ Resolved End Date: _____ ☐ Ongoing

Appendix VIII. Recruitment Flyer

Appendix IX. Food Diaries

Printed Food Diary:

FOOD OR DRINK		Date:		
Amount	Description	Time	Location	Alone or Accompanied

Online Food Diary:

Accessible at: http://www.myfitnesspal.com


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University

Appendix X.

Thomas Jefferson University

Kimmel Cancer Center

CAREFOR Inclusion/Exclusion Criteria Checklist

Inclusion Criteria:

Patients must meet all of the following criteria in order to be considered for entry into the CAREFOR trial.

- *Pathologically proven diagnosis of DCIS or invasive breast cancer*
- *Ability to have breast conservation as determined by the judgment of the radiation oncologist*
- *The patient must be female*
- *Age ≥ 18*
- *If multifocal breast cancer, then it must be able to be resected through a single lumpectomy incision*
- *Appropriate stage for protocol entry, including no clinical evidence for distant metastases, based upon the following minimum diagnostic workup:*
- *History/physical examination, including breast exam and documentation of weight and Karnofsky Performance Status of 80-100% at study entry.*
- *Women of childbearing potential must have a negative serum pregnancy test within 14 days of study entry*
- *Women of childbearing potential must be non-pregnant and non-lactating and willing to use medically acceptable form of contraception during radiation therapy*
- *Patient must capable of and provide study specific informed consent prior to study entry*
- *BMI ≥21*
- *Weight ≥100lbs*
- *No prior history of non-breast invasive malignancies in the past 1year*
- *Patient must not have any of the following severe, active co-morbidity, defined as follows:*
    - *Unstable angina and/or congestive heart failure requiring hospitalization within the last 6 months*
    - *Transmural myocardial infarction within the last 6 months*
    - *Acute bacterial or fungal infection requiring intravenous antibiotics at the time of registration;*
    - *Chronic Obstructive Pulmonary Disease exacerbation or other respiratory illness requiring hospitalization or precluding study therapy within 30 days before registration;*

- *Hepatic insufficiency resulting in clinical jaundice and/or coagulation defects; note, however,that laboratory tests for liver function and coagulation parameters are not required for entry into this protocol*
- *Acquired Immune Deficiency Syndrome (AIDS) or HIV positive based upon current CDC definition; note,however, that HIV testing is not required for entry into this protocol. The need to exclude patients with AIDS or HIV from this protocol is necessary because anti-retrivirals may alter patient metabolism.*

- *Patient must not have active systemic lupus, erythematosus, or any history of scleroderma, dermatomyositis with active rash*
- *No prior radiotherapy to the ipsilateral breast or prior radiation to the region of the breast that would result in overlap of radiation therapy fields*
- *Patient may not have any active Gastrointestinal/Malabsorption disorder at the discretion of the Principal Investigator*
  - *Inflammatory Bowel Disease*
  - *Celiac Disease*
  - *Chronic Pancreatitis*
  - *Chronic Diarrhea or Vomiting*
  - *Active Eating Disorder*
-
- *Not currently taking steroids*
- *No history of or current active drug/alcohol dependence.*
- *No patients with decisional impairment.*

Exclusion Criteria

- *Patient is not a candidate for breast conservation.*
- *Patient is male.*
- *Age <18 years*
- *Patient has evidence of distant metastases*
- *Karnofsky Performance Status less than 80% within 60 days prior to study.*
- *Ipsilateral mammogram done greater than 6 months prior to study.*
- *Women of childbearing potential with a positive serum beta hCG.*
- *Patient has a history of dementia, psychosis or other disorder affecting their mental status to the point where they cannot consent or comply with study guidelines.*
- *BMI < 21*
- *Weight < 100lbs*
- *Unintentional weight loss ≥10% in the last 3 mos*
- *Prior invasive non-breast malignancy (except non-melanomatous skin cancer, carcinoma in situ of the cervix) unless disease free for a minimum of 2 years prior to registration*

- *Two or more breast cancers not resectable through a single lumpectomy incision*
- *Non-epithelial breast malignancies such as sarcoma or lymphoma*
- *Prior radiotherapy to the ipsilateral breast or prior radiation to the region of the breast that would result in overlap of radiation therapy fields*
- *Severe, active co-morbidity, defined as follows:*
  - *Unstable angina and/or congestive heart failure requiring hospitalization within the last 6 months*
  - *Transmural myocardial infarction within the last 6 months*
  - *Acute bacterial or fungal infection requiring intravenous antibiotics at the time of registration;*
  - *Chronic Obstructive Pulmonary Disease exacerbation or other respiratory illness requiring hospitalization or precluding study therapy within 30 days before registration;*
  - *Hepatic insufficiency resulting in clinical jaundice and/or coagulation defects; note, however,that laboratory tests for liver function and coagulation parameters are not required for entry into this protocol*
  - *Acquired Immune Deficiency Syndrome (AIDS) or HIV positive based upon current CDC definition; note,however, that HIV testing is not required for entry into this protocol. The need to exclude patients with AIDS or HIV from this protocol is necessary because anti-retrivirals may alter patient metabolism.*
- *Active systemic lupus erythematosus, or any history of scleroderma, dermatomyositis with active rash*

