

Chapter Three

Materials and Methods

The study was conducted at Khartoum oncology hospital (RICK) .The study conducted from 2014 to 2017 . The rationale for this study is to development tools to assessment and evaluation patient with late stage breast cancer in symptoms control by using symptoms improvement ratio (SIR) to evaluate benefit of Radiotherapy in palliative cases, what is mean by this is that now, in principle it is possible to evaluate the radiotherapy protocol by using simple and fast tools such as questionnaire ,clinical fellow upetc

In the past there were no clear role of radiotherapy in palliative care ,the oncologist controlled the pain and other symptoms by using the chemotherapy drug which increase the body toxicity with uncountable response in area of metastatic .

The main objective of this study is study of radiation therapy treatment effect of palliative metastatic breast cancer using concept symptoms improvement ratio such as Pain response ,improve the quality of life and toxicity .

3.1 Materials

3.1.1 Planning Material :

3.1.1.1. Conventional simulator 2D

A fluoroscopy of patient by using simple planning with two image AP/PA -LAT view of patients to detect the patient separation

the images were performed using two type of machine (Hustise Castter unit , Terasix UPJ machine) .the patients were planning depended on area of metastic .

Some cases were planning manual depending on previous patients images and anatomical land mark .



Figure 3-1 Planning Machine used in Thesis

3.1.2 Treatment Units:

3.1.2.1 Cobalt 60 (EQUINOX-Terabalt)

The cobalt-60 sources are used in many market and product segments. The major application is in the health care industry where irradiators are used to sterilize single use medical products. The medical products are circulated through the shielded room and exposed to the cobalt-60 sources. This treatment sterilizes the medical products which can then be shipped to hospitals for immediate use **Cobalt-60 machine components:** A typical cobalt machine consists of: Stand , Gantry , Source head , Beam stopper , Couch , Control console (Radiation Oncology Physics 2005)

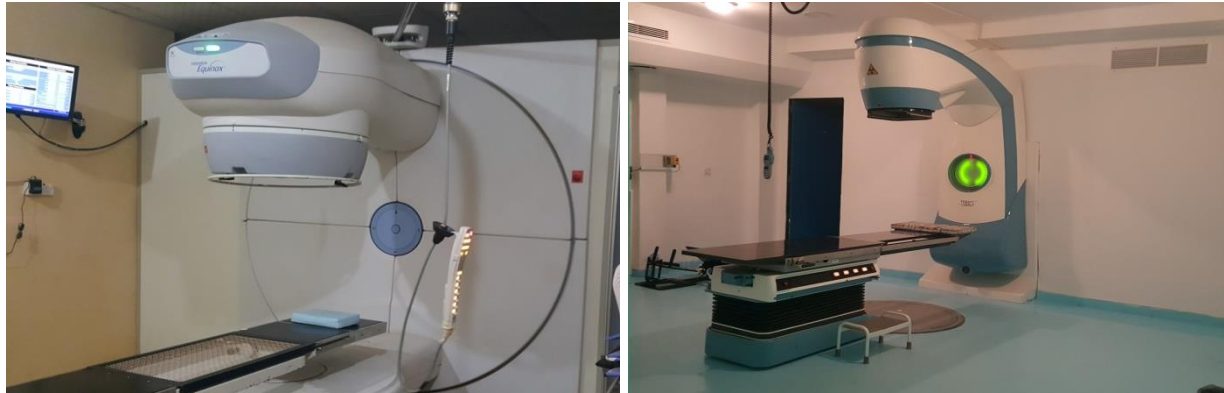


Figure 3-2 Cobalt 60 Machine used in thesis

3.1.2.2 Linear Accelerator (LINEAC)

The linear accelerator is the radiation therapy treatment machine. The linear accelerator also features the revolutionary IMRT (Intensity Modulated Radiation Therapy), a powerful tool in the fight against cancer. IMRT delivers a more precise dose of radiation to the tumor while protecting outlying tissue.

Medical linacs are cyclic accelerators that accelerate electrons to kinetic energies from 6 to 25 MeV using non-conservative microwave RF fields in the frequency range from 103 MHz (L band) to 104 MHz (X band), with the vast majority running at 2856 MHz band linear accelerator with 80 MLC.

