

ABSTRACT

Aim/research questions

The aim of the study was to evaluate CT-based treatment planning *versus* digitised image planning (standard planning technique) for carcinoma of the breast, using the four-field breast technique, in terms of the depth of supraclavicular and axillary nodes, the variability of the breast tissue and the dose inhomogeneity at the matchline.

The variability of the depth of supraclavicular and axillary nodes has not been documented in any local or national studies. When simulating patients for treatment, it is evident that the anatomical variability of patient chest wall thickness, shape and size is a contributing factor towards the final treatment plan and dose distribution achieved. Therefore knowing the correct depth of the nodes and being able to clearly demarcate the breast tissue should result in a favourable dose administration.

The following questions were addressed:

- What is the dose to the supraclavicular nodes from both plans?
- What is the dose to the axillary nodes from both plans?
- How do the plans differ in terms of dose coverage to the supraclavicular and axillary nodes?
- What is the relationship between the depth of the supraclavicular nodes and the patient separation?

- What is the relationship between the depth of the axillary nodes and the patient separation?
- Does the target volume receive adequate dose coverage from the plans?
- How is dose to the heart volume affected by target coverage on both plans?
- How is dose to the lung volume affected by target coverage on both plans?
- What is the dose variability along the matchline?
- Are the plans over dosing?
- Are the plans under dosing?

Motivation

There is no known documentation of studies done in South Africa to assess the variability of breast tissue in patients treated for cancer of the breast. This study aimed to critically compare the digitised image planning technique used to determine the volume of breast tissue to that obtained from the CT planning data. This is important because if the breast tissue is inadequately covered then the dose delivered to the area will be inadequate thus possibly resulting in tumour recurrence.

The irregular three dimensional volumes of the breast and regional lymph nodes make it technically difficult to deliver an equal and adequate dose to the breast tissue and regional lymph nodes. The techniques used for field

matching and assessing matchline inhomogeneity have always been a controversial issue.

Methodology

This study was conducted at three centers, namely the Parklands Radiotherapy Department, Durban, the Durban Oncology Centre, Durban, and the St Anne's Radiotherapy Department, Pietermaritzburg. The treatment planning computers at the Parklands Radiotherapy Department and the Durban Oncology Centre were used only because the beam configuration and beam data are identical.

Those participants referred by the radiation oncologist for radiation therapy, using the four-field breast technique, were selected to participate in this study. The sample size included 30 participants.

The participant had to first undergo the simulation process prior to the CT (computerised tomography) scan being performed. The planning process was then followed. A treatment plan was generated by the planning radiographer using the standard technique. This was referred to as plan 1. The second plan was generated by the researcher to achieve optimal coverage of the breast tissue and nodal regions. This was referred to as plan 2 and was generated using the CT-based planning technique where the approach was to achieve as conformal a plan as possible.

The depth and doses to the supraclavicular nodes, axillary nodes and breast tissue were demarcated on the CT scan slices. All measurements were recorded by the use of planning tools on the treatment planning system.

Results/ Conclusion

- One of the advantages of CT based treatment planning was the ability to adjust the field parameters based on CT information.
- The three dimensional appearance from the CT data accurately defined the anatomical structures.
- The mean depth of the supraclavicular nodes was 3.61cm and the dose from both plans were inadequate.
- The mean depth of the axillary nodes was 3.43cm and the dose from plan 2 was adequate for coverage of the depth of the nodes and plan 1 was not adequate.
- Heart volume was accurately defined.
- Lung volume was accurately defined.
- Matchline dose inhomogeneity was well defined and viewed from many planes.
- Areas of over dosage or under dosage were accurately defined.

Recommendations

This research will serve as a base for further studies and it recommends that the following further research be undertaken:

- With left-sided breast tumours, it is often difficult to reduce the volume of heart in the field. One may consider introducing a heart block to

reduce the dose to the heart. The use of a block may result in inadequate coverage of tissues that are high risk of harboring microscopic disease.

- The use of humeral head shielding has resulted in inadequate dose to the axillary nodes. Further research could possibly investigate the use of an anterior supraclavicular humeral shield and omitting the use of the posterior axillary humeral shield. Whether the dose to the axillary nodes will be adequate or not, is yet to be determined.
- The use of high energy photons for the posterior axillary field is also an area that needs investigation. The patient separation will possibly be a great contributing factor.
- For patients with smaller axillary separation the omission of the posterior axillary field is an area that also needs investigation.
- This study was based on a technical aspect. The assessment of the clinical aspect will be a long term follow-up at least ten years to look at survival rates.

DEDICATION

This dissertation is dedicated to three very special people in my life, my late mum, my late dad and my late brother whom I lost during the last fourteen months.

My mum and dad have always encouraged my studies and career.

My precious brother taught me the true meaning of strength and courage.

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GLOSSARY OF TERMS

Alloy shielding blocks – Heavy metal blocks e.g. Lead, tungsten, or special alloys are used to shape the beam. The blocks transmit only a part of the beam therefore reducing the dose to normal tissues (Bomford *et al.*, 2003:1).

Beams eye view (BEV) – The view of the patient anatomy as seen through the radiation collimator by an imaginary observer at the source location (Webb, 1993:342).

Carcinoma – malignant tumour arising from the epithelium, which are cells that line the surface (Bomford *et al.*, 2003:283).

Computerised Tomography (CT) – Section imaging in which the required image must be reconstructed from projection measurements, usually using a digital computer (Webb, 1993:343).

Conformal therapy – Conformal therapy is a method of modifying the beam to follow the shape of the tumour. The actual shaping is done by multileaf collimators or alloy shielding blocks. This technique also reduces the volume of normal tissue irradiated (Flinton, 1998:4).

Dose-volume histogram (DVH) – Histogram showing the fraction of the target volume raised to a particular dose value or the fraction of the volume receiving the specified dose value or greater (Webb, 1993:344).

Field – Area selected and demarcated to focus the treatment (Dobbs, 1999:1).

Inhomogeneity – Variability of attenuation of an incident radiation beam on the basis of differences in tissue density (Dobbs, 1999:25).

Isocentre – The axis of rotation of a gantry, for example that of a computed tomography (CT) scanner or a machine delivering radiotherapeutic radiation (Webb, 1993:347).

Matchline problems – Potential sites of over dose or under dose where two adjacent radiation fields meet (Webb, 1993:347).

Multileaf collimator (MLC) – X-ray collimator comprising many leaves comprising tungsten and thus able to create an irregularly shaped window through which radiation can pass (Webb, 1993:347).

Organ at risk – Normal tissues which are prone to injury because of heightened radiation sensitivity. Attempts to avoid these organs at risk may significantly influence treatment planning and/or prescribed dose (ICRU 50, 1993:v).

Plan 1 – This was the plan using the digitised image planning technique where all simulated parameters will be entered onto the computed tomography (CT) data, without any modifications to the field size, gantry

angles and collimator angles parameters. Optimisation of the plan will be achieved

Plan 2 – This was the plan using the CT-based planning technique where the approach will be to achieve as conformal a plan as possible. The researcher will have the option to make any beam modification depending on the data from the CT scan images.

Radiation dose - Is the required dose of energy absorbed by the patient, at the tumour site, from the radiation beam (Griffiths and Short, 2000:3).

Radiation treatment planning (RTP) – as applied to external beam therapy is used to describe the work involved in displaying graphically a dose distribution which results when one or more radiation beams converge on the target volume (Bomford *et al.*, 2003:207).

Radiation therapy – Is the administration of ionising radiation as a form of treatment for cancer. It is a synonym for radiotherapy where the aim is to deliver an optimal dose to the tumour whilst sparing the surrounding normal tissue (Dobbs, 1999:1).

Radiotherapy – Treatment of disease with ionising radiation (Travis, 1989:278). The aim is to deliver an optimal dose to the tumour whilst sparing the surrounding normal tissue (Dobbs, 1999:1).

Separation – Is the distance between the entry points of two fields (Dobbs, 1999:3).

Simulator – A machine which emulates the geometry of a treatment machine, but which uses diagnostic energy x-rays to take images of the patient in the treatment position (Webb, 1993:351).

Simulation – The technique used to obtain the treatment parameters, using a simulator (Dobbs, 1999:6).

SAD technique – (Source-Axis Distance) Also known as an isocentric technique. In this technique the axis of machine rotation (isocentre) is placed in the target volume. The gantry of the machine can then be rotated to any angle while the target remains within the field boundaries (Bentel, 1996:45).

Scout View – A digital two-dimensional planar radiograph formed using a CT scanner, operated such that the source and detector do not rotate about the patient (Webb, 1993:350).

Slice Thickness – The thickness of a tomographic section (Webb, 1993:351).

SSD technique – (Source-Skin Distance) The axis of rotation is placed on the patient's skin surface away from the tumour (Bentel, 1996:45).

Target volume – A geometrical concept used for treatment planning and is defined to select appropriate beam sizes and beam arrangements to cover the clinical disease marginal spread of disease and a ‘safety ‘ margin (Dobbs, 1999:16).

Tissue inhomogeneity corrections – Part of the radiotherapy planning process which takes account of the varying x-ray attenuation of different body tissues. CT data is often used to assist this process (Webb, 1993:352).

Tumour – Can be defined as a lesion resulting from the autonomous or relatively autonomous abnormal growth of cells which persists after the initiating stimulus has been removed (Bomford *et al.*, 2003:243).

Tumour Staging – Method of classification of the extent of a malignant tumour on the basis of a description of the extent of the spread of the primary, its movement into lymph nodes and its dissemination to distant structures (refer to Appendix G)
(Hermanek *et al.*, 1999:204,209).

Wedge – A wedge –shaped metal block, usually made from lead, steel or brass, which reduces the radiation intensity progressively across the beam (Flinton, 1998:139).

CHAPTER ONE

BACKGROUND TO THE STUDY

1.1 INTRODUCTION

It is generally accepted that adapting to new techniques and trends often creates resistance and a fear of entering into a world of the unknown.

Technology has evolved considerably over the years and in the medical field it has provided us with great opportunities that could only benefit our patients.

As individuals we either turn away from these opportunities or embrace them and commit to using them to the advantage of the patient.

It became my passion to assess the value of the computerized tomography (CT) scans during the planning of radiation treatment for breast carcinoma (synonym for cancer) as my instinct was that important information relevant to the anatomical location of the nodes, breast tissue and adequate dose coverage was being overlooked. That was the stimulus to this project.

Cancer of the breast is now the most common cancer in women. It has been reported in the National Cancer Registry that between 1993 and 1995, an annual average of 3 785 new cases of patients with breast cancer were recorded in South Africa (Sitas *et al.*, 1998). More recent statistics in South Africa have not been published by the National Cancer Registry.

The controversy over using the four-field breast technique in the treatment of carcinoma of the breast is a topic that creates great debates. The practise worldwide differs from department to department. According to Violet and

Harmer (2004) in a study series that routinely did not irradiate the supraclavicular nodes in pathologically axillary node positive patients, the risk of recurrence of disease was 4.5 –7%. A further study by Violet and Harmer (2004) showed recurrence rates in clinically axillary node positive patients were reduced from 5.8% in those not receiving radiation therapy to 0% in those receiving radiation therapy.

In contrast to the above findings, a study done by Fisher *et al.*, (1985) on a population of 1665 women, showed no differences observed between patients with node positive disease treated by mastectomy only or mastectomy and radiation therapy in combination. Survival in both groups was about 38%. The authors concluded that the variations of local and regional treatment used in their study are not important in determining survival of patients with breast carcinoma.

Radiation therapy plays a very distinct role in the management of patients with breast carcinoma (Hojris *et al.*, 2000 and Overgaard *et al.*, 1997). Radiation therapy is administered following lumpectomy in patients undergoing breast conservation therapy (BCT), postmastectomy and preoperatively for patients with locally advanced disease (Ceilley *et al.*, 2005 and Pierce and Glatstein, 1994). A multidisciplinary approach is absolutely essential for optimal breast conservation treatment (Early Breast Cancer Clinical Trials Collaborative Group [E.B.C.C.T.C.G], 1995). The fundamental principle of radiation therapy is to concentrate the radiation beam to the target tissues and at the same time minimise the dose to normal tissues (Bentel *et al.*, 1999).

The standard technique for the four-field breast treatment refers to the two tangential fields (diagram 1.1a and 1.1b) that are used to treat the breast or chest wall, the direct anterior supraclavicular field (diagram 1.2a) to cover supraclavicular nodes and a posterior axillary field (diagram 1.2b) to include the axillary lymph nodes.

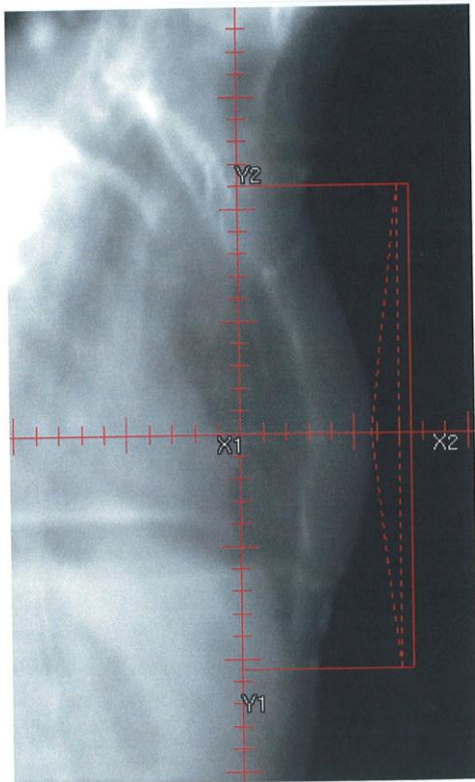
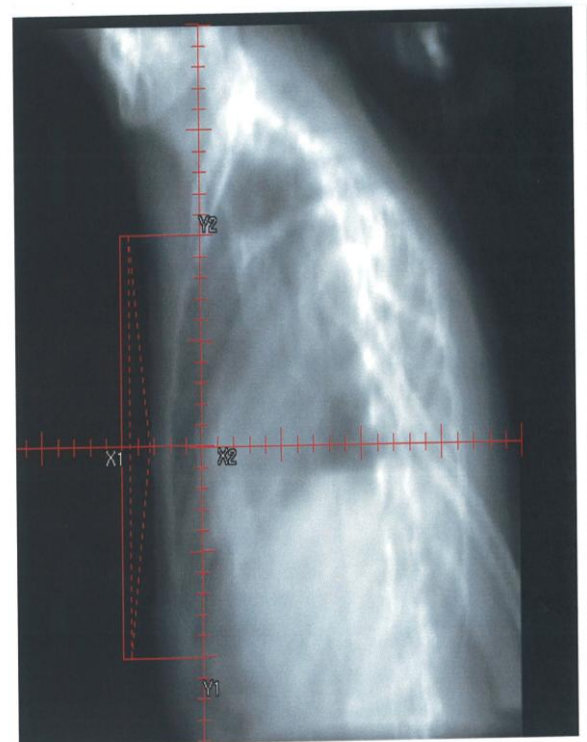


Diagram 1.1a



1.1b

Demonstrates the two tangential fields. Red rectangular area demarcates the treatment field (From participant's beam data).

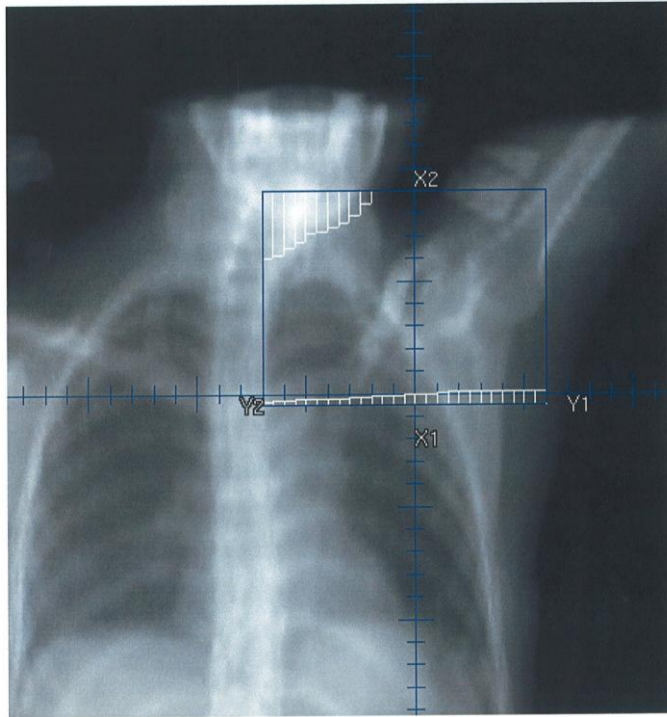


Diagram 1.2 (a)

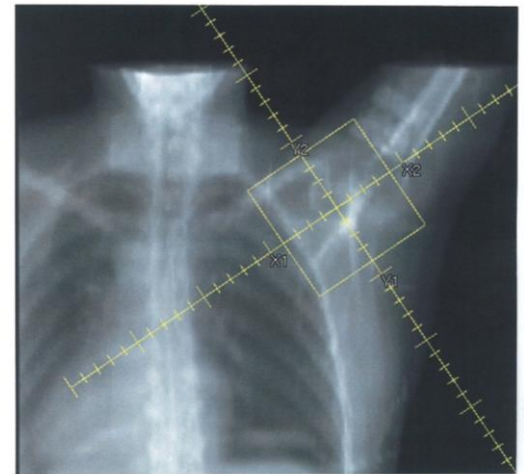
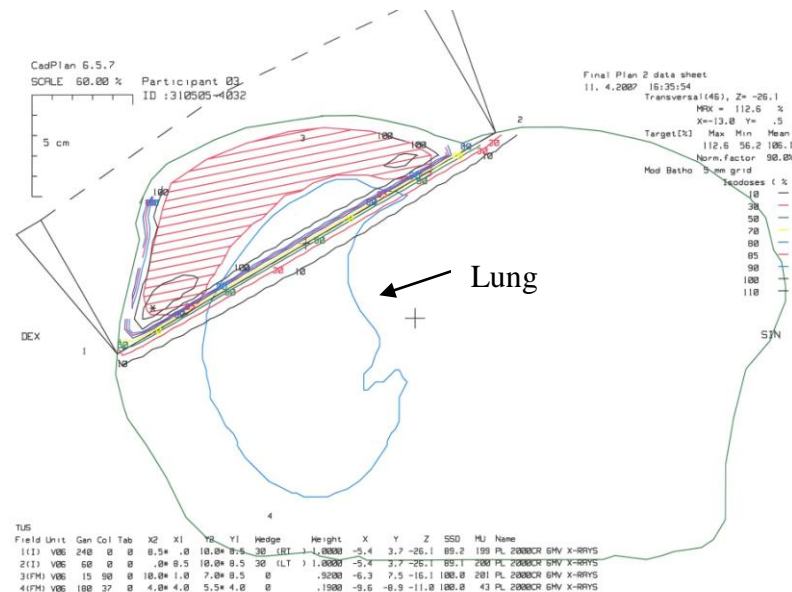


Diagram 1.2 (b)

Shows the anterior supraclavicular field 1.2a demarcated by the blue rectangular area and posterior axillary field 1.2b demarcated by the yellow square field (From participant's beam data).

Currently, the standard technique does not involve the use of CT images for the treatment, instead manual contours which are obtained at the time of simulation are digitised into the treatment planning computer. These manual contours are representative of the patient's body shape and the contours create the impression of a CT scan. A plan is generated once the simulated treatment fields are accurately placed on the contours. The limitations currently experienced by those involved in the treatment planning are due to the lack of adequate contours when using digitised image planning, and the

absence of detailed information about the position of organs at risk in relation to the target volume.



The following criteria were currently used as guidelines for selecting patients for four-field breast technique:

- Tumours greater than 4cm in maximum diameter (Fisher *et al.*, 1985).
- T3/T4 tumours in respect of skin, nipple and pectoral muscle involvement (Perez *et al.*, 2004).
- Four or more lymph nodes involved (Grills *et al.*, 2003, Fortin *et al.*, 2003).
- Positive or close surgical margins (Cowen *et al.*, 2000).
- Extracapsular extension of tumour in lymph nodes (Chao, 2005 and Strom *et al.*, 2005).

(D.J. Hacking, Personal Communication, March 7, 2004)

These criteria are also supported and highlighted in a document published by Strom and Bassett (2002) for the American College of Radiology. The document outlines the practice guidelines for breast conservation therapy in the management of invasive breast carcinoma. It provides an educational tool to assist practitioners in making good decisions on patient management and care and is not intended as a legal standard of care (Strom and Bassett, 2002 and Recht *et al.*, 2001).

Vicini *et al.*, (1997) agree that there is inadequate evidence on the necessity for nodal radiation therapy. In addition, some studies (Galper *et al.*, 2005 and Vicini *et al.*, 1997) suggest that extracapsular extension or the extent of the axillary dissection should also be used to decide on the need for nodal

irradiation. Both studies observed a trend towards decreased nodal failure with nodal irradiation for patients with four or more positive lymph nodes. A very large study conducted by the European Organization for Research and Treatment (EORTC), enrolled 5569 patients who were randomly assigned to undergo a dose of 50Gy to the breast with or without an additional dose of 16Gy. The aim of the study was to determine whether the additional dose reduces the risk of recurrence. The decision to deliver an additional dose of radiation was based on the fact that most recurrences occur in the region of the primary tumour. The results were promising and showed a reduction in the rate of recurrence over a five year period from 19.5% without the additional dose to 10.2% with the additional dose (Bartelink *et al.*, 2001).

The introduction of CT scans has given a different perspective to radiation treatment planning. Furthermore, with the additional information from the CT scans, a more conformal plan may be generated. Conformal planning refers to techniques used to modify the beam to follow the shape of the tumour hence reducing the volume of normal tissue being irradiated (Flinton, 1998). Generally CT-based treatment planning is used routinely for deep seated lesions, for example prostate, bladder and brain. In Parklands Radiotherapy Department, Durban, Durban Oncology Centre, Durban and St Anne's Radiotherapy Department, Pietermaritzburg, CT-based planning is not the standard practice in the radiotherapy treatment planning of patients with breast carcinoma. The question arises as to whether the current standard technique used in these departments is adequate in terms of treating the

nodes to the correct depth and also adequately covering the breast tissue, hence the need for this research.

Matchline problems refer to the potential sites of over dose or under dose where two adjacent radiation fields meet (Webb, 1993). The problem of inhomogeneity at the matchline has been a challenge for many clinicians/practitioners (Hurkmans *et al.*, 2000; Rajasekar *et al.*, 1998 and Hunt *et al.*, 1987). This problem is further complicated by the absence of adequate contours in the standard planning technique used. Generally an assumption is made that the inhomogeneity at the matchline is the same as on the missing contours. The inhomogeneity at the matchline is also controlled by field shaping done using multileaf collimators (MLC) or alloy shielding blocks.

A MLC is an X-ray collimator comprising many leaves (diagram 1.4) made from tungsten and is thus able to create an irregularly shaped window for the radiation to pass through (Webb, 1993). Alloy shielding blocks are heavy metal blocks, for example lead, tungsten, or special alloys used to shape the beam. The blocks transmit only a part of the beam thereby reducing the dose to normal tissues ((Bomford *et al.*, 2003). The field shaping using MLC or alloy shielding blocks is very dependant on the patient shape and size. This is also related to the inhomogeneity observed during the planning stages. The MLC or alloy shielding blocks are modified or edited in an attempt to reduce the areas of over dose or under dose. (Rajasekar *et al.*, 1998).

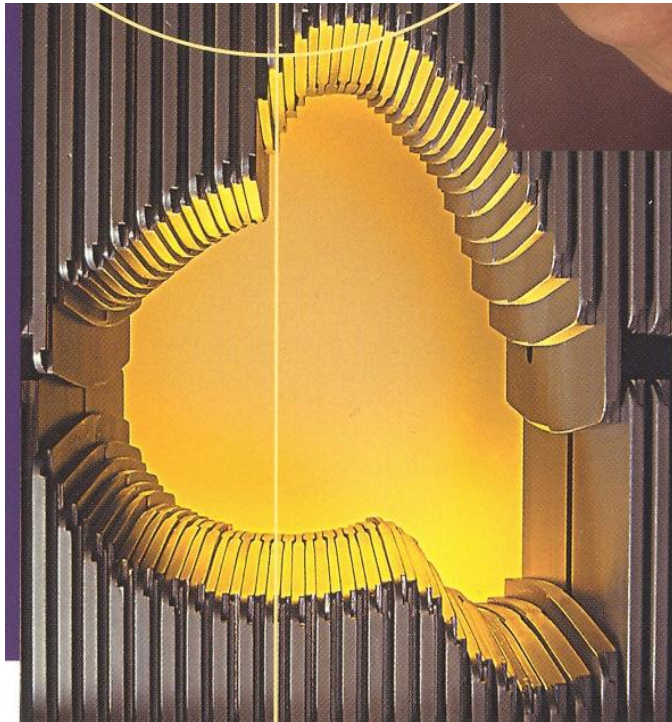


Diagram 1.4 Shows the shape formed by the leaves of the MLC (Varian Medical systems brochure,2001)

The aim of the study was to evaluate CT-based treatment planning *versus* digitised image planning (standard planning technique) for carcinoma of the breast, using the four-field breast technique, in terms of the depth of supraclavicular and axillary nodes, the variability of the breast tissue and the dose inhomogeneity at the matchline.

1.2 MOTIVATION AND SIGNIFICANCE

The variability of the depth of supraclavicular and axillary nodes has not been documented in any local or national studies. When simulating patients for treatment, it is evident that the anatomical variability of patient chest wall thickness, shape and size is a contributing factor towards the final treatment

plan and dose distribution achieved. Therefore knowing the correct depth of the nodes and being able to clearly demarcate the breast tissue should result in optimal dose administration. This study aimed to evaluate the depth of the supraclavicular and axillary nodes from the CT scan, thus giving an indication of adequate or inadequate dose coverage to these nodes. Inadequate dose delivery may compromise the clinical outcome of the patient.

There is no known documentation of studies done in South Africa to assess the variability of breast tissue in patients treated for cancer of the breast. This study aimed to critically compare the digitised image planning technique used to determine the volume of breast tissue to that obtained from the CT data. This is important because if the breast tissue is inadequately covered then the dose delivered to the area will be inadequate thus probably resulting in tumour recurrence.

The irregular three dimensional volumes of the breast and regional lymph nodes make it technically difficult to deliver an equal and adequate dose to the breast tissue and regional lymph nodes. The techniques used for field matching and assessing matchline inhomogeneity have always been a controversial issue. The treatment of the breast with the supraclavicular and axillary field involves the most complex geometric and field matching situation. Rajasekar *et al.*, (1998) in their study clearly state that refinement of techniques can improve control of tumour and minimise the adverse effects of treatment.

1.2.1 CASE REPORT PERFORMED BY THE RESEARCHER

(December 2003, Parklands Radiotherapy Department)

This case report was done to establish the need for embarking on this research.

The patient, a 49 year old female, presented following a right mastectomy and axillary clearance for a locally advanced breast carcinoma. She presented as a stage T3 N3 M0 lesion in the right breast. The histiological findings were reported as a moderately differentiated ductal carcinoma with a 50% oestrogen receptors positivity. Eighteen lymph nodes were identified and all showed the presence of metastases and extracapsular spread, but all surgical margins were free of malignancy.

She was treated with six cycles of adjuvant chemotherapy with taxotere, adriamycin, and cyclophosphamide in view of the poor prognostic factors. She was then started on adjuvant arimidex.

The patient was then referred to the Parklands Hospital Radiotherapy Department for adjuvant radiotherapy treatment to the right chest wall, supraclavicular fossa and axilla to improve the local control. Due to the difficulty in reducing the lung volume during simulation, the radiation oncologist decided that the patient should have a planning CT scan of the chest. This was done in the position as was planned during simulation. Markers were placed on all entry points and borders.

The planning field parameters were transposed onto the CT scan to achieve as homogeneous a dose distribution as possible.

Findings

- The depth of the supraclavicular nodes on the CT scan was 4cm at the level of the apex of the lung. This value was underestimated on the digitised image planning technique by 1cm
- The depth of the axillary nodes on the CT scan was also 4cm anterior to the head of the humerus along the mid vessel. This information was lacking on the digitised image planning technique. On this particular CT data it was questionable as to whether to include the posterior axillary field or not because the separation at the axilla was only 10cm. Where the separation is small, it is often possible to deliver adequate dose posteriorly with the anterior supraclavicular field only. This is avoided due to the high exit dose posteriorly which may increase the dose to normal tissues. There was a discussion with the radiation oncologist and it was debated as to whether an anterior supraclavicular and axillary field combined with a high energy beam, would have been adequate for dose coverage at the depth of the axillary nodes.
- As the lungs were easily visualised, it was simpler to manoeuvre the field angles to optimise the volume of lung in the field of radiation.
- The multileaf collimator (MLC) shaping of the posterior axillary field was unchanged when compared to the simulation radiographs.
- The MLC shaping on the anterior supraclavicular field was shifted both superiorly and medially when compared to the simulation radiographs.

