EVALUATION OF TREATMENT MODALITIES IN RADIOTHERAPY INDUCED ESOPHAGITIS

By

Gale Taylor

A clinical project submitted in partial fulfillment of the requirements for the degree of
MASTERS OF NURSING

WASHINGTON STATE UNIVERSITY
Intercollegiate Center for Nursing Education
April 30th, 1997
To the Faculty of Washington State University:

The members of the Committee appointed to examine
the clinical project of GALE TAYLOR find it satisfactory
and recommend that it be accepted.

Chair

[Signatures]
ACKNOWLEDGMENTS

I would like to express my gratitude to those who have encouraged and supported me in the completion of this clinical project, and during my pursuit of a Master of Nursing degree. First, I want to thank my family, whom without complaint, watched my quest to reach my goal of attaining an advanced degree.

Beyond my family I would like to especially thank Marcy Kelly, RN, RTT for encouraging my pursuit of this topic, her unflagging willingness to answer my questions and, her help in understanding the workings of the radiation therapy department.

To my committee chair a special thanks is extended for assisting me with the journey that this project has taken me. The specific guidance, attention to detail, prodding, and nurturing have helped with the completion of this project. Her insights into the workings of research and her efforts to help smooth the way by joining forces with another student are genius. Thank you Dr. Margaret Bruya.

And finally, a special nod of thanks goes to my fellow student and mentor, Kathleen Kozak, without whom I may have lost my focus and way as we pulled and pushed each other through our studies.
EVALUATION OF TREATMENT MODALITIES IN RADIOTHERAPY INDUCED ESOPHAGITIS

Abstract

by Gale Taylor, BSN
Washington State University
April 30th, 1997

Chair: Dr. Margaret Bruya

Patients who have a diagnosis of non-small cell lung cancer (NSCLC) that necessitates the use of ionizing radiation to the chest and mediastinum unavoidably receive treatment to normal esophageal tissues. Damage to otherwise healthy tissue results as the esophageal mucosa lay within treatment fields. Repeated treatments over the course of prescribed radiation treatments results in radiotherapy induced esophagitis.

The purpose of this project is to contrast the efficacy of two currently used treatment modalities for the treatment of radiotherapy induced esophagitis. Each study subject will be assigned through a random drawing, either Group A, Reynold's Solution, or Group B, sucralfate and fluconazole. Using a repeated measures design, study patients will be asked to provide subjective information regarding the symptoms as they relate to swallowing difficulty (dysphagia) and pain with swallowing (odynophagia). Patients will be asked to provide six (6) recordings of swallowing experiences they have while receiving their prescribed radiotherapy and study medications.
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Carcinomas of the lung are the leading cause of cancer related deaths in both men and women in the United States. Surgery offers the best chance for cure in stages I and II of non-small-cell lung cancer (NSCLC). Only a small percentage of patients are diagnosed with operable early stage disease. Many patients are diagnosed with locally advanced NSCLC that is surgically nonresectable and receive only palliative radiation therapy (Hazuka et al., 1994).

Palliative treatments for some disease states, including NSCLC, result in adverse side effects. Undesirable side effects can be identified and targeted for treatment thereby lessening patient's discomfort. Esophagitis is a major side effect of palliative treatments with radiation therapy.

Radiation therapy to the chest and mediastinum causes mucosal injury resulting in esophagitis. In a substantial number of bronchogenic carcinoma patients, the normal esophagus is unavoidably included within the treatment fields and exposed to ionizing radiation. Dosage levels of 5000 to 6000 rads or CGy (Centi Gray) over a 6 to 8 week period are often delivered to segments of normal esophageal mucosa (Moss, Brand, & Battifora, 1979).

The esophagus is lined with stratified squamous epithelium that is moderately radiosensitive. Radiation therapy induces esophagitis in large part because of the accelerated destruction of the epithelial cells (Allison, Vongtama, Vaughan, & Shin, 1995). Since the mucosa acts as a protective barrier to infection, radiation treatments potentially compromise the esophageal protection from fungal and, or bacterial penetration. Painful swallowing (odynophagia) and mechanical difficulty with swallowing (dysphagia) are often the first symptoms of radiation induced esophagitis...
Radiation Esophagitis (Slaughter, 1988). It has been theorized that gram negative bacteria and yeast do play a role in the pathogenesis of the treatment induced esophagitis (Brady, 1984; Loprinzi, Foote, & Michalak, 1995).

Minimizing this acutely induced treatment related adverse effect, esophagitis, would result in improved quality of life for treatment patients. More efficacious treatment schedules could be maintained as breaks and delays in therapy would be reduced.

**Statement of Problem**

This study investigates the treatment of radiation induced esophagitis. Currently, there is no established preventive measure for this clinically induced problem (Loprinzi et al., 1995). Patients are identified and treated after subjective complaints of dysphagia appear. Treatment is aimed at alleviation of symptoms, maintenance of good nutrition, reduced fatigue, stabilization of weight and, proper hydration (Dunne, 1991).

This study will contrast two treatment plans currently in use. The study will establish the efficacy of each and evaluate if one is superior.

