



# Study of Radiation Therapy Treatment Effect of Palliative Metastatic Breast Cancer (PMBC) using Symptoms Improvement Ratio

Lara Abdelmunim I Abdelrahman\*, Mohamed E Gar Elanabi and Nahla Gafer

College of Medical Radiological Science, Sudan university of Science and Technology, Khartoum, Sudan

\*Corresponding author: Lara Abdelmunim I Abdelrahman, College of Medical Radiological Science, Sudan university of Science and Technology, Khartoum, Sudan

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## Abstract

The study examined the association between Palliative radiotherapy and the improvement of the symptoms associated with metastatic breast cancer. These include metastatic in the spinal cord and associated pain, brain metastases and associated symptoms, bone metastases, Metastatic in the lung and finally spread in organs such as liver and others. The study also dealt with the connection between it and the improvement of the standard of life of the patient and toxic and other important factors and was achieved through a set of international standards questionnaire by which the calibration of the result. The value of radiotherapy for palliation is well known to oncologists but not necessarily to other physicians. Using terms such as symptom improvement ratio (SIR) than traditional response rates might be more appropriate in describing the benefits of palliative radiotherapy to other health care professionals. Late detection and spread of the disease in the late stages of breast cancer due to proliferation causes multiple symptoms this study was conducted in the centre of tumours treatment in Sudan, represented in Khartoum oncology Hospital (RICK) in the period 2014 to 2017. The findings support the hypothesis that radiotherapy is an effective treatment for a proportion of patients with MBC related pain, with 35% of assessable patients experiencing a clinically meaningful improvement in their pain. Of these, 12.5% had a complete improvement in their pain. There were no specific features that differentiated the complete responders from the other patients. Though this may be due to the small number of complete responders. There was no association between pain response and improvement in any other symptoms, therefore, palliative radiotherapy in MBC should only be considered for pain control.

**Keywords:** Palliative radiotherapy; Symptoms improvement; Metastatic breast cancer; Pain control

## Introduction

Breast cancer is the most frequently diagnosed cancer (23% of total cancer cases) and the leading cause of death (14% of deaths), in females, worldwide [1]. According to the Globocan 2008 estimates, approximately 1.37 million women are diagnosed with breast cancer per year. In Sudan breast cancer is the most common case. Table 1 shows the frequency % of the breast Cancer from January 2014 to December 2017 in radiation isotopes centre of Khartoum.

Metastatic breast cancer is also classified as Stage 4 breast cancer. The cancer has spread to other parts of the body. This usually includes the lungs, liver, bones or brain [2]. The spread of cancer usually happens through one or more of the following steps:

**Table 1:** Shows the frequency % of the breast Cancer from January 2014 to December 2017 in radiation isotopes centre of Khartoum.

| Year | Number of patients | Percentage |
|------|--------------------|------------|
| 2014 | 1236               | 17         |
| 2015 | 1247               | 16         |
| 2016 | 1229               | 15         |
| 2017 | 1404               | 20         |

a. Cancer cells invade nearby healthy cells. When the healthy cell is taken over, it too can replicate more abnormal cells.

b. Cancer cells penetrate into the circulatory or lymph system. Cancer cells travel through the walls of nearby lymph vessels or blood vessels.

c. Migration through circulation. Cancer cells are carried by the lymph system and the bloodstream to other parts of the body.

d. Cancer cells lodge in capillaries. Cancer cells stop moving as they are lodged in capillaries at a distant location and divide and migrate into the surrounding tissue.

e. New small Tumours grow. Cancer cells form small Tumors at the new location (called micro metastases) (Table 2).

**Table 2:** Stages and Classifications of breast cancer.

| Stage       | TNM Classifications                 |
|-------------|-------------------------------------|
| Stage 0:    | in situ breast cancer - Tis, N0, M0 |
| Stage I:    | T1, N0, M0                          |
| Stage IIa:  | T0-1, N1, M0, or T2, N0, M0         |
| Stage IIb:  | T2, N1, M0, or T3, N0, M0           |
| Stage IIIa: | T0-2, N2, M0, or T3, N1-2, M0       |
| Stage IIIb: | T4, N (any), M0, or T(any), N3, M0  |
| Stage IV:   | T(any), N(any), M1                  |

### Palliative Radio Therapy for Metastatic Breast Cancer

About 34–50% of patients receiving radiotherapy are of palliative intent (Janjan N, 2008). Similar to other clinical domains, the practice of palliative radiotherapy is always guided by basic ethical principles and available clinical evidence. It requires sophisticated assessment to balance the potential benefits and burdens to the patients with respect to patient’s autonomy and expectations, and consideration of logistical factors Palliative radiotherapy is mainly indicated to relieve various local symptoms in cancer patients; to prevent debilitation such as spinal cord compression and pathological fracture; and to achieve durable loco regional control (Wong K 2004) (Table 3). The effectiveness has been confirmed by cumulative clinical evidence.

