



## Palliative Radiotherapy Between Scientific Evidence and Technological Evolution: Role of Clinic Appropriateness and the Choice of Treatment

<b>Sara Falivene</b>	Radiation Oncology, Second University of Naples, Naples, Italy
<b>Rossella Di Franco</b>	Radiation Oncology, Second University of Naples, Naples, Italy
<b>Francesca Maria Giugliano</b>	Radiation Oncology, Istituto Nazionale per lo Studio e la Cura dei Tumori-Fondazione "Giovanni Pascale" IRCCS, Naples, Italy
<b>Valentina Borzillo</b>	Radiation Oncology, Istituto Nazionale per lo Studio e la Cura dei Tumori-Fondazione "Giovanni Pascale" IRCCS, Naples, Italy
<b>Angela Argenone</b>	Radiation Oncology, Istituto Nazionale per lo Studio e la Cura dei Tumori-Fondazione "Giovanni Pascale" IRCCS, Naples, Italy
<b>Vincenzo Ravo</b>	Radiation Oncology, Istituto Nazionale per lo Studio e la Cura dei Tumori-Fondazione "Giovanni Pascale" IRCCS, Naples, Italy
<b>Paolo Muto</b>	Radiation Oncology, Istituto Nazionale per lo Studio e la Cura dei Tumori-Fondazione "Giovanni Pascale" IRCCS, Naples, Italy

### ABSTRACT

*Purpose: purpose is to assess the impact of radiotherapy with palliative purposes in the department of Radiation Oncology, use of advanced technologies in palliation and impact on management of patients were to be enrolled in medical treatments. Methods and Materials: We have evaluated the treatments made in 2013 in our department. At the Institute can effect treatments in 3DCRT, brachytherapy, and from November 2012 Cyberknife® system is available for SRT and SRS treatments. We have considered impact of treatments with palliative purposes for each type of technique used. Risultati: In 2013, 874 patients were treated: for brain metastases, 149 in total, were performed with 3DCRT technique (Whole Brain) in 22 patients, with special technique in 127 patients including (77% radiosurgery; 23% fractionated stereotactic radiotherapy. SRT have a dominant role in presence of a number of secondary encephalic lesions less than or equal to 4 because SRT is a selective treatment that preserves whole brain, and structures as the brainstem, chiasm, optic nerves, and then fits the cognitive functions and relationships. 110 treatments were done for bone metastases with 3DCRT (68 treated with 8 Gy, 76 with 30 Gy, 44 with 20 Gy, 2 with 40 Gy); in 2012 started the experience with the Cyberknife® system and were treated 199 patients with 3DCRT, 1 patient with the Cyberknife® system for retreatment of spinal metastasis. In 2013, 203 palliative treatments for bone metastases were performed, with 3DCRT technique in 185 patients, 18 with special technique. Conclusion: Our experience shows that palliation is a common indication in radiotherapy, but careful patient selection is essential for the choice of radiotherapy technique and dose fractionation. We should not consider the palliative treatment of secondary importance, so even in the palliation need to promote research and technology to optimize results.*

### KEYWORDS :

#### Introduction

Palliative treatments represent an important share in a Department of Radiation Oncology. One of the missions of our department is to improve quality of life other than overall survival of patients.

Compared to a conventional fractionation, the palliative treatment aims to reach a greater cytotoxic effect on tumor cells and rapid control of the symptom, to this end it is used a higher dose per fraction (3-8 Gy) and a lower number of fractions.(1)

The techniques used in the palliative radiotherapy treatments ranging from external beam techniques with 2D or 3D conformal, to the stereotactic, or brachytherapy. Stereotactic radiotherapy or brachytherapy, get a more favorable spatial distribution of the dose in the tumor and surrounding healthy tissues. Stereotactic radiotherapy (SRT) allows the delivery of high doses of radiation, a considerable saving of the critical organs and can be done in a single session (radiosurgery-SRS) or in multiple fractions (fractionated stereotactic radiotherapy). Stereotactic radiotherapy is used with palliative intent for treatment of few small brain metastases (no more than 3-4), and even sometimes it is preferred to surgery because it allows to treat multiple lesions simultaneously or placed in proximity of critical areas. (2,3)

Stereotactic body radiation therapy (SBRT) is used in the treatment of lung, liver, bone metastases, or recurrent abdominal and thoracic malignancies, always limited in size (less than 3-4 cm) to control pain and/or other symptoms such as bleeding and compression.