  Active Gastrointestinal/Malabsorption disorder at the discretion of the Principal Investigator
  - *Inflammatory Bowel Disease*
  - *Celiac Disease*
  - *Chronic Pancreatitis*
  - *Chronic Diarrhea or Vomiting*
  - *Active Eating Disorder*
- *Current use of steroids*
- *Active drug/alcohol dependence or abuse history.*
- *Decisionally impaired patients.*


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Appendix XI. PROMIS Cancer Fatigue Short Form[REF] and FACT-B Assessment

Table 2. Preliminary PROMIS Cancer Fatigue Short Form

Please respond to each question by checking one box

Item	In the Past 7 Days …	Never	Rarely	Sometimes	Often	Always
FATEXP 20	How often did you feel tired?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
FATEXP 5	How often did you experience extreme exhaustion?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
FATEXP 18	How often did you run out of energy?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
FATIMP 33	How often did your fatigue limit you at work (include work at home)?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
FATIMP 30	How often were you too tired to think clearly?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
FATIMP 21	How often were you too tired to take a bath or shower?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
FATIMP 40	How often did you have enough energy to exercise strenuously?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Abbreviations: PROMIS, Patient-Reported Outcomes Measurement Information System; FATEXP, Fatigue Experience; FATIMP, Fatigue Impact.
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FACT-B (Version 4)

Below is a list of statements that other people with your illness have said are important. **Please circle or mark one number per line to indicate your response as it applies to the past 7 days.**

	PHYSICAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GP1	I have a lack of energy	0	1	2	3	4
GP2	I have nausea	0	1	2	3	4
GP3	Because of my physical condition, I have trouble meeting the needs of my family	0	1	2	3	4
GP4	I have pain	0	1	2	3	4
GP5	I am bothered by side effects of treatment	0	1	2	3	4
GP6	I feel ill	0	1	2	3	4
GP7	I am forced to spend time in bed	0	1	2	3	4

	SOCIAL/FAMILY WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GS1	I feel close to my friends	0	1	2	3	4
GS2	I get emotional support from my family	0	1	2	3	4
GS3	I get support from my friends	0	1	2	3	4
GS4	My family has accepted my illness	0	1	2	3	4
GS5	I am satisfied with family communication about my illness	0	1	2	3	4
GS6	I feel close to my partner (or the person who is my main support)	0	1	2	3	4
Q1	*Regardless of your current level of sexual activity, please answer the following question. If you prefer not to answer it, please mark this box* ☐ *and go to the next section.*					
GS7	I am satisfied with my sex life	0	1	2	3	4

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FACT-B (Version 4)

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

	EMOTIONAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GE1	I feel sad	0	1	2	3	4
GE2	I am satisfied with how I am coping with my illness	0	1	2	3	4
GE3	I am losing hope in the fight against my illness	0	1	2	3	4
GE4	I feel nervous	0	1	2	3	4
GE5	I worry about dying	0	1	2	3	4
GE6	I worry that my condition will get worse	0	1	2	3	4

	FUNCTIONAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GF1	I am able to work (include work at home)	0	1	2	3	4
GF2	My work (include work at home) is fulfilling	0	1	2	3	4
GF3	I am able to enjoy life	0	1	2	3	4
GF4	I have accepted my illness	0	1	2	3	4
GF5	I am sleeping well	0	1	2	3	4
GF6	I am enjoying the things I usually do for fun	0	1	2	3	4
GF7	I am content with the quality of my life right now	0	1	2	3	4

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Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

	ADDITIONAL CONCERNS	Not at all	A little bit	Some-what	Quite a bit	Very much
B1	I have been short of breath	0	1	2	3	4
B2	I am self-conscious about the way I dress	0	1	2	3	4
B3	One or both of my arms are swollen or tender	0	1	2	3	4
B4	I feel sexually attractive	0	1	2	3	4
B5	I am bothered by hair loss	0	1	2	3	4
B6	I worry that other members of my family might someday get the same illness I have	0	1	2	3	4
B7	I worry about the effect of stress on my illness	0	1	2	3	4
B8	I am bothered by a change in weight	0	1	2	3	4
B9	I am able to feel like a woman	0	1	2	3	4
P2	I have certain parts of my body where I experience pain	0	1	2	3	4

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