This is significant as any changes on the MLC will affect the dose inhomogeneity by either overdosing or underdosing the planning target volume.

It was evident from this case report that further evaluation of CT scans in terms of the technical aspect was needed.

In order to create a better understanding of the topic, the researcher decided to address questions relating to each objective. This is carried forward throughout the document so that there is clarity on how the questions relate to the objectives.

Objective 1: To evaluate CT-based treatment planning *versus* digitised image planning for carcinoma of the breast in terms of the depth of the supraclavicular and axillary nodes. The following questions were addressed:

- What is the dose to the supraclavicular nodes from both plans?
- What is the dose to the axillary nodes from both plans?
- How do the plans differ in terms of dose coverage to the supraclavicular and axillary nodes?
- What is the relationship between the depth of the supraclavicular nodes and the patient separation?
- What is the relationship between the depth of the axillary nodes and the patient separation?

Objective 2: To evaluate CT-based treatment planning *versus* digitised image planning for carcinoma of the breast in terms of the variability of the breast tissue. The following questions were addressed:

- Does the target volume receive adequate dose coverage from the plans?
- How is dose to the heart volume affected by target coverage on both plans?
- How is dose to the lung volume affected by target coverage on both plans?

Objective 3: To evaluate CT-based treatment planning *versus* digitised image planning for carcinoma of the breast in terms of the dose inhomogeneity at the matchline. The following questions were addressed:

- What is the dose variability along the matchline?
- Are the plans over dosing?
- Are the plans under dosing?

Chapter 2, the literature review, provides an insight into research conducted that relates to treatment of breast carcinoma using the four-field breast technique. It also covers the anatomy and lymphatic drainage of the breast. An explanation of the simulation technique involved in field placement and treatment planning is also detailed in this chapter. Chapter 3, the methods and design, describes the selection of the population, dose reference values and statistical methods used. Chapter 4, documents the data analysis and

results that were obtained from the study. Chapter 5, the discussion, presents a detailed report on the study. Chapter 6 focuses on the significance of the results, limitations of the study and recommendations for future research.

CHAPTER TWO

LITERATURE REVIEW

2.1 INTRODUCTION

According to the American Cancer Society statistics, breast cancer is the most common malignant disease in American women. It affects an estimated 213 000 new patients each year in the United States of America. Breast cancer is diagnosed in about 1300 men each year in America (Uschold, 2004). It has been reported in the National Cancer Registry that between 1993 and 1995, an annual average of 3 785 new cases of patients with breast cancer were recorded in South Africa (Sitas *et al.*, 1998).

The treatment of breast carcinoma involves a multidisciplinary approach. According to Dobbs (1999), radiation therapy can be defined as the administration of treatment using ionising radiation. It is a synonym for radiotherapy where the aim is to deliver an optimal dose to the tumour whilst sparing the surrounding normal tissue (Yu *et al.*, 2005). Radiation therapy plays a very distinct role in the management of patients with breast carcinoma (Hojris *et al.*, 2000 and Overgaard *et al.*, 1997). It is administered following lumpectomy in patients undergoing breast conservation therapy (BCT), postmastectomy and preoperatively for patients with locally advanced disease (Ceilley *et al.*, 2005 and Bentel *et al.*, 1999).

Also included in the management of breast carcinoma is systemic chemotherapy and hormonal therapy. Chemotherapy is the administration of anti-cancer drugs either intravenously (injected into a vein) or by mouth. The

drugs travel in the bloodstream and move throughout the entire body (National Comprehensive Cancer Network [NCCN], 2000). Hormonal therapy is the use of an anti-oestrogen drug to block the effect of oestrogen or to lower oestrogen levels. Oestrogen, a hormone produced by the ovaries, promotes growth of some breast carcinomas (National Comprehensive Cancer Network, [NCCN] 2000). More than 60 years passed before it could be demonstrated that oestrogens are concentrated in oestrogen responsive tissues. Contrary to this, not all tissues containing oestrogen are hormonally responsive. Only about 55-60% of the advanced breast carcinoma patients with oestrogen in their tumour tissues have been initially reported to respond to hormonal therapy (Thorpe, 1988).

Most studies use the multidisciplinary approach for management of breast carcinoma. The management is obviously dictated by the stage of the disease and the regimen selected incorporates chemotherapy, hormonal therapy and radiotherapy (Jager *et al.*, 1999, Overgaard *et al.*, 1999 and Ragaz *et al.*, 1997).

The objectives of radiation therapy in the management of breast carcinoma are to minimise the risk of loco-regional recurrence while simultaneously minimising the risk of treatment related normal tissue injury (Pierce *et al.*, 1992 and Fowble *et al.*, 1991). This is highlighted in these studies as often tissue complications change or alter the management of the patients.

Emani *et al.*, (1991) also emphasize the importance of the radiation oncologist having a good knowledge of tolerance of normal tissue and organs when administering radiation therapy. In order to reach this goal, careful and accurate treatment planning is critical (McShan *et al.*, 1995). Although upgraded field matching techniques and CT-based treatment planning have been introduced in many centres, minimal modifications have been made until recently with the emergence of image-based treatment planning and advanced radiotherapy delivery techniques (Arthur *et al.*, 2006). The techniques used for the treatment of breast carcinoma are standard, but the position of the treatment field is very dependant on the patients' anatomy, volume of breast tissue at risk and the acceptability of dose inhomogeneity in terms of normal tissue injury (Buchholz *et al.*, 2003).

The standard four-field breast technique involves the use of two tangential fields (chapter 1, diagram 1.1) that are skimmed across the breast or chest wall to cover all remaining breast tissue following breast conservation, or the whole breast bed following mastectomy, the direct anterior supraclavicular field (chapter 1, diagram 1.2a) to include the supraclavicular nodes and a posterior axillary field (chapter 1, diagram 1.2b) to include the axillary lymph nodes.

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The controversy of radiation therapy to the supraclavicular and axillary nodes stems from two very interesting theories. The one theory, the Halstedian theory refers to the orderly “centrifugal” progression of the disease therefore the involvement of the axillary nodes is considered local disease and the

supraclavicular nodes as regional disease. The other theory, Fisher's theory views breast carcinoma as a systemic disease, thus locoregional disease does not exist. The two contradicting theories had a great impact on the evolution of breast carcinoma management and treatment (Kiricuta, 2004). A review of the anatomy is necessary as the progression of the disease to the nodal areas impacts on the management and treatment of breast carcinoma.

2.2 ANATOMY

The female breast lies on the anterior chest wall superficial to the pectoralis major muscle (Warwick and Williams, 1973). A thin layer of mammary tissue extends from the midline laterally to the latissimus dorsi muscle and superiorly to the clavicle (Gosling *et al.*, 2002). The majority of the protuberant breast extends mediolaterally from the midline to near the midaxillary line (Mathers *et al.*, 1996). The cranial-caudal borders of the breast are from the second anterior rib to the sixth anterior rib (Buchholz *et al.*, 2003).

The upper-outer quadrant of the breast may extend into the region of the low axilla and is commonly known as the Tail of Spence. This anatomical feature leads the upper outer quadrant of the breast to contain a greater percentage of total breast tissue when compared to the other quadrants. The glandular tissue is supported by fibrous septae known as Cooper's suspensory ligaments. These septae connect the breast parenchyma to the overlying skin and pectoralis fascia (Buchholz *et al.*, 2003).

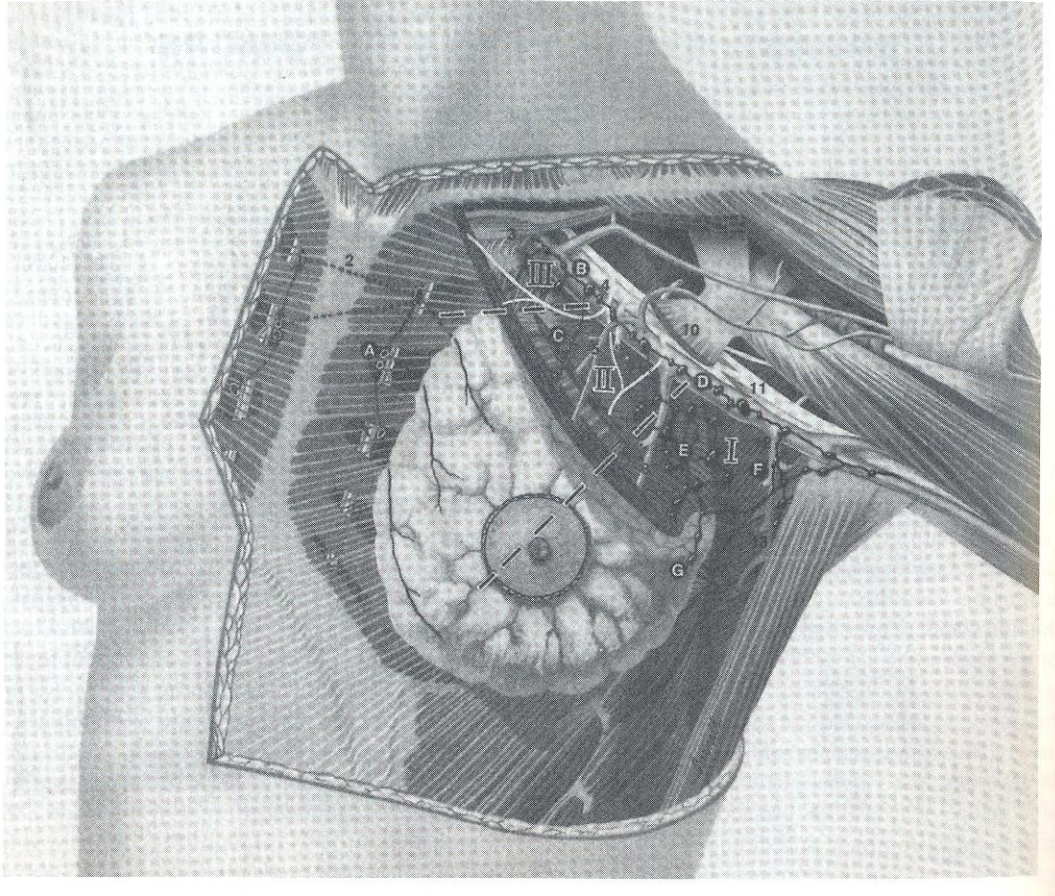


Diagram 2.1 Demonstrates the anatomy of the breast

Bulchholz, T.A., Strom, E.A. and McNeese, M.D. 2003. Radiation

Oncology : Rationale, technique ,results. 8th edition, (edited by Cox J.D.

and Kian Ang, K) Mosby.

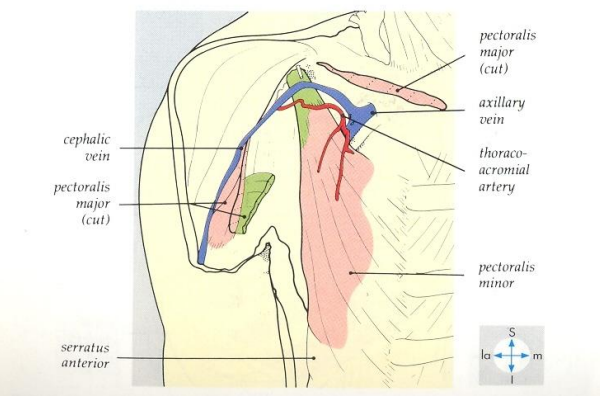
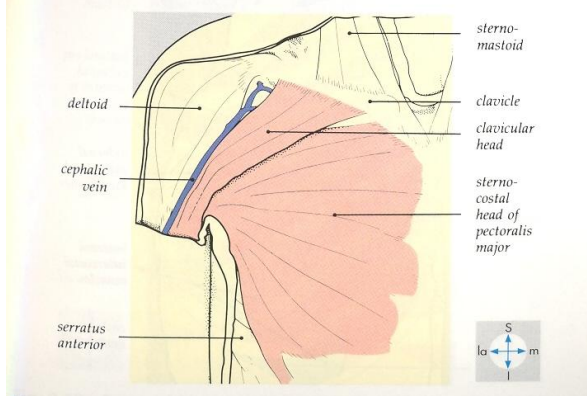
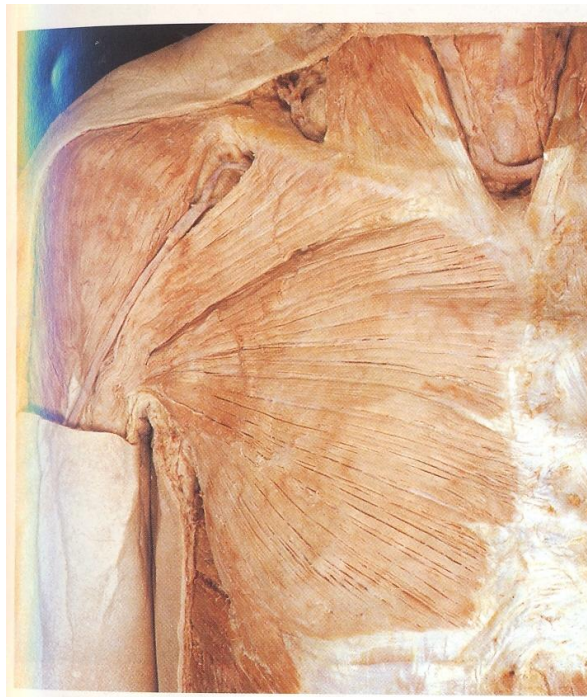


Diagram 2.2 Shows the coronal section of the breast. Good visualisation of the muscles and ligaments

Gosling, J.A., Harris, P.F., Whitmore,I. and Willan,P.L.T. 2002. Human Anatomy. Fourth Edition. Mosby

The glandular elements consist of 15-20 lobes arranged radially, each draining into a lactiferous duct. These ducts open independently onto the surface of the nipple. The nipple is surrounded by an area of pink skin called the areola (Gosling *et al.*, 2002).

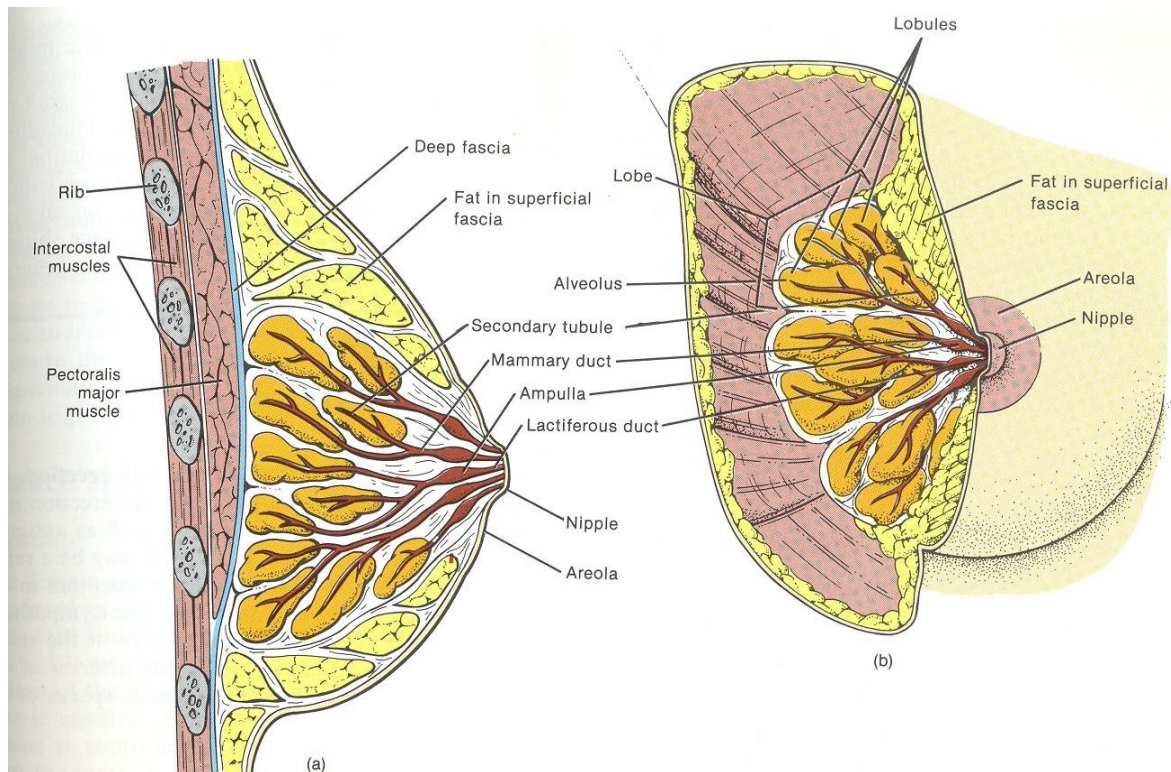


Diagram 2.3(a) Sagittal section and (b) anterior view showing the ducts

Tortora, G.J. and Anagnostakos, N.P. 1987. Principles of Anatomy and Physiology. Fifth edition. Harper and Row Publishers, New York.

2.3 NEUROVASCULAR SUPPLY

Blood is supplied to the breast from the segmental arteries and veins, also known as the intercostal vessels (Clifford *et al.*, (2002). The large lateral thoracic, internal thoracic, thoraco-acromial and superior epigastric arteries have branches supplying the breast (Gosling *et al.*, 2002). The venous drainage of the breast is to the intercostals, internal thoracic and axillary veins. The breast is innervated by branches of the intercostal nerves from the second thoracic vertebra to the seventh thoracic vertebra. The important

physiological changes in the breast are mediated not by nerves but by circulating hormones (Mathers *et al.*, 1996).

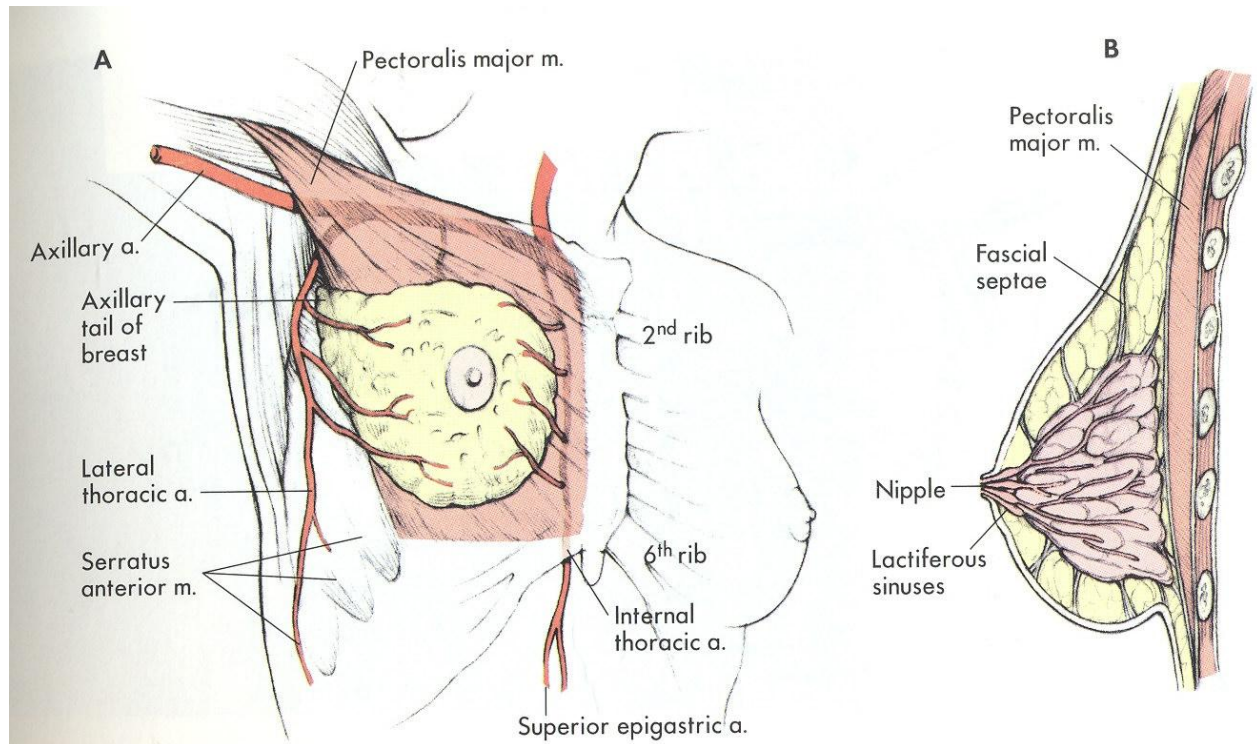


Diagram 2.4 Shows the blood supply to the breast

**Mathers, L.H., Chase, R.A., Dolph, J., Glasgow, E.E. and Gosling, J.A.
1996. Clinical Anatomy Principles. Mosby.**

2.4 LYMPHATIC DRAINAGE

In view of the fact that breast tumors metastasize through the lymphatic channels that drain the breast, it is of utmost importance to understand the routes of lymphatic drainage in the management and treatment of breast carcinoma. The breast is known to have a rich lymphatic plexus with primary drainage to the lymph nodes of the axilla, internal mammary chain, and

supraclavicular fossa. Lymph nodes draining the breast can also be identified within the substance of the breast and below the pectoralis major muscle (Buchholz *et al.*, 2003).

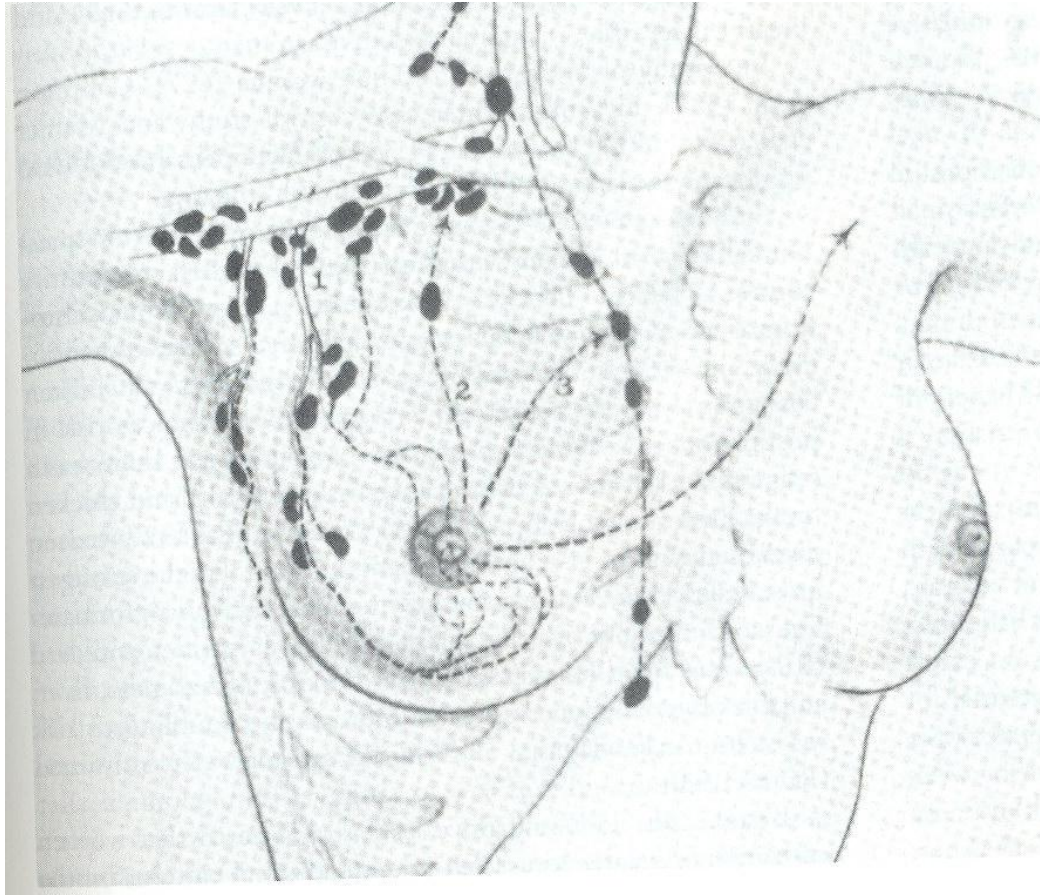


Diagram 2.5 Anatomy of the lymphatics of the routes of the breast

**Perez, C.A., Brady, L.W., Halperin, E.C. and Schmidt-Ullrich, R.K. 2004.
Principles and Practice of Radiation Oncology. Fourth edition, USA
Lippincott Williams and Wilkins.**

Two sets of lymphatic channels are associated with the breast. The first group of lymphatics is superficial and drains the skin covering the breast. The second is a deep group that drains the internal breast tissues. The superficial

and deep groups of lymphatics communicate with each other extensively (Uschold, 2004).

The axillary lymph nodes are divided into three levels. Level I nodes are those below the inferolateral border of the pectoralis minor muscle and are also referred to as the low axillary nodes. Level II are those directly beneath the pectoralis minor muscle and are also known as the midaxillary nodes. Level III are those superior to the pectoralis minor muscle and are also referred to as the apical or subclavicular nodes (Buchholz *et al.*, 2003).

The common route by which cancer spreads to the supraclavicular nodes is through the axillary chain (Clifford *et al.*, 2002). Supraclavicular node involvement usually indicates advanced regional disease. Large lymphatic trunks pass from the subclavicular nodes at the axillary apex medially through the small anatomic triangle. This is formed by the subclavian vein, the subclavian muscle tendon and the chest wall (Gosling *et al.*, 2002).

Retrograde spread may occur into other supraclavicular nodes as lymph nodes in this region become obstructed with tumour. The nodes at greatest risk of involvement are often difficult to palpate because they lie behind the sternocleidomastoid muscle. The more lateral nodes are easier to examine (Buchholz *et al.*, 2003).

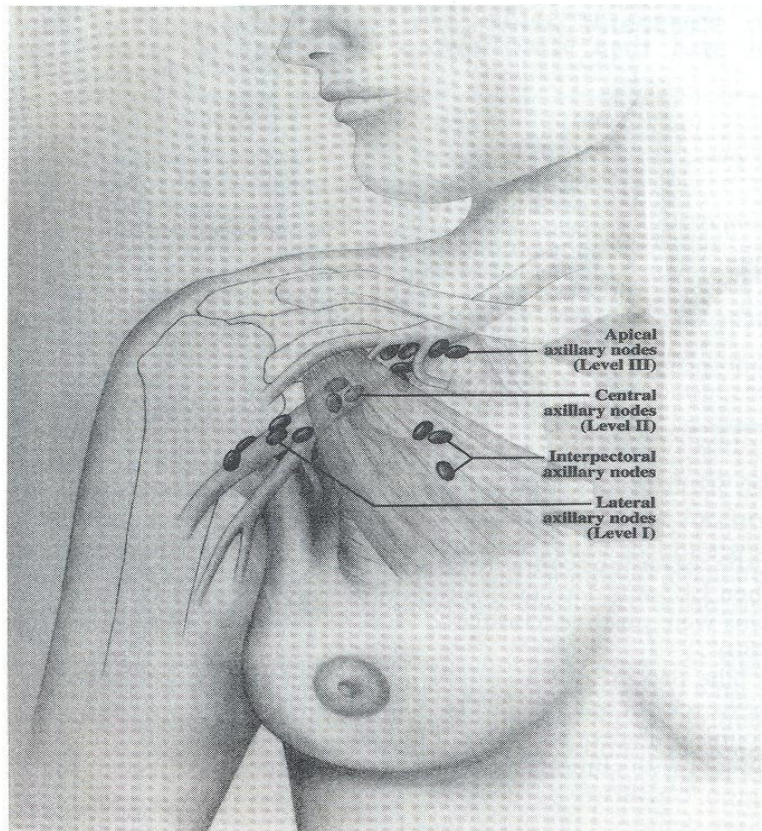


Diagram 2.6 Shows the position of level I, II and III nodes

Bulchholz, T.A., Strom, E.A. and McNeese, M.D. 2003. Radiation

Oncology : Rationale, technique ,results. 8th edition, (edited by Cox J.D. and Kian Ang, K) Mosby.

2.5 EPIDEMIOLOGY AND AETIOLOGY

2.5.1 Epidemiology

Breast cancer is the most common cancer in the western countries. According to current statistics, approximately one in eight women will develop breast cancer at some point during their lifetime (Buchholz *et al.*, 2003). World wide there are in the region of one million new cases reported annually. Buchholz *et al.*, (2003) report that the incidence of invasive breast cancer has steadily

increased up until 1988 and has remained constant since. Over the same period the incidence of non-invasive breast cancer has significantly increased. The incidence of ductal carcinoma in situ has continued to increase and is still increasing by 6% per year (Buchholz *et al.*, 2003).

2.5.2 Aetiology

Although the aetiology of breast carcinoma is non specific and basically unknown (Pervan *et al.*, 1995) many factors have been identified that may be related. These as stated by Mieny (2003) could be divided into viral, genetic and hormonal.