**Table 3:** Indication of palliative radiotherapy.

|   |
|---|
| <b>Pain relief:</b><br>Metastatic bone pain<br>Painful lymphadenopathy<br>Pain due to soft tissue infiltration by cancers<br>Neuropathic pain due to nerve compression and infiltration |
| <b>Rescue of neurological deficit</b><br>Spinal cord compression<br>Brain metastases  |
| <b>Relief of pressure symptoms</b><br>Thoracic tumours:<br>SVCO<br>Upper airway obstruction<br>Dysphagia<br>Collapse of lung  |
| <b>Reduced the increased intracranial pressure secondary to brain metastases</b><br>Retroperitoneal tumours<br>Relief of hydronephrosis   |
| <b>Pelvic tumours</b><br>Relief of hydronephrosis<br>Urinary retention<br>Intestinal obstruction  |
| <b>Control of fungation and ulceration of metastatic or primary skin cancers</b>  |
| <b>Haemostasis:</b><br>Haemoptysis<br>Bleeding rectal or gynaecological cancers<br>Bleeding skin cancers  |
| <b>Prophylaxis of impending symptoms</b><br>Prevention of spinal cord compression<br>Prevention of pathological fracture<br>Prevention of pending pressure symptoms                     |
| <b>Durable control of advanced locoregional disease beyond cure.</b>  |

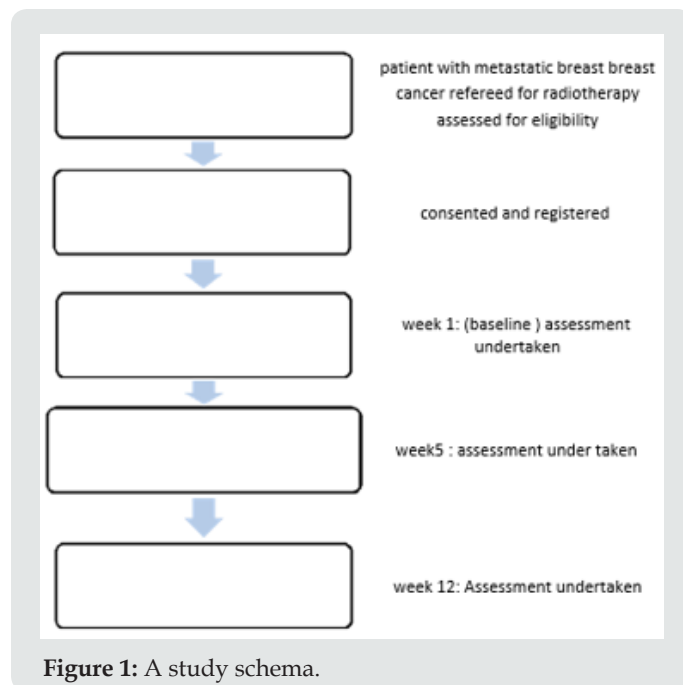
### Principle of Palliative Radiotherapy

The intention of giving radiotherapy for palliation of symptoms is improvement in quality of life by decreasing or eradicating symptoms. This will not be achieved if the treatment itself induces a lot of side effects. Also, patients with metastatic cancer have a reduced life span, this may only be months, and therefore the treatment itself should not consume a major portion of the patients remaining lifespan. The major benefit of radiotherapy is the speed with which symptom improvement develops and the certainty of response. Sufficient radiation dose must be given to ensure that the symptom response will last for the rest of the patient’s life. Too low a dose means retreatment at some later time is needed.

Hence guiding principles are:

1. Accurate anatomical localization of the symptomatic tumour deposit.
2. Simple treatment techniques and field arrangements.
3. Short hypo fractionated treatment regimes.
4. Moderate dose treatment to achieve a good predictable response and to keep treatment toxicity to a minimum.
5. Consider the patient’s overall life expectancy when determining the treatment aims and treatment duration.

### Materials and Methods



**Figure 1:** A study schema.

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 RT 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 follow up. The patients were planning and treatment by 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 Metastatic. Some cases were planning manual depending on previous patients' images and anatomical land mark. The patient was treating in both cobalt 60 unit or linear accelerator unit. 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 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. 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. 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. 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 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.