**Statement of Purpose**

This investigation evaluates the efficacy of two separate treatment plans to diminish discomforts associated with painful and difficult swallowing attributable to radiotherapy induced esophagitis. The study goals will be to evaluate two standard treatments which are: 1.) sucralfate 1 gram in suspension four times a day with fluconazole 100 mg daily for 14 days after symptoms of esophagitis appear and, 2.) Reynold's Solution 10cc four times a day to be swished and swallowed after symptoms appear (See Table 1 Reynold's Solution). The study will evaluate the efficacy of reduction of symptoms of each of the previously outlined protocols.
TABLE 1

Reynold's Solution

Proportion of Medication per each Pint

<table>
<thead>
<tr>
<th>Medication</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>erythromycin 400mg/5cc</td>
<td>240cc</td>
</tr>
<tr>
<td>nystatin oral suspension</td>
<td>60cc</td>
</tr>
<tr>
<td>hydrocortisone 221mg</td>
<td>diluted in 10 cc alcohol</td>
</tr>
<tr>
<td>diphenhydramine syrup</td>
<td>170cc</td>
</tr>
</tbody>
</table>

Medication delivered per 10 cc dose

<table>
<thead>
<tr>
<th>DRUG</th>
<th>STRENGTH</th>
<th>DOSAGE</th>
<th>FREQUENCY GIVEN</th>
<th>PREPARATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>erythromycin</td>
<td>400mg/5cc</td>
<td>400 mg</td>
<td>Four times/day orally</td>
<td>Liquid suspension</td>
</tr>
<tr>
<td>nystatin solution</td>
<td>100,000iu/cc</td>
<td>125,000</td>
<td>Four times/day orally</td>
<td>Liquid suspension</td>
</tr>
<tr>
<td>hydrocortisone</td>
<td>221 mg/10cc</td>
<td>4.6 mg</td>
<td>Four times/day orally</td>
<td>Liquid suspension</td>
</tr>
<tr>
<td>diphenhydramine</td>
<td>12.5mg/5cc</td>
<td>8.85 mg</td>
<td>Four times/day orally</td>
<td>Liquid suspension</td>
</tr>
</tbody>
</table>
Literature Review

Radiotherapy began over a century ago with the discovery of "x-ray" by Wilhelm Roentgen in 1895. The discovery of radium by the Curies followed in 1896 and this eventually lead to the modern practice of the medical subspecialty of radiation therapy (Perez, & Brady, 1987). As these new discoveries were studied and radiotherapy evolved, the destructive powers of radiation became recognized. The first recorded death from radiation exposure was documented in 1904.

The modern day linear accelerators of radiation therapy departments are much more refined. Despite technological advances with equipment and treatment plans, adverse side effects continue to occur. Adverse side effects of radiation therapy dictate anticipation and treatment.

Curative and palliative radiation therapy is directed toward the most oppressive of signs and symptoms that destroy patient's quality of life and may lead to a shortened life span before the natural course of their disease. Purposes for radiotherapy include pain reduction, release of nerve compression, termination of hemorrhages, resolution of ulceration, reduction of bothersome discharge, reduction of disfigurement, relief of digestive or respiratory obstruction, and offers hope of cure for some diagnoses.

Descriptions of suspected radiation induced esophagitis can be found as early as 1922. Coutard and Hautant reported evidence of advanced laryngeal cancer treatment and cure to the International Congress of Oncology in Paris. Subsequently, many texts and publications have cited incidence and histological examples of esophagitis associated with radiation (Moss et al., 1979; Levitt & Tapley, 1984; Perez & Brady, 1987).

As treatment techniques were refined, so too were the treatments for the adverse side effects associated with radiation therapy. Studies began with animal models in the late 1970's and have continued to present times (Moss et al., 1979; Pass et al., 1994;
Loprinzi et al., 1995). As a result of this research, levels of minimally tolerated radiation were established and treatment modalities of adverse effects have been determined.

Human subjects studies can be found within the literature beginning in the 1990's. Clinical studies with human subjects have been completed to determine the uses of standard and accelerated radiation treatment protocols. Treatment protocols were evaluated with regard to toxicities from therapy (Bishop et al., 1994). Evaluation of combine chemotherapy with radiotherapy protocols have been studied as well (Hazuka et al., 1994; Ball et al., 1995; Greco, Stroup, & Hainsworth, 1995). Evaluation of the uses of intraoperative delivery of radiation therapy in human subjects has also been published (Pass et al., 1994). Specific medical treatment for the adverse side effect of radiation induced esophagitis with analgesics (Dunne, 1991) and antifungals combined with antiulcer medications (Laine et al., 1993; Allison et al., 1995; Taal, Olmos, Boot, & Hoefnagel, 1995) have been reported.

Research Questions

There are two central questions to be addressed in this study:

1.) Is the treatment of subjectively reported pain with swallowing (odynophagia) associated with suspected radiation induced esophagitis, more effectively treated with Reynold's Solution or a combination of sucralfate (Carafate) and fluconazole (Diflucan), see experimental model Figure 1 (Appendix A)?

2.) Is the treatment of subjectively reported difficulty with swallowing (dysphagia) associated with suspected radiation induced esophagitis more effectively treated with Reynold's Solution or a combination of sucralfate (Carafate) and fluconazole (Diflucan), see experimental model Figure 1 (Appendix A)?
Definitions of Terms

**Esophagitis**: any subjective alteration in swallowing or sensations of discomfort.

**Radiotherapy**: a treatment modality wherein tissues are purposively exposed to irradiation.

**Rads**: the amount of irradiation that is received in a prescribed dosage.

**CGy**: stands for Centi Gray and is used interchangeable with rads.

**Ionizing Radiation**: any type of radiation capable of removing electrons from an atom with which it interacts.

**Radiosensitive**: how affected certain tissues are to the effects of radiation therapy treatments. In that vein, if tissue is highly radiosensitive it will show a large effect to the treatment.