From the literature review it would appear that up to 10% of breast carcinomas are genetically related (Jacobs and Gibson, 1998). The sisters and daughters of a woman with breast cancer have a threefold increased risk of acquiring the disease. The risk is increased ten times for women who have a mother and a sister affected (Bomford and Kunkler, 2003).

The acquired factors include benign breast disease, menstruation, oral contraceptive use and hormonal replacement therapy, age at time of first pregnancy, lactation, diet, weight and radiation (Mieny *et al.*, 2003). A number of benign conditions in the breast increase the risk of breast carcinoma. The greater the number of years of menstruation, the higher the risk of breast carcinoma. Bomford and Kunkler (2003) report that there is a small increase in risk for women who take the oral contraceptive pill and for ten years after cessation. The risk increases threefold in women who have their first babies

over the age of 30. It is also stated that women who have breast-fed their children are slightly less prone to breast carcinoma (Bomford and Kunkler, 2003). Also of importance is that a diet high in animal fats may cause the development of breast carcinoma (Pervan *et al.*, 1995). It is thought that the risk is increased in obese postmenopausal women due to the increased quantities of oestrogen stimulating malignant transformation of the breast (Clifford *et al.*, 2002). Exposure to ionizing radiation increases the risk of breast carcinoma. This was evident when those irradiated by the atomic bombs dropped by Nagasaki and Hiroshima showed an increased risk of breast carcinoma with dose (Bomford and Kunkler, 2003).

2.6 PATHOLOGY OF THE BREAST

Most breast carcinomas arise in the upper outer quadrant of the breast. They are usually solitary although multifocal carcinomas may occur in the same or opposite breast. Carcinomas may be well circumscribed or diffusely infiltrating (Neal and Hoskin, 2003).

Microscopically, breast carcinomas may be classified as 'lobular' arising in the lobules at the termination of the duct system or 'ductal' which arise from the extralobular elements of the glandular tissue (Perez *et al.*, 2004). In situ carcinoma is diagnosed when all the malignant cells are confined within the lumen of the duct and do not breach the basement membrane. With invasive carcinomas, the malignant cells breach the basement membrane (Neal and Hoskin, 2003).

The following are common types of breast carcinoma

- Ductal carcinoma in situ – It is the most common type of noninvasive breast carcinoma. The cancer cells stay confined to the ducts and do not spread through the walls of the ducts into the fatty tissue of the breast (Clifford *et al.*, 2002, Strom and Basett, 2001 and National comprehensive cancer network, 2000).
- Lobular carcinoma – This type of carcinoma starts in the milk-producing glands. The cells can spread beyond the breast to other parts of the body. Almost 10-15% of invasive breast carcinomas are invasive lobular carcinomas (Clifford *et al.*, 2002, Strom and Basett, 2001 and National comprehensive cancer network, 2000).
- Inflammatory carcinoma – In this type of carcinomas, the tissues appear inflamed. This inflammation is due to spread of cancer cells within lymphatic channels of the skin. Inflammatory carcinomas account for 1% of invasive breast carcinomas (Clifford *et al.*, 2002, Strom and Basett, 2001 and National comprehensive cancer network, 2000).
- Paget's disease of the breast - This starts as an intraductal carcinoma which grows up into the lactiferous duct and involves the skin of the areola. Paget cells are large, hyperchromatic cells surrounded by a clear ring, caused by intracellular accumulation of mucopolysaccharides (Clifford *et al.*, 2002 and Mieny, 2003).

The status of the axillary lymph nodes is the most important prognostic factor for patients with early stage breast carcinoma (Cheng *et al.*, 2002).

Extracapsular extension of tumour cells is a common finding on histopathologic review of axillary contents in patients with node positive breast carcinoma (Hetelekidis *et al.*, 2000 and Wong *et al.*, 2000).

Also of importance as a prognostic indicator is the surgical margin status (Cowen *et al.*, 2000). Positive surgical margins in the literature are not always well defined, and are often regarded as the presence of either invasive carcinoma and/or intraductal carcinoma in situ in the surgical margin (Cowen *et al.*, 2000). In contrast to this, a few studies have demonstrated that surgical margin status does not influence local control (Vargas *et al.*, 2005 and Jobsen *et al.*, 2003). No clear difference has been made in the literature with regard to the value of positive surgical margins with either invasive carcinoma or in situ carcinoma or both in patients with breast carcinoma (Vargas *et al.*, 2005 and Jobsen *et al.*, 2003).

2.7 STAGING SYSTEMS

Two staging systems are widely used internationally for breast cancer: the American Joint Committee on Cancer (AJCC) and the Union Internationale Contre le Cancer (UICC) systems (Perez *et al.*, 2004). The AJCC system has made major changes in staging in order to improve on treatment outcomes. Some of the changes were made to include:

- Micrometastases are distinguished from isolated tumour cells on the basis of size and histologic evidence of malignant activity.
- Identifiers have been added to indicate the use of sentinel lymph node dissection.

- Lymph node status is designated according to the number of involved axillary lymph nodes.
- Metastases to the infraclavicular lymph nodes have been added as N3. Metastases to the supraclavicular lymph nodes have been reclassified as N3 rather than M1.
- Microscopic involvement of the internal mammary nodes detected by sentinel lymph node dissection is classified as N1. Macroscopic involvement of the internal mammary nodes detected by imaging studies or by clinical examination is classified as N2 if it occurs in the absence of metastases to the axillary lymph nodes. If it occurs in the presence of metastases to the axillary lymph nodes it is classified as N3.

(Perez *et al.*, 2004)

(Appendix G for detailed staging)

The concern by oncologists and pathologists is that the current staging system used for breast carcinoma does not include in the calculation of tumour size additional tumour found at the time of re-excision. This may result in under staging and under treatment of patients with breast cancer.

2.8 CT-BASED TREATMENT PLANNING

At Parklands Hospital, Radiotherapy department in KwaZulu-Natal, the standard technique does not involve the use of CT images for the treatment planning, instead manual contours that are obtained at the time of simulation, are representative of the patient's body shape and the contours create the impression of a CT scan. Great emphasis is placed on this crucial step of the

planning process because the accuracy of the final treatment plan is dependant on the precise recording and imaging of the simulation data (Appendix F). A plan is generated once the simulated treatment fields are accurately placed on the contours.

The vital importance of CT scans for treatment planning has become evident over the past few years due to the heightened awareness of tissue tolerance and accurate anatomical mapping. Many authors have shown the advantages derived from CT-based planning. (Madu *et al.*, 2001, Pierce *et al.*, 1997 and Gebarski *et al.*, 1982,).

Dunlap *et al.*, (1997) examined the dose distribution of 119 breast patients to determine whether a standard plan could be used instead of individualised computer plans. The study results demonstrated that the variation in dose distribution was related to the variation in the patient shape and size of chest wall and thus recommended the use of individualised computer plans (Dunlap *et al.*, 1997).

Prior to the introduction of CT scanners, estimation of the depth of the nodes was based on the clinical knowledge of the radiation oncologist. The advancement of imaging modalities has had a great impact on radiotherapy treatment planning (Kozak *et al.*, 2006 and Chui *et al.*, 2005). CT-based treatment planning is important and is being used more routinely for target delineation because it permits visualisation of the intrathoracic contents

encompassed by the proposed treatment fields (Mundt and Roeske, 2005 and Bulchholtz *et al.*, 2003).

A study performed by Bentel *et al.*, (2000) explored the dosimetric consequences of the variability of depth of the supraclavicular and axillary nodes. The results showed the depth to be related to the patient's size in the anterior-posterior diameter. Bentel *et al.*, (2000) clearly state the need for further research in this area. In many radiotherapy departments, extension of microscopic disease beyond the capsule of the axillary nodes has been an indication to irradiate the axilla. However, very little data exists to justify this practice (Grills *et al.*, 2003).

A study done at the Duke University Medical Center, Durham, North Carolina to assess the frequency and magnitude of the tangential field border shifts in breast cancer patients undergoing routine CT-based treatment planning, showed that the position of the breast tissue varied widely in patients with breast cancer (Bentel *et al.*, 1999). The authors felt that routine CT-based treatment planning is feasible, helpful and enabled them to better design the treatment fields, obtain contour information for dosimetry as well as anatomic information for dose prescription depth (Bentel *et al.*, 1999).

2.9 ADVANTAGES OF CT-BASED TREATMENT PLANNING

The advantages of CT scans in the treatment planning of breast carcinoma were documented by Boyages *et al.*, (2000) and Buchholz *et al.*, (2003).

CT-based treatment planning allows for reconstruction of the true dose in

three dimensions within the entire treated volume. This also allows for better control of doses to the heart and lung which are the critical structures (Kong *et al.*, 2002). It gives the opportunity to correct for lung inhomogeneity and changes in contour at multiple levels. The advantages derived from precise lung and heart volume extent within the treatment field is seen in the treatment planning histograms.

The other advantage of CT scan based planning is that it allows the radiotherapist to design breast fields virtually on the basis of CT data sets from individual patients. Because the breast volume is difficult to distinguish from the surrounding connective tissue on CT, it is imperative that the results of physical examination also be taken into account in the design of treatment fields (Buchholtz *et al.*, 2003).

2.10 DISADVANTAGES OF CT-BASED TREATMENT PLANNING

The disadvantages of CT-based treatment planning are the cost of the CT scan to the patient and the time factor involved should the patient be scanned at a venue away from where the planning was done.

2.11 ADVANTAGES OF THE CURRENT STANDARD TECHNIQUE

The advantages of the current digitised image planning or standard technique used in KwaZulu-Natal are the saving of the cost of the CT scan and the reduced time involved in the treatment planning.

2.12 DISADVANTAGES OF THE CURRENT STANDARD TECHNIQUE

The disadvantages using the current standard technique is derived from the researcher's personal experience in Durban, KwaZulu-Natal based private and public sector practises as well as from reviewing the literature. The following problems have become evident:

- The lack of anatomical detail due to the two dimensional appearance on the orthogonal films (Griffith and Short, 2000).
- The inability to reproduce a true three dimensional image set due to the lack of contours (Boyages *et al.*, 2000).
- The depth for treatment of supraclavicular and axillary nodes is from a clinical examination only.
- The patient becomes restless due to lengthy simulation time.
- The heart volume is not accurately defined (Buchholz *et al.*, 2003).
- The lung volume is not accurately defined (Buchholz *et al.*, 2003).
- The matchline dose inhomogeneity is only viewed in one plane.
- The inability to accurately define areas of over dosage or under dosage
- The inability to accurately calculate volumetric dose distribution (Buchholtz *et al.*, 2003).

Therefore, from reviewing the literature it became evident that further research was necessary to evaluate CT-based treatment planning for carcinoma of the breast versus digitised image planning, using the four-field breast technique in terms of the depth of supraclavicular and axillary nodes, the coverage of the breast tissue and dose inhomogeneity at the matchline. The benefits that have been reported for radiation therapy in breast carcinoma

in terms of local control and survival are based on non CT-planned techniques. It will be vital to document clinical benefits either in improved outcomes or reduced morbidity to justify the extra costs (time and money) in CT-based treatment planning.

2.13 SUPRACLAVICULAR AND AXILLARY NODAL COVERAGE

The controversy surrounding the clinical decision whether to include the regional nodes in the radiation therapy fields is documented by many authors (Katz *et al.*, 2006, Cheng *et al.*, 2002, Goodman *et al.*, 2001, Halverson *et al.*, 1993 and Recht *et al.*, 1991).

A study performed by Smitt and Goffinet (1999) established that for primary control of disease the tangential fields are adequate. But this does not provide adequate dose to the axillary tissue. Reznik *et al.*, (2005) and Reed *et al.*, (2005) also commented on the lack of axillary coverage and dose contribution from the tangential fields only.

A study done by Hoskin *et al.*, (1992) on 347 patients justified the use of radiation therapy to the regional nodes. This is also supported by Recht and Houlihan (1995). On the other hand a study done by Latosinsky and Bear (2001) questioned the use of radiation therapy in lowering the recurrences in node positive carcinoma of the breast. The aim was to use trained surgical oncologists to provide 'better quality' surgery in the hope of making adjuvant radiation therapy unnecessary.

A randomised study by the Danish Breast Cancer Group (Overgaard *et al.*, 1997) on 1 708 high risk pre-menopausal breast cancer patients demonstrated that postoperative radiotherapy improved distant disease free survival. The study also reported on improved overall survival of 9% and a reduced incidence of loco-regional disease. This is also supported in the literature by Violet and Harmer (2004) who stated that there may be improved survival in high risk patients receiving regional nodal radiation therapy.

2.14 TARGET VOLUME DELINEATION

The planning target volume (PTV) or target volume (TV) (which is synonymous) is outlined by the radiation oncologist. This is a geometrical concept and it is defined to select appropriate beam sizes and beam arrangements. It is of great consequence that the PTV is clearly defined by the radiation oncologist as the PTV is used for dose planning and dose specification. Ideally the dose should be delivered only to the PTV. However, this goal is very hard to achieve due to the limitations in radiation treatment technique.

Target volume delineation can sometimes vary between oncologists due to different margins being added to the clinical target volume (CTV). The CTV is a tissue volume that contains a demonstrable palpable disease and/or subclinical microscopic malignant disease (ICRU 50, 1993).

Recommendations are also made in the International Commission on Radiation Units and Measurements (ICRU) reports 50 and 62. Diagram 2.7 is an example of the CTV outlined by the radiation oncologist through the

planning volume. Chao (2005) suggests for those patients undergoing lumpectomy to use the ipsilateral breast as the target volume. The external boundaries of the palpable breast tissue and the tumour bed scar should be outlined with radio-opaque wire. The entire breast plus a 3 to 5 cm margin should be CT scanned.

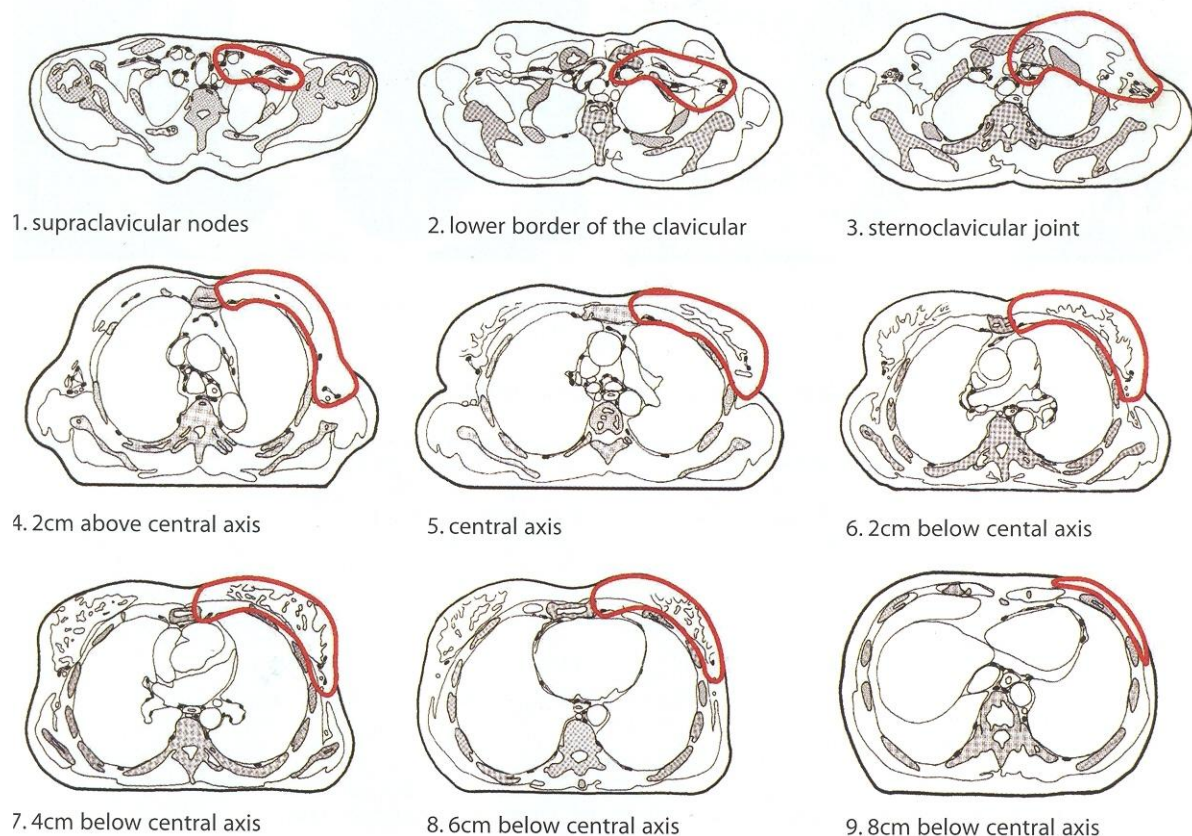


Diagram 2.7 Demonstrates CTV in nine representative CT axial sections through the planning volume.

Kiricuta, I.C. 2004. Clinical Target Volumes in Conformal and Intensity Modulated Radiation Therapy. A clinical guide to cancer treatment.

Target volume selection and delineation in breast cancer conformal radiotherapy. Edited by Gregoire, V., Scalliet, P. and Ang, K.K. Springer-Verlag Berlin Heielberg.

A very interesting article by Struikmans *et al.*, (2005) demonstrates the discrepancies in target volume delineation when outlined by five different observers. Eighteen patients with left sided breast carcinoma participated in this study. The largest differences between observers were noted for the cranial and the posterior extension of the tumour volume. The authors recommended that each institute set-up guidelines on variability when defining target volumes.

A study conducted by Jephcott *et al.*, (2004) critically assessed PTV dose coverage by different techniques. In the final analysis it was found that the technique with the single anterior field generated a plan with poor PTV dose coverage in 60% of cases. The four-field technique provided adequate PTV coverage and a limited dose to the medial posterior neck. On the other hand the technique produced areas in excess of 120% in 90% of cases.

2.14.1 Dose homogeneity

The aim when delivering radiation therapy is to have as homogeneous a dose as possible within the PTV. The different tissue densities and the dose absorption effect present a challenge in maintaining a homogeneous dose. In principle some heterogeneity has to be accepted during the treatment planning process. The ICRU report 62 (1999) recommends that the heterogeneity be kept within +7% (maximum dose) and -5% (minimum dose) of the prescribed dose (ICRU 62, 1999). The maximum dose is significant in relation to possible side effects and the minimum dose is significant in relation to tumour control.

In some planning cases it is virtually impossible to achieve this degree of homogeneity. It then becomes the responsibility of the radiation oncologist to decide whether this can be accepted or not. The clinical decision of accepting higher doses can be substantiated as an advantage when the higher dose is in an area where tumour had been present.

2.15 ORGANS AT RISK

Organs at risk are normal tissues whose radiation sensitivity may significantly influence treatment planning and the prescribed dose (ICRU 62, 1999).

During the administration of radiation therapy one is faced with the challenge of sparing normal tissue from excessive radiation dose. The two important organs that are referred to are the heart and the lungs as these organs often determine the placement of the radiation fields during treatment planning. The total doses that are administered are also governed by the tolerance limits of these organs.

A real concern arises when radiation doses are combined with other modalities like chemotherapy. These combinations can lead to severe late effects in different vital organs. The literature now places a great deal of emphasis on the volume of organ irradiated, in addition to the dose administered (ICRU 50, 1993).

For each organ at risk, it is imperative that the maximum dose, together with the volume of the organ receiving that dose be documented. Sometimes part of the organ or even the whole organ is irradiated to doses above the

accepted tolerance limits. In that case, the volume that receives at least the tolerance dose should be recorded (ICRU 50, 1993).

Many studies have attempted to specify radiation therapy tolerance doses for the various tissues and structures of the body. The minimal tolerance dose (TD 5/5) and maximal tolerance dose (TD 50/5) refer to severe complication rate of 5% and 50% respectively, within five years of radiation therapy completion (Nicolaou, 2003).

For the purpose of the current study the reference tolerance doses have been adapted from the table of normal tissue tolerance to therapeutic irradiation. The minimum tolerance dose to one third of the affected side lung is 45Gy (Chao *et al.*, 2002). This refers to the dose required to produce a severe complication rate of 5% within 5 years of completion of treatment.

2.15.1 Dose to lungs

Due to the proximity of the lungs, a small amount of lung is inevitably irradiated but the depth is carefully screened during simulation to ensure that a minimum volume is irradiated. The direct anterior supraclavicular field is positioned to cover the supraclavicular nodes and a posterior axillary field to cover the axillary lymph nodes. The complex geometry of this approach poses a great technical challenge to both the radiation oncologist and the planning radiographer (Chao *et al.*, 2002).

When doses of radiation therapy exceed tolerance levels, pulmonary reactions are expressed clinically as a pneumonitic process 1-3 months after the completion of therapy. This can become a critical problem if both lungs are involved (Nicolaou, 2003). In addition, as much as 9% of irradiated breast carcinoma patients suffer from radiation-induced lung sequelae (Kong *et al.*, 2002).

The risk of inducing pneumonitis during radiation therapy to the breast is a matter of concern. In light of this, Nicolini *et al.*, (2005) investigated the potential benefit of a conformal technique with non-coplanar fields to minimise the dose to the lungs. The conventional tangential technique can reduce the dose to the ipsilateral lung at the risk of increasing the dose to the contralateral breast. A significant reduction in lung dose was achieved by the use of two non-coplanar fields in this study.

2.15.2 Dose to the heart

Ischaemic heart disease is the most significant challenge in the treatment of carcinoma of the breast (Hojris *et al.*, 1999). Patients treated with radiation therapy can develop cardiomyopathy and present with severe signs and symptoms of pericardial disease, along with constriction and severe heart failure (Nicolaou, 2003 and Rutqvist *et al.*, 1992). The reference dose for the heart tolerance for the study done by Hojris *et al.*, (1999) was 50Gy to one third of the heart. Although Chao *et al.*, (2002) refers to 60Gy to one third of the heart as the tolerance dose, it was decided by the oncologists that 50Gy would be more precautionous for this study. This refers to the dose required to

produce a severe complication rate of 5% within five years of completion of treatment.

The data from the study done by Prosnitz and Marks (2005) suggest that radiation therapy induced cardiac injury may still occur with modern techniques. Furthermore, cardiac abnormalities may be seen in patients with extremely small fractions of the left ventricle of the heart included within the radiation field. Five percent of the left ventricle corresponds to approximately 2% to 3% of the heart. This percentage is difficult to see on a dose volume histogram and would be considered safe by most radiation oncologists (Prosnitz and Marks, 2005).

2.16 MATCHLINE DOSIMETRY

Matchline dosimetry refers to the dose obtained when two or more fields are matched. Unfortunately one is always faced with matchline problems which relate to potential sites of over dose or under dose where two adjacent radiation fields meet (Webb, 1993).

Matchline dosimetry has been a very controversial issue in many radiotherapy departments due to the complex geometry of the treatment technique. Hunt *et al.*, (1987) studied the matchline dose distributions by comparing four different geometric alignment techniques in order to determine the most acceptable matchline dose uniformity. The study concluded that careful beam alignment techniques for breast cancer are essential. When tangential fields are allowed to diverge into the supraclavicular field, overdoses as high as 150% or

underdoses of similar magnitude are possible. By geometrically aligning the supraclavicular field to the tangential fields, average matchline doses are reduced to approximately 110% of the prescription (Hunt *et al.*, 1987).

Lu *et al.*, (2003) also discuss the problems encountered in matching fields. Although proposed solutions are sought, often these solutions present other difficulties in terms of increasing doses to critical structures and set-up discrepancies. The proposed technique describes a precise match while removing constraints on the tangent's length and decreasing scatter dose (Lu *et al.*, 2003).

The dose at the matchline is also very dependant on the shape of the MLC or alloy blocks and the degree of manoeuvring the shape. The contributing effect of the MLC or block shape to the dose inhomogeneity at the matchline will become evident in either a positive or negative way.

2.17 SUMMARY AND MAIN AIMS

A multidisciplinary approach is absolutely essential for optimal breast conservation treatment (Early Breast Cancer Trialists' Collaborative Group, 1995). The fundamental principle of radiation therapy is to concentrate the radiation beam to the target tissues and at the same time minimising the dose to normal tissues (Bentel *et al.*, 1999). Although there is general agreement on the optimal management for breast carcinoma, no consensus has been reached on the need for regional nodal irradiation (Vicini *et al.*, 1997). CT

based treatment planning is becoming more routine in most departments and certainly the benefits are evident.

The aim of the study was to evaluate CT-based treatment planning *versus* digitised image planning for carcinoma of the breast, using the four-field breast technique, in terms of the depth of the supraclavicular and axillary nodes, the variability of the breast tissue and the dose inhomogeneity at the matchline.

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The literature reviewed aimed to further strengthen the impact of this study by addressing the objectives set-out:

- To evaluate CT-based treatment planning *versus* digitised image planning for carcinoma of the breast in terms of the depth of the supraclavicular and axillary nodes.
- To evaluate CT-based treatment planning *versus* digitised image planning for carcinoma of the breast in terms of the variability of the breast tissue.
- To evaluate CT-based treatment planning *versus* digitised image planning for carcinoma of the breast in terms of the dose inhomogeneity at the matchline.

CHAPTER THREE

RESEARCH METHODS AND DESIGN

3.1 INTRODUCTION

This chapter describes the research study population and the selection criteria that were used. In addition, the methodology is highlighted as well as the underlying reasons for the research parameters. In conclusion, consideration is given to the data analysis methods used.

3.2 LOCATION OF THE STUDY

This study was conducted at three centers, namely the Parklands Radiotherapy Department, Durban, the Durban Oncology Centre, Durban, and St Anne's Radiotherapy Department, Pietermaritzburg. The treatment planning computers at the Parklands Radiotherapy Department and the Durban Oncology Centre were used only because the beam configuration and beam data are identical.

3.3 PERMISSION TO CONDUCT THE STUDY

Letters were sent to all the oncologists who refer patients to the selected venues to obtain permission to use their patients in this study (Appendices A(i)-A(iii)). Letters were also sent to the hospital managers informing them of the aims of this study and to obtain permission to use the radiotherapy facilities. Applications were made to the ethics committees of the three hospitals (Appendices A(iv)-A(vi)) and the ethics committee at the Durban University of Technology (Appendix L).

3.4 INVITATION TO PARTICIPATE

All participants were provided with an information letter (Appendix C) and were given every opportunity to ask questions prior to signing an informed consent (Appendix B) to participate.

3.5 SPONSORS

The cost of the computed tomography (CT) scans that were required for this research, was covered in part by a research grant from Drs Lake, Smit and Partners (Appendix A (viii-xi)).

The cost of the stationery required for this research was covered by Parklands Hospital (Appendix A (vii)).

3.6 DATA COLLECTION

Primary data were collected over a period of one year. The recruitment of participants was very dependant on the referral patterns from the radiation oncologist.

The primary data collected were:

- Personal and demographic data of the research participants
- Supraclavicular and axillary nodal measurements and doses
- Breast measurements and doses
- Matchline measurements and doses
- Dose inhomogeneity
- Heart doses

- Lung doses

3.7 PARTICIPANT INFORMATION SHEET, INFORMED CONSENT, AND DATA COLLECTION SHEET

A participant information sheet (Appendix C) and an informed consent form (Appendix B) were designed by the researcher. All participants read the patient information sheet and signed the informed consent form.

Two data collection sheets were designed by the researcher. The one sheet was designed to record all participants' demographics and clinical parameters (Appendix D) and the other to record all participants' treatment plan parameters (Appendix E).

3.8 ETHICAL ISSUES

The participants were presented with an information letter detailing the requirements to conduct the study (Appendix C). Verbal and written informed consent was obtained from all participants (Appendix B). Participants were reassured that confidentiality would be maintained at all times and that the data would only be available to the researcher. Participants were also informed that their participation in the study was voluntary and should they wish to withdraw at any point, their treatment would not be compromised.

Participants had to undergo a CT scan. No contrast media was administered. From the National Council of Radiation Protection and Measurement (Travis, 1989), the average effective dose equivalent from a single CT examination is

1.10 μ Sievert. The annual collective effective dose equivalent allowed to the public is 3.70 Sievert (Travis, 1989). The exposure risks for CT scans were therefore minimal when compared to 50 Sievert (50 000 000 μ Sievert) that was received from the course of treatment that the participants underwent. In support of this comment is the literature from a study done by Hart and Wall (2002).

The researcher ensured confidentiality by not disclosing the identity of the participants. All files were coded with the participants' details. No names were stored with the data. Computer files and discs will be kept securely for five years until such time that it is ethically and legally permissible to destroy them. The research proposal was approved by the ethics committee of the Faculty of Health Sciences at the Durban Institute of Technology (now called Durban University of Technology).

