

# Radiation for Palliation: Role of Palliative Radiotherapy in Alleviating Pain/Symptoms in a Prospective Observational Study at Two Tertiary Care Centers

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## Abstract

**Purpose:** Approximately one-third of patients attending the tertiary care center require palliative management. The purpose of this study was to investigate the role of palliative radiation in alleviating the pain and symptoms and improvement in quality of life (QOL). **Methods:** This was a prospective study aimed to evaluate patients attending two oncology centers and those who require palliative radiation. During 3 years, 1365 patients attended radiation oncology center for various malignancies. Of these patients, 304 patients were treated with palliative radiation for various indications. These patients were followed up for a period of up to 6 months for symptom relief and improved QOL. **Results:** About 22% of patients received palliative radiation primarily for carcinoma lung, breast, and prostate malignancy. Analysis revealed elderly patients in the age group of 50–70 being the most commonly affected and most common presentation was pain, swelling, and headache. The most common site of metastases was bone including the spine and brain. Most commonly employed schedule of palliative radiation was 30 Gy in 10 fractions and 20 Gy in 5 fractions. Patients responded well to palliative radiation and had improved pain relief and QOL. **Conclusions:** Palliative radiation is an important part of the management of cancer care and when given improves QOL, and significant pain relief.

**Keywords:** Palliation, palliative radiotherapy, quality of life

## INTRODUCTION

The WHO defines palliative care as “an approach that improves the quality of life (QOL) of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial, and spiritual.”<sup>[1]</sup> Patients with advanced cancer often suffer from considerable symptoms such as pain, breathlessness, cough, swelling, ulceration, bleeding, neurological deficits, and decreased mobility. These symptoms are not relieved by traditional WHO step ladder pattern of pain relief and require specialized palliative radiation for alleviating these symptoms. Since these symptoms are quite complex, interventions including pharmacological, opinion of other specialists, aids in the management of symptom control, managing side effects, and improving QOL. Patients were recruited at two tertiary care institution’s between 2015 and 2017. All patients attending the

radiotherapy department were analyzed and those requiring palliative radiation were included in this study.

Palliative radiotherapy is indicated in the treatment of painful bony metastases, symptomatic brain metastases, spinal cord, nerve root compression, superior vena cava syndrome (SVCO), hematuria, hemoptysis, and hematemesis. Palliative radiation improves pain relief, neurologic functions, and thus improving QOL in patients with metastatic cancers. The study used the prospective database to evaluate and explore the benefits palliative radiotherapy achieves in alleviating pain and symptoms due to metastatic disease.

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### Access this article online

Quick Response Code:



Website:  
www.jpalliativecare.com

DOI:  
10.4103/IJPC.IJPC\_35\_19

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**How to cite this article:** Kumar A, Mukundan H, Bhatnagar S, Sarin A, Taneja S, Sahoo S. Radiation for palliation: Role of palliative radiotherapy in alleviating pain/symptoms in a prospective observational study at two Tertiary Care Centers. *Indian J Palliat Care* 2019;25:391-7.