**Dysphagia**: a difficulty swallowing.

**Pain**: An unpleasant or distressing sensation due to bodily injury or disorder than can range from minor to severe.

**Palliative treatment**: a treatment with the goal being relief of symptoms rather than a cure of the underlying process

**Stratified squamous epithelial**: the layer of cells that line the esophagus.

**Sucralfate/Difulcan Therapy**: a currently used medication combination for the treatment of esophagitis.

**Mucosal injury**: any alteration in the normal function of the mucosal lining by edema, ulceration, stricture, or perforation.

**Reynold's Solution**: a current used medication combination for the treatment of esophagitis (see Table 1).

**Odynophagia**: a strong feeling of burning, squeezing pain with swallowing.
Significance to Nursing

The practical problems of treatment of non-small cell lung cancer (NSCLC) with radiation includes induced esophagitis. The need to lessen the effects of esophagitis may result in better nutritional maintenance for clients, stabilization of weight, reduced treatment related fatigue, proper hydration, decreased discomfort, fewer admissions for treatment induced side effects (Dunne, 1991), and continuous treatments given without delays as side effects resolve. By looking for expected side effects and promptly treating them with the most efficacious modality nurses can expect optimal outcomes.
Chapter 2

Carcinomas of the lung are the leading cause of cancer related deaths in both men and women in the United States. Surgery offers the best chance of cure in stages I and II of non-small-cell lung cancer (NSCLC). Only a small percentage of patients are diagnosed with operable early stage disease. Many patients are diagnosed with locally advanced NSCLC that is surgically nonresectable and receive only radiation therapy (Hazuka et al., 1994).

Palliative treatments for some disease states, including NSCLC, result in adverse side effects. Undesirable side effects can be identified and targeted for treatment thereby lessening patient's discomfort. Esophagitis is a major side effect of palliative treatments with radiation therapy.

Radiation therapy to the chest and mediastinum causes mucosal injury resulting in esophagitis. In a substantial number of bronchogenic carcinoma patients, the normal esophagus is unavoidably included within the treatment fields and exposed to ionizing radiation. Dosage levels of 5000 to 6000 rads or CGy (Centi Gray) over a 6 to 8 week period are often delivered to segments of normal esophageal mucosa (Moss et al., 1979).

The esophagus is lined with stratified squamous epithelium that is moderately radiosensitive. Radiation therapy induces esophagitis in large part because of the accelerated destruction of the epithelial cells (Allison et al., 1995). Since the mucosa acts as a protective barrier to infection, radiation treatments potentially compromise the esophageal protection from fungal and, or bacterial penetration. Painful swallowing (dysphagia) and mechanical difficulty with swallowing are often the first symptoms of radiation induced esophagitis (Slaughter, 1988). It has been theorized that gram negative
bacteria and yeast do play a role in the pathogenesis of the treatment induced esophagitis (Brady, 1984; Loprinzi et al., 1995).

Minimizing this acutely induced treatment related adverse effect, esophagitis, would result in improved quality of life for treatment patients. More efficacious treatment schedules could be maintained as breaks and delays in therapy would be reduced.

**Design**

An experimental design will be used. Subjects will be randomly assigned to each treatment group through a simple random assignment system. Prior to enrollment of any subjects, treatment group assignments by a random selection will be recorded and stored within the study's locked file. As subjects enter the study, they will be placed within their treatment group (See Experimental Model Figure 1, Appendix A) with accordance to the above mentioned selection. Only the research team will have access to the listing of how patients will be assigned.

**Study Setting**

This study will be completed in the Northwestern Region of the United States within a major regional hospital's Outpatient Oncology Department as well as a satellite clinic with support services provided within the departments and by the physician group (See Appendix B). Up to ten patients will be enrolled in each of the separate treatment groups. Patient identification, informed consents and, study datum will be collected within these departments.

**Study Sample**

The sample includes persons greater than 18 years of age with a diagnosis of non-small cell lung cancer (NSCLC) confirmed by biopsy. These individuals must not be
candidates for surgery have a treatment plan that includes radiotherapy and, with less than 10% loss of their normal body weight. They must not have preexisting complaints of odynophagia, dysphagia, or esophagitis for at least one year prior to enrollment into the study. All subjects must sign an informed consent (see Appendix C).

Data Collection Procedures

As patients are referred into the Radiation Therapy Oncology department for initial consultation, either the physicians, departmental nurse, or researcher will provide potential study subjects with the letter of invitation to participate (See Appendix D).

After initial screening of subjects, demographic information will be gathered (See Appendix E), informed consents signed (See Appendix C) and participants randomized into groups. Study subjects will be instructed on the proper use of the visual analog measurement format to be used within this study (See Appendix F). Each subject will receive verbal and written instruction on how to document their degree of pain with swallowing (odynophagia) and difficulty swallowing (dysphagia).

Data will be collected every four days during the prescribed treatment course for a total of six (6) recordings. Each study subject will be asked to provide information regarding their subjective observations on swallowing difficulty and pain with swallowing beginning with their first radiotherapy treatment and ending on day twenty one (21) of their treatment course.