3.9 SELECTION OF RESEARCH POPULATION

Female patients presenting with primary breast carcinoma with a primary tumour (T) T1,T2 or T3, and regional lymph nodes (N) (Hermanek *et al.*, 1999) N1 or N2 were selected. The selection of participants was done using the convenience sampling method. In this method the participants are selected at the convenience of the researcher (Daly et al.,1991). The reasons for selecting this method were twofold. The four-field breast technique is not routinely selected for all patients with carcinoma of the breast therefore it was not possible to use a random sampling method. Secondly, in 2003 the total number of female patients treated for breast carcinoma at Parklands

Radiotherapy Department, Durban Oncology Centre and St Anne's Radiotherapy Department respectively was 223. From this number only 38 patients were referred for four-field breast technique. All the other patients were treated using two or three-field breast technique. Those patients referred by the radiation oncologist for radiation therapy, using the four-field breast technique, were therefore selected to participate in this study.

Therefore the sample size included 30 participants. Although this is a small sample size, whether the data shows a statistical significance or not, any numerical difference would be clinically important (Personal Communication, Dr D.J. Hacking). Therefore $n=30$ is the maximum and optimal number of participants available.

3.9.1 Inclusion criteria

Only those patients with primary breast carcinoma who had undergone a lumpectomy or a mastectomy were included in this study. Participants selected included those patients who were diagnosed with breast cancer with histological confirmation, and staged using the TNM classification (Clifford *et al.*, 2002) and who met the following criteria:

- Tumours greater than 4cm in maximum diameter because it is suggestive of more advanced disease (Fisher *et al.*, 1985).
- T3/T4 tumours in respect of skin, nipple and pectoral muscle involvement (Perez *et al.*, 2004).
- Four or more lymph nodes involved, is suggestive of more advanced disease (Grills *et al.*, 2003, Fortin *et al.*, 2003).
- Positive or close surgical margins, suggesting a higher risk of local failure of more advanced disease (Cowen *et al.*, 2000).
- Extracapsular extension measuring over 2mm (Chao, 2005).

Only those patients referred for four-field breast technique were included in this study.

3.9.2 Exclusion criteria

Male patients were not included in this study due to the fact that the shape of the chest wall differs slightly from that of the female breast. The researcher was concerned that this may contribute to skewing of the results for dose inhomogeneity.

Participants who presented with bilateral breast cancers were not selected because the positioning needs to be changed for bilateral breast treatment as both arms are extended and supported above the head. The arms are more extended than for treatment of one side only otherwise the patient will not fit through the CT gantry.

3.10 RESEARCH QUESTIONS ADDRESSED

The following research questions were addressed:

- What is the dose to the supraclavicular nodes from both plans?
- What is the dose to the axillary nodes from both plans?
- How do the plans differ in terms of dose coverage to the supraclavicular and axillary nodes?
- What is the relationship between the depth of the supraclavicular nodes and the patient separation?
- What is the relationship between the depth of the axillary nodes and the patient separation?
- Does the target volume receive adequate dose coverage from the plans?
- How is the heart volume affected by target coverage on both plans?
- How is the lung volume affected by target coverage on both plans?
- What is the dose variability along the matchline?
- Are the plans over dosing?
- Are the plans under dosing?

3.11 METHODOLOGY

- The participants' clinical characteristics were recorded on a data sheet (Appendix D). This information was important because the management of cancer is dependant on many of these characteristics.

It was recorded from the participant's information file. Permission was obtained from the oncologists (Appendices A(i)-A(iii)) to gain access to the participant's information file.

- The radiation fields for the standard technique were defined at simulation.

3.11.1 Simulation Technique

Simulation techniques differ between departments hence it is impossible to describe all the techniques used in breast treatment. The technique described by Bentel *et al.*, (1999) involves the patient undergoing a CT scan prior to the simulation. The markers are placed on the skin as tentative field borders.

These borders are often adjusted in order to achieve good coverage of the breast tissue. This technique is possible if there is a dedicated CT scanner in the radiotherapy department as the radiation oncologist needs to be present to demarcate the field borders. Not many radiotherapy departments have CT scanners which means that the radiation oncologist has to be available at the time when the patient is being scanned elsewhere. This creates logistical problems if the CT scan department is not within the vicinity of the radiotherapy department.

3.11.2. Simulation technique used for this research

The participant was positioned on the breastboard on the simulator couch. The breastboard angle chosen was such that the anterior chest wall was almost horizontal to the table, thus alleviating a collimator angle. The arm

position on the breastboard of the affected side was selected so that when the participant's arm was extended above the head it was almost at right angles.

The position of the arms for axillary radiation therapy was important as there was displacement of the axillary nodes away from the chest wall and as well as in relation to the humeral head. This was also emphasized in the study by Pergolizzi *et al.*, (2004) which showed a displacement of almost 6.4cm from the chest wall when the arms were extended above the head. This was for the lower nodes whereas the upper group showed a smaller variation. A statistically significant difference in node displacement between the two positions of the arms was demonstrated using the analysis of variance.

- Participant was in a comfortable position (diagram 3.1). The unaffected hand was placed on the abdomen. The participant was also given a knee-rest which helped ease any stress on the spine.

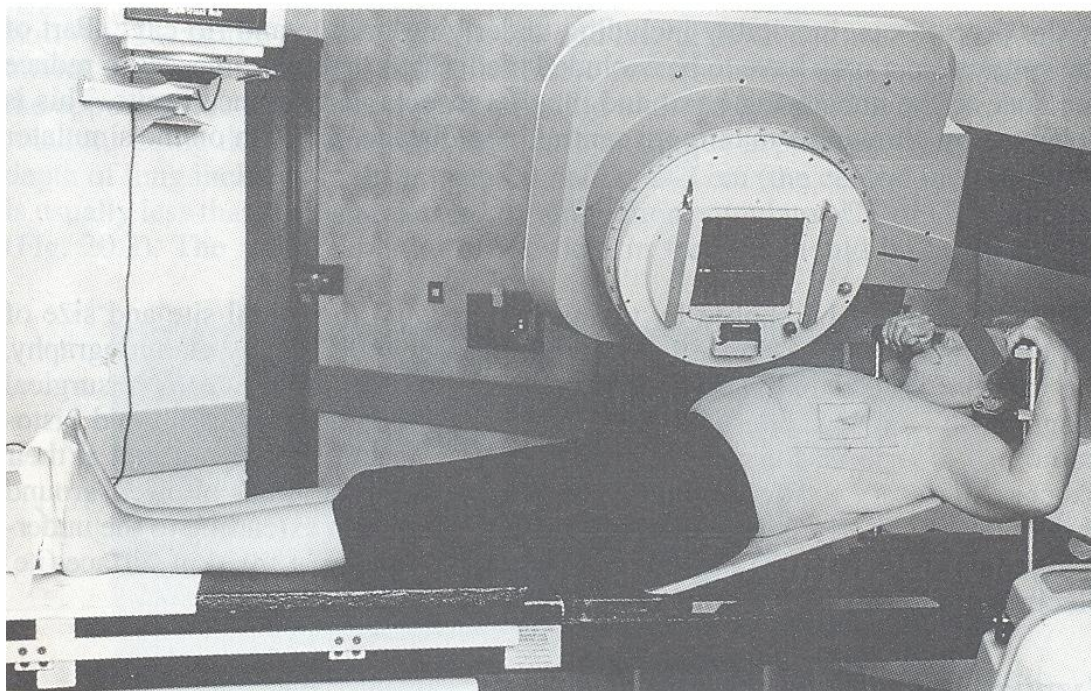


Diagram 3.1 : Shows the position on the breastboard.

(Dobbs, J., Barrett, A. and Ash, D. 1999. Practical Radiotherapy Planning. Third edition. Oxford University Press Inc., New York).

- A clinical midline was set-up and drawn on the participant's skin which extended from the mid sternal notch to the xiphisternum. The level for the matchline was determined by verifying using a radiographic imager. The position of the field and the amount of lung in the field was confirmed. The level for the matchline was in fact the superior border of the tangential breast fields. The radiation oncologist then demarcated the inferior, medial and lateral borders for the tangential fields.
 - Inferior border was 1 –2cm caudal to the inframammary fold

- Medial border was at midline of the participant , and was determined by palpation of the suprasternal notch and the xiphoid process
 - Lateral border was corresponding to midaxillary line
 - Matchline was first or second intercostal space
- (Uschold, 2004)

- The next step was to set a length on the tangential fields so that the field edges matched the superior and inferior marks. This gave the centre level of the glancing fields.
- Markers were placed on the medial and lateral borders where they intersected with the level. The field centre was positioned on the medial mark at centre level and the table was raised so that the range finder reading was 100cm to the skin surface.
- The gantry was angled so that the markers were superimposed on one another. The field was screened to obtain the precise gantry angle and to verify the amount of lung in the field. Between two and two and a half centimetres are usually accepted by the radiation oncologists.
- The gantry angle was recorded and the position of the medial field was checked to ascertain adequate coverage of the breast.
- The gantry was positioned back to 0 degrees. The table was raised until the lateral laser passed through the lateral marker on the skin. The distance scale was read at the medial marker (a) was recorded on a separate simulator sheet (Appendix F). All measurements were recorded on the simulator sheet. Using the callipers, the distance

between the medial border and lateral border markers (b) was measured. The table height was adjusted so that the raise read $\frac{1}{2}$ (a). The table was offset from the medial border by the distance that was calculated using the formula $\sqrt{(b^2 - a^2)}$, based on a simple Pythagorean association. The raise was read off at the offset. The gantry was angled to the simulated medial angle. The field length was set to cover the superior and inferior marks. The width was set to cover the breast anteriorly. The field was once again verified using the radiographic imager. The field borders were drawn on the participant's skin and a radiograph was taken, using the simulator, for record purposes.

- Using the field light the lasers, offset and the opposite angle, which represented the lateral oblique field, were drawn. A radiograph of the lateral oblique angle was taken. The gantry was then moved to the zero position so that the anterior radiograph was exposed.
- The simulator couch was then moved to the superior border of the glancing field which became the matchline. Wire markers were placed on the superior border and following the shape of the medial border. The radiation oncologist demarcated the borders for the supraclavicular field.
 - Superior border was on the edge of skin
 - Inferior border was the first or second intercostal space
 - Medial border was the midpoint of the suprasternal notch

- Lateral border was the vertical line at the level of the anterior axillary fold

The centre of the supraclavicular field was along the matchline. The inferior half of the field was blocked off using alloy shielding or multileaf collimators to create a half beam block. Only the superior half of the field was used for treatment. The gantry was angled 15 degrees medially to avoid the spinal cord. The field was set to read 100cm on the skin and was verified by using the radiographic imager before a radiograph was taken.

The axillary field was then simulated. The radiation oncologist positioned the field for the posterior axillary boost. The gantry was moved anteriorly and set to read 100cm on the skin. The field was verified by screening before a radiograph was taken. The fields were then marked anteriorly on the skin. The landmarks were recorded and the collimator angles were noted. The opposite angles were recorded for the posterior field. It was important for the treatment set-up that the lasers of the glancing fields were extended to this level because it helped to reproduce the participant's position for treatment.

3.11.3 Planning Procedure

Participants had a CT scan of the breast in the treatment position.

Radiopaque markers were positioned on the superior and inferior borders of the breast field, lasers, offsets and centres as defined at simulation. The scans (with a 5mm slice thickness) extended from the supraclavicular region

to the most inferior part of the lungs. A scout view taken at the time of the CT scan was also obtained which depicted the area that had been scanned.

- The CT scan slices were then loaded onto the treatment planning system by the researcher.
- All body contours and organs of risk were outlined by the researcher.
- The planning target volumes were outlined and checked by the radiation oncologist.
- A treatment plan was generated by the planning radiographer using the standard technique. This was referred to as plan 1 in this research and was generated using the digitised image planning technique where all simulated parameters were entered onto the CT data, without any modifications to the parameters.
- The second plan was generated by the researcher to achieve optimal coverage of the breast tissue and nodal regions. This was referred to as plan 2 in this research and was generated using the CT-based planning technique where the approach was to achieve as conformal a plan as possible. The researcher had the option to use any beam modification depending on the data from the CT scan images.

In order to avoid any bias, the CT-based treatment plans were all generated by the researcher to achieve optimal coverage of the breast tissue and nodal regions. .
- The researcher then compared plan 1 with plan 2 in order to compute the endpoint variables. A data sheet (Appendix E) was used to record the variables.

- From a consistency point, it was important that all treatment plans (plan 1) were produced by the same planning radiographer. Therefore the plans generated at the Durban Oncology Centre were performed by the same planning radiographer for each participant from this particular centre. The treatment plans (plan 1) that were generated at the Parklands Radiotherapy Department were performed by the same planning radiographer for each participant from this particular centre. The CT-based plans (plan 2) for all participants were generated by the researcher.

The glancing fields were planned on the central slice until the distribution was acceptable. Different wedges were used and the most suitable was selected for the final plan. Each field was given a weight which was indicative of the dose from each field.

The supraclavicular field was entered on the matchline slice. The block or MLC shape was input from the simulator film. The axillary field parameters were entered on the centre of the posterior axillary level. The field weighting of the supraclavicular to the axillary was approximately 3:1. This varied with participant shape and size. The block or MLC shape was input from the simulator film. The dose distribution was calculated for all slices. The final planning involved adjusting the block or MLC shape to achieve the optimal dose distribution at the different levels. The final plan was checked and passed by the oncologist.

3.11.4 Measurements for Supraclavicular Nodes

All measurements were recorded for plan 1 and plan 2

- The position of the supraclavicular nodes was discussed with the radiologist as this was an important and difficult point of measurement.
- The depth was measured at the defined reference point. This was referred to as reference point 1 and was measured 1cm anterior to the apex of the lung and at the level of the 2nd rib, sternoclavicular joints.
- The dose was then measured at reference point 1.
- The field separation was measured at this level.
- The measurements were made possible by the use of planning tools on the treatment planning system.

3.11.5 Measurements for axillary nodes

All measurements were recorded for plan 1 and plan 2.

- The position of the axillary nodes was discussed with the radiologist as this was an important and difficult point of measurement.
- The depth was measured at the defined reference point. This was referred to as reference point 2 and was measured anterior to the humeral head, along the vascular bundles which comprises the vein, artery and the lymphatics (Mathers *et al.*, 1996). The centre of which was the reference point. The radiologist also suggested that using the lateral aspect of the latissimus dorsi muscle was a good guideline.
- The dose was then measured at reference point 2.
- The field separation was measured at this level.

- The measurements were made possible by the use of planning tools on the treatment planning system.

3.11.6 Measurements for Breast Tissue

- A histogram was generated for each plan (Appendix H and I).
- All doses and percentage volumes were translated off the histogram.
- The dose received by 100% of the target volume (D100) was recorded.
- The dose received by 95% of the target volume (D95) was recorded.
- The dose received by 90% of the target volume (D90) was recorded.
- The dose received by 85% of the target volume (D85) was recorded.
- The dose received by 80% of the target volume (D80) was recorded.
- The dose received by 70% of the target volume (D70) was recorded.
- The dose received by 60% of the target volume (D60) was recorded.
- The dose received by 50% of the target volume (D50) was recorded.
- The percentage volume covered by the 50Gy dose was recorded.
- The field separation was measured at this level.
- The maximum, minimum and mean doses for the breast were translated off the histogram.
- The maximum, minimum and mean doses for the heart were translated off the histogram (Appendix J).
- The dose to 33% of the heart volume (D33) was recorded.
- The percentage volume of the heart receiving 50Gy (V50) was recorded.
- The maximum, minimum and mean doses of the lung for the affected side breast were translated off the histogram (Appendix K).

- The dose to 33% of the lung for the affected side breast was recorded.
- The percentage volume of the lung for the affected side breast receiving 45Gy ($V_{45\text{Gy}}$) was recorded.

3.11.7 Measurements of dose inhomogeneity

All measurements for dose inhomogeneity were recorded for plan 1.

- The dose was measured at reference point 3 which was defined at 3cm lateral to the offset and on the matchline.
- The dose was measured at reference point 4 which was defined at the offset and on the matchline.
- The dose was measured at reference point 5 which was defined at 3cm medial to the offset and on the matchline.
- The dose was measured at reference point 6 which was defined at 1cm below the matchline and in line with the offset.
- The dose was measured at reference point 7 which was defined at 1cm above the matchline and in line with the offset.
- The maximum, minimum and mean doses for the matchline were translated off the plan.
- The maximum, minimum and mean doses for the axilla were translated off the plan.
- The measurements were made possible by the use of planning tools on the treatment planning system.
- Doses were also translated off the histogram.

3.12 METHOD OF DATA ANALYSIS

Data were entered and analysed using the Statistical Package for the Social Sciences (SPSS) version 11.5 (SPSS Inc., Chicago, Ill, USA). Demographic and clinical parameters were described using frequency tables and bar charts and pie charts for the categorical variables, and quantitative variables were summarized using mean, standard deviation and range.

The raw data were checked for normality using the Kolmogorov-Smirnov test. Since all variables passed the normality assumption, parametric statistical tests were used. A two-sided significance level of 0.05 was used throughout. One-sample t-tests were used to compare the mean of each plan at each site to a reference value. Paired t-tests were used to compare means of plan 1 to plan 2. Pearson's correlation and linear regression was used to determine and quantify relationships between quantitative variables for each plan separately. Relationships were shown graphically by means of scatter plots.

CHAPTER FOUR

RESULTS

4.1 Introduction

This chapter reports the results of the data analysis. The descriptive statistics for the independent variables namely age, menopausal status, oestrogen receptor status, progesterone receptor status, tumour size and histology are presented first. The dependent variables namely the depth of the supraclavicular nodes, the depth of the axillary nodes, breast tissue coverage and dose inhomogeneity are then presented. An analysis is also presented on the research questions relevant to each of the dependant variables.

The aims of the study were:

- To evaluate CT-based treatment planning versus digitised image planning for carcinoma of the breast in terms of the depth of the supraclavicular and axillary nodes.
- To evaluate CT-based treatment planning versus digitised image planning for carcinoma of the breast in terms of the variability of the breast tissue.
- To evaluate CT-based treatment planning versus digitised image planning for carcinoma of the breast in terms of the dose inhomogeneity at the matchline.

The following research questions were addressed:

- What is the dose to the supraclavicular nodes from both plans?

- What is the dose to the axillary nodes from both plans?
- How do the plans differ in terms of dose coverage to the supraclavicular nodes?
- How do the plans differ in terms of dose coverage to the axillary nodes?
- What is the relationship between the depth of the supraclavicular nodes and the patient separation?
- What is the relationship between the depth of the axillary nodes and the patient separation?
- Does the target volume receive adequate dose coverage from the plans?
- How is dose to the heart volume affected by target coverage on both plans?
- How is dose to the lung volume affected by target coverage on both plans?
- What is the dose variability along the matchline?
- Are the plans over dosing?
- Are the plans under dosing?

4.2 Results - Demographic and clinical parameters

Thirty participants were recruited into this study. The mean age was 57.9 years with a standard deviation of 12.5 years. The minimum age was 36 years and the maximum age was 82 years.

The vast majority of the participants were post menopausal (76.6%, n=23), while 20% (n=6) were pre menopausal. One participant who was 40 years old (3.3%) had an unknown menopausal status. The menopause status of the participants is shown in Figure 4.1.

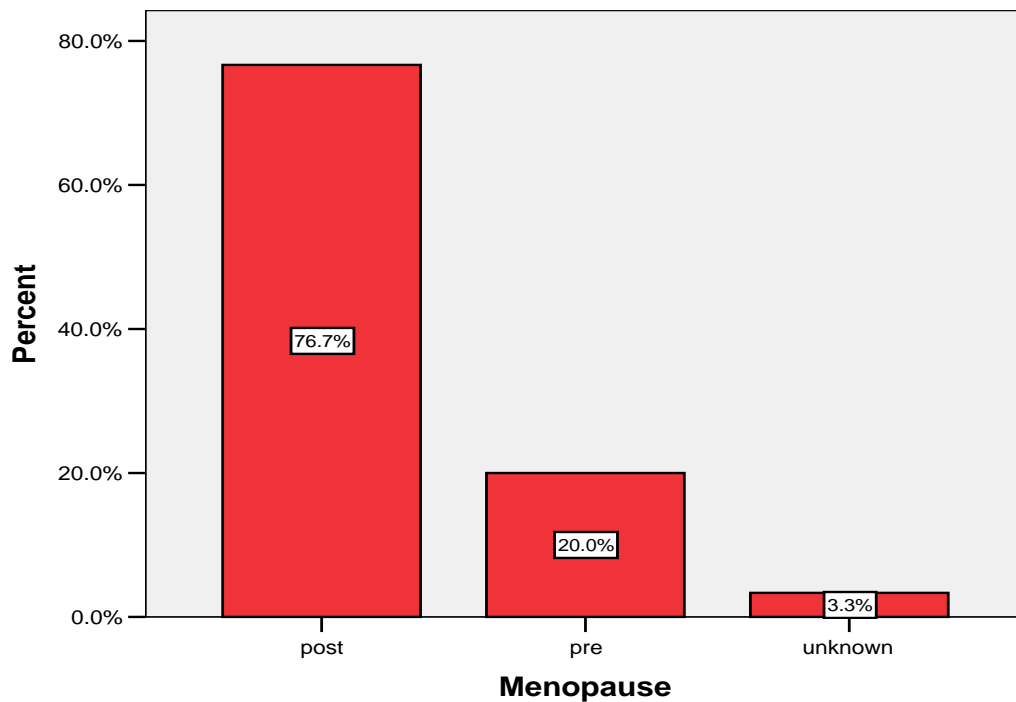


Figure 4.1: Percentage of participants by menopause stage (n=30)

Oestrogen receptor (OR) status for this population was 63.3% positive (n=19), while 50% (n=15) were Progesterone receptor (PR) status positive (Figures 4.2 and 4.3).

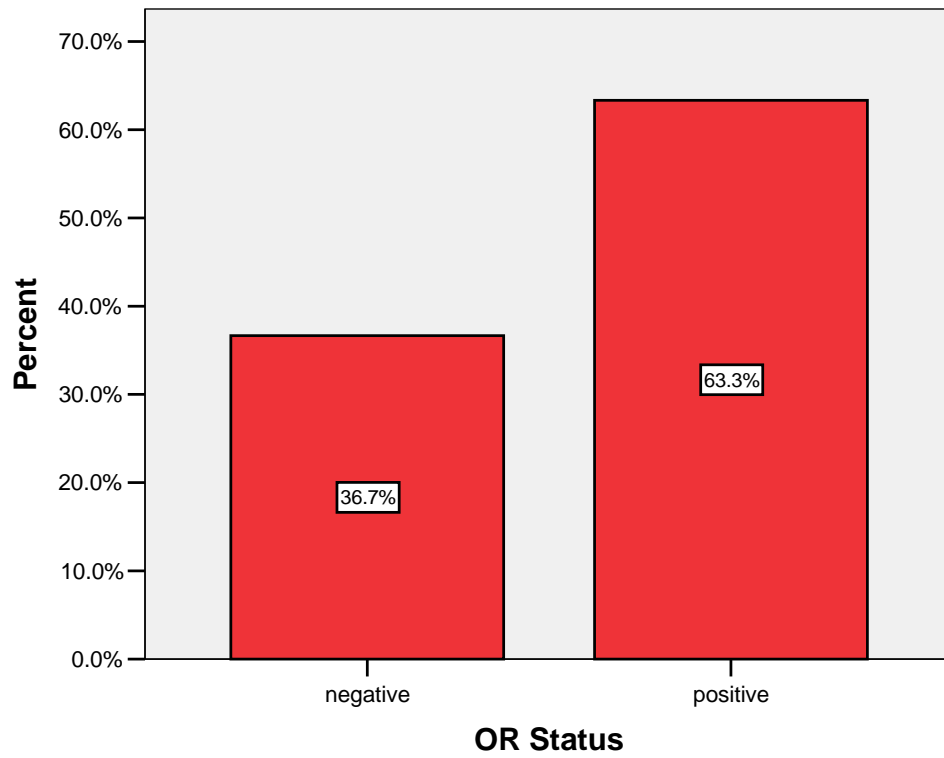


Figure 4.2: OR status of participants (n=30)

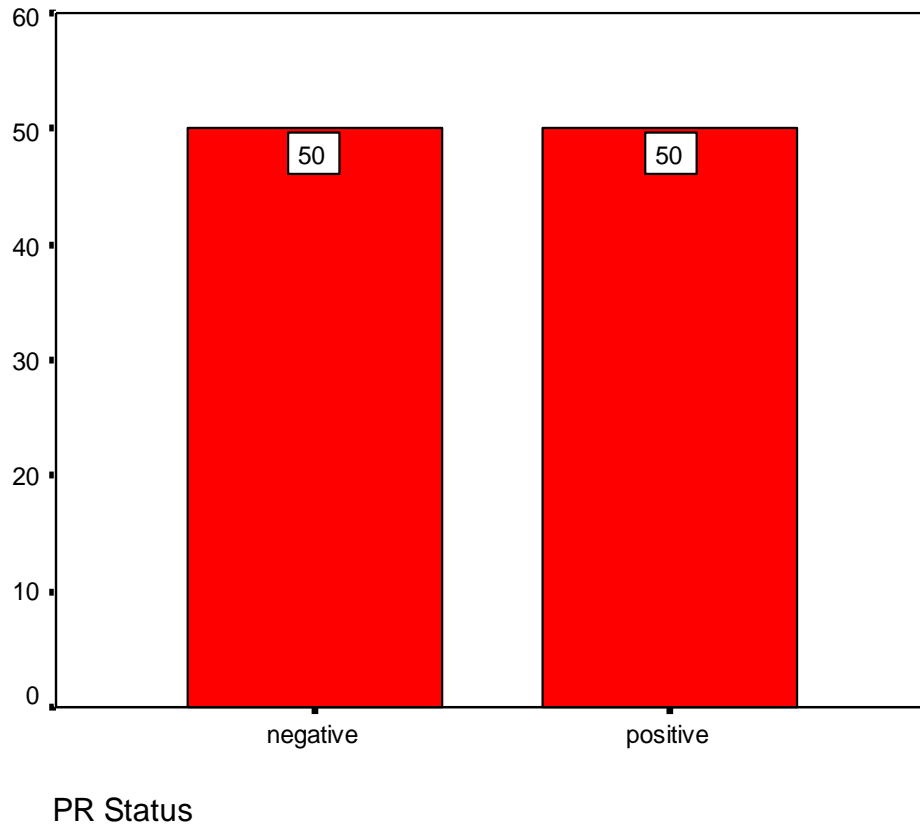


Figure 4.3: PR status of participants (n=30)

In just over half the participants (53.3%, n=16), the tumour was located in the left breast. Mastectomy was the predominant surgery (73.3%, n=22), while only 8 (26.7%) had lumpectomy.

Mean tumour length was 3.65 cm with a standard deviation of 1.84, (range 1 to 8 cm), while mean tumour breadth was 3.50 cm with a standard deviation of 1.96, (range 1 to 8 cm).

The average number of total nodes removed during surgery was 8.6 (range 0 to 25).) One participant had 25 nodes removed of which 21 nodes were

positive for disease. The average number of positive nodes was 4 (range 0 to 21).

The histological findings were predominantly ductal carcinoma (n=26, 86.7%), with only 4 participants (13.3%) presented with lobular carcinoma.

Forty percent of participants showed lymphatic invasion of the tumour (n=12), Table 4.1, and 26.7% (n=8) showed vascular invasion of the tumour (Table 4.2).

Table 4.1: Lymph invasion

	Frequency	Percent
No	17	56.7
unknown	1	3.3
Yes	12	40.0
Total	30	100.0

Table 4.2: Vascular invasion

	Frequency	Percent
No	21	70.0
unknown	1	3.3
Yes	8	26.7
Total	30	100.0

The surgical margins were clear (no tumour cells in surgical margins) in 76.6% (n=23) and close (tumour cells present within 1-2mm of surgical margins) in 23.3% (n=7). This is depicted in Figure 4.4.