### Questionnaires: Brief Pain Inventory (BPI)

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 [3,4] 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 [4].

### Short Form Mc Gill 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 [5]. A short form version was developed in 1987 [6]. In 2009, this was further modified in order to develop a single measure for both neuropathic and non-neuropathic pain. [7] Amongst other purposes, it was planned that this questionnaire, SF-MPQ2, could be used in treatment response studies 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 [8]. It has been extensively validated [9,10]. 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 allaying 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 (Table 4).

**Table 4:**

| Symptoms                  | Patient group | Average low SIR | High point in base line | Low point in base line | Average high SIR |
|---------------------------|---------------|-----------------|-------------------------|------------------------|------------------|
| Partial bone pain relief  | B             | 70              | 100                     | 0                      | 90               |
| Complete bone pain Relief | B             | 28              | 100                     | 0                      | 80               |
| Relief chest pain         | D             | 59              | 100                     | 0                      | 86               |
| Brain metastatic          | C             | 50              | 100                     | 0                      | 70               |
| Spinal cord compression   | A             | 64              | 100                     | 0                      | 73               |

**Quality of Life Questionnaire (EORTC QLQ-C30): The EORTC**

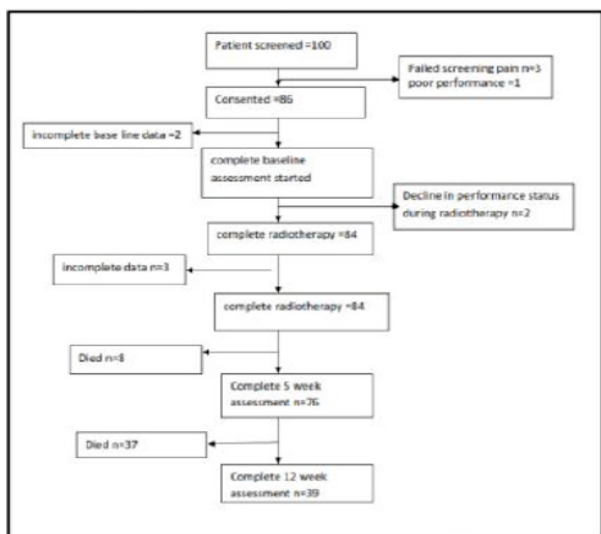
QLQ-C30 is a validated questionnaire designed to assess the quality of life of cancer patients [10]. It incorporates nine multi-item scales: five functional scales (physical, role, cognitive, emotional and social); three symptom scales (fatigue, pain, and nausea and vomiting); and a global health and 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 (Table 5).

**Table 5:**

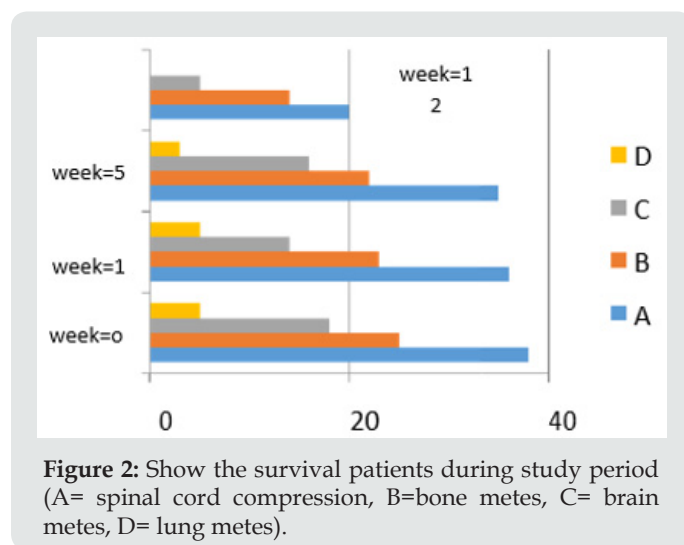
| Metastatic site    | Code | Frequency |
|--------------------|------|-----------|
| Spinal compression | A    | 38        |
| Bone Metastatic    | B    | 25        |
| Brain metes        | C    | 18        |

