RESEARCH ARTICLE

Retreatment with radiotherapy for symptomatic bone, brain or visceral metastases

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Abstract

Background   The need for reirradiation in the metastatic disease appears when other modalities of treatment lose their efficacy. The aim of reirradiation in the metastatic disease is mainly palliative to control a particular symptom. However, this theoretical benefit must be confronted against the risk of an undesirable toxicity.

Materials and Methods   Experience with reirradiation for symptomatic bone, brain or visceral metastases are reviewed. Twenty-two patients were found to have a second palliative radiotherapy on the same location. Locatión of metastases were visceral in 5 (23 %) patients, brain in 4 (18 %) patients, spine in 1 (4.5 %) patient and bone metastasis other than spine in 12 (54.5 %) patients. Median dose delivered in the first treatment was 30 Gy (range 20–30 Gy) and 20 Gy for the second treatment (range 6–32.4 Gy).

Results   A good symptomatic response after first irradiation (complete response or disappearance of >50 % of symptoms) was reached in 21 (95.5 %) of the 22 patients analyzed. After second irradiation, 82 % (18 patients) achieved a good response, 3 (14 %) patients had a moderate response (relief of symptoms <50 %) whereas no response was observed in 1 (4 %) patient. Acute toxicity was limited to grade 1–2 proctitis in 2 and 3 patients after the first and second irradiation, respectively. No cases of late toxicity after the first or second irradiation were recorded.

Conclusion   A second treatment with palliative radiotherapy is feasible and well tolerated and offers the possibility of symptomatic relief in a high percentage of patients with symptomatic metastases.

Keywords   Symptomatic metastases · Palliative reirradiation · Response rates · Toxicity profile

Introduction

Retreatment by radiotherapy comprises both first treatment to the primary cancer site followed by treatment to a metastasis at any other site at any time and the so-called reirradiation, defined as two treatments of the same primary or metastatic tumor location separated in time. The need for reirradiation appears when other modalities such as surgery, chemotherapy or supportive care are considered ineffective. The ultimate goal of reirradiation can be either curative in the case of a persistent tumor or local tumor recurrence suitable of a curative approach, or merely palliative to control a particular symptom [1]. Reirradiation, particularly after radical radiotherapy, has been traditionally faced against the reluctance of most radiation oncologists because of the risk of inducing severe iatrogenic complications. However, in the last years, a wide body of clinical data is refuting this particular dogma evidencing that many normal tissues do really show recovery after radiation damage. These evidences support, in part, the use of reirradiation for palliative purposes in daily clinical practice. Feasibility and clinical benefit of reirradiation have been highlighted by different groups, leading to consider it a valid treatment option in the palliative setting [2–5].

   The aim of the current paper is to describe patterns of palliative reirradiation, clinical results and potential

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complications after a second radiotherapy course on the same site as primary observed at our institution.

Materials and methods

We examined an existing radiotherapy database at the Universitary Hospital Ramon y Cajal (Madrid, Spain) containing demographic data, clinical diagnoses, sites and doses of radiotherapy. We retrospectively reviewed the records of 9,966 patients treated between 2001 and 2010 identifying 129 patients who received palliative radiotherapy in two or more occasions. Of these, in 22 patients, the second palliative radiotherapy was performed on the same location as the first, being the subject for this analysis. We deliberately excluded those patients in whom either treatment was performed with radical intent. Treatment sites were recorded according to the metastasis location into a limited number of sites: vertebral metastasis, bone metastasis other than vertebral, brain and visceral metastases. Treatment procedure is well established. As a general rule in our department, a three-dimensional CT-based planning was performed for every treatment. Radiotherapy was delivered by megavoltage units, either Co-60 unit or linear accelerator. All patients had signed an informed consent before each treatment. Complete characteristics of analyzed patients are detailed in Table 1.