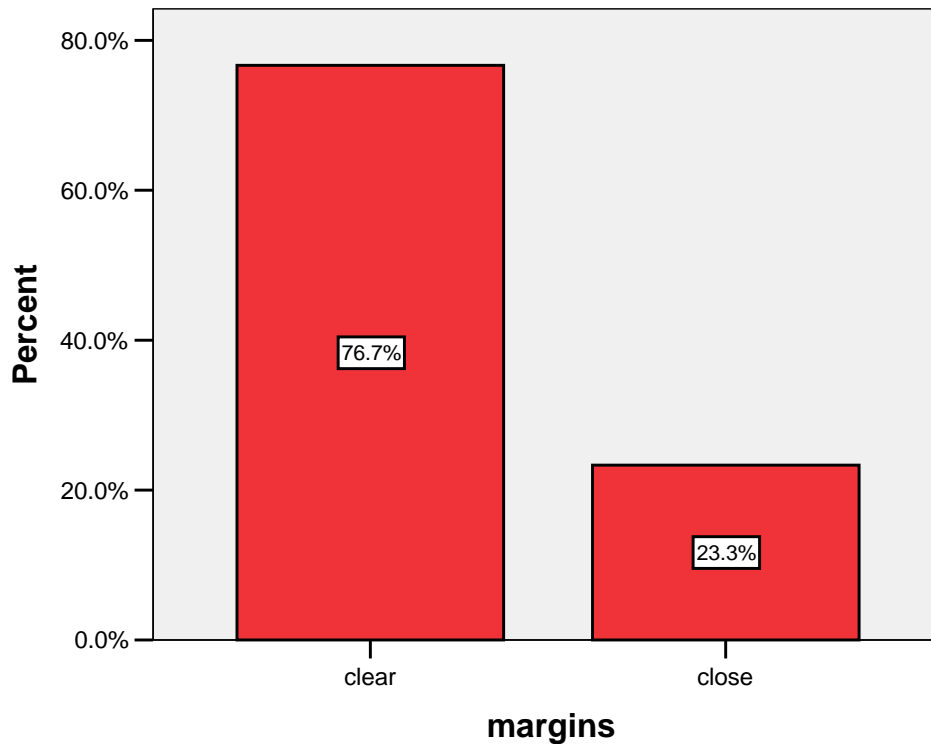


Figure 4.4: Surgical margins in study participants (n=30)

Table 4.3 displays the analysis of the tumour (T) staging. The most common T stage was 2 (n=16, 53.3%). There were 20% (n=6) with T1 tumours, 16.7% (n=5) with T3 tumours and 10% (n=3) with T4 tumours. The most common nodal (N) status was N1 which accounted for 50% of the participants (n=15). There were 16.7% (n=5) with N0 nodal status and 30% (n=9) with N2 nodal status. This is depicted in Table 4.4. One participant had an unknown nodal status. There were no participants with metastasis as this was also an exclusion criterion.

Table 4.3: Stage (T) showing tumour status

	Frequency	Percent
1	6	20.0
2	16	53.3
3	5	16.7
4	3	10.0
Total	30	100.0

Table 4.4: Stage (N) showing nodal status

	Frequency	Percent
0	5	16.7
1	15	50.0
2	9	30.0
unknown	1	3.3
Total	30	100.0

Figure 4.5 shows the tumour grading. Grade II (56.67%, n=17) was the most frequently presenting grade, followed by grade III (n=11, 36.7%). There were 3.33% of the participants whose grade was unknown to this study.

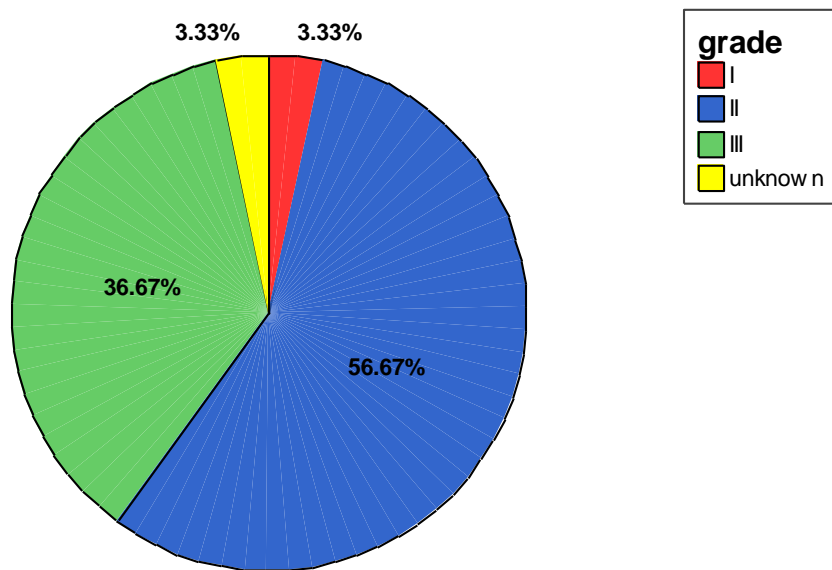


Figure 4.5: Pie chart showing percentage of participants by grade of tumour

Twenty six participants had chemotherapy (86.7%). Of those having chemotherapy, the median number of cycles was 8 (range 3 to 8). Four participants were unsuitable for chemotherapy due to their age and performance status. This was a consideration by the oncologist. Sixty percent (n=18) had hormone therapy.

4.3 Objective 1

To evaluate CT based treatment planning versus digitised image planning for carcinoma of the breast in terms of the depth of the supraclavicular and axillary nodes.

4.3.1 Research question: What is the dose to supraclavicular nodes from both plans?

Plan 1 which was generated using the digitised image planning technique had a mean dose of 45.52Gy at the reference point of the supraclavicular nodes, which was highly statistically significantly lower than the reference value of 50Gy ($p < 0.001$). The 95% CI for plan 1 was from 46.81Gy to 44.23Gy.

Plan 2 which was generated using the CT-based planning technique where the approach was to achieve as conformal a plan as possible, had a slightly higher mean dose than plan 1, of 46.42Gy at the reference point of the supraclavicular nodes. However, there was still a significant difference between this dose and the 50Gy reference ($p = 0.001$) since the 95% CI did not overlap 50Gy (48.33 to 44.51). This is shown in Table 4.5.

Thus it was concluded that both plans gave significantly lower dose than the required 50Gy, although plan 2 was closer to the 50Gy than plan 1. This small difference may be reflected as a statistically significant difference yet not clinically significant from an oncology point of view.

Table 4.5: One sample t-test comparison of dose at supraclavicular nodes for plan 1 and plan 2 comparing to reference value of 50Gy

	N	Mean	Std. Deviation	Std. Error Mean	95% CI for mean		t statistic	p value
					Upper limit	Lower limit		
dose at reference point 1 supraclavicular nodes in Gray P1	30	45.52	3.62	0.66	46.81	44.23	-6.786	<0.001
dose at reference point 1 supraclavicular nodes in Gray P2	30	46.42	5.33	0.97	48.33	44.51	-3.69	0.001

4.3.2 Research question: What is the dose to the axillary nodes from both plans?

Table 4.6 below shows that plan 1 had a highly significantly lower mean dose at the reference point of the axillary nodes than the reference value of 50Gy ($p < 0.001$). The mean dose for plan 1 at the reference point of the axillary nodes was 35.03Gy (95% CI 41.93Gy to 28.12Gy). Since the 95% CI did not overlap with the reference value of 50Gy, it can be concluded at the 95% level of confidence that the sample mean was significantly different to 50Gy.

Plan 2 had a significantly higher mean dose than the reference value of 50Gy ($p < 0.001$). The mean dose for plan 2 at the reference point was 52.51Gy (95% CI 53.34Gy to 51.67Gy) showing no overlap of the confidence interval with the reference value of 50Gy.

Although neither plan was getting 50Gy dose at the reference point of the axillary nodes, Plan 1 was clinically significant in terms of inadequate dose for tumour control. Plan 2 would be acceptable from an oncology perspective.

Table 4.6: One sample t-test comparison of dose at axillary nodes for plan 1 and plan 2 comparing to reference value of 50 Gy

	N	Mean	Std. Deviation	Std. Error Mean	95% CI for mean		t statistic	p value
					Upper limit	Lower limit		
Dose at reference point 2 axillary nodes in Gray P1	30	35.03	19.29	3.52	41.93	28.12	-4.251	<0.001
dose at reference point 2 axillary nodes in Gray P2	30	52.51	2.34	0.43	53.34	51.67	5.879	<0.001

4.3.3 Research question: How do the plans differ in terms of dose coverage to the supraclavicular and axillary nodes?

Plan 1 and 2 were not significantly different from each other for mean dose at the reference point of the supraclavicular nodes ($p=0.340$). The mean difference between the two plans was 0.897Gy.

However, for axillary node dose the two plans differed highly significantly ($p<0.001$). The mean difference between the doses of the two plans was 17.48Gy.

Thus there was no statistical difference between the doses of the two plans for the supraclavicular nodes, but for the axillary nodes there was a highly significant difference, with plan 2 giving a higher dose than plan 1.

Table 4.7: Paired t-test for comparison of mean dose in plan 1 and plan 2 for supraclavicular and axillary nodes

	Paired Differences					t	df	p value (2-tailed)
	Mean	Std. Deviati on	Std. Error Mean	95% CI				
				Lower	Upper			
dose at supraclavicular nodes P1 - dose at supraclavicular nodes P2	-0.897	5.059	0.924	-2.79	0.99	-0.97	29	0.340
dose at axillary nodes P1 - dose at axillary nodes P2	-17.48	19.19	3.503	-24.6	-10.32	-5.00	29	<0.001

4.3.4 Research question: What is the relationship between the depth of the supraclavicular nodes and the patient separation?

Mean depth of the supraclavicular nodes was 3.61 cm with a standard deviation of 1.14 cm (range 1.91 to 6.24 cm).

Plan 1:

The Pearson's correlation coefficient between separation at the matchline centre and depth of the supraclavicular nodes was 0.870 ($p < 0.001$). Thus

there was a strong and significant relationship between the two variables. A regression equation was determined for prediction of depth of the nodes based on the separation. The equation was:

Depth of supraclavicular nodes (cm) = $(0.579 \times \text{field separation at matchline (cm)}) - 6.539$.

The relationship is shown graphically in Figure 4.6.

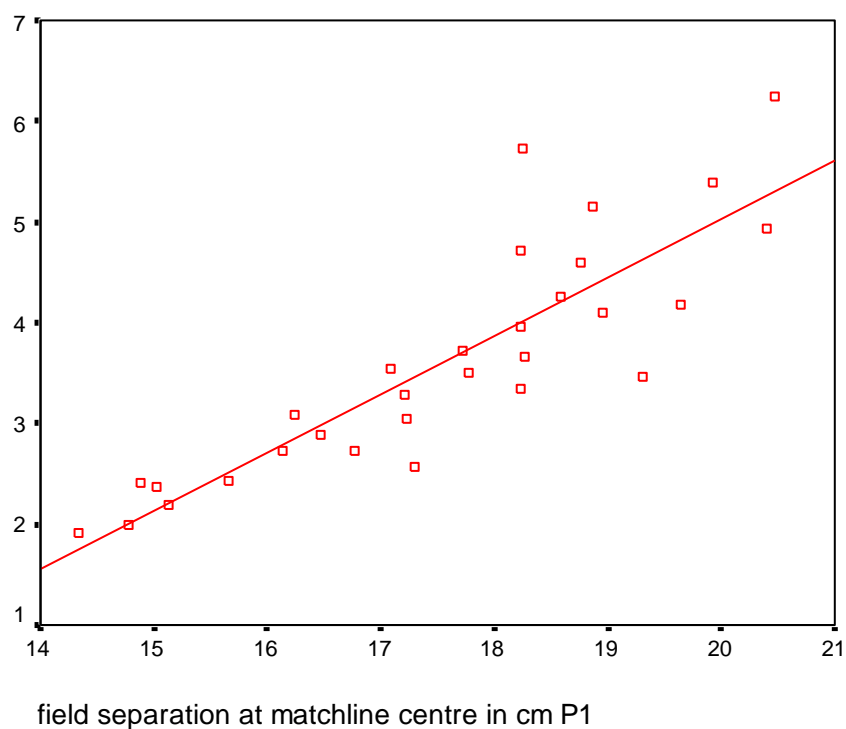


Figure 4.6: Scatter plot of field separation at matchline by depth of supraclavicular nodes in plan 1

Plan 2:

The Pearson's correlation coefficient between separation at the matchline centre and depth of the supraclavicular nodes was 0.871 ($p < 0.001$) for plan 2.

Thus there was a strong and significant relationship between the two variables. A regression equation was determined for prediction of depth of the nodes based on the separation. The equation was:

Depth of supraclavicular nodes (cm) = $(0.5879 \times \text{field separation at matchline (cm)}) - 6.699$.

The relationship is shown graphically in Figure 4.7.

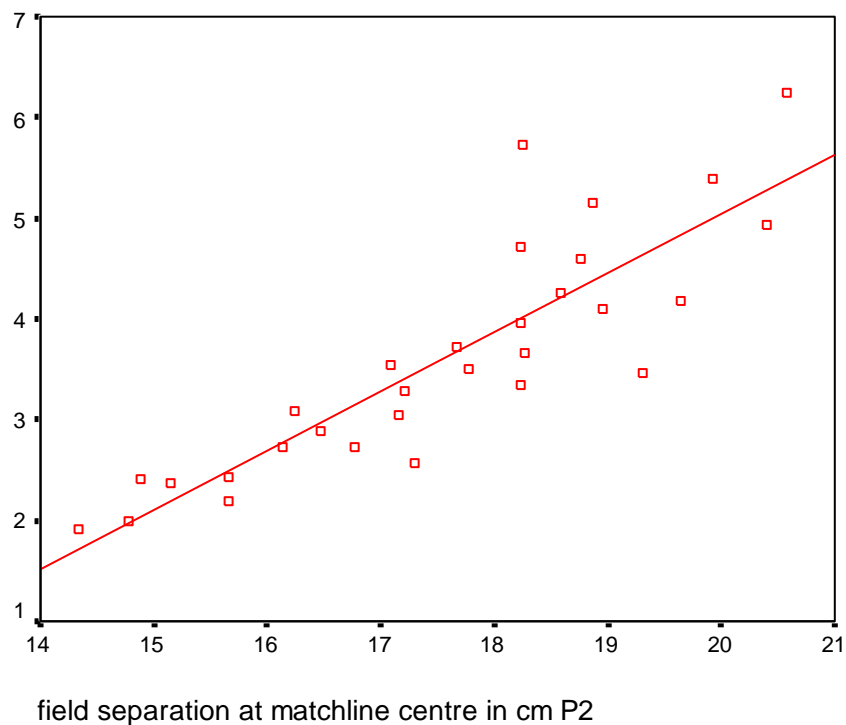


Figure 4.7: Scatter plot of field separation at matchline by depth of supraclavicular nodes in plan 2

4.3.5 Research question: What is the relationship between the depth of the axillary nodes and the patient separation?

The mean depth of the axillary nodes was 3.43 cm with a standard deviation of 0.84 cm (range 2.05 to 5.25 cm).

Plan 1

The Pearson's correlation coefficient between separation at the axillary centre and depth of the axillary nodes was 0.641 ($p < 0.001$) for plan 1. Thus there was a moderate and significant relationship between the two variables. A regression equation was determined for prediction of depth of the nodes based on the separation. The equation was:

Depth of axillary nodes (cm) = $(0.285 \times \text{field separation at axillary centre (cm)}) - 1.011$.

The relationship is shown graphically in Figure 4.8.

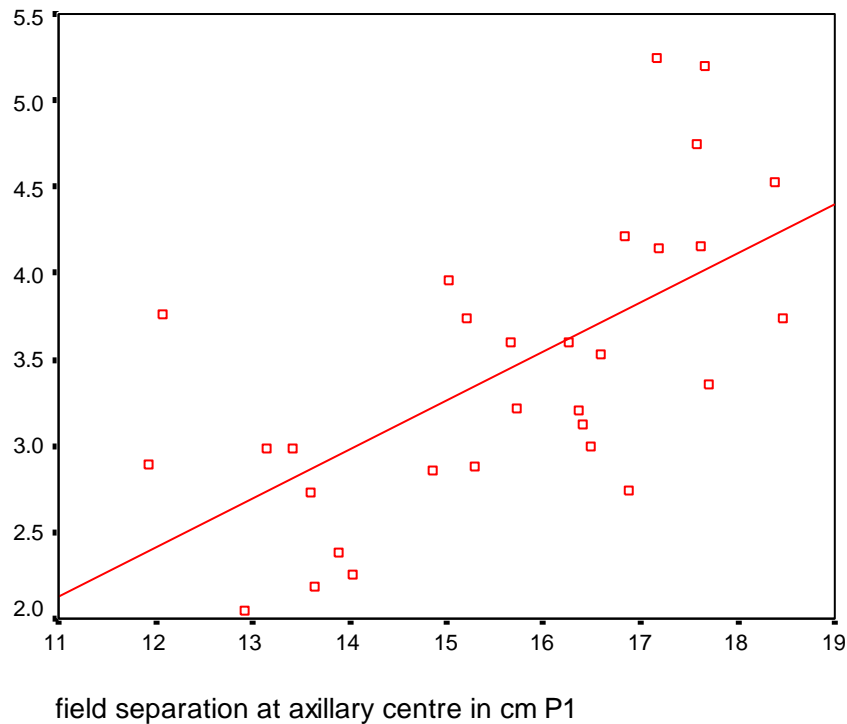


Figure 4.8: Scatter plot of field separation at axillary centre by depth of axillary nodes in plan 1

Plan 2

The Pearson's correlation coefficient between separation at the axillary centre and depth of the axillary nodes was 0.630 ($p < 0.001$) for plan 2. Thus there was a moderate and significant relationship between the two variables. A regression equation was determined for prediction of depth of the nodes based on the separation. The equation was:

$$\text{Depth of axillary nodes (cm)} = (0.281 \times \text{field separation at axillary centre (cm)}) - 0.963.$$

The relationship is shown graphically in Figure 4.9

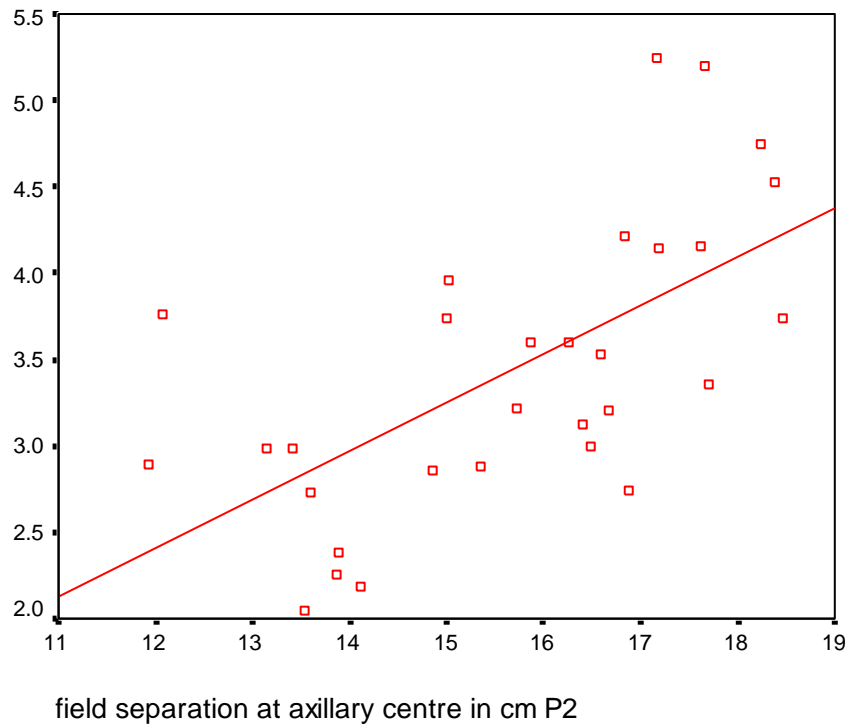


Figure 4.9: Scatter plot of field separation at axillary centre by depth of axillary nodes in plan 2

4.4 Objective 2:

To evaluate CT based treatment planning versus digitised image planning for carcinoma of the breast in terms of the variability of the breast tissue (target volume).

4.4.1 Research question: Does the target volume receive adequate dose coverage from the plans?

To answer this objective paired t-tests were done to compare the mean dose between the two plans at each target volume. The results of the analysis are shown in Table 4.8. At all target volumes there was a statistically significant

difference in the mean dose, with the dose of plan 2 being higher than that of plan 1 in all cases.

Table 4.8: Paired t-test for comparison of mean doses between plans

	Plan	Mean	N	Std. Deviation	Std. Error Mean	p value
Dose given to 100% of target	Plan 1	4.68	30	3.68	0.67	0.008
	Plan2	6.98	30	5.31	0.97	
Dose given to 95% of target	Plan 1	21.64	30	13.11	2.39	<0.001
	Plan2	35.59	30	10.34	1.89	
Dose given to 90% of target	Plan 1	33.19	30	12.17	2.22	<0.001
	Plan2	44.85	30	7.11	1.30	
Dose given to 85% of target	Plan 1	40.93	30	9.00	1.64	<0.001
	Plan2	48.21	30	4.80	0.88	
Dose given to 80% of target	Plan 1	45.23	30	6.97	1.27	<0.001
	Plan2	49.96	30	2.89	0.53	
Dose given to 70% of target	Plan 1	49.28	30	3.83	0.70	0.001
	Plan2	51.53	30	0.85	0.15	
Dose given to 60% of target	Plan 1	51.09	30	1.84	0.34	0.001
	Plan2	52.23	30	0.70	0.13	
Dose given to 50% of target	Plan 1	52.08	30	1.41	0.26	0.005
	Plan2	52.89	30	0.66	0.12	

The percentage target volume receiving a dose of 50Gy was compared between the two plans using paired t-tests. There was a highly significant difference between the mean volumes of the two plans ($p < 0.001$). This is shown in Table 4.9.

Table 4.9: Paired t-test for comparison of mean volume receiving 50Gy dose between plans

	Plan	Mean	N	Std. Deviation	Std. Error Mean	p value
Percentage target volume receiving 50Gy	Plan 1	70.1267	30	12.59707	2.29990	<0.001
	Plan 2	82.4300	30	6.49908	1.18656	

The relationship between field separation for the breast and percentage volume receiving 50Gy was examined separately for each plan using Pearson's correlation.

Plan 1:

Table 4.10 shows that there was no correlation between the two variables for plan 1 ($r = 0.194$, $p=0.306$).

Table 4.10: Pearson's correlation between field separation at breast centre and percentage target volume receiving 50Gy in plan 1

		field separation at breast centre in cm P1
percentage target volume receiving 50Gy in % P1	Pearson Correlation	0.194
	p (2-tailed)	0.306
	N	30

Plan 2:

Table 4.11 shows that there was no correlation between the two variables for plan 2 ($r = 0.202$, $p=0.285$).

Table 4.11: Pearson's correlation between field separation at breast centre and percentage target volume receiving 50Gy in plan 2

		field separation at breast centre in cm P2
percentage target volume receiving 50Gy in % P2	Pearson Correlation	0.202
	p (2-tailed)	0.285
	N	30

The summary statistics and comparison of the plans with regard to maximum, minimum and mean dose for breast centre are shown in Table 4.12. There was no difference between the maximum dose of the two plans ($p=0.773$), however, the minimum doses ($p<0.001$) as well as the mean doses ($p<0.001$) were highly significantly different, with plan 2 showing higher minimum and mean doses than plan 1.

Table 4.12: Comparison of maximum, minimum and mean doses for breast centre between plan 1 and plan 2

		Mean	N	Std. Deviation	Std. Error Mean	t statistic	p value
Maximum dose point breast centre in Gray	Plan 1	55.1467	30	2.67807	.48895	-0.292	0.773
	Plan 2	55.2967	30	.96935	.17698		
Minimum dose point breast centre in Gray	Plan 1	9.6617	30	10.05077	1.83501	-5.453	<0.001
	Plan 2	21.9783	30	13.62409	2.48741		
Mean dose point breast centre in Gray	Plan 1	47.2700	30	5.28701	.96527	-5.234	<0.001
	Plan 2	50.7183	30	2.82914	.51653		

4.4.2 Research question: How is dose to the heart volume affected by target coverage on both plans?

Heart doses were compared between plan 1 and plan 2 separately for left and right breast tumours.

4.4.2.1 Left breast tumours:

For left breast tumours there was no significant difference between plan 1 and plan 2 with regard to maximum dose to the heart ($p=0.106$). However, minimum and mean dose to the heart were significantly different between the plans ($p<0.001$) with plan 2 giving a higher minimum and mean dose. The dose to one third of the heart was borderline non significantly different between plan 1 and 2 ($p=0.054$), with plan 2 having a slightly higher dose.

The percentage of the heart receiving 50Gy was significantly higher in plan 2 than plan 1 ($p=0.022$).

Table 4.13a: Comparison of dose to the heart parameters between plan 1 and plan 2 for left breast tumours (n=16)

		Mean (Gy)	N	Std. Deviation	Std. Error Mean	t statistic	p value
Maximum dose to heart in Gray	Plan 1	49.8750	16	6.59308	1.64827	-1.718	0.106
	Plan 2	52.7375	16	1.20934	.30233		
Minimum dose to heart in Gray	Plan 1	.9125	16	.20616	.05154	-4.607	<0.001
	Plan 2	1.1000	16	.21292	.05323		
Mean dose to heart in Gray	Plan 1	5.0562	16	2.47870	.61968	-4.498	<0.001
	Plan 2	7.5438	16	2.49505	.62376		
Dose to one third of the heart	Plan 1	3.3000	16	.91506	.22876	-2.089	0.054
	Plan 2	3.8437	16	1.44590	.36147		

Table 4.13b: Comparison of dose to the heart parameters between plan 1 and plan 2 for left breast tumours (n=16)

		Mean (%)	N	Std. Deviation	Std. Error Mean	t statistic	p value
Percentage volume of heart receiving 50Gy	Plan 1	1.6063	16	1.78119	.44530	-2.566	0.022
	Plan 2	2.4250	16	1.71901	.42975		

4.4.2.2 Right breast tumours:

Table 4.14 shows that there were no statistically significant differences between plan 1 and plan 2 for right breast tumours with regard to the doses to the heart when compared by the paired t-test.

Table 4.14a: Comparison of dose to the heart parameters between plan 1 and plan 2 for right breast tumours (n=14)

		Mean (Gy)	N	Std. Deviation	Std. Error Mean	t statistic	p value
Maximum dose to heart in gray	Plan 1	13.5071	14	13.31688	3.55908	-0.751	0.446
	Plan 2	16.9571	14	17.55294	4.69122		
Minimum dose to heart in gray	Plan 1	.4143	14	.15119	.04041	-1.175	0.261
	Plan 2	.7214	14	.92335	.24678		
Mean dose to heart in gray	Plan 1	1.8214	14	.86307	.23067	-0.362	0.723
	Plan 2	1.9357	14	.58652	.15676		
Dose to one third of the heart	Plan 1	1.8714	14	.91183	.24370	-0.713	0.489
	Plan 2	2.0429	14	.24718	.06606		

Table 4.14b: Comparison of dose to the heart parameters between plan 1 and plan 2 for right breast tumours (n=14)

		Mean (%)	N	Std. Deviation	Std. Error Mean	t statistic	p value
Percentage volume of heart receiving 50Gy	Plan 1	.0714	14	.26726	.07143	1.000	0.336
	Plan 2	.0000	14	.00000	.00000		

4.4.3 Research question: How is dose to the lung volume affected by target coverage on both plans?

Affected lung doses were compared between the plans using paired t-tests in Table 4.15 below. It can be seen that the maximum dose to the affected lung did not differ significantly between the two plans ($p=0.144$), but the minimum and mean doses did differ significantly ($p=0.007$ and $p<0.001$ respectively) with plan 2 giving the higher dose.

Similarly the dose to one third of the affected lung, as well as the percentage volume of the affected lung receiving 45Gy also was significantly higher in plan 2 than plan 1.

Table 4.15: Comparison of parameters for dose to the affected lung between plan 1 and plan 2

		Mean	N	Std. Deviation	Std. Error Mean	t statistic	p value
maximum dose to affected lung in gray	Plan 1	55.0033	30	2.43034	.44372	-1.500	0.144
	Plan 2	55.6767	30	1.49151	.27231		
minimum dose to affected lung in gray	Plan 1	.7067	30	.22118	.04038	-2.884	0.007
	Plan 2	.7967	30	.29064	.05306		
mean dose to affected lung in gray	Plan 1	12.9500	30	2.68954	.49104	-5.353	<0.001
	Plan 2	14.7267	30	2.77214	.50612		
dose to one third of affected lung in gray	Plan 1	10.2967	30	6.66584	1.21701	-3.141	0.004
	Plan 2	13.6900	30	8.95642	1.63521		
percentage volume of affected lung receiving 45Gy	Plan 1	7.2333	30	3.45317	.63046	-6.806	<0.001
	Plan 2	11.0433	30	4.20646	.76799		

4.5 Objective 3:

To evaluate CT based treatment planning versus digitised image planning for carcinoma of the breast in terms of the dose inhomogeneity at the matchline

4.5.1 Research question: What is the dose variability along the matchline?

4.5.1.1 Reference point 3

Table 4.16 shows that the mean inhomogeneity was not different between plan 1 and plan 2 at reference point 3 ($p=0.466$).

Table 4.16: Paired t-test for comparison of mean inhomogeneity between plan 1 and plan 2 at reference point 3

	Mean	N	Std. Deviation	Std. Error Mean	t statistic	p value
matchline inhomogeneity dose P1	51.50	30	4.57	0.83	-0.739	0.466
matchline inhomogeneity dose P2	52.09	30	3.23	0.59		

4.5.1.2 Reference point 4

Table 4.17 shows that the mean inhomogeneity was highly significantly different between plan 1 and plan 2 at reference point 4 ($p < 0.001$). The inhomogeneity was higher in plan 2 than plan 1.