As their symptoms of esophagitis begin to develop, usually after having received approximately 3000 cGY (Perez, & Brady, 1987) of their prescribed radiation treatments, prescriptions for either Reynold's Solution 10 ml four times a day or sulcralfate 1 gram in suspension four times a day with fluconazole 100mg daily for fourteen (14) days will be given and instructions on how to take their medications will be reviewed. Treatment of all groups will end two weeks after radiation therapy has stopped.

Data will be collected on up to twenty (20) subjects or the number of subjects that are available to enter the study during the enrollment period of four (4) months.
The investigator will be available to departmental workers and study participants via a voicemail phone system. This phone system number will be provided to subjects with the informed consent.

As data is compiled it will be stored for future analysis and kept within a locked study file. The paper visual analog scales will also be stored within the above mentioned locked file.

All records will be destroyed within six (6) month of the completion of the study's analysis. Storage of datum for the above mentioned six months will allow for retrieval of datum if questions arise. Final elimination of datum at the end of six (6) will assure continued patient confidentiality.

Instrumentation

Pain and or discomfort are difficult to measure. Pain is highly subjective and uniquely individual (Frank-Stromborg, 1988). The visual analogue scale is commonly used to measure intensity or pain. Patients will be asked to place a mark on a 10cm visual analogue scale at the point that best describes their perceived pain intensity and difficulty with swallowing.

Subjects will be asked to record their symptoms on a schedule of once every four (4) days during the first twenty one (21) days of their prescribed radiotherapy schedule. Recordings will begin on the first day of the prescribed radiotherapy treatments. Recordings of data will continue on every fourth (4th) day for the remainder of the study period. This should represent six (6) recordings.
HOW MUCH
PAIN WITH
SWALLOWING?

<table>
<thead>
<tr>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>no pain</td>
</tr>
</tbody>
</table>

HOW MUCH
DIFFICULTY SWALLOWING?

<table>
<thead>
<tr>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>no swallowing</td>
</tr>
<tr>
<td>difficulty</td>
</tr>
</tbody>
</table>

The data collected is considered to be interval level as one end of the scale is zero with the other end representing the opposite of zero or the most intense phenomenon. By measuring the placement of the markings one can gauge the intensity of the measured phenomenon (Wewers, Rachfal, & Ahijevych, 1990).

The visual analogue scale (VAS) is valuable to assess the intensity of a subjective phenomenon and to monitor changes in the subjective phenomenon over time. Many researchers have used the VAS scale and report that this tool is sensitive to measures of pain with a demonstrated reliability on repeated measurements ($r = 0.95$, $p < 0.001$).
Additionally, when the VAS was compared to a numerical rating scale the validity correlated well (Frank-Stromborg, 1988). Another advantage to the VAS is the ease of use for subjects, its versatility and, relatively little time to record the data.

**Human Subjects Considerations**

The study presented above follows all of the policies set forth by Washington State University. Additionally, this project follows the guidelines set forth by the Intercollegiate Center for Nursing Education (ICNE) for the completion of a clinical research project as is required for the completion of the advanced practice Family Nurse Practitioner Master's Degree. Washington State University's Human Subjects Summary Review Form is appended (see Appendix G).

The proposal set forth has been approved by the University's Institutional Review Board (IRB) and has been found acceptable for implementation with human subjects. Further approval has come from the Director of the Department of Radiation Therapy Oncology and Sacred Heart Hospital (see Appendix B).

Research subjects who agree to participate in this study will sign the consent form (See Appendix C). Each subject will have the opportunity to ask questions. Subjects will be made aware of the purpose of the research study and understand the criteria for subject selection. All procedures will be explained and descriptions of the risks and benefits reviewed. Alternatives to study participation will be discussed and options to withdrawal from the study are clearly stated. Assurances of strict anonymity and confidentiality are outlined prior to their individual written consents.
References


Radiation Esophagitis 23


APPENDIX A

FIGURE 1
EXPERIMENTAL MODEL

ESOPHAGITIS

Arm I:
Reynold's Solution @ time
patient has symptoms

Arm II:
Sucralfate/Fluconazole @ time
patient has symptoms
December 11, 1996

Dear Ms. Taylor,

I have reviewed your proposed research project and find it pertinent and of interest to my clinical practice. Additionally, I have had my clinical partners review the proposal and they concur with my desire to proceed.

To that end, I would like you to know that we look forward to implementation of this clinical research.

The thorny problems of unavoidable adverse side effects of radiotherapy dictate anticipation and timely effective treatment. By reviewing two currently utilized treatments of subjectively reported radiotherapy esophagitis we can evaluate your results and perhaps change our clinical practices accordingly.

Please know that we will assist you in any manner that we can.

Sincerely,

Donald Schmutz, M.D.
Director Radiation Oncology Department
Sacred Heart Medical Center
APPENDIX C

EVALUATION OF TREATMENT MODALITIES IN RADIOTHERAPY INDUCED ESOPHAGITIS

INFORMED CONSENT

A. Invitation to participate

You are invited by Gale Taylor, Graduate Student at the Intercollegiate Center for Nursing Education (ICNE) to take part in a research study regarding treatment of radiation induced esophagitis. Your agreement to take part in this study is voluntary and of your own free will. The ICNE and Washington State University Institutional Review Board (IRB) have approved the use of human subjects for this study.

B. Purpose of the study

This study is examining two commonly used treatments of radiation induced esophagitis. You are asked to take part in this study because you will be receiving radiation to your upper chest, including your esophagus. If you agree to take part and be a subject in this study, you will be randomly assigned to one of two treatment groups. You will be asked to record information regarding any pain or difficulty with swallowing.