The response to treatment is difficult to assess in the context of palliative irradiation and reirradiation. Response Evaluation Criteria in Solid Tumors (RECIST), commonly used to determine the degree of tumor response to the treatment administered, lack the same utility in a palliative situation [6]. The aim of palliative treatment is not just to achieve a complete or partial disappearance of the tumor by imaging tests but to obtain a significant symptomatic relief in the patient. Therefore, its applicability in assessing the response to both the first irradiation and the subsequent palliative reirradiation is doubtful. Instead, groups that have examined the efficacy of retreatment for symptomatic control chose simple measuring scales, considering a complete response when the patient is totally asymptomatic after treatment. In our particular case, we decided to use a valuation scale similar to that used by the group of Mithal et al. to analyze the effectiveness of treatment. These authors defined a complete response as "complete freedom from pain with no analgesic requirements." They defined a partial response as "improved pain but analgesic medicine still required [7]." We considered a "good response" if the symptoms disappeared completely or more than 50 %, "moderate response" if the disappearance of symptoms is less than 50 % and "no response" if there is no improvement in the disappearance of symptoms after treatment. Response to treatment was recorded 4 weeks after radiotherapy, with a

Table 1 Patients and treatments' characteristics

	n (%)
Age (years; median)	57 (range 34–85)
Gender	
Female	13 (59)
Male	9 (41)
Primitive tumor location	
Lung	7 (31)
Breast	6 (26)
Prostate	3 (13)
Colorectal	2 (10)
Stomach	1 (5)
Bladder	1 (5)
Skin melanoma	1 (5)
Neuroendocrine Merkel cell carcinoma	1 (5)
Metastatic disease location	
Bone metastases	13 (59)
Visceral metastases	5 (23)
Brain metastases	4 (18)

Radiotherapy schedules	n (%)	$BED_{\alpha\beta=2}$
First palliative treatment		
10 × 300 cGy	12 (54)	75 Gy$_2$
5 × 400 cGy	8 (36)	60 Gy$_2$
6 × 500 cGy	1 (5)	105 Gy$_2$
10 × 250 cGy	1 (5)	56.3 Gy$_2$
Second palliative treatment		
10 × 300 cGy	8 (36)	75 Gy$_2$
5 × 400 cGy	7 (31)	60 Gy$_2$
1 × 800 cGy	3 (14)	40 Gy$_2$
5 × 300 cGy	2 (9)	37.5 Gy$_2$
1 × 600 cGy	1 (5)	24 Gy$_2$
18 × 180 cGy	1 (5)	61.6 Gy$_2$

good response being the complete disappearance or reduction of symptoms greater than 50 %.

The time interval between radiation episodes was defined as the time between the end of the first treatment and the start of the second course of radiotherapy. Overall survival was defined from the moment of first attendance to the date of death or last follow-up. Acute and late toxicities were recorded according to the RTOG/EORTC criteria [8].

Different treatment schedules with diverse dose and fractionation schemes were used. To facilitate comparison between different regimens, all the schedules were recalculated to the biologically effective dose (BED) according to the linear-quadratic model using the following formula:

$$BED = n \cdot d(1 + d/\alpha/\beta)$$

with n = number of fractions, d = dose per fraction, α = linear (first order, dose dependent) component of cell killing, β = quadratic (second order, dose dependent) component of cell killing, and α/β ratio = the dose at which both components of cell killing are equal [9].

The BED represents the physical dose required for a given effect if the dose was delivered by infinitely small doses per fraction or, in the case of continuous radiation rates, at a very low dose rate. Thus, BED can be used to equate or compare different fractionation schedules. Brain and spinal cord, which are considered as late-reacting tissues, have a small α/β value of 2–3 Gy. According to the previous experience reported from other groups, we calculated the BED with α/β ratio of 2 Gy ($BED_{\alpha\beta=2}$) with no correction for the possible recovery of tolerance from the first radiation exposure. In this model, a dose of 50 Gy given in single daily fractions of 2 Gy is equivalent to a BED of 100 Gy_2 [10, 11].