Table 4.17: Paired t-test for comparison of mean inhomogeneity between plan 1 and plan 2 at reference point 4

	Mean	N	Std. Deviation	Std. Error Mean	t statistic	p value
matchline inhomogeneity dose P1	49.66	30	3.33	0.61	-4.052	<0.001
matchline inhomogeneity dose P2	52.26	30	2.46	0.45		

4.5.1.3 Reference point 5

Table 4.18 shows that the mean inhomogeneity was highly significantly different between plan 1 and plan 2 at reference point 5 ($p < 0.001$). The inhomogeneity was higher in plan 2 than plan 1.

Table 4.18: Paired t-test for comparison of mean inhomogeneity between plan 1 and plan 2 at reference point 5

	Mean	N	Std. Deviation	Std. Error Mean	t statistic	p value
matchline inhomogeneity dose P1	49.43	30	4.15	0.76	-4.059	<0.001
matchline inhomogeneity dose P2	52.63	30	2.87	0.52		

4.5.1.4 Reference point 6

Table 4.19 shows that the mean inhomogeneity was not significantly different between plan 1 and plan 2 at reference point 6 ($p = 0.079$).

Table 4.19: Paired t-test for comparison of mean inhomogeneity between plan 1 and plan 2 at reference point 6

	Mean	N	Std. Deviation	Std. Error Mean	t statistic	p value
matchline inhomogeneity dose P1	51.55	30	4.53	0.83	-1.822	0.079
matchline inhomogeneity dose P2	52.14	30	3.57	0.65		

4.5.1.5 Reference point 7

Table 4.20 shows that the mean inhomogeneity was significantly different between plan 1 and plan 2 at reference point 7 ($p=0.001$). Plan 2 had a slightly higher mean inhomogeneity than plan 1.

Table 4.20: Paired t-test for comparison of mean inhomogeneity between plan 1 and plan 2 at reference point 7

	Mean	N	Std. Deviation	Std. Error Mean	t statistic	p value
matchline inhomogeneity dose P1	49.19	30	6.51	1.19	-3.848	0.001
matchline inhomogeneity dose P2	50.92	30	5.16	0.94		

There was a highly significant difference between plan 1 and plan 2 with regard to maximum, minimum, and mean dose at the matchline ($p<0.001$).

This is shown in Table 4.21 below. In all comparisons, plan 2 gave a higher dose than plan 1.

Table 4.21: Comparison of maximum, minimum and mean dose at matchline between plan 1 and plan 2

		Mean	N	Std. Deviation	Std. Error Mean	t statistic	p value
maximum dose point matchline in Gray	Plan 1	55.5010	30	3.07667	.56172	-4.158	<0.001
	Plan 2	57.8083	30	1.34863	.24623		
minimum dose point matchline in Gray	Plan 1	25.8433	30	10.33198	1.88635	-5.619	<0.001
	Plan 2	34.0350	30	6.65123	1.21434		
mean dose point matchline in Gray	Plan 1	46.1583	30	3.82197	.69779	-5.935	<0.001
	Plan 2	49.0100	30	2.73856	.49999		

The minimum and mean doses at the axilla were statistically significantly different between the two plans ($p < 0.001$ and $p = 0.001$ respectively).

However, there was no difference between the plans with respect to maximum dose at the axilla (Table 4.22).

Table 4.22: Comparison of maximum, minimum and mean dose at axilla between plan 1 and plan 2

		Mean	N	Std. Deviation	Std. Error Mean	t statistic	p value
maximum dose point axilla in gray	Plan 1	57.6800	30	.91497	.16705	-1.587	0.123
	Plan 2	58.1000	30	1.26757	.23142		
minimum dose point axilla in gray	Plan 1	31.8183	30	16.57106	3.02545	-4.701	<0.001
	Plan 2	45.9533	30	8.55509	1.56194		
mean dose point axilla in gray	Plan 1	50.2750	30	4.99173	.91136	-3.740	0.001
	Plan 2	54.1333	30	1.34538	.24563		

4.5.2 Are the plans over dosing?

To answer this objective, the mean inhomogeneity for all reference points in both plans were compared to the upper reference value of 53.75Gy, in accordance with ICRU recommendations.

The ICRU report 62 (1999) recommends that the heterogeneity be kept within +7% (maximum dose) and -5% (minimum dose) of the prescribed dose (ICRU 62, 1999). The maximum dose is significant in relation to possible side effects and the minimum dose is significant in relation to tumour control.

Table 4.23 shows that all means were significantly lower than the reference value of 53.75Gy. Thus it was concluded that the plans were not overdosing.

Table 4.23: One sample t-test for comparison of mean inhomogeneity at reference points in plan 1 and plan 2 to an upper reference value of 53.75Gy.

	Test Value = 53.75					
	t	df	p value (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
Matchline inhomogeneity dose at ref point 3 in gray P1	-2.695	29	0.012	-2.2500	-3.9573	-.5427
Matchline inhomogeneity dose at ref point 3 in gray P2	-2.818	29	0.009	-1.6600	-2.8646	-.4554
Matchline inhomogeneity dose at ref point 4 in gray P1	-6.733	29	<0.001	-4.0933	-5.3367	-2.8500
Matchline inhomogeneity dose at ref point 4 in gray P2	-3.317	29	0.002	-1.4900	-2.4087	-.5713
Matchline inhomogeneity dose at ref point 5 in gray P1	-5.697	29	<0.001	-4.3200	-5.8709	-2.7691
Matchline inhomogeneity dose at ref point 5 in gray P2	-2.144	29	0.041	-1.1233	-2.1948	-.0519
Matchline inhomogeneity dose at ref point 6 in gray P1	-2.658	29	0.013	-2.1967	-3.8869	-.5064
Matchline inhomogeneity dose at ref point 6 in gray P2	-2.466	29	0.020	-1.6067	-2.9394	-.2739

Matchline inhomogeneity dose at ref point 7 in gray P1	-3.838	29	0.001	-4.5600	-6.9899	-2.1301
Matchline inhomogeneity dose at ref point 7 in gray P2	-3.001	29	0.005	-2.8267	-4.7534	-.9000

4.5.3 Are the plans under dosing?

To answer this question, the mean inhomogeneity for all reference points in both plans were compared to the lower reference value of 47.5Gy by means of a one-sample t-test. Since means under 47.5Gy were of interest, only negative t values were considered (positive t values meant that the mean was higher than the reference value).

Table 4.24 shows that there were no negative t values. Thus it was concluded that none of the means were significantly less than 47.5Gy, and that there was no under dosing.

Table 4.24: One sample t-test for comparison of mean inhomogeneity at reference points in plan 1 and plan 2 to a lower reference value of 47.5Gy.

	Test Value = 47.5					
	t	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
matchline inhomogeneity dose at ref point 3 in gray P1	4.792	29	<0.001	4.0000	2.2927	5.7073
matchline inhomogeneity dose at ref point 3 in gray P2	7.793	29	<0.001	4.5900	3.3854	5.7946
matchline inhomogeneity dose at ref point 4 in gray P1	3.548	29	0.001	2.1567	.9133	3.4000
matchline inhomogeneity dose at ref point 4 in gray P2	10.597	29	<0.001	4.7600	3.8413	5.6787
Matchline inhomogeneity dose at ref point 5 in gray P1	2.545	29	0.017	1.9300	.3791	3.4809
matchline inhomogeneity dose at ref point 5 in gray P2	9.786	29	<0.001	5.1267	4.0552	6.1981
matchline inhomogeneity dose at ref point 6 in gray P1	4.905	29	<0.001	4.0533	2.3631	5.7436
matchline inhomogeneity dose at ref point 6 in gray P2	7.126	29	<0.001	4.6433	3.3106	5.9761
matchline inhomogeneity dose at ref point 7 in gray P1	1.422	29	0.166	1.6900	-.7399	4.1199
matchline inhomogeneity dose at ref point 7 in gray P2	3.634	29	0.001	3.4233	1.4966	5.3500

CHAPTER FIVE

DISCUSSION

5.1 Introduction

The results that were obtained from the data and presented in the form of tables, figures, graphs and statements in Chapter 4 are discussed in the current chapter.

5.2 Demographic and clinical parameters

The annual risk for development of carcinoma of the breast increases exponentially up to the age of menopause. After the age of 80, the annual incidence of breast carcinoma begins to show a slight decline (Buchholz *et al.*, 2003).

The mean age for the study was 57.9 years. The minimum age was 36 years and the maximum age was 82 years.

The menopausal status of the patients is also a significant prognostic indicator and, although this was not a defined objective for this study, it is an important factor in terms of long term disease free survival for future studies. The vast majority of the participants were post menopausal (76.6%), while 20% were pre menopausal. One participant who was 40 years old had an unknown menopausal status (chapter 4, figure 4.1).

The oestrogen (OR) status for this population was 63.3% positive while the progesterone (PR) status was 50% positive (refer chapter 4, figures 4.2 and 4.3). Thorpe (1988) in his report refers to the study by Overgaard *et al.*,

(1999) on the Danish Breast Cancer Cooperative Group (DBCCG) project where OR and PR statuses were found to be significant prognostic variables for pre menopausal women under 50 years of age. In contrast, in the post menopausal women, neither receptor status was found to be a significant prognostic factor in the low risk group. In the high risk, post menopausal women, however OR status was a significant prognostic indicator for recurrence free survival; moreover, it appeared to be independent of lymph node status.

The average number of total nodes removed was 8.6 (range 0 to 25), which in terms of widely accepted standards would be considered an inadequate sample. One participant had 25 nodes removed of which 21 nodes were positive. The average number of positive nodes was four. Katz *et al.*, (2006) report on an analysis of 224 patients, 42 of which had involvement of four or more axillary nodes. Interestingly, the patients with four or more involved axillary nodes were also associated with risk factors of lymphovascular invasion.

Forty percent of the participants showed lymphatic invasion of the tumour (chapter 4, table 4.1). Wong *et al.*, (2000) attempted to assess clinical or pathological factors that predict extent of involvement in carcinoma of the breast. The only strong predictor for finding four or more positive nodes was the presence of lymphatic invasion.

The surgical margins for this population were clear in 76.6% and close in 23.3% (chapter 4, figure 4.4). The management for close margins will remain as for positive margins. The value of positive surgical margins on local control was a predictive factor in a study conducted by Jobsen *et al.*, (2003). The outcome was an endorsement of the view that positive surgical margins did impair long term local control. However, further analysis revealed that this was restricted to young women only, with a local recurrence rate of 36.9% at 5 years for women less than or equal to 40 years and positive surgical margins as compared to 2.6% for older women. This could be an area for further study.

Stage T2 was the most common stage with 53.3% of the participants and N1 with 50%. Grade II was the most frequently presenting grade with 56.67%.

5.3 Objective 1

To evaluate CT-based treatment planning *versus* digitised image planning for carcinoma of the breast in terms of the depth of the supraclavicular and axillary nodes.

5.3.1 Research question: What is the dose to the supraclavicular nodes from both plans?

The results (chapter 4, table 4.5) showed that both plans achieved significantly lower doses than the prescribed 50Gy. Plan 1 had a mean dose of 45.52Gy and plan 2 a mean dose of 46.42Gy. Although, the mean dose for plan 2 was closer to the prescription dose of 50Gy than plan 1, this small

difference is not a statistically significant difference. Therefore a type 1 error, yet not significant from an oncology point. This dose 46.42Gy is still considered an acceptable dose in terms of tumour control therefore plan 2 is more acceptable than plan 1). The accepted dose inhomogeneity, according to ICRU recommendations is between 47.5Gy (5% below) and 53.5Gy (7% above) for a prescription of 50Gy. According to the ICRU guidelines the dose from both plans to the supraclavicular nodes were inadequate.

Madu *et al.*, (2001) in a study to define the supraclavicular nodes, examined the implications for CT-based treatment planning. The study strengthens the argument for CT-based treatment planning and brings to light the benefits derived from it. The accurate definition of the position of the nodal regions from CT scanning paves the way for precision planning. The results from this study showed an improvement with the conformal plans in terms of nodal dose coverage. The conformal plans demonstrated 100% of the supraclavicular volume was covered by the 90% isodose when compared to the standard technique which showed 93.3% of the supraclavicular volume covered by the 90% isodose. Also of importance was the observation that as the depth at which the supraclavicular nodes were situated, increased, the percentage of the supraclavicular volume encompassed within the 90% isodose significantly decreased for the standard plans *versus* the conformal plans. This is significant as it could be a contributing factor to under dosing in the supraclavicular region resulting in recurrence of the tumour.

5.3.2 Research question: What is the dose to the axillary nodes from both plans?

The mean dose for plan 1 was 35.03Gy and plan 2 was 52.51Gy (chapter 4, table 4.6). When compared to the prescription dose of 50Gy, plan 2 had a significantly higher mean dose than plan 1. In the clinical situation a mean dose of 35.03Gy would be totally unacceptable as it is not considered as a curative dose or even adequate for tumour control. On reviewing the plans for plan 1 method, it was evident that all plans generated with humeral head shielding as per the request of the oncologist showed that the axillary nodes were inadvertently under dosed. This is a valid observation because in the absence of a CT scan, it is impossible to accurately define the axillary nodes. This problem is more evident due to the fact that the position of the axillary nodes also changes with the arm position.

The accepted dose inhomogeneity, according to ICRU recommendations is between 47.5Gy (5% below) and 53.5Gy (7% above) for a prescription of 50Gy. The dose 52.51Gy from plan 2 is clinically significant in terms of control of disease. Therefore to answer the research question, the dose to the axillary nodes from plan 1 is inadequate and unacceptable but is adequate from plan 2.

Smitt and Goffinet (1999) closely studied the axillary coverage of six patients using conformal planning techniques. The dose delivered to the axilla of more than 90% of the prescribed dose was achieved in only one of the six patients. This occurred in a thin woman with relatively small breasts. The mean nodal

dose ranged from 73% - 95% of the prescribed dose. Under dosing occurred primarily in the deep posterior-superior region of the axilla.

In positioning the patient for this technique, the arm is extended above the head (chapter 3, diagram 3.1). This position is very important as the anatomical location of the axillary nodes differs from that seen in text books when the arm is positioned alongside the body (diagram 5.1 and diagram 5.2).

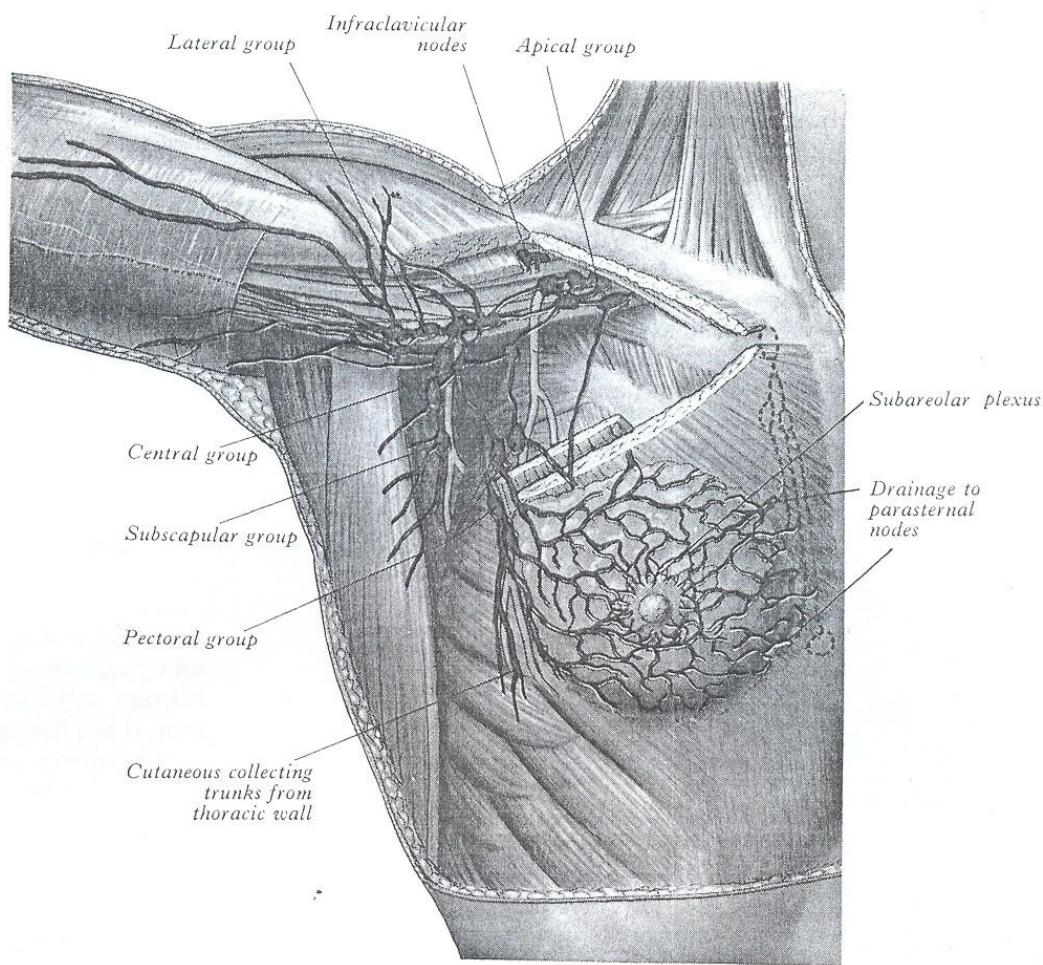


Diagram 5.1 Demonstrates the position of the lymph nodes when the arm is extended.

Warwick, R. and Williams, P.L. 1973. Gray's Anatomy. Thirty fifth edition. University of London. Longman.

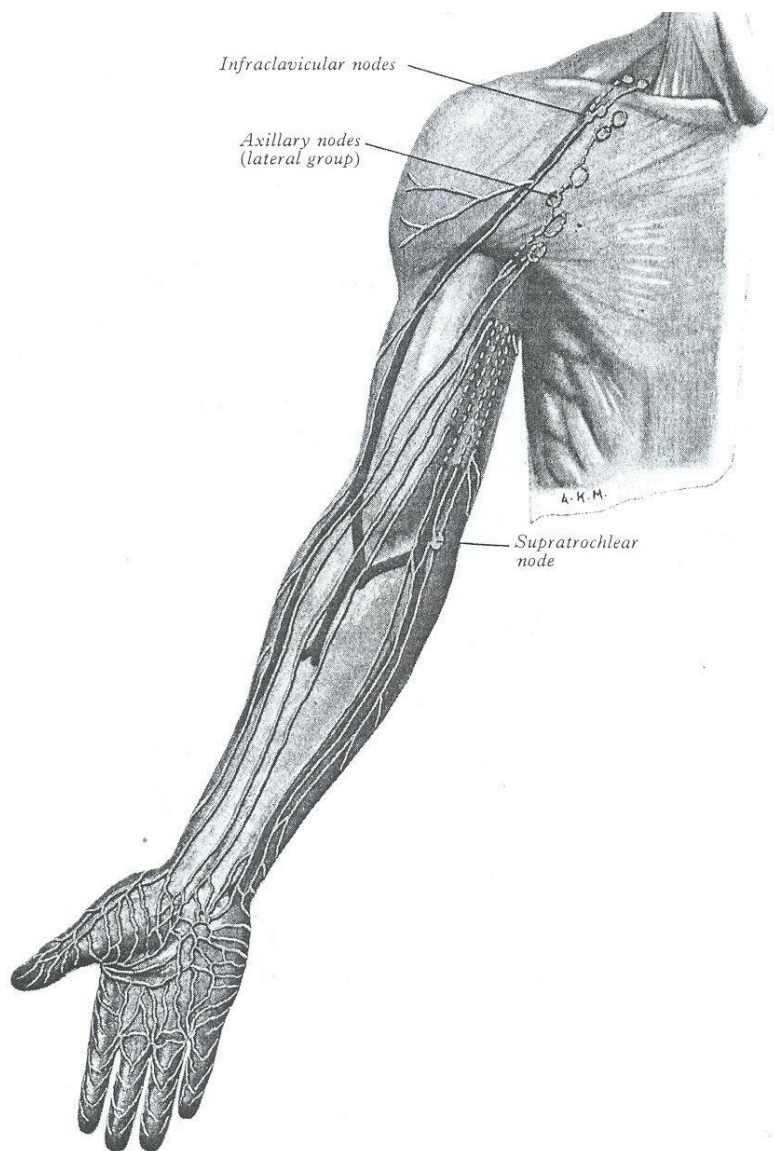


Diagram 5.2 Demonstrates the position of the lymph nodes when the arm is alongside the body.

Warwick, R. and Williams, P.L. 1973. Gray's Anatomy. Thirty fifth edition. University of London. Longman.

From the CT scan (diagram 5.3) it is evident that the advantage of the right arm extended above the head being that the axillary nodes move higher or

superiorly, away from the chest wall thus reducing on the volume of lung being irradiated. When compared to the left side, where the left arm is alongside the body, it is clearly seen volume of left lung is greater than the volume of the right lung.

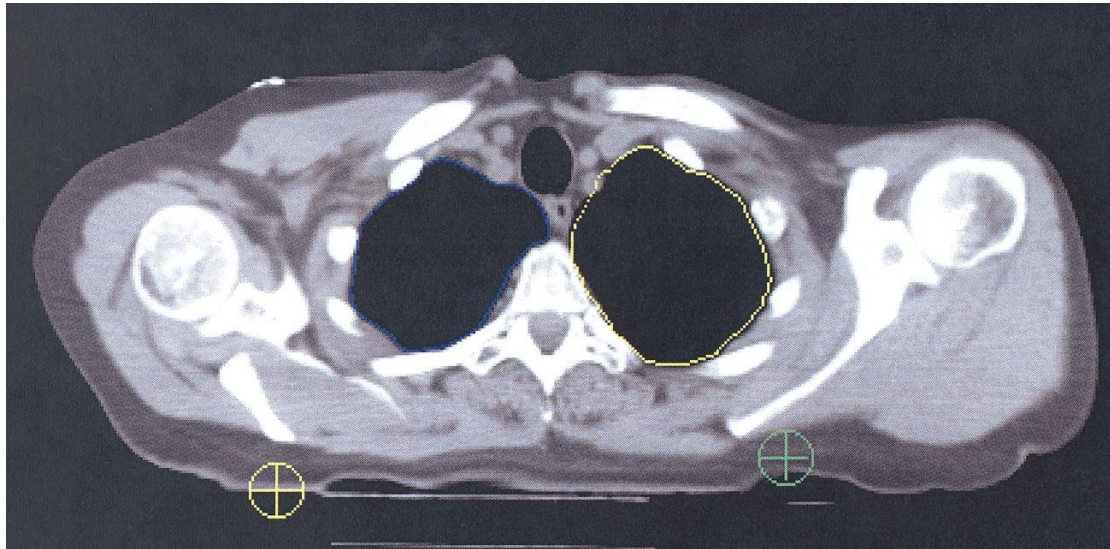


Diagram 5.3 Demonstrates the volume of right lung being less when the right arm is positioned above the head (From a participant's plan data).

Pergolizzi *et al.*, (2004) evaluated the position of the arm and the impact of displacement of the axillary nodes away from the chest wall. The authors also strongly recommended the use of CT scan planning when planning patients with arms positioned above the head. The outcome of the study showed a greater distance between the nodes and the chest wall. The concern expressed by Pergolizzi *et al.*, (2004) was the close proximity of the nodes to the humeral head hence they recommend that a shielding block be avoided when three-dimensional planning is not being used. As mentioned earlier a similar trend was noticed in this study on the plan 1 participants where the

mean dose was 35.03Gy due to the use of humeral head shielding being used.

5.3.3 Research question: How do the plans differ in terms of dose coverage to the supraclavicular and axillary nodes?

Plans 1 and 2 were not significantly different from each other for mean dose at the reference point of the supraclavicular nodes. However, for the dose to the axillary nodes, the two plans differed highly significantly. The mean difference between the doses of the two plans was 17.48Gy.

There was no statistical difference between the mean doses of the two plans (chapter 4, table 4.7) for the supraclavicular nodes, making both plans acceptable. Unlike the plans for the axillary nodes, plan 1 would not be accepted for administering treatment, whereas plan 2 would be the plan of choice giving a higher dose.

5.3.4 What is the relationship between the depth of the supraclavicular nodes and the patient separation?

Mean depth of the supraclavicular nodes in this study was 3.61cm with a standard deviation of 1.14 cm (range 1.91 to 6.24 cm).

This was in contrast to the findings of Madu *et al.*, (2001) where the depth of the supraclavicular nodes ranged between 3.9cm to 8.3cm and the study by Bentel *et al.*, (2000) where the depth of the supraclavicular nodes ranged between 2.4cm to 9.5cm. In the study by Bentel *et al.*, (2000) the depth appeared to be associated with patient size. Furthermore, there was a linear

relationship between the supraclavicular lymph node depth and the patient separation. A similar trend was seen by the researcher in relation to the depth of the supraclavicular lymph nodes and the patient separation (chapter 4, figures 4.6 and 4.7).

There was a strong and significant relationship between the two variables. Both plan 1 and plan 2 were not significantly different from each other for mean dose at the reference point of the supraclavicular nodes ($p=0.340$). The mean difference between the two plans was 0.897Gy.

5.3.5 What is the relationship between the depth of the axillary nodes and the patient separation?

The mean depth of the axillary nodes was 3.43cm with a standard deviation of 0.84 cm (range 2.05 to 5.25 cm). There was a moderate and significant relationship between the two variables for both plan 1 (chapter 4, figure 4.8) and plan 2 (chapter 4, figure 4.9).

In contrast to this finding, Bentel *et al.*, (2000) found that the depth of the axillary lymph nodes ranged from 1.4cm to 8cm with a mean of 4.3cm. This was most likely due to the varying range in the patient size, separation and shape.

5.4 OBJECTIVE 2

To evaluate CT based treatment planning *versus* digitised image planning for carcinoma of the breast in terms of the variability of the breast tissue (target volume).

5.4.1 Research question: Does the target volume receive adequate dose coverage from the plans?

The coverage of the target volume is important for tumour control and therefore it is imperative that the target volume delineation is accurate. The use of CT-based planning in patients with carcinoma of the breast is limited by a practitioner's ability to radiographically identify the breast tissue and target volume. This is often a problem in older women. However, tissues with increased density are commonly seen on CT scan images. The study done by Bentel *et al.*, (1999) also assessed the use of CT-based planning as this was not the routine practise. The borders were identified as 1-2cm medially and posteriorly to the lateral/posterior extent of the palpable breast tissue. On assessment of post CT planning it was found that in 48% of the patients the medial margin was inadequate therefore there was a lack of tumour volume coverage. One of the main points of this study was the anatomic variability in patients with carcinoma of the breast which confirmed that the degree of variability was independent of the geometric margin selected.

The variability of delineations of target volume has been challenged by many authors. Hurkmans *et al.*, (2001) in an attempt to decrease the variability

delineated by different oncologists suggest that a lead wire be placed around the palpable target volume before CT scanning.

When comparing the mean dose between the two plans the results (chapter 4, table 4.8) showed that the dose for each specified percentage of target volume there was a statistically significant difference in the mean dose, with the dose of plan 2 being higher than that of plan 1, in all cases. The ideal situation will be to have the $D_{100\%} = V_{100\%}$. The $D_{100\%}$ (dose to 100% of the target volume) showed very low mean doses. In fact, for plan 1, up to $D_{85\%}$, the doses were totally unacceptable. The $D_{85\%}$ for plan 1 was 40.93Gy and plan 2 was 48.21Gy. Plan 1 from a clinical viewpoint would not be adequate for tumour control. On the other hand, although the dose for plan 2 was 48.21Gy which is below the prescription dose of 50Gy, it still is within the lower limits (47.5Gy) of the ICRU recommendation. From a clinical viewpoint, this dose would be adequate for tumour control. Assuredly, the literature showed similar trends in other studies. Bulchholz *et al.*, (2003) comments on the guidelines used at M.D. Anderson Cancer Centre for target volume coverage whereby the CT-based planning is performed to assure that the target volume is encompassed by the 90% isodose curve.

Kozak *et al.*, (2006) also compared the dosimetry of two different conformal techniques for carcinoma of the breast. The PTV coverage for both techniques was excellent and there was no statistically significant differences in the PTV volumes receiving 100% or 90% of the prescribed dose (i.e., V_{100} and V_{90}). In all case, 95% of the PTV received 90% of the prescribed dose.

The results of this study (chapter 4, table 4.9) also showed the percentage target volume receiving a dose of 50Gy was highly significantly difference between the mean volumes of the two plans ($p < 0.001$). $V_{50\text{Gy}}$ for plan 1 was 70.12% and 82.43% for plan 2. From the researcher's viewpoint this was a surprise finding as one would expect the conformal plan to produce a much better coverage of the target volume. This was probably due to the prioritisation of critical structure avoidance over the delivery of dose to the target volume. This would be influenced by variability in the anatomy of the participants involved.