**Table 1: Patient characteristics**

Parameter	Group	Cobalt-60 (137/763)	LINAC (167/602)	Cobalt-60%	LINAC (%)
<b>a. Age and sex</b>					
Age	10-30	4	7	2.9	4.1
	31-50	21	53	15.32	31.63
	51-70	86	79	62.77	47.30
	71-90	27	28	19.7	16.76
Sex	Male	89	100	64.96	59.88
	Female	49	67	35.76	40.11
<b>b. Primary site, metastatic site, presentation, PS at the time of presentation, and treatment site</b>					
Primary site	Lung	35	49	25.54	29.34
	Colon/rectum	9	8	6.56	4.79
	Breast	37	27	27	16.16
	Prostate	16	18	11.6	10.77
	Misc (Gyn, GI, CUPS, lymphoma, myeloma, H and N, RCC, thyroid, GU and NET)	40	65	29.19	38.92
Metastatic site	Bone	95	107	69.34	64.07
	Brain	34	42	24.81	25.14
	Visceral (liver/spleen)	17	2	12.40	1.19
	Misc (LN, lung, abdominal wall, ADR, bleeding P/R, P/V, hematuria, hematemesis, SVCO)	48	21	35.03	12.57
Presentation	Altered sensorium/abnormal behaviour	7	9	5.10	5.3
	Pain	33	111	24.08	66.46
	Dysphagia	8	1	5.8	0.59
	Mass/lesion/swelling	19	4	13.86	2.39
	Headache	22	31	16.05	18.56
	Hematuria/hematemesis/bleeding	19	3	13.86	1.76
	Misc (weight loss, cough, weakness, fatigue, dyspnoea, LUTS)	84	80	61.31	47.90
PS at presentation ECOG scale	2	66	147	48.17	88.02
	3	70	19	51.09	11.37
	4	2	1	1.4	0.59
Treatment site	Brain	28	42	20.43	25.14
	Chest/mediastinum/axilla/breast	16	10	11.67	5.9
	Face and neck	1	7	0.72	4.19
	LL (pelvis/femur)		35		20.95
	Abdomen (epigastric region, paraaortic)	1	1	0.72	0.59
	Eye		1		0.59
	Upper limb (clavicle, humerus, scapula, temporal bone)	5	4	3.64	2.39
	Spine	56	67	40.8	40.11
	Ribs	2		1.4	
<b>c. Radiation doses</b>					
Radiation dose	4 Gy/2#	1		0.72	
	8 Gy/1#	7	17	5.1	10.17
	9 Gy/3#	2	2	1.4	1.19
	12 Gy/6#		1		0.59
	20 Gy/5#	44	31	32.11	18.56
	21 Gy/7#		1		0.59
	21 Gy/3#	1		0.72	
	24 Gy/8#	2		1.4	
	25 Gy/10#		1		0.59
	30 Gy/10 #	78	111	56.93	66.46
	33 Gy/11#		1		0.59
	36 Gy/12#	1		0.72	
	39 Gy/13#		1		0.59
	45 Gy/20#	1		0.72	
45 GY/25#		1		0.59	

*Contd...*

**Table 1: Contd...**

Parameter	Group	Cobalt-60 (137/763)	LINAC (167/602)	Cobalt-60%	LINAC (%)
<b>d. Response assessment</b>					
Response assessment	Postradiation				
	Improved	121	156	88.32	93.41
	Not improved	16	11	11.67	6.58
Response at 3 months	CR	2	1	1.4	0.59
	PR	64	110	46.71	65.86
	PD	69	49	50.36	29.34
	Death	2	7	1.45	4.19
	Did not receive radiation	1	-	0.72	
	Response at 6 months	CR	2	1	1.45
	PR	63	110	45.98	65.86
	PD	64	32	46.71	19.16
	Death	8	24	5.83	14.37
	Did not receive radiation	1	-	0.72	
Primary end point (pain relief/symptom relief)	Improved	105	144	76.64	86.22
	Not improved	31	23	22.62	13.77
	Did not receive radiation	1	-	0.72	
Secondary end point (improved QOL)	Improved	86	132	62.77	79.04
	Not improved	50	35	36.49	20.95
	Did not receive radiation	1	-	0.72	
	Death	1	-	0.72	

QOL: Quality of life, LINAC: Linear accelerator, PD: Progressive disease, CR: Complete response, PR: Partial response, ECOG: Eastern Cooperative Oncology Group, GI: Gastrointestinal, GU: Genitourinary, SVCO: Superior vena cava syndrome, Gyn: Gynecological, CUPS: Carcinoma of unknown primary site, RCC: Renal cell carcinoma, LUTS: Lower urinary tract syndrome, NET: Neuroendocrine tumors, LN: Lymph node, ADR: Adrenals, P/V: Per vaginum, P/R: Per rectum, PS: Performance status, LL: Lower limb

### Objectives of the study

The intent and objective was to investigate the patterns of palliative radiation therapy in patients and their outcome. The primary objective was pain and/or symptom relief and secondary objective was improvement in QOL.

## METHODS

### Data collection

The study used the inpatient and outpatient registered in the radiotherapy department of two tertiary care centers over 3 years. Those patients requiring palliative radiation were identified and discussed in the multidisciplinary tumor board meeting. This was a prospective study and analysis, in which all patients attending the radiotherapy department were recruited and those requiring palliative intent radiation were included. One center treated patients with Cobalt 60 (Co-60) equipment and the other center treated with linear accelerator (LINAC).

### Population

The study evaluated a wide spectrum of primary malignancies requiring palliative radiation to various sites for various indications.