In these cases, the evaluation and the control of the movements of target is a very important question being SBRT a very precise and conformational technique so the use of a personalized system of immobilization (such as thermoplastic custom masks and "body frame") is fundamental.

Aim of this paper is to assess the impact of radiation therapy with palliative purposes in the department of Radiation Oncology, the use of advanced technologies in palliation and the impact of the use of these techniques in the management of patients not eligible to curative treatments.

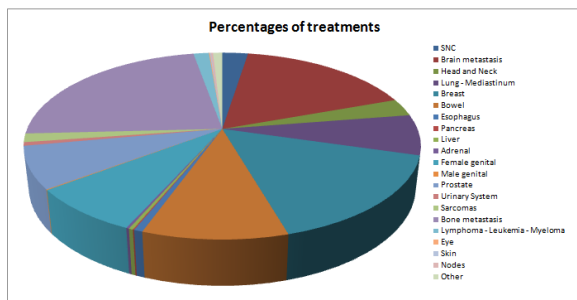
#### Methods and Materials

We have evaluated all treatments made in 2013 at the Department of Radiotherapy of the Istituto Nazionale per lo Studio e la Cura dei Tumori - Fondazione "Giovanni Pascale" - IRCCS - of Naples. At the Institute can effect treatments in 3DCRT with linear accelerator LINAC equipped with 120 MLC dynamic therapy (IMRT), and LINAC 6mV

system with MLC-IMRT-IGRT-Arc, and brachytherapy. From November 2012 Cyberknife® system is available for SRT and SRS treatments. We have divided the treatments according to the primary tumor and according to the purpose of the indication and we have compared them with the treatments of previous two years. Then we have considered the impact of the treatments with palliative purposes for each type of technique used. In particular we have focused our interest on the pathology in which palliation is preponderant purpose (bone and brain metastases) and we have noted if the presence in the department of an advanced technology as Cyberknife® system since November 2012 have had an impact on selection and management of these patients compared to the two previous years.

**Results**

In 2013 at the Department of Radiotherapy of the Istituto Nazionale per lo Studio e la Cura dei Tumori - Fondazione "Giovanni Pascale" - IRCCS - of Naples, 874 patients were treated. Fig.1 shows the percentages of patients divided according to the type of pathology.

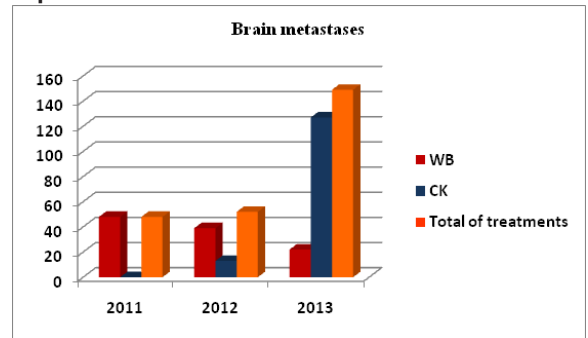


**Fig.1 percentages of patients divided according to type of pathology**

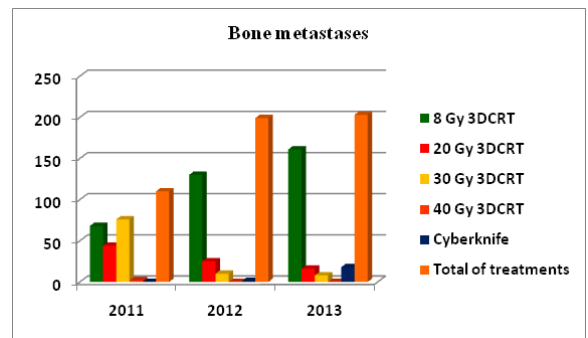
For each group of patients is reported the percentage of radiation treatments made with palliative purpose (Table 1).