C. Explanation of protocol

After agreeing to take part in this study, you will need to sign this consent form. You will be asked to record your symptoms of pain with swallowing and swallowing difficulty every four days. At the time that you notice these symptoms you will be
randomly assigned to one of two separate treatment groups. Each group will be assigned a medical treatment plan currently used to treat symptoms of esophagitis as prescribed by your radiation therapy oncologist and I will be evaluating which is the most effective for treatment relief. The self-report forms will take less than two (2) minutes to fill out. You will be asked to provide the information regarding your symptoms once every four (4) days during your prescribed radiation therapy treatments. These recordings will begin on the first day of your treatments. I will ask you to record your symptoms every fourth (4th) day thereafter until day twenty one (21) of your prescribed treatment. In addition, you are being asked to answer questions about yourself which are included on the demographic questionnaire. If you have adverse health related problems arise, are unable to tolerate the treatments or, have significant delays or breaks within your actual radiation therapy treatments, you may not be able to take part in or be asked to stop participating in the study.

D. Potential risks and discomforts

You may become uncomfortable because of the seriousness of your conditions, fatigued as treatment progresses, mental stress related to your diagnosis, and an inability to tolerate your treatment protocol. These risks and discomforts are decreased by having all study related interactions occur within the Radiation Therapy Oncology Department.

All support services, such as, dietary counseling, pastoral care, social services, transport services, financial counseling, laboratory care, volunteer counseling through the Can Surmount Program, and your medical oncologist are available to you. My education includes being a baccalaureate prepared registered nurse with over eighteen (18) years
of experience with oncology patients.

You may also become uneasy about telling me about your symptoms as they progress. I have made every effort to provide complete confidentiality and privacy so no one will know you have taken part in this study. All of your personal information is protected by identifying you with a study number. Your name and study number are kept in separate files, and are available only to myself and the research team as needed. All research information and personal identifying information will be kept in locked files that can be opened only by myself and the research team if need be.

If you do experience any adverse reactions while in this study such as respiratory difficulty, rash associated with your medication, or emotional distress related to the protocol, you should immediately call your radiation oncologist to report them. Appropriate interventions will be made at that time to assist you with problems as they occur.

You may choose not to continue at any time during the study. Your choice not to continue will not affect your relationship as a treatment patient of the radiation therapy oncology department, your relationship with your radiation therapy oncologist nor your relation with your treatment nurses and technicians. You may choose to answer as many or as few of the questions as you would like. You may stop or withdraw from the study at any time.

E. Potential benefits

You will benefit by receiving one of two identified and established treatment of radiation induced esophagitis.
F. **Assurance of confidentiality**

Information obtained as part of this study will be strictly private and confidential. The information will be used only for research. The number code with your name will be available only to myself and research team. The completed information taken from subjects will be kept in a locked file and destroyed six (6) months after the completion of the study. At no time, will your study number and personal information be available to anyone but the researchers. Study results will be reported only as a part of a larger group.

G. **Withdrawal from the study**

Your agreement to take part in this study is voluntary. If you agree to take part, you may choose to stop and withdraw your consent at any time.

H. **Informed consent**

1. I, as shown by my signature below, fully understand the study goals, procedures and risks that go along with taking part in this study.

2. I, as shown by my signature below, understand that taking part in this study is of my own free will and that I may stop at any time.

3. I, as shown by my signature below, give permission to Gale Taylor to use and then destroy the information and disseminate finding from this study. I understand that the investigator and other professionals who work with the investigator agree to protect the privacy and confidentiality of the information gathered during this study within the limits of Washington State Law.
I have read and understand the above conditions. I have had the chance to ask questions about the study and the methods used to collect the study information. These questions have been answered to my satisfaction. I have read and understand the study and have received a copy of this form.

I may contact Gale Taylor at 509-455-2090 extention 8651, then follow the voice prompts to leave a message or, Dr. M. Bruya, (Committee Chairwoman) at ICNE, 509-324-7273, to get information or ask questions I may have about this study at any time.

_________________________  ____________
Subject's Signature        Date

_________________________  ____________
Investigator's Signature   Date
APPENDIX D:
Letter of Invitation to Participate

Dear Sir or Madam,

Hello. My name is Gale Taylor. I am currently working toward completion of a graduate program of study in nursing. As part of my studies I have had the opportunity to propose a research project.

Briefly, the study I have proposed involves the evaluation of how effective two separate treatment plans are for a commonly occurring side effect of radiation therapy. The side effect being investigated is subjectively reported esophagitis or difficulty with swallowing and/or pain with swallowing as a result of having received your prescribed radiotherapy. The two treatments to be contrasted are used to relieve the above mentioned symptoms.

If you agree to participate in this study you will be randomly assigned to one of the two groups. You will receive one of two medication combinations to treat the side effect of esophagitis.

Your participation is voluntary and by your written consent. Your name will be kept confidential at all times and will only be know to study investigators. Any publication to research findings will be devoid of any reference to individuals and will, in fact, give participants anonymity. The benefits to you as a study patient will likely be minimal as you will be receiving one of two already utilized standard treatments. Future patients may gain greater benefits than you as we will be able to sort out which of the two treatments plans is the most effective.

If after reading this letter you are not interested in participation in this study please just let us know. You are under no obligation to participate and will not experience any change of standard treatment care because of preferring not to participate.

If you are interested in participating in the study please notify either your Radiotherapy Oncologist or the departmental nurse so that further information can be made available to you. Thank for your consideration.