### Covariates studied

Patient- and tumor-related variables studied were age, sex, primary site of disease, metastatic site, presentation of metastatic disease, performance status at presentation (Eastern Cooperative Oncology Group Scale) and also the factors evaluated were treatment site, doses of radiation delivered,

response assessment post treatment at third and six months. The primary end point was pain and/or symptom relief and secondary end point was improvement in QOL.

## RESULTS

Two tertiary centers were involved in this study and prospective data was evaluated over 3 years. Center A treated patients with cobalt 60 equipment (Co-60) and Center B with LINAC [Table 1].

A total of 602 patients were treated on LINAC over 3 years and of which, 167 patients were treated with palliative intent and 763 patients were treated on Cobalt 60 and of which, 137 patients were treated with palliative intent.

The most common malignancy was carcinoma lung followed by the breast, prostate and colon, and rectum. The most common sites of metastases were bone followed by the brain and visceral metastases. The most common radiation doses used was 30 Gy in 10 fractions followed by 20 Gy in 05 fractions. Response was assessed immediately postradiation and at 3 months and 6 months.

A total of 304 patients were treated (167 - LINAC, 137 - Cobalt-60) with palliative intent radiation. Majority were in the age group of 51–70 years (62% - Cobalt, 47% - LINAC arm). About 64% of patients were male in cobalt arm and 35% of females, whereas 59% were male in LINAC arm and 40% were females.

Majority of patients were carcinoma lung in both groups (25% and 29%) followed by the breast (11% and 10%) and

colon/rectum (6% and 4%). However, miscellaneous sites contributed to a large number (29% and 38%). Bony site was the predominant site of metastases in both groups (69% and 64%), followed by central nervous system metastases (24% and 25%) and visceral Mets (12% and 1%). Miscellaneous sites also contributed to a large number (35% and 12%). Pain was the most common presenting symptom in both groups (24% and 66%) followed by the headache (16% and 18%). Miscellaneous presentations including headache, altered sensorium, swelling, dysphagia, gastrointestinal (GI) symptoms, genitourinary symptoms, weight loss, fatigue, lower urinary tract syndrome, and dyspnea were also primary presentations. Majority of patients had poor performance status at the time of presentation.

The most common site of palliative radiation was to spine due to either compression fracture or multiple metastases contributing to 40% in both groups followed by the brain with 20%–25% of patients receiving whole-brain radiation in both groups. The most common palliative radiation schedule used was 30 Gy in 10 fractions (56% and 66%) followed by 20 Gy in 05 fractions in 32% and 18% patients, respectively. Various other fractionation schedules were also employed depending on the indication and performance status of patients of which 8 Gy in one fraction was the most common contributing to 5% and 10% in cobalt and LINAC group, respectively.

### Response assessment

The response was assessed using patients assessment of pain/symptom relief. About 88% and 93% patients, respectively, in cobalt and LINAC group had immediate pain/symptom relief post radiation. However, this decreased to 46% and 65% at the end of 3 months and remained so at the end of 6 months. About 6% and 14% of patients died at the end of 6 months in cobalt and LINAC group, respectively, due to progressive disease or other comorbidities. Overall 76% of patients in Cobalt group and 86% of patients in LINAC group had improvement in symptoms and 62% of patients experienced improved QOL in cobalt group vis a vis 79% in the LINAC group.

### Duration and timing of palliative radiation

The duration of palliative radiation for the entire study ranged from 1 day to 30 days. It did not vary by age sex, race, comorbidity, marital status, and socioeconomic status.

## DISCUSSION

In today's advanced technological world where there is progress in all fields of oncology including surgery, chemotherapy and radiotherapy, the role of individual specialties in curative versus palliative management is not well defined with all claiming to achieve success. However, there is a consensus that in a metastatic setting the intent of treatment will remain palliative in the improvement of QOL. With advancement in radiotherapy techniques from 2D to now conformal treatments, the overall idea remains alleviation of symptoms and improved QOL. Doses and fractionation schedules vary on the performance status of patient and prognosis depends on

the primary site of disease and how widespread the metastases is at presentation.