Results

We identified 22 patients, 13 men and 9 women, with a mean age of 57 years (range 34–85 years) eligible for analysis. In 3 (14 %) patients, diagnosis of metastases coincided with the initial diagnosis of tumor.

The primary tumor was located in lung in 7 (32 %) patients, breast in 6 (27 %) patients, prostate in 3 (14 %) patients. The primary tumor was colorectal in 2 (9 %) patients and bladder, stomach and skin melanoma and cutaneous Merkel cell carcinoma in 1 (4.5 %) patient each. The metastatic disease was located in visceral in 5 (23 %) patients, brain in 4 (18 %) patients, spine in 1 patient (4.5 %); bone metastasis other than spine was found in 12 (54.5 %) patients (Table 2).

The ability of cancer patients to perform ordinary tasks may be used as a prognostic factor. The Karnofsky Performance Status Scale (KPS) was designed to measure the level of patient activity and medical care requirements [12]. The Karnofsky Performance scores range from 0 to 100 %. A higher score means the patient is better able to carry out daily activities. We determined the KPS in our patients before each treatment. We observed a median KPS of 60 % (range 40–70 %) before first irradiation that decreased to a median KPS of 50 % (range 30–70 %) before reirradiation. Thirteen patients presented with a KPS of 60–70 % at the time of the first irradiation whereas only 6 patients presented with KPS of 60–70 % before the second irradiation, although this difference was not statistically significant.

Median dose delivered in the first treatment was 30 Gy (range 20–30 Gy) and 20 Gy for the second treatment (range 6–32.4 Gy). Treatment schedules most frequently used for the first irradiation were 10 × 300 cGy (54 %),

5 × 400 cGy (36 %), 6 × 500 cGy (5 %) and 10 × 250 cGy (5 %). For reirradiation, the schemes employed were 10 × 300 cGy (36 %), 5 × 400 cGy (31 %), 1 × 800 cGy (14 %), 5 × 300 cGy (9 %), 1 × 600 cGy (5 %) and 18 × 180 cGy (5 %). The choice of radiotherapy schedules was left to the discretion of the treating radiation oncologist. We found no significant differences in the use of a radiation scheme regarding the characteristics of each patient, tumor location or KPS. However, it is true that there was a tendency to use more shortened radiotherapy schedules in patients with low KPS, although this difference was not statistically significant ($p = 0.075$).

Planning target volumes (PTVs) for both irradiations were defined according to the tumor site. For bone metastasis, PTV encompassed metastasic bone lesion with 1 cm of margin in all directions. For visceral reirradiations (i.e., bladder, skin, lymph nodes), the PTV comprised either macroscopic tumor with 1–2 cm of margin (skin lesions, lymph node metastases) or the complete affected organ (bladder). Finally, for brain metastases, the PTV for both irradiations was the whole brain.

The mean BED for the first treatment was 75 Gy_2 (range 56–105 Gy_2, $\alpha/\beta = 2$). The mean BED for the second treatment was 60 Gy_2 (range 24–1,205 Gy_2, $\alpha/\beta = 2$). Average accumulated BED for both irradiation was 133.15 Gy_2 (range 99–210 Gy_2, $\alpha/\beta = 2$).

Clinical response to radiotherapy

The response to the radiation was scored as previously described by looking at the reduction of symptoms requiring treatment (i.e., pain, bleeding or neurologic symptoms). After the first treatment, a good symptomatic response (complete response or disappearance of >50 % of the symptoms) was reached in 21 (95.5 %) of the 22 patients analyzed.

After the second irradiation, the percentage of patients who achieved a good response again was of 82 % (18 patients). In 3 (14 %) patients, this response was rated as moderate (relief of symptoms <50 %) and no response in 1 (4 %) patient.

Toxicity analysis

The toxicities of the first and second irradiation were scored according to the RTOG/EORTC criteria for acute and late complications.