**The Results**

**Table 6:** Shows cancer Metastatic site for patients’ evaluation in this study.



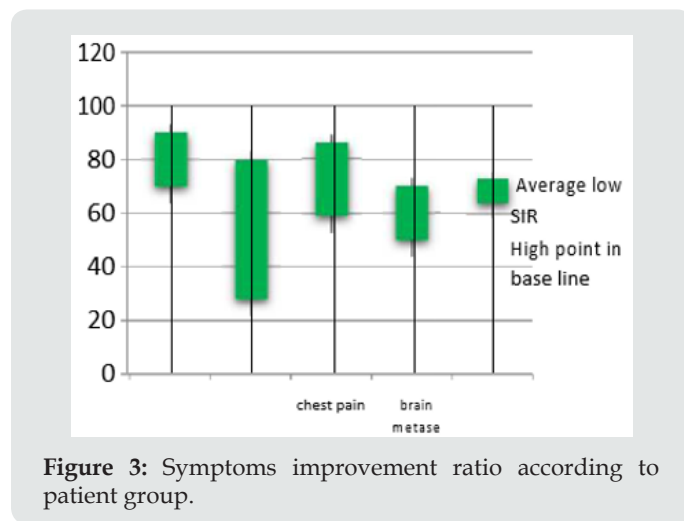
Thirty-nine patients returned completed questionnaires (of 100 expected, deceased patients excluded) during the initial 12 weeks study period (Table 6) (Figure 2).



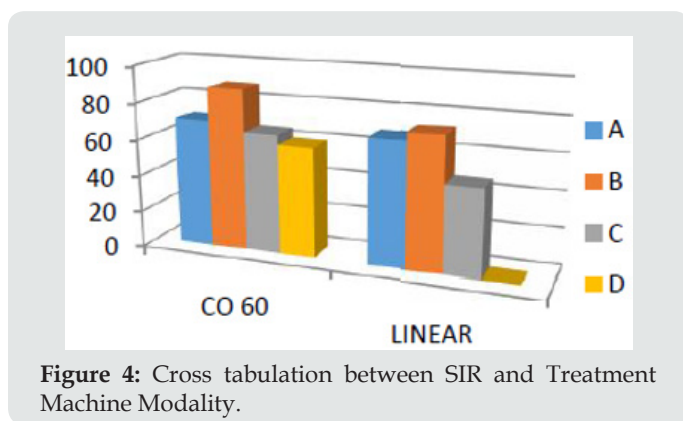
**Figure 2:** Show the survival patients during study period (A= spinal cord compression, B=bone metes, C= brain metes, D= lung metes).

**Symptoms Improvement Ratio (SIR)**

This concept corresponds with Metastatic site and symptoms related to it, the table below show in group A there were high rate symptoms improvement, but it can be change in group B and C (Figures 3 & 4).



**Figure 3:** Symptoms improvement ratio according to patient group.



**Figure 4:** Cross tabulation between SIR and Treatment Machine Modality.

## Conclusion

In metastatic breast cancer patients suffer from many symptoms related with site of metastasis such as pain, dyspnea, bleeding, problem with vision .... etc., this symptoms effect in patient's daily life by decrease the quality of life and increase pain and toxicity. Some time the chemotherapy can't control the localized pain or compression, also the oncologist didn't prefer to be used it because the toxicity will be increase and the few responses. Palliative radiotherapy plays important role in management of this symptoms, symptoms improvement ratio will help all to evaluation the benefit of radiotherapy in palliative cases. A major goal of palliative radiotherapy is controlling the symptoms by given the tumour dose the lethal dose with simple treatment planning and treatment. However, patient's symptoms such as pain, compression and brain Metastatic symptoms can be controlled by radiotherapy. The study was conducted at different oncology hospitals in Sudan (Khartoum oncology hospital (RICK), for specific purpose of acquiring data for study. The study was conducted from 2014 to 2017. Symptoms improvement ratio (SIR) has been develop and become more and more popular in cancer management team. The SIR represents, in absolute terms, the proportion of patients who, following treatment, have a clearly documented improvement in one or more predetermined objective and evaluable symptoms. It represents the average or approximate rate of clinically significant improvement in a specific symptom such as pain.

## Recommendations

The researcher recommended that develop of Palliative Radiotherapy program base use Symptoms improvement ratio concept as reference concept to evaluation the role of radiotherapy in controlled the symptoms in palliative cases when deliver radiotherapy for patients in late stage breast cancer as palliative treatment many factors should be consider:

- a. Implantation of stander palliative radiotherapy program

in each oncology hospital play important role in success the RT treatment.

- b. The time is important factor which effect in patient's response, time between the symptoms appearance and treat with first session.

- c. The radiotherapy regime which describe the suitable field size with minimum number of fractions should be chosen.

- d. Follow up the patient should be consider in all palliative case to manage any incident before it appears.

## Acknowledgment

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