Sincerely,

Gale Taylor, BSN
Graduate Student ICNE
WSU Spokane Campus
APPENDIX E

PATIENT DEMOGRAPHIC QUESTIONNAIRE

Date

1.) Name (or ID #) __________

2.) Age __________

3.) Gender: Female ____
   Male ____

4.) Today's Weight __________

5a.) Have you been a smoker in your lifetime? Yes ____
     No ____

5b.) If yes, number of years of smoking? ______

5c.) If yes, number of packs per day? ______

6.) Do you have a sore throat? Yes ____
    No ____

7.) Do you have difficulty swallowing? Yes ____
    No ____

8.) Have you had radiation therapy treatments in the past 12 months? Yes ____
    No ____

9.) Have you had chemotherapy treatments in the past 12 months? Yes ____
    No ____

10.) Do you have allergies to any of the following:
     Erythomycin Yes ____
          No ____
     Diphenhydramine Yes ____
           No ____
     Nystatin Yes ____
            No ____
     Sucralfate Yes ____
            No ____
     Hydrocortisone Yes ____
           No ____
     Fluconazole Yes ____
            No ____
APPENDIX F

DATA COLLECTION WORKSHEET

This worksheet is designed to measure how much pain and difficulty you may be experiencing during the initial phases of your prescribed radiation therapy course. Please answer each question by making a vertical (up and down) mark through each horizontal line. Each horizontal line has a range from zero (0) to the highest amount of pain and difficulty you can imagine. After reading each question place a mark on the exact point on the horizontal line that would best describe your experiences in relationship to the zero point.

1. How much pain with swallowing

   ______________________________________________________________________

   zero  worst imaginable

2. How much swallowing difficulty

   ______________________________________________________________________

   zero  worst imaginable
APPENDIX G

Human Subject Review Summary Form

University procedures require Institutional Review Board (IRB) review and approval of research involving human subjects. If a project is exempt, a completed copy of the first two pages of the Human Subject Review Summary Form must be submitted to the OGRD. No research can be initiated until approval has been obtained from the IRB. If the project is not exempt, 18 copies of this entire form must be filed with the OGRD (Phone 335-9661; Zip 3140). The IRB approval must be kept on research data for THREE YEARS after completion of the research. This form is available at OGRD on 3.5" disk. (Revised 2/95)

Principal Investigator: Gale E. Taylor
Academic Title: Graduate FNP Student

Department/Division: Nursing/Masters
Zip Code: 99022
Telephone: 509-244-3257

Project Title: Evaluation of Treatment Modalities in Radiotherapy Induced Esophagitis

Anticipated Starting Date: January 1997
Anticipated Termination Date: May 1997

Is the project seeking funds? Yes [ ] No [x] Granting agency: __________________________ Principal Investigator on grant: __________________________

RESEARCH QUALIFYING FOR EXEMPTION FROM FEDERAL REGULATIONS FOR THE PROTECTION OF HUMAN SUBJECTS (Quoted from the Code of Federal Regulations, Title 45, Part 46.101)

i. Check the type of exemption application to the project:
   0. No exemption. [x]  

1. Research conducted in established or commonly accepted educational settings involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or on the comparison among instructional techniques, curricula, or classroom management methods.

2. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior, unless: (i) information obtained is recorded in such a manner that the human subjects can be identified, directly or through identifiers linked to the subjects; and (ii) any disclosure of the subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

3. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (2) of this section, if: (i) The human subjects are elected or appointed public officials or candidates for
public office; or (ii) federal statute(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

4. Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

5. Research and demonstration projects which are conducted by or subject to the approval of the department or agency heads, and which are designed to study, evaluate or otherwise examine: (i) Public benefit or service programs; (ii) Procedures for obtaining benefits or services under those programs, (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs.

6. Taste and food quality evaluation and consumer acceptance studies. (i) If wholesome foods without additives are consumed or (ii) if a food is consumed that contains a food ingredient at or below the level of and for a use found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U. S. Department of Agriculture.

II. Abstract:

A. Briefly describe the purpose, procedures and research design (be sure to include what the subjects will do) (use the back side if necessary): The purpose of the research is to contrast the efficacy of two currently used treatment modalities for the treatment of subjectively reported radiotherapy induced esophagitis. Each study subject will be randomized through a random drawing, either Group A with Reynold's solution or Group B with sucralfate/diflucan, drawn every time a patient enters the study. Using a repeated measures design, study patients will be asked to provide subjective information regarding the symptoms as they relate to swallowing difficulty and/or pain with swallowing (dysphagia). Patients will be asked to provide six (6) recordings of the swallowing experiences they have while receiving their prescribed radiotherapy and their randomized study medications.
B. Check the method to be used:

1. Survey (Submit a copy) _ Check how administered: Self X Telephone ___ Personal Interview ___ Other ___

2. Observational ___ Public Record ___ Taste Evaluation ___ Pathological or Diagnostic Specimens ___

3. Experimental ___

4. Other ___ Describe __________________________

C. Is data anonymous ___ or confidential X ___? (See page 4) Describe how anonymity or confidentiality will be maintained (e.g., coded to a master list and separated from data, locked cabinet, office, restricted computer, etc.)? Who will have access to the data? Each subject will be identified by code number and randomized into each of the study groups by previously mentioned method. The master list of coded numbers as correlated to patient name will be locked in a separate fire proof box from the data. Access to data of the study will be granted to researcher, research chairperson and committee members as necessary.