Two (9 %) and 3 patients (14 %) with pelvic metastases experienced acute rectal grade 1–2 toxicity attributable to radiotherapy after the first and the second treatment, respectively. No patients suffering from late complications neither after the first treatment nor after reirradiation were observed.

Table 2 Individual characteristics of treatment and outcome of the 22 patients included

N	Primitive tumor	Metastatic location	Treatment intention	First irradiation	BED$_{\alpha/\beta=2}$ (Gy)	KPS-1 (%)	Response	TTI (months)	Second irradiation	BED$_{\alpha/\beta=2}$ (Gy)	KPS-2 (%)	BED$_{\alpha/\beta=2}$ (Gy)	Response	OST (months)	Status
1	Bladder	Visceral	Hemostatic	10 × 300 cGy	75	60	Good	12	5 × 400 cGy	60	50	135	Good	19	DoD
2	Colorectal	Visceral	Antialgic	10 × 300 cGy	75	60	Good	7	10 × 300 cGy	75	60	150	Good	55	DoD
3	Stomach	Osseous	Antialgic	5 × 400 cGy	60	50	Good	9	10 × 300 cGy	75	50	135	Good	78	DoD
4	Prostate	Osseous	Antialgic	10 × 300 cGy	75	60	Good	35	5 × 300 cGy	37.5	50	112.5	Good	74	AwD
5	Lung	Visceral	SVCS	10 × 300 cGy	75	40	Good	3	10 × 300 cGy	75	40	150	Good	28	DoD
6	Lung	Brain	CNS metastases	10 × 300 cGy	75	50	Good	3	5 × 300 cGy	37.5	50	112.5	Good	11	DoD
7	Lung	Osseous	Antialgic	5 × 400 cGy	60	60	Moderate	3	1 × 800 cGy	40	50	100	Good	9	DoD
8	Cutaneous Melanoma	Visceral	Lymph-node metastases	6 × 500 cGy	105	60	Good	23	6 × 500 cGy	105	60	210	Good	151	DoD
9	Breast	Osseous	Antialgic	10 × 300 cGy	75	70	Good	43	10 × 300 cGy	75	70	150	Good	125	DoD
10	Colorectal	Osseous	Antialgic	10 × 300 cGy	75	60	Good	7	1 × 600 cGy	24	50	99	Poor	19	AwD
11	Breast	Osseous	Antialgic	5 × 400 cGy	60	60	Good	18	5 × 400 cGy	60	50	120	Good	141	AwD
12	Breast	Brain	CNS metastases	10 × 300 cGy	75	50	Good	17	5 × 400 cGy	60	50	135	Good	64	AwD
13	Prostate	Osseous	Antialgic	10 × 300 cGy	75	60	Good	35	10 × 300 cGy	75	60	150	Good	59	DoD
14	Breast	Osseous	Antialgic	5 × 400 cGy	60	50	Good	12	1 × 800 cGy	40	50	100	Good	55	DoD
15	Lung	Brain	CNS metastases	10 × 250 cGy	56.3	60	Good	19	10 × 300 cGy	75	60	131.3	Good	34	DoD
16	Breast	Osseous	SCC	10 × 300 cGy	75	40	Good	56	5 × 400 cGy	60	40	135	Good	168	AwD
17	Lung	Osseous	Antialgic	5 × 400 cGy	60	50	Good	7	5 × 400 cGy	60	50	120	Moderate	61	AwD
18	Lung	Osseous	Antialgic	5 × 400 cGy	60	50	Good	11	1 × 800 cGy	40	50	100	Moderate	38	DoD
19	Lung	Osseous	Antialgic	10 × 300 cGy	75	60	Good	12	5 × 400 cGy	60	50	135	Moderate	95	DoD
20	Breast	Brain	CNS metastases	10 × 300 cGy	75	60	Good	54	10 × 300 cGy	75	60	150	Good	137	DoD
21	Cutaneous Merkel cell carcinoma	Visceral	Lymph-node metastases	5 × 400 cGy	60	50	Good	4	18 × 180 cGy	61.6	50	121.6	Good	15	DoD
22	Prostate	Osseous	Antialgic	5 × 400 cGy	60	60	Good	12	5 × 400 cGy	60	50	120	Good	57	DoD