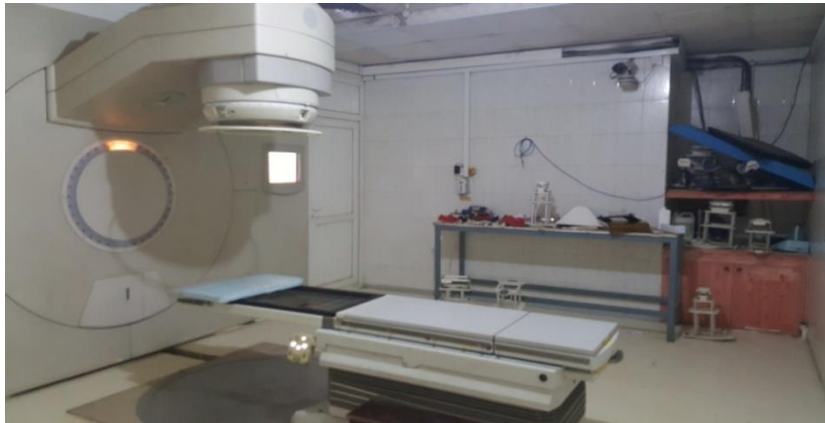


Figure 3-3 Linear accelerator Machine used in thesis

3.1.3 Treatment Planning System (TPS) Pinnacle3

fast ,accurate and interactive treatment planning tools have made Philips pinnacle 3 radiation treatment planning system in performance and reliability .pinnacle3 powerful visualization tools are evident in the crisp volumetric rendering of the image displayed volumetric rendering is ability to compute and render all the image information in the image data set available .

plan modification and optimization -isodose curves ,3D dose clouds and dose volume histogram (DVH) are update real time as beam weight ,treatment prescription or normalization points are modified .

3.1.4 Other tools :

- Personal computer with Intel Core i5 at MHz ,8G RAM ,1TB HDD 64 CD - DVD Drive ,windows 8
- hp printer and scanner
- SPSS version 13

3.2 Methods

3.2.1 Sampling The study include 100 patients date was brought from Khartoum oncology hospital (RICK) for specific purpose of acquiring date for this study .the date taken from patient

3.2.2 Study Design

it is analytical study where the data collected prospectively .which was amongst the metastatic breast cancer patients in Sudan. Study of radiotherapy regimes for the treatment of in patients with MBC. A study schema is shown in Figure 3-4

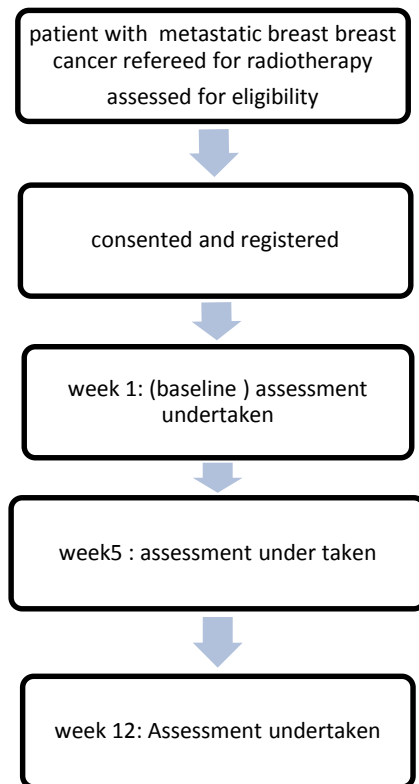


Figure 3-4 Study design

More frequent patient improvement assessments were considered to help identify the optimal time to assess response. Evaluate the radiation dose, dose distribution for palliative cases in both linear and Cobalt-60

3.2.2.1 Pre study assessment

One of the challenges of conducting a study examining a pain intervention in patients with advanced cancer is that changes in analgesia may occur during the study period. In such cases, it becomes very difficult to disentangle any improvements in pain as a result of the study intervention from any changes in concomitant analgesia. One of the ways this can be addressed is by stabilizing pain and analgesia prior to study entry. This approach was adopted for potential

Patients in this study. Prior to study consent, patients were reviewed by Drs. Nahla gaffer and Dr Mohaga (Palliative Medicine), often with multiple visits or telephone consultations over several weeks, enabling background analgesia to be optimized and pain stabilized, where possible, before study entry. This also resulted in some patients' analgesia improving to the extent that their pain was no longer severe enough for study entry. Following optimization of analgesics, if patients were eligible, written informed consent was obtained. Study assessments and time points are outlined in Table 3-1.

3.2.3 Baseline visit

At the baseline visit, an assessment of performance status was made along with a physical examination. All previous treatments for Metastatic breast cancer MBC – surgery, chemotherapy or radiotherapy - were documented along with the medication history which listed all medicines taken in the previous 24 hours. Baseline toxicity

assessment was performed and all study questionnaires were completed. In order to improve compliance, rather than leaving the patient to complete the questionnaires, a researcher completed the questionnaires based on the answers received from the patient.

Take blood samples from patients at baseline and week 12. The aims of these blood tests were twofold. The first aim was to explore the possibility that proteins could be identified which might help to predict a response to radiotherapy. The second aim was to explore the possibility of toxicity due to radiotherapy.