The relationship between field separation for the breast and percentage volume receiving 50Gy was examined separately for each plan using Pearson's correlation co-efficient. Plan 1 (chapter 4, table 4.10) and plan 2 (chapter 4, table 4.11) showed that there was no correlation between the two variables.

The summary statistics and comparison of the plans with regard to maximum, minimum and mean dose for breast centre are shown in chapter 4, table 4.12. There was no difference between the maximum dose of the two plans ($p = 0.773$), however, the minimum doses ($p < 0.001$) as well as the mean doses ($p < 0.001$) were highly significantly different, with plan 2 showing higher minimum and mean doses than plan 1.

5.4.2 Research question: How is the heart volume and dose affected from target coverage on both plans?

5.4.2.1 Left breast tumours:

For left breast tumours there was a non significant difference between plan 1 and plan 2 (chapter 4, table 4.13) with regard to maximum dose to the heart ($p=0.106$). However, minimum and mean doses to the heart showed a significant difference between the plans ($p<0.001$) with plan 2 giving a higher minimum and mean dose. This can be put down to the realisation that target volume under dosing was occurring with non CT-based planning. The increased target volume coverage results in higher minimum and mean cardiac doses, especially if the only planning constraint was a Dmax dose.

For the same reason, the percentage of the heart receiving 50Gy was significantly higher in plan 2 (2.42Gy) than plan 1 (1.60Gy). This was due to the fact that with the conformal planning more of the heart was in the field in trying to achieve optimal coverage of the target volume. The mean dose to 33% of the heart was 3.3Gy for plan 1 and 3.84Gy for plan 2. The dose to one third of the heart was borderline non- significantly different between plan 1 and 2 ($p=0.054$), with plan 2 having a slightly higher dose. The literature (Chao *et al.*, 1999) states that 33% of the heart can tolerate a dose of 60Gy, this being the minimal tolerance dose for severe complication rate of 5% within 5 years of completion of radiotherapy. Therefore both plans (in the current study) were still well within the tolerance limits.

The study by Kozak *et al.*, (2006) which reported on the dosimetric comparison of two conformal techniques showed in patients with left-sided breast lesions, the heart volumes receiving 20Gy, 10Gy and 5Gy never exceeded 0%, 1% and 2%, respectively. These results differs from the study probably due to the volume of heart contoured. It was not possible to determine whether the entire heart with the vessels or, only the heart was contoured in the study by Kozak et al. The study also strongly suggests that the conformal techniques will not contribute to excess cardiac mortality. No statistically significant differences in the volumes of heart or lung receiving greater than 5Gy were observed between the two conformal techniques.

5.4.2.2 Right breast tumours:

Table 4.14 shows that there were no statistically significant differences between plan 1 and plan 2 for right breast tumours with regard to the doses to the heart when compared by paired t-test. The mean dose to 33% of the heart was 1.87Gy from plan 1 and was 2.04Gy from plan 2. This was well within the tolerance dose of the heart.

5.4.3 Research question: How is the lung volume affected from target coverage on both plans?

The lung doses of the affected side breast were compared between the plans using paired t-tests in Table 4.15 below. It can be seen that the maximum dose to affected lung did not differ significantly between the two plans ($p=0.144$), but the minimum and mean doses did differ significantly ($p=0.007$ and $p<0.001$ respectively) with plan 2 giving the higher dose.

Similarly the dose to 33% of the affected lung was significantly higher in plan 2 (13.69Gy) than in plan 1 (10.29Gy). The volume of the affected lung receiving 45Gy was also significantly higher in plan 2 (11.04Gy) than in plan 1 (7.23Gy). Although there was a statistically significant difference between the variables, both plans were acceptable from a clinically significant viewpoint and within the tolerance guidelines stated by Chao *et al.*, (1999).

According to the tolerance guidelines (Chao *et al.*, 1999), 33% of the lung can tolerate 45Gy with a 5% complication rate at 5 years. The expected side effects would be above 60Gy and may present as lung fibrosis. Yet, the study by Ragaz *et al.*, (1997) showed limited lung fibrosis in most of the irradiated patients. This complication was possibly related to the cumulative dose of the chemotherapy.

Kozak *et al.*, (2006) showed good results to lung volumes from conformal planning. The affected side lung volume receiving 20Gy averaged just 1% and not any of the cases did the volume receiving 20Gy exceed 3%, thus resulting in low risk of acute lung toxicity.

5.5 OBJECTIVE 3

To evaluate CT-based treatment planning *versus* digitised image planning for carcinoma of the breast in terms of the dose inhomogeneity at the matchline

5.5.1 What is the dose variability along the matchline?

The goal of treatment planning is to achieve the most homogeneous dose distribution throughout the target volume. This has shown to be quite a challenge during the study. The dose variability should ideally be as close as possible to the 100%. The accepted dose inhomogeneity, according to ICRU recommendations is between 47.5Gy (5% below) and 53.5Gy (7% above) for a prescription of 50Gy.

5.5.1.1 Reference point 3

This was a point chosen 3cm lateral to the offset demarcated on the breast. Chapter 4, table 4.16 shows that the mean inhomogeneity was not different between plan 1 and plan 2 at reference point 3 ($p=0.466$). The mean inhomogeneity for plan 1 was 51.50Gy and for plan 2 was 52.09Gy. These values are relatively low and within the limits of the ICRU recommendations. The dose variability at reference point 3 for both plans showed a good result.

5.5.1.2 Reference point 4

This was a point chosen at the offset demarcated on the breast. Chapter 4, table 4.17 shows that the mean inhomogeneity was highly significantly different between plan 1 and plan 2 at reference point 4 ($p<0.001$). The mean inhomogeneity was 49.66Gy for plan 1 and 52.26Gy for plan 2. Although the results are statistically significant, clinically this was seen as a good result and was within the limits of the ICRU recommendations.

5.5.1.3 Reference point 5

This was a point chosen 3cm medial to the offset demarcated on the breast.

Chapter 4, table 4.18 shows that the mean inhomogeneity was highly significantly different between plan 1 and plan 2 at reference point 5 ($p < 0.001$). The mean inhomogeneity was 49.43Gy for plan 1 and 52.63Gy for plan 2. Although the results are statistically significant, clinically this was seen as a good result and was within the limits of the ICRU recommendations.

5.5.1.4 Reference point 6

This was a point chosen 1cm inferior to the matchline demarcated on the breast. Chapter 4, table 4.19 shows that the mean inhomogeneity was not significantly different between plan 1 and plan 2 at reference point 6 ($p = 0.079$). The mean inhomogeneity for plan 1 was 51.55Gy and for plan 2 was 52.14Gy. These values are relatively low and within the limits of the ICRU recommendations. The dose variability at reference point 6 for both plans showed a good result.

5.5.1.5 Reference point 7

This was a point chosen 1cm superior to the matchline demarcated on the breast. Chapter 4, table 4.20 shows that the mean inhomogeneity was a significant difference between plan 1 and plan 2 at reference point 7 ($p = 0.001$). The mean inhomogeneity for plan 1 was 49.19Gy and for plan 2 was 50.92Gy. Although the results are statistically significant, clinically this was seen as a good result and within the limits of the ICRU recommendations.

There was a highly significant difference between plan 1 and plan 2 with regard to maximum, minimum, and mean dose at the matchline ($p < 0.001$). This is shown in chapter 4, table 4.21. In all comparisons, plan 2 gave a higher dose than plan 1. Plan 2 on one of the participants generated a maximum hot spot of 116.2%. Rajasekar *et al.*, (1998) reported on maximum doses as high as 125%. However, in an attempt to reduce the hot spot a partial transmission block was placed in the field to absorb the hot spot. The % transmission selected was dependant on the patient separation at the axilla. The minimum dose for plan 1 was 25.84Gy and plan 2 was 34.03Gy. These results were both clinically and statistically significant.

Hunt *et al.*, (1987) caution researchers on over doses as high as 150% or under doses of similar magnitude, should beam alignment be ignored. By geometrically aligning the beams matchline doses are reduced to approximately 110%.

The minimum and mean doses at the axilla were statistically significantly different between the two plans ($p < 0.001$ and $p = 0.001$ respectively). The minimum dose for plan 1 was 31.81Gy and for plan 2 was 45.95Gy. From a clinical viewpoint plan 1 was unacceptable as the minimum dose was too low. Plan 2 was also slightly low, not acceptable by ICRU recommendations, but possibly the best compromise in attempting to keep doses to the heart and lungs to the minimal. The mean doses were within the ICRU recommendations. However, there was no difference between the plans with respect to maximum dose at the axilla (chapter 4, table 4.22).

5.5.2 Are the plans over dosing?

The mean inhomogeneity for all reference points in both plans were compared to the upper reference value of 53.75Gy by means of a one-sample t-test.

Chapter 4, table 4.23 shows that all means were significantly lower than the reference value of 53.75Gy hence it was concluded that the plans were not over dosing.

5.5.3 Are the plans under dosing?

The mean inhomogeneity for all reference points in both plans were compared to the lower reference value of 47.5Gy by means of a one-sample t-test. Since means under 47.5Gy were of interest, only negative t values were considered (positive t values meant that the mean was higher than the reference value).

Chapter 4, table 4.24 shows that there were no negative t values. Thus it was concluded that none of the means were significantly less than 47.5Gy, and that there was no under dosing.

CHAPTER SIX

CONCLUSIONS AND RECOMMENDATIONS

6.1 INTRODUCTION

The results obtained in chapter 4 gave strength to the practice of digitised-based planning, whereby CT scans are not routinely performed. The study reaffirms and increases the confidence level that what is being done is still good practice. The benefits of CT-based treatment planning have had a great impact on precision and accuracy during the planning stages. This is by no means a criticism of the current technique used. In fact, it is pleasing to note that there is tremendous expertise amongst those involved in the clinical management of the patient.

Many oncologists have trained when CT scanning was only being developed, so the clinical setup was an important and accurate aspect. A great deal was dependant on their knowledge of anatomy in reference to surface markers. The introduction of CT images provided more self assurance to the oncologists in terms of defining areas for treatment.

6.2 CONCLUSIONS AND SIGNIFICANCE

The aim of this study was to evaluate computerised tomography (CT) based treatment planning *versus* digitised image planning (standard planning technique) for carcinoma of the breast, using the four-field breast technique, in terms of the depth of supraclavicular and axillary nodes, the variability of the breast tissue and the dose inhomogeneity at the matchline.

- One of the advantages of CT based treatment planning was the freedom for adjusting parameters in order to achieve optimal coverage of the tumour volume.
- The three dimensional appearance from the CT data accurately defined the anatomical structures.
- The depth for treatment of supraclavicular and axillary nodes was easily determined from the CT data.
- Heart volume was accurately defined from the CT data.
- Lung volume was accurately defined from the CT data.
- Matchline dose inhomogeneity was well defined from the CT data and was viewed from many planes.
- Areas of over dosage or under dosage were accurately defined from the information gained from the CT data.

6.3 SUMMARY OF CONTRIBUTIONS/RECOMMENDATIONS

This study has contributed significantly in highlighting the benefits derived from CT-based treatment planning. Although from the results in chapter 4, plans 1 and 2 did not differ significantly for each objective but the vast amount of information that became available from the CT data was most valuable in terms of doses to the critical organs. Even though there was a relationship between the depth of the nodes and patient separation it became evident from the results that each patient be planned individually to the required depth.

The most significant findings to emerge from this thesis were:

- The dose to the supraclavicular nodes were statistically inadequate for both plan 1 and plan 2. But clinically the dose was adequate for control of disease.
- The dose to the axillary nodes from plan 1 was inadequate for tumour control but plan 2 was acceptable.
- There was no statistical difference between the mean doses of the two plans for the supraclavicular nodes therefore making both acceptable. Unlike the plans for the axillary nodes, plan 1 was not accepted for administering treatment, therefore plan 2 was the plan of choice giving a higher dose.
- There was a linear relationship between the depth of the supraclavicular lymph nodes and the participant separation.
- There was a moderate and significant relationship between the depth of the axillary lymph nodes and the participant separation.
- When comparing the mean dose between the two plans from the target volume coverage, the results showed that the dose for each specified percentage of target volume there was a statistically significant difference in the mean dose, with the dose of plan 2 being higher than that of plan 1, in all cases.
- For left breast tumours there was a non significant difference between plan 1 and plan 2 with regard to maximum dose to the heart. However, minimum and mean doses to the heart showed a significant difference between the plans with plan 2 giving a higher minimum and mean dose.

- For right breast tumours mean dose to 33% of the heart was 1.87Gy from plan 1 and was 2.04Gy from plan 2. This was well within the tolerance dose of the heart.
- The maximum dose to the lung of the affected breast did not differ significantly between the two plans, but the minimum and mean doses did differ significantly with plan 2 giving the higher dose.
- Similarly the dose to 33% of the lung of the affected breast was significantly higher in plan 2 (13.69Gy) than in plan 1(10.29Gy). The volume of the affected lung receiving 45Gy was also significantly higher in plan 2 (11.04Gy) than in plan 1(7.23Gy). Although there was a statistically significant difference between the variables, both plans were acceptable from a clinically significant viewpoint and within the ICRU guidelines.
- The dose variability at reference point 3 for both plans showed a good result.
- The mean inhomogeneity at reference point 4 was 49.66Gy for plan 1 and 52.26Gy for plan 2. Although the results are statistically significant, clinically this was seen as a good result and within the limits of the ICRU recommendations.
- The mean inhomogeneity at reference point 5 was 49.43Gy for plan 1 and 52.63Gy for plan 2. Although the results are statistically significant, clinically this was seen as a good result and within the limits of the ICRU recommendations.
- The dose variability at reference point 6 for both plans showed a good result.

- The mean inhomogeneity at reference point 7 for plan 1 was 49.19Gy and for plan 2 was 50.92Gy. Although the results are statistically significant, clinically this was seen as a good result and within the limits of the ICRU recommendations.
- There was a highly significant difference between plan 1 and plan 2 with regard to maximum, minimum, and mean dose at the matchline. In all comparisons, plan 2 gave a higher dose than plan 1. Plan 2 on one of the participants generated a maximum hot spot of 116.2%.
- The minimum and mean doses at the axilla were statistically significantly different between the two plans. The minimum dose for plan 1 was 31.81Gy and for plan 2 was 45.95Gy. From a clinical viewpoint plan 1 was unacceptable as the minimum dose was too low. Plan 2 was also slightly low, not acceptable by ICRU recommendations, but possibly the best compromise in attempting to keep doses to the heart and lungs to the minimal. The mean doses were within the ICRU recommendations. However, there was no difference between the plans with respect to maximum dose at the axilla.
- All reference points mean doses were significantly lower than the reference value of 53.75Gy. Thus it was concluded that the plans were not over dosing.
- All reference points mean doses were significantly lower than the reference value of 47.5Gy. Thus it was concluded that the plans were not under dosing.

6.4 LIMITATIONS

The following aspects contributed to limitations during the research process:

- Elderly or obese participants presented a problem as the breast tended to fall laterally. This created great difficulty as it was impossible to include the entire breast without also including a large volume of lung tissue.
- The reproducibility of the set-up was also challenged for participants with large breasts and this resulted in the participants being re-simulated.
- Dose homogeneity within a large breast was difficult to obtain and therefore more planning time was allocated for the final plan.
- This study concentrated on the technical aspect only. The assessment of the clinical aspect will be a long term follow-up of at least ten years to evaluate survival rates.
- Fortunately, the research participants had their CT scans sponsored. Patients without a medical aid may find the cost implication of the CT scan a financial strain.
- The digitised planning method demonstrated that the use of the humeral head shielding was very close to the axillary nodes and in some cases resulted in under dosage to the nodes.
- Obese participants posed a problem on the CT scanner as the largest breast board angle that could be used was 12.5 degrees. Any angle higher than this meant that the participant was unable to enter into the gantry space. Lowering the angle was not the ideal solution as the steepness of the chest wall further complicated the planning process.

- Participants from Durban Oncology had to travel to Parklands Hospital for their CT scans.
- The absence of external lasers made the set-up very difficult therefore extra time was required for the CT scan.

6.5 FUTURE RESEARCH

This research should serve as a base for further studies and it is recommended that the following further research be undertaken:

- With left-sided breast tumours, it is often a difficulty with reducing the volume of heart in the field. One may consider introducing a heart block to reduce the dose to the heart. The use of a block may result in inadequate coverage of tissues that are high risk of harboring microscopic disease.
- The use of humeral head shielding resulted in inadequate dose to the axillary nodes. Further research could possibly investigate the use of an anterior supraclavicular humeral shield and omitting the posterior axillary humeral shield. Whether the dose to the axillary nodes will be adequate or not, is yet to be determined.
- The use of high energy photons for the posterior axillary field is also an area that needs investigation. The patient separation will possibly be a great contributing factor.
- For patients with smaller separation the omission of the posterior axillary field is an area that also needs investigation.

- This study was based on a technical aspect. The assessment of the clinical aspect will be a long term follow-up of at least ten years to evaluate survival rates.

This research has made the researcher aware of the many gaps and areas of unanswered questions in the management and treatment of patients with carcinoma of the breast.

Concluding Statements

This study has highlighted the importance of CT- based planning in the treatment of carcinoma of the breast. Precise definition of target volumes and nodal regions can minimize the dose to uninvolved areas. A knowledge of the depth of the supraclavicular and axillary nodes results in a plan of exceptional quality. The advantage of identifying the areas of inhomogeneity on the CT scans, means that the treatment plan may be adjusted accordingly.

It is imperative that each department draw up their own guidelines in terms of delineation of target volumes, in keeping with ICRU recommendations. The use of CT scans to achieve this has helped with precise definition and accurate treatment planning. The use of conformal therapy is also gaining momentum and will further improve the results. Conformal radiation therapy refers to the delivery of radiation which conforms in three dimensions to the shape of the defined target or targets while at the same time minimizes dose to normal tissues (Madu *et al.*, 2001).

The way forward from conformal radiation therapy is intensity-modulated radiation therapy (IMRT). It is a new technique for dose optimization and is expected to achieve better dosimetric results compared to those of standard planning. It is promising that IMRT should result in either the improvement of local disease control due to improved coverage of the tumour volume or reduced normal tissue dose while achieving the same tumour coverage (Madu *et al.*, 2001).

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APPENDICES

APPENDIX A(i)



Dr Dayle Hacking
Durban Oncology Center
Jan Smuts Highway

Dear Dr Hacking

REQUEST FOR PERMISSION TO CONDUCT STUDY

I am currently registered as a Masters student at the Durban Institute of Technology in the Department of Radiography. I would like to embark on a research project towards a Masters.in Radiography. I have already obtained a National Diploma in Radiography (Therapy), a Higher Diploma in Radiography (Therapy) and a B.Tech in Radiography (Therapy).

The proposed title of my project is: **A study is to evaluate CT-based treatment planning versus digitised image planning for carcinoma of the breast, using the four-field breast technique, in terms of the depth of supraclavicular and axillary nodes, the variability of the breast tissue and the dose inhomogeneity at the matchline.**

I intend selecting at least 30 patients for this study. This study is not structured to alter the course of treatment in any way. I intend assessing the technical aspect of treatment planning therefore my study will include only those patients referred to planning for four-field breast technique. I plan to commence the data collection in November this year and complete the process by September 2005.

I strongly believe that this study will benefit both the patients and the doctors in terms of expanding on the technique used to achieve optimal coverage of target volumes.

This study will provide the opportunity to evaluate the use of CT scans for treatment planning and bring the department in line with international practice. There will be no additional cost to the patient or the hospital.

I hereby apply for permission to undertake this research as it will include some of the patients referred to Durban Oncology Centre for radiotherapy treatment.

My proposal has been reviewed by the Department of Radiography and approved by the Research committee of the Faculty of Health Sciences, at the Durban Institute of Technology. Appropriate ethical approval has been obtained.

My research proposal is attached for your perusal.

Your support and permission (in writing) to perform this study at Durban Oncology Centre will be greatly appreciated.

Yours sincerely

Yogi Govender

1. Student

Mrs Y. Govender
B.Tech Radiography
Tel (H) : 031 - 4647521
(W) : 031 - 2424128
Cell : 0836323176
E-mail : jmurray@kzn.netcare.co.za
Signature : _____

2. Internal Supervisor

Ms Nalene Naidoo
B. Tech. Radiography (final year
completion:M.Tech)
Tel (H) : 031 – 5782125
(W) : 031 – 2042922
E-mail : NaleneN@dit.ac.za
Signature : _____

3. External Supervisor

Dr D. Hacking
M.B.Ch.B., F.F. Rad. T. (SA)
Tel (H) : 031 – 2087098
(W) : 031 - 2618221
E-mail : dayle@durbanoncology.co.za
Signature : _____

APPENDIX A(ii)



Dr Rob de Bruyne
Hopelands Cancer Center
Hopelands Road
Overport
Durban
4000

Dear Dr de Bruyne

REQUEST FOR PERMISSION TO CONDUCT STUDY

I am currently registered as a Masters student at the Durban Institute of Technology in the Department of Radiography. I would like to embark on a research project towards a Masters degree in Radiography. I have already obtained a National Diploma in Radiography (Therapy), a Higher Diploma in Radiography (Therapy) and a B. Tech in Radiography (Therapy).

The proposed title of my project is: **A study is to evaluate CT-based treatment planning versus digitised image planning for carcinoma of the breast, using the four-field breast technique, in terms of the depth of supraclavicular and axillary nodes, the variability of the breast tissue and the dose inhomogeneity at the matchline.**

I intend selecting at least 30 patients for this study. This study is not structured to alter the course of treatment in any way. I intend assessing the technical aspect of treatment planning therefore my study will include only those patients referred to planning for four-field breast technique. I plan to commence the data collection in November this year and complete the process by September 2005.

Dr D. Hacking (Radiation Oncologist) has offered me his support in supervising the project.

I strongly believe that this study will benefit both the patients and the doctors in terms of expanding on the technique used to achieve optimal coverage of target volumes.

This study will provide the opportunity to evaluate the use of CT scans for treatment planning and bring the department in line with international practice. There will be no additional cost to the patient or the hospital.

I hereby apply for permission to undertake this research as it will include patients referred by your practise to Parklands Hospital, Radiotherapy Department.

My proposal has been reviewed by the Department of Radiography and approved by the Research committee of the Faculty of Health Sciences, at the Durban Institute of Technology. Appropriate ethical approval has been obtained.

My research proposal is attached for your perusal.

Your support and permission (in writing) to perform this study at Parklands Hospital, Radiotherapy Department will be greatly appreciated.

Yours sincerely

Yogi Govender

1. Student

Mrs Y. Govender
B.Tech Radiography
Tel (H) : 031 - 4647521
(W) : 031 - 2424128
Cell : 0836323176
E-mail : jmurray@kzn.netcare.co.za
Signature : _____

2. Internal Supervisor

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(W) : 031 – 2042922
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Signature : _____

3. External Supervisor

Dr D. Hacking
M.B.Ch.B., F.F. Rad. T. (SA)
Tel (H) : 031 – 2087098
(W) : 031 - 2618221
E-mail : dayle@durbanoncology.co.za
Signature : _____

APPENDIX A(iii)



Dr Gregory Landers
Parklands Hospital
Overport
Durban
4000

Dear Dr Landers

REQUEST FOR PERMISSION TO CONDUCT STUDY

I am currently registered as a Masters student at the Durban Institute of Technology in the Department of Radiography. I would like to embark on a research project towards a Masters degree in Radiography. I have already obtained a National Diploma in Radiography (Therapy), a Higher Diploma in Radiography (Therapy) and a B. Tech in Radiography (Therapy).

The proposed title of my project is: **A study is to evaluate CT-based treatment planning versus digitised image planning for carcinoma of the breast, using the four-field breast technique, in terms of the depth of supraclavicular and axillary nodes, the variability of the breast tissue and the dose inhomogeneity at the matchline.**

I intend selecting at least 30 patients for this study. This study is not structured to alter the course of treatment in any way. I intend assessing the technical aspect of treatment planning therefore my study will include only those patients referred to planning for four-field breast technique. I plan to commence the data collection in November this year and complete the process by September 2005.

I strongly believe that this study will benefit both the patients and the doctors in terms of expanding on the technique used to achieve optimal coverage of target volumes.

This study will provide the opportunity to evaluate the use of CT scans for treatment planning and bring the department in line with international practice. There will be no additional cost to the patient or the hospital.

I hereby apply for permission to undertake this research as it will include patients referred by your practise to Parklands Hospital, Radiotherapy Department.

My proposal has been reviewed by the Department of Radiography and approved by the Research committee of the Faculty of Health Sciences, at the Durban Institute of Technology. Appropriate ethical approval has been obtained.

My research proposal is attached for your perusal.

Your support and permission (in writing) to perform this study at Parklands Hospital, Radiotherapy Department will be greatly appreciated.

Yours sincerely

Yogi Govender

1. Student

Mrs Y. Govender
B.Tech Radiography
Tel (H) : 031 - 4647521
(W) : 031 - 2424128
Cell : 0836323176
E-mail : jmurray@kzn.netcare.co.za
Signature : _____

2. Internal Supervisor

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completion:M.Tech)
Tel (H) : 031 – 5782125
(W) : 031 – 2042922
E-mail : NaleneN@dit.ac.za
Signature : _____

3. External Supervisor

Dr D. Hacking
M.B.Ch.B., F.F. Rad. T. (SA)
Tel (H) : 031 – 2087098
(W) : 031 - 2618221
E-mail : dayle@durbanoncology.co.za
Signature : _____

APPENDIX A(iv)



Mrs Joan Murray
Parklands Radiotherapy Manager
75 Hopelands Road
Overport
Durban
4000

Dear Mrs Murray

REQUEST FOR PERMISSION TO CONDUCT STUDY

I am currently registered as a Masters student at the Durban Institute of Technology in the Department of Radiography. I would like to embark on a research project towards a Masters degree in Radiography. I have already obtained a National Diploma in Radiography (Therapy), a Higher Diploma in Radiography (Therapy) and a B. Tech in Radiography (Therapy).

The proposed title of my project is: **A study is to evaluate CT-based treatment planning versus digitised image planning for carcinoma of the breast, using the four-field breast technique, in terms of the depth of supraclavicular and axillary nodes, the variability of the breast tissue and the dose inhomogeneity at the matchline.**

I intend selecting at least 30 patients for this study. This study is not structured to alter the course of treatment in any way. I intend assessing the technical aspect of treatment planning therefore my study will include only those patients referred to planning for four-field breast technique. I plan to commence the data collection in November this year and complete the process by September 2005.

Dr D. Hacking (Radiation Oncologist) has offered me his support in supervising the project. I strongly believe that this study will benefit both the patients and the doctors in terms of expanding on the technique used to achieve optimal coverage of target volumes.

This study will provide the opportunity to evaluate the use of CT scans for treatment planning and bring the department in line with international practice. There will be no additional cost to the patient or the hospital.

I hereby apply for permission to undertake this research using the planning equipment at Parklands Hospital, Radiotherapy Department and Durban Oncology Centre.

My proposal has been reviewed by the Department of Radiography and approved by the Research committee of the Faculty of Health Sciences, at the Durban Institute of Technology. Appropriate ethical approval has been obtained.

My research proposal is attached for your perusal.

Your support and permission (in writing) to perform this study at Parklands Hospital, Radiotherapy Department and Durban Oncology Centre will be greatly appreciated.

Yours sincerely

Yogi Govender

1. Student

Mrs Y. Govender
B.Tech Radiography
Tel (H) : 031 - 4647521
(W) : 031 - 2424128
Cell : 0836323176
E-mail : jmurray@kzn.netcare.co.za
Signature : _____

2. Internal Supervisor

Ms Nalene Naidoo
B. Tech. Radiography (final year
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(W) : 031 – 2042922
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Signature : _____

3. External Supervisor

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M.B.Ch.B., F.F. Rad. T. (SA)
Tel (H) : 031 – 2087098
(W) : 031 - 2618221
E-mail : dayle@durbanoncology.co.za
Signature : _____

APPENDIX A(v)



Mr Philip O' Ehley
Hospital Manager
Parklands Hospital
75 Hopelands Road
Overport
Durnan
4000

Dear Mr O'Ehley

REQUEST FOR PERMISSION TO CONDUCT STUDY

I am currently registered as a Masters student at the Durban Institute of Technology in the Department of Radiography. I would like to embark on a research project towards a Masters degree in Radiography. I have already obtained a National Diploma in Radiography (Therapy), a Higher Diploma in Radiography (Therapy) and a B. Tech in Radiography (Therapy).

The proposed title of my project is: **A study is to evaluate CT-based treatment planning versus digitised image planning for carcinoma of the breast, using the four-field breast technique, in terms of the depth of supraclavicular and axillary nodes, the variability of the breast tissue and the dose inhomogeneity at the matchline.**

I intend selecting at least 30 patients for this study. This study is not structured to alter the course of treatment in any way. I intend assessing the technical aspect of treatment planning therefore my study will include only those patients referred to planning for four-field breast technique. I plan to commence the data collection in November this year and complete the process by September 2005.