D. Nature of the data collected?

Subjects under 18 years of age? No

Subjects confined in a correctional or detention facility? No

Is pregnancy a prerequisite for serving as a subject? No

Are fetuses in utero subjects in this research? No

Subjects presumed to be not legally competent? No

Are personal records (medical, academic, etc.) used without written consent? No

Are data from subjects (responses, information, specimens) directly or indirectly identifiable? And place subject at risk (criminal or civil liability) or damaging to subjects' financial standing, employability or reputation? No

Will specimens obtained from an autopsy used in the research? No

Will subjects be asked sensitive questions about sexual experiences? No

Will questions be asked about alcohol or drug use? No

Will alcohol or drugs be administered? Yes

Will blood/body fluids be drawn? No

If yes to any of the above, please explain rationale: Subjects will be randomized into one of two treatment groups wherein the efficacy of two currently used medication regimes for subjectively reported radiotherapy induced esophagitis will be contrasted and analyzed. Medications are prescribed by the patient's physician on a routine basis. The randomization of
prescribed medications is the variable of interest.

E. Will any ethnic group or gender be excluded from the study pool?  No.
   If yes, please explain:

Principal Investigator: The information provided above is accurate and the project will be conducted in accordance with applicable Federal, State, and University regulations.
   Signature  Gale Taylor  Date 12-16-96

Faculty Sponsor (if principal investigator is a student): The research is in accordance with applicable Federal, State, and University regulations.
   Signature  Margaret Child Rising  Date 16 Dec. 96

Chair, Director, or Dean: The research is in accordance with applicable Federal, State, and University regulations.
   Signature  Marion Sturges  Date 16 Dec. 96

Institutional Review Board: This project has been properly filed as required by Federal, State, and University procedures.
   Signature  Dennis D. Green  Date 10 Jan. 97

WSU IRB APPROVED

DATE 1-13-97
INITIALS MMD
III. DESCRIPTION OF THE POPULATION:

A. Approximate number 15-20

B. Age range over 18 years

C. How will subjects be selected or recruited? This study will be completed in the Northwestern region of the United States within a regional hospital's Outpatient Oncology Department and satellite clinic. Up to ten patients will be enrolled in each of the separate treatment groups. Patient identification, informed consents and, study datum will be collected within these departments.

The sample includes persons over 18 years with a diagnosis of non-small cell lung cancer (NSCLC) confirmed by biopsy. These individuals must not be candidates for chemotherapy or surgery, with less than 10% loss of their normal body weight. They must not have preexisting complaints of dysphagia or esophagitis for at least one year prior to enrollment into the study. All subjects must sign an informed consent.

D. Will the subjects be compensated (include extra credit)? If yes, how much, when and how. Must they complete the project to be paid? No.

E. Are any of the subjects not competent to give consent (e.g., minors, prisoners, institutionalized)?
   If yes, how will consent be obtained? From whom? Are there procedures for gaining assent?
   (Submit copy of Assent Form.) No. See consent form provided following Human Subjects Review Summary Form.

F. Will a written consent form be obtained? Yes X  No
   If yes, please attach consent form (refer to components of a consent form included in OGRD Memo 4).
   If no: How will consent be obtained? Why is this method being used?

IV. DECEPTION. If any deception (withholding of complete information) is required for the validity of this activity, explain why this is necessary and attach a debriefing statement. Subjects will be randomized in the fashion mentioned previously into one of two treatment groups. Prior to being randomized they will not know which group they will participate in and will therefore need to sign the consent without foreknowledge of their group assignment.

V. ASSESSMENT OF RISKS AND BENEFITS.

A. Describe any potential risks and describe how you will minimize these risks. These include stress, social, legal, discomfort, invasion of privacy, or embarrassment, and side effects. Subjects may become uncomfortable because of the seriousness of their conditions, fatigued as treatment progresses, mentally stressed as related to their diagnosis and develop the inability to tolerate their treatment protocols. These risks and discomforts
are decreased by having all study related interaction occur within the Radiation Therapy Oncology Department. All support services, such as, dietary counseling, pastoral care, social services, transport services, financial counseling, laboratory care, volunteer counseling through the CanSurmount Program and medical oncologist are available to subjects within the oncology department.

Every effort will be made to provide complete confidentiality and privacy so no one will know whom study subjects are. Private examination rooms are available to potential subjects to discuss the study, consent, and ongoing concerns that may arise during the course of the study.

B. In the event that any of these potential risks occur, how will it be handled (e.g., compensation, counseling, etc.)? As above, if any risks occur, services will be available to study subjects via prompt referral to needed services which are already in place in the oncology departments.
C. Will this study interfere with any subjects’ normal routine (e.g., school attendance, medical treatment, etc.)? No.

D. Describe the expected benefits to society and to the individual subjects? Study subjects will benefit by receiving one of two identified and established treatments for subjectively reported radiotherapy induced esophagitis. Potential benefits may be a more efficacious treatment of subjectively reported esophagitis for future patients. Individually, these patients will benefit from use of these commonly prescribed, established clinical methods, neither of which have been compared to each other.

E. If blood or other specimens will be taken? No.
   Which specimens? ____________________________
   ____________________________
   What are the qualifications of the person who will draw the specimen? __________
   ____________________________
   ____________________________
   How often? ____________________________
   ____________________________
   How much? ____________________________
   ____________________________
   Describe the procedure for drawing the specimen.