3.2.4 Week 1 visit

Patients were seen eight (+/-three) days after the start of radiotherapy for their week 1 visit. At this consultation, current medication was recorded, including analgesics in the past 24 hours. Any toxicity from radiotherapy was documented and the questionnaires were repeated. Current symptoms were documented. Following the week 1 visit, patients received weekly phone calls in order to monitor symptoms and assess analgesic requirements.

3.2.5 Week 5 visit

Patients were seen 35 (+/-5) days from the start of radiotherapy. At this visit, all the study visits performed at week 1 were repeated. In addition.. However, if patients were unable to attend, efforts were made to see them at home. After the week 5 visit, the weekly phone calls continued until the week 12 visit.

3.2.6 Week 12 visit

At the week 12 visit, all assessments undertaken at week 5 were repeated.. Following this visit, patients were discharged back to their local oncology teams and study involvement ceased. During the course of the study, if patients' analgesia required to be altered, this was done as per usual clinical practice

3.3. Patient

3.3.1 Inclusion criteria

1. ≥ 18 years of age
2. Histological or MBC diagnosis* of breast carcinoma
3. Able to complete study assessments
4. Life expectancy of at least 3 months based on clinical judgment
5. ECOG Performance Status 0-2
6. Worst pain $>4/10$ (0-10 Numeric rating scale) corresponding to the index site.

3.3.2 Exclusion criteria

1. Received chemotherapy or radiotherapy in the preceding six weeks
2. Planned chemotherapy during the period of the study that is likely to alter pain during the course of the study
3. Psychotic disorders or cognitive impairment
4. Co-existing lung tumors at the time of study entry
5. Pregnancy or breastfeeding. Likely to alter pain at the index site during the duration of the study

3.3.3 Sample Size and Type:

The study included 100 patients (appendix A) Patients data was brought from (Khartoum oncology hospital (RICK), Data was taken from patients questionnaires pre radiotherapy, week 1,5,12

The patient were female patients which diagnosis with MBC and the tumor spread and cause specific symptoms. The e median age (IQR) was 45 (35-55) years.

The 100 patients were treated in metastatic area with radiotherapy treatment as localized treatment to control the symptoms, 70 % Treatment in LINEAC, and 30% in cobalt 60.

3.4. Method of Data Collection:

3.4.1 Questionnaires:

3.4.1.1 Brief Pain inventory (BPI)

All questionnaires utilized in this study are attached in Appendix.

The BPI is a multi-dimensional pain assessment tool. It was designed to serve two purposes; to measure the intensity of pain and to assess the level of interference of pain on daily function. It was developed for use in cancer patients and has been extensively validated in both cancer and non-cancer patients (Cleeland, C.S. 1994 - Portenoy, R.K1999)

All questions in the BPI relate to the previous 24 hours. The section on pain intensity asks the worst, least and average pain as well as the pain right now. Subjects are asked to score each answer from 0-10 where 0 is “no pain” and 10 is “pain as bad as you can imagine”. It also asks the participant to rate the percentage of pain relief they

experience from whatever pain treatments or medications they are currently on, ranging from 0-100.

The second section of the BPI focuses on the level of interference of pain on the subject's lifestyle, namely their general activity, mood, walking ability, normal work, relations with other people, sleep and enjoyment of life. Again the scores are from 0-10 with 0 corresponding to "does not interfere" and 10 representing "completely interferes" with each question that has been asked.

Once the questionnaire has been completed, the total BPI score can be calculated and repeated to assess the impact of an intervention on the subject's pain. For the study, the total score at baseline was calculated. A pain response was taken as a 30% drop in BPI score from the baseline assessment (Portenoy, R.K1999)

3.4.1.2 Short form McGill Pain Question (SF-MPQ)

The MPG is a scale for assessing pain using verbal descriptors. It was designed to allow patients to express the intensity and quality of their pain (Melzack, R.,1975) . A short form version was developed in 1987(Melzack,1987) ., In 2009, this was further modified in order to develop a single measure for both neuropathic and non-neuropathic pain.(Dworkin, R.H2009), Amongst other purposes, it was planned that this questionnaire, SF- MPQ2, could be used in treatment response studies

3.4.1.3 lead Assessment of Neuropathic symptoms and sign (LANSS)

The LANSS was developed in 2001 as a tool to identify patients who are likely to have neuropathic pain (Bennett, M2001) .,It has been extensively validated (Kaki,

A.M2005- Yucel, A.,2004) .The assessment consists of two sections; a pain questionnaire and sensory testing. In the pain questionnaire, subjects are asked five yes/no questions concerning their pain. With the sensory testing, the subject is examined for allodynia and for altered pin-prick threshold. Combining the scores for the questionnaire and the sensory testing gives a maximum score of 24. A score of >12 suggests that neuropathic mechanisms are likely to be contributing to the patient's pain, whereas a score of <12 suggests that neuropathic mechanisms are unlikely to be contributing to the patient's pain.