### Brain and spinal metastases

Brain metastases is very common form of metastases with incidence ranging from 170,000 to 200 000 per annum as per the US registry. The most common primary site is lung followed by the breast. Metastatic brain tumor outnumber primary brain tumors by a factor of 10 to 1 with autopsy series demonstrating 10%–30% incidence rate for all patients with cancer.<sup>[2,3]</sup> Patients presents with neurologic signs and symptoms of the headache, weakness, ataxia, seizures, speech/swallowing difficulty, hemiparesis, and ataxia.<sup>[4]</sup> Patients are evaluated with magnetic resonance imaging (MRI) brain along with complete systemic workup. Performance status and extracranial disease affects prognosis. Radiation Therapy Oncology Group (RTOG), RPA analysis by Gaspar *et al.* is a useful tool for assessment.<sup>[5]</sup> Patients are managed with cerebral decompression and adjuvant whole-brain radiotherapy with various fractionation schedules, most common being 30 Gy in 10 #.<sup>[6-9]</sup> Role of stereotactic radiosurgery (SRS) boost to the metastatic sites is emerging and data are not yet mature; however, SRS boost may be combined with whole brain radiation and is considered standard of care after local therapy with surgical resection and or SRS (RTOG 9508).<sup>[10,11]</sup> There is a role of repeat whole-brain radiation with doses up to 20 Gy with some neurological benefits.<sup>[12]</sup> Patient may experience dementia post whole-brain radiation and this should be kept in mind while giving re-irradiation. More than 20,000 cases of spinal cord compression are diagnosed in United States every year with the incidence of 5%–14% of all cancer patients.<sup>[13,14]</sup> It is a medical emergency and immediate intervention is required. Most patients have limited survival and only one-third survive beyond 1 year.<sup>[15,16]</sup> Fuller *et al.* revealed that most common malignancy is breast followed by the lung and prostate cancers with 29%, 17%, and 14% incidence.<sup>[17]</sup> Thoracic spine is most commonly involved (59%–78%) followed by the lumbar spine (16%–33%) and cervical spine (4%–15%). The most common presentation is backache, weakness, sensory deficits, and autonomic dysfunction. Patients are evaluated with MRI scan and managed with steroids, surgery, and palliative radiation. The most common dose fractionation schedule is 30 Gy in 10 #.<sup>[18]</sup> Based on the study by Rades *et al.*,<sup>[19]</sup> single fraction of 8 Gy is useful for patients with limited survival and 30 Gy in 10 # should be used for all other patients. Many fractionation schedules have been used for the management of spinal cord compression; however, the most commonly employed schedule is 30 Gy in 10 fractions.

### Bone

Bony metastases are a common cause of pain and significantly reduce QOL. As per the US registry, more than 100,000 patients are affected annually.<sup>[20,21]</sup> About 70% bony metastases are from the breast, prostate, and lung.<sup>[22]</sup> Other sites include thyroid, melanoma, and kidneys. GI primary is found in 5%–15% of cases<sup>[23]</sup> and hematological malignancies such as myeloma and lymphoma also contribute to bony metastases. Prognosis is



generally poor in patients with bony metastases and has short median survival duration of 6 months only. Patients having bone only metastases from prostate and breast may survive up to 04 years.<sup>[22,24,25]</sup> Axial skeleton is the most commonly affected and frequent sites being spine, pelvis, and ribs. Lumbar spine is the most commonly affected.<sup>[26-29]</sup> In appendicular skeleton proximal femurs are commonly affected followed by humerus. Acral sites are rarely affected. Patients present with slow, insidious pain which is progressive and is well localized. Patient may also present with radiation pain. Evaluation is done by general examination, radiographs, contrast-enhanced MRI, bone scan, positron emission tomography-computed tomography (CT) scans, and contrast-enhanced CT scan. Management includes use of the WHO step ladder pattern of pain management, surgery for pathological fractures, spine stabilization, steroids, bisphosphonates, palliative radiation therapy, hemi-body irradiation, use of radiopharmaceuticals, strontium 89, and samarium – 153 therapy.