VI. PROJECT CHECKLIST
   A. Will any investigational new drug (IND) be used? Yes  No  X  
   B. Will any other drugs be used? Yes  X  No  

   C. Will alcohol be ingested by the subjects? Yes  No  X  
      If yes, what type? Refer to guidelines for administration of ethyl alcohol in human experimentation available from the OGRD.

   D. Will audio-visual tapes, audio tapes, or photographs be taken? Yes  No  X  
      If yes: which of the above? Where will tapes or photographs be stored? When will this material be destroyed? How will confidentiality be maintained?
INFORMED CONSENT

A. Invitation to participate

You are invited by Gale Taylor, Graduate Student at the Intercollegiate Center for Nursing Education (ICNE) to take part in a research study regarding treatment of radiation induced esophagitis. Your agreement to take part in this study is voluntary and of your own free will. The ICNE and Washington State University Institutional Review Board (IRB) have approved the use of human subjects for this study.

B. Purpose of the study

This study is examining two commonly used treatments of radiation induced esophagitis. You are asked to take part in this study because you will be receiving radiation to your upper chest, including your esophagus. If you agree to take part and be a subject in this study, you will be randomly assigned to one of two treatment groups. You will be asked to record information regarding any pain or difficulty with swallowing.

C. Explanation of protocol

After agreeing to take part in this study, you will need to sign this consent form. You will be asked to record your symptoms of pain with swallowing and swallowing difficulty every four days. At the time that you notice these symptoms you will be randomly assigned to one of two separate treatment groups. Each group will be assigned a medical treatment plan currently used to treat symptoms of esophagitis as prescribed by your radiation therapy oncologist and I will be evaluating which is the most effective for treatment relief. The self report forms will take less than two (2) minutes to fill out. You will be asked to provide the information regarding your symptoms once every four (4)
days during your prescribed radiation therapy treatments. These recordings will begin on
day one (1) of your treatments. I will ask you to record your symptoms every fourth
(4th) day thereafter until day twenty one (21) of your prescribed treatment. In addition,
you are being asked to answer questions about yourself which are included on the
demographic questionnaire. If you have adverse health related problems arise, are unable
to tolerate the treatments or, have significant delays or breaks within your
actual radiation therapy treatments, you may not be able to take part in or be asked to
stop participating in the study.

D. Potential risks and discomforts

You may become uncomfortable because of the seriousness of your conditions,
fatigued as treatment progresses, mental stress related to your diagnosis, and an inability
to tolerate your treatment protocol. These risks and discomforts are decreased by having
all study related interactions occur within the Radiation Therapy Oncology Department.
All support services, such as, dietary counseling, pastoral care, social services, transport
services, financial counseling, laboratory care, volunteer counseling through the Can
Surmount Program, and your medical oncologist are available to you. My education
includes being a baccalaureate prepared registered nurse with over eighteen (18) years
of experience with oncology patients.

You may also become uneasy about telling me about your symptoms as they
progress. I have made every effort to provide complete confidentiality and privacy so no
one will know you have taken part in this study. All of your personal information is
protected by identifying you with a study number. Your name and study
number are kept in separate files, and are available only to myself and the research team as needed. All research information and personal identifying information will be kept in locked files that can be opened only by myself and the research team if need be.

If you do experience any adverse reactions while in this study such as respiratory difficulty, rash associated with your medication, or emotional distress related to the protocol, you should immediately call your radiation oncologist to report them. Appropriate interventions will be made at that time to assist you with problems as they occur.

You may choose not to continue at any time during the study. Your choice not to continue will not affect your relationship as a treatment patient of the radiation therapy oncology department, your relationship with your radiation therapy oncologist nor your relation with your treatment nurses and technicians. You may choose to answer as many or as few of the questions as you would like. You may stop or withdraw from the study at any time.

E. Potential benefits

You will benefit by receiving one of two identified and established treatment of radiation induced esophagitis.

F. Assurance of confidentiality

Information obtained as part of this study will be strictly private and confidential. The information will be used only for research. The number code with your name will be available only to myself and research team. The completed information taken from subjects will be kept in a locked file and destroyed six (6) months after the completion of
subjects will be kept in a locked file and destroyed six (6) months after the completion of
the study. At no time, will your study number and personal information be available to
anyone but the researchers. Study results will be reported only as a part of a larger
group.

G. Withdrawal from the study

Your agreement to take part in this study is voluntary. If you agree to take part,
you may choose to stop and withdraw your consent at any time.

H. Informed consent

1. I, as shown by my signature below, fully understand the study goals,
procedures and risks that go along with taking part in this study.

2. I, as shown by my signature below, understand that taking part in this study is
of my own free will and that I may stop at any time.

3. I, as shown by my signature below, give permission to Gale Taylor to use and
then destroy the information and disseminate finding from this study. I understand that
the investigator and other professionals who work with the investigator agree to protect
the privacy and confidentiality of the information gathered during this study within the
limits of Washington State Law.

I have read and understand the above conditions. I have had the chance to ask
questions about the study and the methods used to collect the study information. These
questions have been answered to my satisfaction. I have read and understand the study
and have received a copy of this form.
voice prompts to leave a message or, Dr. M. Bruya, (Committee Chairwoman) at ICNE, 509-324-7273, to get information or ask questions I may have about this study at any time.

_________________________  ________________
Subject's Signature          Date

_________________________  ________________
Investigator's Signature     Date