TUMORS	TOTAL	PALLIATION	%
SNC	170	149	87
Head and Neck	27	2	8
Lung - Mediastinum	61	35	57
Breast	141	0	0
Bowel	87	4	5
Esophagus	5	1	20
Pancreas	1	0	/
Liver	3	2	67
Adrenal	2	2	100
Femal genital	70	0	/
Male genital	1	0	/
Prostate	64	0	/
Urinary System	5	3	60
Sarcomas	13	5	38
Bone	202	202	100
Lymphoma – Leukemia - Myeloma	10	0	/
Eye	1	1	100
Skin	1	0	/
Nodes	2	2	100
Other	8	5	63
Tot. patients	874	413	
	100%	47%	

**Figure 2 showed the number of patients with brain metastases treated in the period 2011-2013 and the technique used.**



In 2013, the treatments for brain metastases, 149 in total, were performed with 3DCRT technique (Whole Brain) in 22 patients, with special technique in 127 patients including 77% using single fraction radiosurgery - SRS (range 10-24 Gy), 23% using fractionated stereotactic radiotherapy with multiple fractions (3% with 2 fractions - range 18-21 Gy; 17% with 3 fractions - range 18-24Gy; 3% with 5 fractions - range 20-25Gy). We have detected an increase in the number of patients treated during 2013 and that SRT have a dominant role in the presence of a number of secondary encephalic lesions less than or equal to 4 because SRT is a selective treatment that preserves as much as possible whole brain, but also structures as the brainstem, chiasm, optic nerves, and then fits the cognitive functions and relationships essential for the maintenance of an acceptable quality of life.



In 2011 (Figure 3), 110 treatments were done for bone metastases with 3DCRT (68 patients treated with 8 Gy, 76 treated with 30 Gy, 44 treated with 20 Gy, 2 treated with 40 Gy); in 2012 started the experience with the Cyberknife® system and were treated 199 patients with 3DCRT (130 patients treated with 8 Gy, 25 treated with 20 Gy, 10 treated with 30 Gy), 1 patient was treated with the Cyberknife® system for retreatment of spinal metastasis. In 2013, 203 palliative treatments for bone metastases were performed with 3DCRT technique in 185 patients (161 with 8 Gy, 16 with 20 Gy, 8 with 30 Gy). While 18 with special technique (9 patients were re-treated with a single fraction of 8 Gy; 1 patient re-treated with a single fraction of 9 Gy; 3 patients re-treated with a single fraction of 10 Gy; 2 patients treated with a single fraction of 16 Gy; 2 patients treated with 20 Gy in 5 fractions; 1 patient treated with 30 Gy in 5 fractions).

We have seen that the management of bone metastases too, is changed significantly in recent years thanks to new scientific evidence about the effectiveness of various types of fractionation, in fact, treatment with 8 Gy single fraction increased by a rate of 62% in 2011 to 65% in 2012 to 79% in 2013. Simultaneously, the number of patients with bone metastases treated was increased, and the best selection of the same also allowed the use of treatments in selected cases with special techniques.

**Discussion**

According to the World Health Organization the purpose of palliative care is to improve the quality of life for patients through the prevention and relief of suffering(4). In 2000, a survey carried from the "Palliative and supportive care" group of AIRO showed that 30-50% of the

treatments performed in Italian centers of radiotherapy have palliative purpose. The treatments were 50% bone metastases, 23% brain metastases, 15% mediastinal masses, 7% visceral metastases and 5% disease responsible for bleeding (5). The multidisciplinary approach is an essential prerequisite for a correct management of the patient who requires palliative care. In palliative radiotherapy dose fractionation has an important role because the reduction of the number of accesses of the patient reduces stress and it can then improve the quality of life. Hypofractionation with the increase of a single dose and the reduction of the total number of fractions aims to achieve a greater cytotoxic effect on tumor cells and a more rapid relief on the symptom (6).