Liver metastases present with pain, nausea, and vomiting and most commonly arises from colorectal malignancies. Surgery, radiofrequency ablation, and irradiation with respiratory gating have been used for palliation.<sup>[30,31]</sup>

Biliary obstruction due primarily to pancreatic malignancies or large lymph nodes causing extrinsic compression can lead to pruritus, jaundice, anorexia, and weight loss. Management included endoscopic stents, percutaneous transhepatic drainage procedures, and celiac plexus blocks. The use of irradiation for palliation and extending life of stents may be used. Intraluminal brachytherapy may extend stent patency and survival in inoperable cholangiocarcinoma.<sup>[32,33]</sup>

Role of radiation in adrenal metastases is not very clear; however, some studies suggested that palliative doses of radiation with 30 Gy in 10 # may achieve some palliative benefit.<sup>[34]</sup> Splenomegaly presents with abdominal pain, anemia, and thrombocytopenia. Splenic radiation is generally done for patients with leukemias and myeloproliferative disorders.<sup>[35]</sup> Total dose given is not more than 6 Gy.

Bleeding from various causes also is managed with palliative doses of radiation. They can be of venous ooze or frank ulceration causing bleeding. There can be hemoptysis or hematemesis which needs urgent intervention either in the form of surgical ligation or palliative radiation. Various studies using various fractionation schedules have demonstrated efficacious results with the use of palliative hypo fractionated regimes. Reduction of bleeding occurs within 24–48 h of the first treatment.

Cancer pain is a significant cause of morbidity and decreased QOL and more than half patients attending oncology center experience pain requiring some form of pain management either pharmacological or interventional.<sup>[36,37]</sup> Radiation is a valuable modality in the management of cancer pain and is used in palliative setting when there is involvement of bone, soft tissues, or nerves.<sup>[38]</sup> Medically pain is managed with

the help of the WHO pain ladder, American pain society guidelines, or NCCN guidelines. In addition, patients may be managed with palliative radiation, neuraxial blocks, and neuroablative techniques.<sup>[39-41]</sup> Complementary therapies such as acupuncture and music therapy may be beneficial.<sup>[42]</sup> SVCO is a medical emergency requiring immediate therapeutic intervention. About 80% of cases are from carcinoma lung<sup>[43]</sup> followed by lymphoma accounting for 10%–18% of cases and benign causes such as thyroid diseases account for 2%–3% of cases. Patients with SVCO has very poor prognosis and only 10%–20% survive for 2 years. Patients are managed with steroids and use of radiation as soon as possible. Patients experience dramatic relief of symptoms and some studies have shown 25% survival rates at 1 year and 10% at 3 years.

The goal of palliative care is to relieve symptoms effectively and efficiently and to maintain the maximum QOL for the duration of the patient's life. The interventions recommended depend on the patient's clinical status, severity of disease, and the location of the symptomatic site. Radiotherapy has an important role to play as a cost effective and simple method to relieve symptoms caused by bone or brain metastases, tumor bleeding, or visceral/lymphovascular obstruction due to cancer.

In our study, elderly patients in the age group of 50–70 were the most commonly affected, male preponderance was seen, and performance status was generally poor. The most common primary site of malignancy was the lungs, breast, and prostate and most common sites of metastases were bony including spinal metastases and brain metastases. Patients presented with pain, headache, swelling, and various other miscellaneous symptoms including weight loss, fatigue, and generalized malaise. Most common palliative radiation schedule implemented was 30 Gy in 10 fractions and 20 Gy in 05 fractions; however, other schedules were also used depending on the indication, site, and performance status of the patient. Patients generally responded well to the treatment and had improved QOL. Palliative radiation is an effective and important modality in the management of metastatic malignancy and has a pivotal role in cancer associated pain. Thus, radiation palliation is once again proven to be effective modality in overall well-being and in improving QOL in terminally and end of life care situations.

#### Limitations of the study

The data represented subjective patient and physician impressions regarding response.

#### CONCLUSIONS

Palliative care in oncology is considered best approach in patients with bony and brain metastases; however, the real outcomes are hard to define and measure. Patient specific validation is useful but most of them are not fully validated. Radiation oncologist should have a formal course in hospice and palliative care during training. The outcome of palliative radiation in bony metastases is well documented and ASTRO guidelines are useful tool for evaluation. Technological

advances have opened up newer possibilities for support and the management of palliative care especially in brain metastases with the use of SRS and gamma knife. SRS has also been used in spine, liver, and lung metastases with good results. Patients receiving early palliative radiation has shown to have improved QOL, decreased depression rates, and better survival. ASCO guidelines states that palliative care should be considered early in the course of illness in metastatic setting and patients should visit hospice centers if survival is felt to be <6 months.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

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