Dr D. Hacking (Radiation Oncologist) has offered me his support in supervising the project. I strongly believe that this study will benefit both the patients and the doctors in terms of expanding on the technique used to achieve optimal coverage of target volumes.

This study will provide the opportunity to evaluate the use of CT scans for treatment planning and bring the department in line with international practice. There will be no additional cost to the patient or the hospital.

I hereby apply for permission to undertake this research using the planning equipment at Parklands Hospital, Radiotherapy Department and Durban Oncology Centre.

My proposal has been reviewed by the Department of Radiography and approved by the Research committee of the Faculty of Health Sciences, at the Durban Institute of Technology. Appropriate ethical approval has been obtained.

My research proposal is attached for your perusal.

Your support and permission (in writing) to perform this study at Parklands Hospital, Radiotherapy Department and Durban Oncology Centre will be greatly appreciated.

Yours sincerely

Yogi Govender

1. Student

Mrs Y. Govender
B.Tech Radiography
Tel (H) : 031 - 4647521
(W) : 031 - 2424128
Cell : 0836323176
E-mail : jmurray@kzn.netcare.co.za
Signature : _____

2. Internal Supervisor

Ms Nalene Naidoo
B. Tech. Radiography (final year
completion:M.Tech)
Tel (H) : 031 – 5782125
(W) : 031 – 2042922
E-mail : NaleneN@dit.ac.za
Signature : _____

3. External Supervisor

Dr D. Hacking
M.B.Ch.B., F.F. Rad. T. (SA)
Tel (H) : 031 – 2087098
(W) : 031 - 2618221
E-mail : dayle@durbanoncology.co.za
Signature : _____

APPENDIX A(vi)



Mr Malcolm Beech
Hospital Manager
St Anne's Hospital
4000

Dear Mr Beech

REQUEST FOR PERMISSION TO CONDUCT STUDY

I am currently registered as a Masters student at the Durban Institute of Technology in the Department of Radiography. I would like to embark on a research project towards a Masters degree in Radiography. I have already obtained a National Diploma in Radiography (Therapy), a Higher Diploma in Radiography (Therapy) and a B. Tech in Radiography (Therapy).

The proposed title of my project is: **A study is to evaluate CT-based treatment planning versus digitised image planning for carcinoma of the breast, using the four-field breast technique, in terms of the depth of supraclavicular and axillary nodes, the variability of the breast tissue and the dose inhomogeneity at the matchline.**

I intend selecting at least 30 patients for this study. This study is not structured to alter the course of treatment in any way. I intend assessing the technical aspect of treatment planning therefore my study will include only those patients referred to planning for four-field breast technique. I plan to commence the data collection in November this year and complete the process by September 2005.

Dr D. Hacking (Radiation Oncologist) has offered me his support in supervising the project. I strongly believe that this study will benefit both the patients and the doctors in terms of expanding on the technique used to achieve optimal coverage of target volumes.

This study will provide the opportunity to evaluate the use of CT scans for treatment planning and bring the department in line with international practice. There will be no additional cost to the patient or the hospital.

I hereby apply for permission to undertake this research as some of the patients will be undergoing treatment at St Anne's Hospital, Radiotherapy Department.

My proposal has been reviewed by the Department of Radiography and approved by the Research committee of the Faculty of Health Sciences, at the Durban Institute of Technology. Appropriate ethical approval has been obtained.

My research proposal is attached for your perusal.

Your support and permission (in writing) to perform this study will be greatly appreciated.

Yours sincerely

Yogi Govender

1. Student

Mrs Y. Govender
B.Tech Radiography
Tel (H) : 031 - 4647521
(W) : 031 - 2424128
Cell : 0836323176
E-mail : jmurray@kzn.netcare.co.za
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2. Internal Supervisor

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completion:M.Tech)
Tel (H) : 031 – 5782125
(W) : 031 – 2042922
E-mail : NaleneN@dit.ac.za
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3. External Supervisor

Dr D. Hacking
M.B.Ch.B., F.F. Rad. T. (SA)
Tel (H) : 031 – 2087098
(W) : 031 - 2618221
E-mail : dayle@durbanoncology.co.za
Signature : _____



St Anne's Hospital

331 Burger Street, Pietermaritzburg • PO Box 595, Pietermaritzburg 3200, South Africa
Telephone: +27 (0) 33 897-5000 • Fax: +27 (0) 33 897-5001 • Website: <http://www.netcare.co.za>
P.R. No.: 5808197

20 December, 2004

Mrs Y Govender
9C Netley Place
QUEENSBURGH
4093

Dear Yogi

REQUEST FOR PERMISSION TO CONDUCT STUDY

I refer to the written request to conduct the research project towards your Master's Degree in Radiotherapy and hereby grant permission for you to conduct such research studies at the St Anne's Linac Joint Venture Radiotherapy Unit.

Kindly ensure that patient confidentiality protocols are adhered to at all times.

I wish you every success towards obtaining your Masters Degree.

Yours sincerely

MALCOLM BEECH
HOSPITAL GENERAL MANAGER

BP

cc Joan Murray



APPENDIX A(vii)



Mr Philip O' Ehley
Hospital Manager
Parklands Hospital
75 Hopelands Road
Overport
Durnan
4000

Dear Mr O'Ehley

I wish to express my gratitude to you for agreeing to sponsor the stationery for my research project.

The proposed title of my project is: **A study is to evaluate CT-based treatment planning versus digitised image planning for carcinoma of the breast, using the four-field breast technique, in terms of the depth of supraclavicular and axillary nodes, the variability of the breast tissue and the dose inhomogeneity at the matchline.**

Dr D. Hacking (Radiation Oncologist) has offered me his support in supervising the project. I strongly believe that this study will benefit both the patients and the doctors in terms of expanding on the technique used to achieve optimal coverage of target volumes.

My proposal is being reviewed by the Department of Radiography at the Durban Institute of Technology. I will forward my proposal and relevant documentation to you as soon as I obtain approval from the Durban Institute of Technology.

I feel quite confident that this study will justify the gain from the clinical outcome simply because if the patient data shows no significant statistical difference, then any numerical difference would be clinically important.

Your support is greatly appreciated.

Yours sincerely

Yogi Govender

1. Student

Mrs Y. Govender
B.Tech Radiography
Tel (H) : 031 - 4647521
(W) : 031 - 2424128
Cell : 0836323176
E-mail : jmurray@kzn.netcare.co.za
Signature : _____

2. Internal Supervisor

Ms Nalene Naidoo
B. Tech. Radiography (final year
completion:M.Tech)
Tel (H) : 031 – 5782125
(W) : 031 – 2042922
E-mail : NaleneN@dit.ac.za
Signature : _____

External Supervisor

Dr D. Hacking
M.B.Ch.B., F.F. Rad. T. (SA)
Tel (H) : 031 – 2087098
(W) : 031 - 2618221
E-mail : dayle@durbanoncology.co.za
Signature : _____

APPENDIX A(viii)



13 September 2004

Ms Karen McKenzie
Practice Manager
St Augustine X-ray Department
St Augustine Hospital

Dear Karen

REQUEST SPECIAL RATES FOR CT SCANS FOR RESEARCH

I am currently registered as a Masters student at the Durban Institute of Technology in the Department of Radiography. I would like to embark on a research project towards a Masters degree in Radiography. I have already obtained a National Diploma in Radiography (Therapy), a Higher Diploma in Radiography (Therapy) and a B. Tech in Radiography (Therapy).

The proposed title of my project is: **A study to evaluate the computerised tomography (CT) based treatment planning versus digitised image planning (standard planning technique) for carcinoma of the breast, using the four-field breast technique, in terms of the depth of supraclavicular and axillary nodes, the variability of the breast tissue and the dose inhomogeneity at the matchline.**

I intend selecting at least 30 patients for this study. This study is not structured to alter the course of treatment in any way. I intend assessing the technical aspect of treatment planning therefore my study will include only those patients referred to planning for four-field breast technique. I intend commencing with the data collection once I obtain approval from Durban Institute of Technology.

Dr D. Hacking (Radiation Oncologist) has offered me his support in supervising the project. I strongly believe that this study will benefit both the patients and the doctors in terms of expanding on the technique used to achieve optimal coverage of target volumes. From the literature review it is evident that those departments using CT-based planning have commented positively on its uses. This will mean that all breast patients for this technique, in the future, will require CT scans for the treatment planning.

I have a budget of R9 000-00 from the research department to include the CT scans as well as stationery. I would be very grateful to your practice if you

would consider a special rate for the scans to keep within the budget. I do realise that this creates a huge cost implication to your practice. The patients will not require contrast media and films to be printed. The scans have to be performed at 5mm intervals from level of sixth cervical to include the whole breast.

I am currently working on my proposal which has to be approved by the Research committee of the Faculty of Health Sciences, at the Durban Institute of Technology. Appropriate ethical approval will also be obtained. A copy of my research proposal will be available for your perusal once approved.

Your support in this study will be greatly appreciated.

Yours sincerely

Yogi Govender

Ph: 031-2424128 (W)

1. Student

Mrs Y. Govender
B.Tech Radiography
Tel (H) : 031 - 4647521
(W) : 031 - 2424128
Cell : 0836323176
E-mail : jmurray@kzn.netcare.co.za
Signature : _____

2. Internal Supervisor

Ms Nalene Naidoo
B. Tech. Radiography (final year completion:
M.Tech)
Tel (H) : 031 – 5782125
(W) : 031 – 2042922
E-mail : NaleneN@dit.ac.za
Signature : _____

3. External Supervisor

Dr D. Hacking
M.B.Ch.B., F.F. Rad. T. (SA)
Tel (H) : 031 – 2087098
(W) : 031 - 2618221
E-mail : dayle@durbanoncology.co.za
Signature : _____

LAKE, SMIT PARTNERS Inc.

SPECIALISTS IN DIAGNOSTIC RADIOLOGY

PR. No. 3805948 Reg. No. 2003/031449/21 Vat. No. 4100209818

Copy: Dr S Kidgell - Partner
Cheryl Weir - Accounts Manager.

20 September 2004

Dear Yogi,

YOUR REQUEST FOR ASSISTANCE FOR YOUR MASTERS THESIS.

The Partners have favourably considered your request for assistance in your Thesis on the benefits of four field breast planning.

As discussed, I confirm the following provisions:

1. PLANNING MODE - SCANNED ON PLANNING TABLE.
2. AP SCOUT OF CHEST FOR EACH PATIENT.
3. 5mm SLICES FROM C6/7 - +/- T12.
4. RADIOGRAPHERS TO PUSH IMAGES OVER THE NETWORK TO PARKLANDS ONCOLOGY.
5. TOTAL NUMBER OF PATIENTS = 30 (OVER +/- 1 YEAR)
6. ACCOUNTS TO BE SENT TO DIT - Yogi to supply details.
7. +/- 15 MIN PER SCAN REQUIRED - YOGI IN ATTENDANCE.
8. NO CONTRAST - NOT IV NOR ORAL
9. NO FILMS REQUIRED.
10. NO REPORT REQUIRED.

The cost for each CT scan as set out above will be R280.00. We wish you the very best of luck with your research.

Kind Regards



Karen McKenzie
Radiographic Manager

APPENDIX A(x)



Ms Karen McKenzie
Practice Manager
St Augustine X-ray Department
St Augustine Hospital

Dear Karen

I would like to express my gratitude to you and your practice for agreeing to scan the patients for my research at a reduced rate.

I feel quite confident that this study will justify the gain from the clinical outcome simply because if the patient data shows no significant statistical difference, then any numerical difference would be clinically important.

My proposal is being reviewed by the Department of Radiography at the Durban Institute of Technology. I will forward my proposal and relevant documentation to you as soon as I obtain approval from the Durban Institute of Technology.

Your support is greatly appreciated.

Yours sincerely

Yogi Govender

1. Student

Mrs Y. Govender
B.Tech Radiography
Tel (H) : 031 - 4647521
(W) : 031 - 2424128
Cell : 0836323176
E-mail : jmurray@kzn.netcare.co.za
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2. Internal Supervisor

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(W) : 031 - 2618221
E-mail : dayle@durbanoncology.co.za
Signature : _____



Mr Philip O'Ehley
Hospital Manager
Parklands Hospital
75 Hopelands Road
Overport
Durnan
4000

NIRESH BECHAN

Dear Mr O'Ehley

REQUEST FOR PERMISSION TO CONDUCT STUDY

I am currently registered as a Masters student at the Durban Institute of Technology in the Department of Radiography. I would like to embark on a research project towards a Masters degree in Radiography. I have already obtained a National Diploma in Radiography (Therapy), a Higher Diploma in Radiography (Therapy) and a B. Tech in Radiography (Therapy).

The proposed title of my project is: **A study is to evaluate CT-based treatment planning versus digitised image planning for carcinoma of the breast, using the 4-field breast technique, in terms of the depth of supraclavicular and axillary nodes, the variability of the breast tissue and the dose inhomogeneity at the matchline.**

I intend selecting at least 30 patients for this study. This study is not structured to alter the course of treatment in any way. I intend assessing the technical aspect of treatment planning therefore my study will include only those patients referred to planning for 4-field breast technique. I plan to commence the data collection in November this year and complete the process by September 2005.

Dr D. Hacking (Radiation Oncologist) has offered me his support in supervising the project. I strongly believe that this study will benefit both the patients and the doctors in terms of expanding on the technique used to achieve optimal coverage of target volumes.

This study will provide the opportunity to evaluate the use of CT scans for treatment planning and bring the department in line with international practice. There will be no additional cost to the patient or the hospital.


I hereby apply for permission to undertake this research using the planning equipment at Parklands Hospital, Radiotherapy Department and Durban Oncology Centre.

My proposal has been reviewed by the Department of Radiography and approved by the Research committee of the Faculty of Health Sciences, at the Durban Institute of Technology. Appropriate ethical approval has been obtained.

My research proposal is attached for your perusal.

Your support and permission (in writing) to perform this study at Parklands Hospital, Radiotherapy Department and Durban Oncology Centre will be greatly appreciated.

Yours sincerely



Yogi Govender

1. Student

Mrs Y. Govender
B.Tech Radiography
Tel (H) : 031 - 4647521
(W) : 031 - 2424128
Cell : 0836323176
E-mail : jmurray@kzn.netcare.co.za
Signature : _____

2. Internal Supervisor

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3. External Supervisor

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M.B.Ch.B., F.F. Rad. T. (SA)
Tel (H) : 031 – 2087098
(W) : 031 - 2618221
E-mail : dayle@durbanoncology.co.za
Signature : _____



Appendix A(xi)



9C Netley Place
Queensburgh
4093

04 January 2005

Ms Karen McKenzie
Radiographic Manager
St Augustine X-ray Department
St Augustine Hospital

Dear Karen

Re : Payment of CT scans for research project

I have consulted with my supervisor with regards to payment for the CT scans. Please have the accounts sent to :

Yogi Govender (Research Fund)
Parklands Hospital
Radiotherapy Department
75 Hopelands Road
Overport
Durban

I will submit the accounts to the Durban Institute of Technology on a monthly basis.

Your support in this study is greatly appreciated.

Yours sincerely

Yogi Govender

Ph : 031-2424128 (W)

APPENDIX B



INFORMED CONSENT

I, hereby voluntarily give consent to participate in the research titled:

A study is to evaluate CT-based treatment planning versus digitised image planning for carcinoma of the breast, using the four-field breast technique, in terms of the depth of supraclavicular and axillary nodes, the variability of the breast tissue and the dose inhomogeneity at the matchline.

Researcher : Mrs Y. Govender
Supervisor : Dr D. Hacking
Co-supervisor : Ms. Nalene Naidoo

Please circle the appropriate answer

1. Have you read and understood the information sheet?

Yes / No

2. Have you had the opportunity to ask questions?

Yes / No

3. Have you had an opportunity to discuss the study?

Yes / No

4. Who have you spoken to?

5. Have you received satisfactory answers to your questions?

Yes / No

6. Do you understand that you can withdraw out of the study at any time, without a reason?

Yes / No

7. Do you understand that should you withdraw from the study, your medical care or legal rights will not be affected?

Yes / No

8. Do you understand that there is no financial implication on you to participate in the study?

Yes / No

9. Do you understand and agree to voluntarily participate in the study?

Yes / No

10 Do you agree not to discuss this research project with any other individuals, except family members.

Yes / No

If you have answered No to any of the above, please obtain any necessary information before signing.

Name of Researcher

Date

Signature

Name of Participant:

Date

Signature

Name of Witness

Date

Signature

APPENDIX C



PARTICIPANT INFORMATION LETTER

I am a masters student at the Durban Institute of Technology and pursuing a research study in order to fulfil the requirements to complete a Masters degree.

The proposed title of my study is: **To evaluate CT-based treatment planning versus digitised image planning for carcinoma of the breast, using the four-field breast technique, in terms of the depth of supraclavicular and axillary nodes, the variability of the breast tissue and the dose inhomogeneity at the matchline.**

Before you decide whether to participate it is important for you to understand why the research is being done and what it will involve. If you do not wish to participate your medical care will not be affected in any way. Please take the time to read the following information carefully. Please ask if there is anything that is not clear or if you would like more information.

AIM OF THE STUDY

The aim of the study is to evaluate the benefits of CT scans in the treatment of carcinoma of the breast using the four-field technique.

PROCEDURE

Approval will be obtained from hospital managers, oncologists, ethics committee and the heads of departments prior to commencement of this study.

This study does not impact on your planned treatment prescription, You will be asked to sign a document to say that you fully understand the procedure and that you agree to participate in the study.

During the planning stages you will be requested to have a CT scan done at Entabeni Hospital X-ray Department. All arrangements will be made prior to the scan. The researcher will be present at the time of the scan. You will be positioned in the same position as when marked-up for the treatment on the simulator. You will not be exposed to any intravenous or oral contrast medium. The procedure will be approximately fifteen minutes and you will not experience any pain or discomfort during this time.

CONFIDENTIALITY

Your dignity and confidentiality will be respected at all times. All information recorded about you during the course of the study will be treated confidentially. The study will not harm you in any way. You have the right to request access to your personal data and, if needed, the right to request changes to any information that is not correct and/or is incomplete.

Information will be recorded on paper and on a computer database by the researcher. In agreeing to take part in this study you agree to this access to your records and for your data to be held on computer by the researcher.

BENEFITS

You will not be exposed to any risks by participating in this study. The implementation of CT scans for breast cancer will definitely provide more information to the doctors but the actual impact this will have on treatment technique will only be determined at the end of the study. The information may also be published. Confidentiality will be maintained at all times, no publication will refer to you by name, and it will not be possible to identify you.

RISKS AND DISCOMFORTS

The CT scan is an additional procedure that is required in order to collect the data. There will be no risks or discomforts from the CT scan. The benefits versus the risks are constantly being weighed. Your exposure to the scan in terms of dose limits will be kept as low as reasonably achievable.

COST

There will be no financial implications to you.

VOLUNTARY PARTICIPATION / WITHDRAWAL

Please understand that your decision to participate in this study is voluntary. Should you wish to withdraw as a participant, your treatment will not be compromised. You can withdraw out of the study at any time, without a reason.

ETHICS APPROVAL

You can be assured that confidentiality will be maintained at all times. The data will only be available to the researcher. Applications will be made to the ethics committees of the three hospitals and the ethics committee at the Durban Institute of Technology.

Should you have any queries, please do not hesitate to contact me.

Yogi Govender

B.Tech Radiography
Tel (H) : 031 - 4647521
(W) : 031 - 2424128
Cell : 0836323176
E-mail : jmurray@kzn.netcare.co.za
Signature : _____

2. Internal Supervisor
:M.Tech)

Ms Nalene Naidoo
B. Tech. Radiography (final year completion
Tel (H) : 031 – 5782125
(W) : 031 – 2042922
E-mail : NaleneN@dit.ac.za
Signature : _____

3. External Supervisor

Dr D. Hacking
M.B.Ch.B., F.F. Rad. T. (SA)
Tel (H) : 031 – 2087098
(W) : 031 - 2618221
E-mail : dayle@durbanoncology.co.za
Signature : _____

APPENDIX D

CLINICAL CHARACTERISTICS - DATA SHEET

(Required for treatment management of the carcinoma)

Participant code: _____

Age _____

Menopause:

Pre _____

Post _____

Unknown _____

Oestrogen receptor status

Positive _____

Negative _____

Unknown _____

Progesterone receptor status

Positive _____

Negative _____

Unknown _____

Location of primary tumour : _____

Surgery: Fine needle aspiration biopsy _____

Biopsy _____

Mastectomy _____

Lumpectomy _____

Histology : Tumour size _____

Lymph nodes removed _____

Positive nodes _____

Histological type _____

Tumour differentiation _____

Lymphatic invasion _____

Vascular invasion _____

Margins _____

Stage : **T** **N** **M**

Grade : _____

Chemotherapy : _____

Number of cycles _____

Hormonal therapy _____

APPENDIX E

DATA SHEET – PLAN PARAMETERS

RT / LT

	Plan 1	Plan 2
Supraclavicular nodes		
dose at ref point 1		
dose at ref point 2		
depth of 100% isodose		
Field separation at matchline centre		
Axillary nodes		
dose at ref point 1		
dose at ref point 2		
dose at ref point 3		
depth of 100% isodose		
Field separation at axillary field centre		
Breast tissue coverage		
100% of volume		
95% of volume		
90% of volume		
85% of volume		
80% of volume		
70% of volume		
60% of volume		
50% of volume		
% volume receiving 50Gy		
Field separation for breast or chest wall		
Matchline inhomogeneity		
Dose at ref point 1		
Dose at ref point 2		
Dose at ref point 3		
Dose at ref point 4		
Dose at ref point 5		
Maximum dose point – centre breast		
Minimum dose point - centre breast		
Mean dose - centre breast		
Maximum dose point - matchline		
Minimum dose point - matchline		
Mean dose - matchline		

Maximum dose – axilla centre		
Minimum dose – axilla centre		
Mean dose – axilla centre		
Maximum dose to heart		
Minimum dose to heart		
Mean dose to heart		
Dose to 1/3 of heart		
Maximum dose to lung (affected side)		
Minimum dose to lung (affected side)		
Mean dose to lung (affected side)		
Dose to 1/3 of lung (affected side)		
Maximum dose to lung (unaffected side)		
Minimum dose to lung (unaffected side)		
Mean dose to lung (unaffected side)		
Beam Energy		

APPENDIX F

DATA SHEET – SIMULATOR

(Parameters required in order to generate the digitised image plan)

Participant code: _____

Position
Level :+ Breast
Matchline
Axilla

	Inf B	Med B	Lat B	S/Clav	Axilla
Field size					
Gantry angle					180
Collimator angle		0	0	0	
Film distance					
Interfield distance					
Raise at offset					
Raise at midline					
Midline to offset					
Centre to centre					
Laser to laser					
Laser to breastboard surface					
Longitudinal table reading					

49.4. AMERICAN JOINT COMMITTEE ON CANCER STAGING OF BREAST CANCER

Tumor (T)

Rules for classifying the primary tumor (T) are the same for clinical and for pathologic classification. If the measurement is made by physical examination, the examiner will use the major headings (T1, T2, or T3). If other measurements, such as mammographic or pathologic measurements, are used, the subsets can be used. Tumors should be measured to the nearest 0.1-cm increment.

- Primary tumor cannot be assessed
- No evidence of primary tumor
- Carcinoma *in situ*

(CIS) Ductal carcinoma *in situ*

(CIS) Lobular carcinoma *in situ*

Paget's) Paget's disease of the nipple with no tumor

Paget's disease associated with a tumor is classified according to the size of the tumor.

Tumor 2 cm or less in greatest dimension

a Microinvasion 0.1 cm or less in greatest dimension

b Tumor more than 0.1 cm but not more than 0.5 cm in greatest dimension

c Tumor more than 0.5 cm but not more than 1 cm in greatest dimension

d More than 1 cm but not more than 2 cm in greatest dimension

e Tumor more than 2 cm but not more than 5 cm in greatest dimension

f Tumor more than 5 cm in greatest dimension

Tumor of any size with direct extension to chest wall[†] or skin, only as described below

g Extension to chest wall, not including pectoralis muscle

h Edema (including *peau d'orange*) or ulceration of the skin of the breast or satellite skin nodules confined to the same breast

i Both (T4a and T4b)

j Inflammatory carcinoma

Regional Lymph Nodes (N)

Regional lymph nodes cannot be assessed (e.g., previously removed)

No regional lymph node metastasis

Metastasis to movable ipsilateral axillary lymph node(s)

Metastasis to ipsilateral axillary lymph node(s) fixed or matted, or in clinically apparent^a ipsilateral internal mammary nodes in the absence of clinically evident axillary lymph node metastasis

Metastasis in ipsilateral axillary lymph nodes fixed to one another (matted) or to other structures

Metastasis only in clinically apparent^a ipsilateral internal mammary nodes and in the absence of clinically evident axillary lymph node metastasis

Metastasis to ipsilateral infraclavicular mammary lymph node(s) with or without axillary lymph node involvement, or in clinically apparent^a ipsilateral internal mammary lymph node(s) and in the presence of clinically evident axillary lymph node metastasis; or metastasis in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement

i Metastasis in ipsilateral infraclavicular lymph node(s)

j Metastasis in ipsilateral internal mammary lymph node(s) and axillary lymph node(s)

k Metastasis in ipsilateral supraclavicular lymph node(s)

Pathologic Classification (pN)

Regional lymph nodes cannot be assessed (e.g., previously removed or not removed for pathologic study)

No regional lymph node metastasis histologically, no additional examination for isolated tumor cells (ITC)

ITC are defined as single tumor cells or small cell clusters not greater than 0.2 mm, usually detected only by immunohistochemical (IHC) or molecular methods but which may be verified on hematoxylin-and-eosin stains. ITCs do not usually show evidence of malignant activity (e.g., proliferation or abnormal reaction).

(i-) No regional lymph node metastasis histologically, negative IHC

(i+) No regional lymph node metastasis histologically, positive IHC, no IHC cluster greater than 0.2 mm

(mol-) No regional lymph node metastasis histologically, negative molecular findings [reverse transcriptase polymerase chain reaction (RT-PCR)]

(mol+) No regional lymph node metastasis histologically, positive molecular findings (RT-PCR)

Metastasis in 1 to 3 axillary lymph nodes, and/or in internal mammary nodes with microscopic disease detected by sentinel lymph node dissection but not clinically apparent^b

mi Micrometastasis (greater than 0.2 mm, none larger than 2.0 cm)

a Metastasis in 1 to 3 axillary lymph nodes

b Metastasis in internal mammary nodes with microscopic disease detected by sentinel node dissection but not clinically apparent^c

c Metastasis in 1 to 3 axillary lymph nodes and in internal mammary lymph nodes with microscopic disease detected by sentinel lymph node dissection but not clinically apparent^c (If associated with greater than 3 positive axillary lymph nodes, the internal mammary nodes are classified as pN3b to reflect increased tumor burden.)

Metastasis in 4 to 9 axillary lymph nodes, or in clinically apparent^b internal mammary lymph nodes in the absence of axillary lymph node metastasis

a Metastasis in 4 to 9 axillary lymph nodes (at least one tumor deposit greater than 2.0 mm)

b Metastasis in clinically apparent^b internal mammary lymph nodes in the absence of axillary lymph node metastasis

Metastasis in 10 or more axillary lymph nodes, or in infraclavicular lymph nodes, or in clinically apparent^b ipsilateral internal mammary lymph nodes in the presence of 1 or more positive axillary lymph nodes; or in more than 3 axillary lymph nodes with clinically negative microscopic metastasis in internal mammary lymph nodes or in ipsilateral supraclavicular lymph nodes

ia Metastasis in 10 or more axillary lymph nodes (at least one tumor deposit greater than 2.0 mm), or metastasis to the infraclavicular lymph nodes

ib Metastasis in clinically apparent^b ipsilateral internal mammary lymph nodes in the presence of 1 or more positive axillary lymph nodes; or in more than 3 axillary lymph nodes and in internal mammary lymph nodes with microscopic disease detected by sentinel lymph node dissection but not clinically apparent^c

ic Metastasis in ipsilateral supraclavicular lymph nodes

Metastasis (M)

Metastasis cannot be assessed

No distant metastasis

Metastasis

Clinically apparent is defined as detected by imaging studies (excluding lymphoscintigraphy) or by clinical examination or grossly visible pathologically.

Clinically apparent is defined as detected by imaging studies (excluding lymphoscintigraphy) or by clinical examination.

Clinically apparent is defined as not detected by imaging studies (excluding lymphoscintigraphy) or by clinical examination.

Steele FL, Page DL, Fleming ID, et al., eds. *AJCC cancer staging manual*, 6th ed. New York: Springer-Verlag, 2002:227-228, with permission.