3.4.1.4 Quality of Life Questionnaire (EORTC QLQ-C30)

The EORTC QLQ-C30 is a validated questionnaire designed to assess the quality of life of cancer patients(Aaronson, N.K2003).It incorporates nine multi-item scales: five functional scales (physical, role, cognitive, emotional and social); three symptom scales (fatigue, pain, and nausea and vomiting); and a global health and quality- of-life scale.

As can be seen in the paragraphs above, with the exception of the NRS for night sweats, all of the questionnaires used in the study have been validated. The first step in the validation process involves a questionnaire being reposed as a potential way of measuring a symptom, e.g. pain. The validation comes when the questionnaire is tested on a different set of patients and similar results are obtained.

3.4.1.5 APAC African IPOS Questionnaire:

Is a validated questionnaire designed to assess the pain of cancer patients the pain rate from 0 = no pain to 5= worst during last three day divided to two sections one complete by patients and the other complete by his family .

	Baseline	Week1	Week5	Week12
Day	1	8+/- 3 days	35+/-5 days	84+/-5
Informed consent	×			
vital signs	×	×	×	×
Medical history	×	×	×	×
Treatment history	×	×	×	×
Physical examination	×	×	×	×
Toxicity assessment	×	×	×	×
Study questionnaires	×	×	×	×
Brief pain inventory	×	×	×	×
LANSS	×	×	×	×
MPQ	×	×	×	×
EORT QLQC30-31	×	×	×	×
APAC-IOPS	×	×	×	×

Table 3-1 Study Assessment

3.5. Data Analysis Method :

The data was analyzed by using statistical package .Statistical Package for social Studies (SPSS) under window using t -test and cross -correlation test measure the pain response, toxicity and QOL

3.5.1. Study Endpoints

3.5.1.1. Primary

As the primary aim of the prospective study was to examine if radiotherapy is an effective treatment for MBC, the primary endpoint was to assess if there was a clinically significant improvement in pain 5 weeks following radiotherapy. A clinically significant improvement in pain was defined as a > 30% reduction from baseline in total BPI score (Portenoy, R.K., 2003)

3.5.1. 2. Secondary

There were a large number of secondary endpoints, all of which were exploratory in nature. The rationale for this was to inform future randomized studies examining radiotherapy in MBC. Endpoints were assessed at weeks 1, 5 and 12 weeks post radiotherapy with the primary analysis at week 5, unless otherwise stated.

Secondary endpoints were as follows:

To examine the effect of radiotherapy on pain at weeks 1 and 12 post radiotherapy, assessed using the BPI. A clinically significant improvement in pain was defined as a > 30% reduction from baseline in total BPI score (Cleeland, C.S.1994)

To examine the effect of radiotherapy on quality of life using the EORTC QLQ- C30 questionnaire (version 3.0) including lung cancer module EORTC QLQ-LC13 [135]

3.5.2 Primary End point:

The researcher assessment the patient in(week 5) , 86 patients were evaluate. The primary endpoint, based on an intention to treat analysis . who had a clinically significant improvement in pain 5 weeks post radiotherapy

3.5.2 Secondary end point :

At this point (week 12) the researcher correspond the radiotherapy treatment role in symptoms controlled with pain response ,improve of Quality of life was measured by the patient-completed EORTC Core Quality of Life Questionnaire (QLQ-C30 version 2) Improvement was defined as a change in reported baseline symptom levels from moderate or severe (67–100 points) to none or little (0–33 points) , Control of symptoms was defined as stable symptom levels between 1 and 33 points, while prevention of symptoms was assumed when patients did not report symptoms during the study period. A similar approach was used for the global QoL scale. Here, four score level ranges were defined: 0–24, 25–49, 50–74 and 75–100, with 0 being the worst and 100 the best possible score. and toxicity the patients underwent clinical examination with an evaluation of PS, weight and blood tests. Local investigators recorded nadir values of haemoglobin, leucocyte and platelet counts, the number of transfusions, leukopenic infections, thrombocytopenic bleedings, events of phlebitis during the study treatment period and hospital admissions due to

chemotherapy side effects. all this result will analysis according to symptoms improvement ration

3.6 Date storage method :

- In the researcher personal computer(PC)
- In the treatment planning system hard disk pinnical3
- Personal information keep safe and secret

3.7 Ethical Issue :

- Permission of radiotherapy department has been granted
- No patient data will be published
- Permission of physics department has been granted
- Permission of statistic department has been granted