Various schemes have been used in hypofractionation radiotherapy of bone metastases, brain metastases, in advanced cancers of the lung, rectum, bladder, brain. Another important question is about the proper timing of initiation of palliative cancer care, in fact, palliative therapy should begin soon as possible, be done in a short period of time and without serious acute side effects. For this purpose is often necessary use of complex techniques such as conformal radiotherapy or special techniques such as stereotactic radiotherapy and brachytherapy. Stereotactic radiotherapy, in fact, allows to administer high doses of radiation to the tumor in a single fraction (radiosurgery - SRS) or in limited fractions (fractionated stereotactic radiotherapy - SRT), with a high dose gradient such as to obtain a better control of the disease and a high savings surrounding healthy tissue (7). It is used in the palliative treatment of brain metastases of small size and limited number. Correct patient selection must be completed before the indication for SRS. KPS, age, control of the primary disease and absence of extracranial metastasis, as indicated dall'RTOG, represent the most important factors that allow a selection of the cases in which to perform the radiosurgical treatment (8).

Stereotactic body radiation therapy (SBRT), however, can be used for the palliative treatment of metastatic lung, liver, bone and recurrent abdominal and thoracic malignancies, with the advantage of irradiating lesions difficult to reach with traditional methods and with a duration of therapeutic cycle very short (one week) (9). In this case the size of the lesions must be limited (<3-4 cm), and a low KPS or a widespread disease and progression of primary tumors represent a contraindication (10). The American Society for Therapeutic Radiology and Oncology (ASTRO) has published specific guidelines. Another common indication for palliative radiotherapy is the pain from bone metastases, in fact it reduces pain symptoms after a short treatment schedule and after radiotherapy, improvement in not only tumor re-

lated symptoms but also the patient's quality of life (QOL) is expected (11,12).

Several randomized clinical trials comparing multiple fractions and a single fraction of 8 Gy have shown similar effects on pain-relieving effects on painful bone metastasis (13-18).

A meta-analysis reported that single fraction and multiple fractions damage overall pain response for 60% and 61% of patients respectively (19). The Dutch Bone Metastases Study Group presented that reirradiation of painful bone metastasis was effective and retreatment response was 63%. 50-70% of patients undergoing re-irradiation showed pain-relieving effects (20). Reirradiation in the total dose should not exceed that which is acceptable by organs at risk, such as the spinal cord and brainstem. Stereotactic body radiotherapy (SBRT) in the vertebral metastasis allows the shaped dose distribution sparing the spinal cord from high irradiation dose. When used SBRT might be re-irradiation is required in previously irradiated sites. In patients with single bone metastasis, primary lesion controlled, and favorable prognosis, treatment aiming at long-term symptom control is also considered (21-23). In fact emerges the role of SBRT in the management of spinal oligometastasis, spinal radioresistant (24). The highly precise radiotherapy for bone metastasis is also important in terms of local control (25).

The SBRT provides high biological effectiveness doses to metastatic spine disease with a steep dose gradient, and saving the adjacent critical organs.

Our experience shows that palliation is a common indication for radiotherapy, but also shows that careful patient selection is essential and is required for the choice of radiotherapy technique and dose fractionation.

The entire course of treatment should take into account the ultimate goal of treatment, the quality of remaining life of the patient. Therefore it is important to program the start of the treatment more rapidly as possible, with a reduced number of sessions and with techniques which limit the possible side effects acute. At the same time we should not consider the palliative treatment of secondary importance compared to those with radical or adjuvant purposes, so even in the palliation need to promote research and technology to optimize results, pertanto l'appropriatezza clinica nella scelta del tipo di trattamento e del tipo di tecnica è fondamentale nella radioterapia palliativa.

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