SCC spinal-cord compression, SVCS superior vena cava syndrome, CNS central nervous system, BED biologically effective dose, KPS Karnofsky Performance Status, TTI time interval between both treatments (months), OST overall survival time (months), DoD death of disease, AwD alive with disease

No association was found between the occurrence of complications and the physical dose administered, both cumulative and in each treatment separately, as well as with the $BED_{\alpha\beta=2}$.

Survival analysis

The median time interval (MTI) between the diagnosis of the primary tumor and the metastatic disease subject of the first irradiation was 41 months (range 0–121 months). The MTI between the two irradiations was 12 months (range 3–56 months).

At the moment of the last follow-up, 6 (27 %) patients are alive while 16 (73 %) patients had died. The median survival time (MST) for the entire series was 58 months (range 9–168 months). The MST after the first irradiation was 17 months (range 5–63) while MST was only 3 months (range 1–9) after second radiotherapy. The actuarial overall survival rates at 12 and 24 months are 48 and 10 %, respectively (95 % CI 29–88 %).

Univariate analysis revealed a statistically significant association for patients with initial diagnosis of breast cancer and a higher 12-month actuarial survival rates as compared to other primary tumor sites (Log-Rank, $p = 0.015$). Likewise, when the interval between two irradiations was greater than 12 months, actuarial survival at 1 year was significantly higher ($p = 0.001$) (Table 3). We did not find any other significant association with survival among the rest of factors analyzed, including location of metastatic disease, KPS before each treatment, physical dose administered or the BED calculated for both of the treatments separately as well as the cumulative BED for the two irradiations.

Discussion

Palliative radiation therapy is one of the major contributions to the burden of care in a Department of Radiation Oncology. The 2001 Swedish survey on employment patterns of radiotherapy evidenced that 46 % of the treatments were administered with palliative intent [13]. Similarly, data from an analysis in the Canadian province of Ontario confirmed that 53 % of the radiotherapy treatments had initial palliative intent [14]. The Spanish experience, published by Esco et al. [15] showed that 27 % of the administered treatments were with palliative intent. The discrepancy with the data reported by researchers in other countries where palliative radiotherapy comprises 40–50 % of the treatments would lay, according to the authors, the lack of available treatment units.

Bone and cerebral metastases represent almost three quarters of palliative radiation treatments. In our series, the

Table 3 Results of univariate analysis for overall survival

	Actuarial 1-year overall survival (%)	p value
Primitive tumor location		
Lung	0	0.015
Breast	41.7	
Stomach	0	
Colorectal	0	
Bladder	0	
Prostate	33	
Skin melanoma	0	
Neuroendocrine Merkel cell carcinoma	0	
Metastatic disease location		
Bone metastases	61	0.124
Brain metastases	50	
Visceral metastases	40	
Time interval between both irradiations		
≥12 months	18	0.001
<12 months	0	

anatomical location more frequently retreated was the bone in 13 (59 %) cases followed by the brain in 4 (18 %) cases, consistent with published data. The main goal of palliative care is to achieve symptomatic relief, although this is not necessarily associated with increased survival. The results of numerous studies have shown that radiation therapy achieved adequate relief and symptom control in patients with bone and/or visceral metastases treated with palliative intent associating an acceptable tolerance and a low profile in both acute and late toxicities. In this context, it can be considered that radiotherapy as palliative treatment is cost efficient [12, 16].

In recent years, directly related to the progress of anti-neoplastic therapy, survival of patients with metastatic advanced cancer is increasing. This fact is of special relevance in the most prevalent tumors such as breast cancer in women and prostate cancer in men. With increasing frequency, there is the need for reirradiation in patients with cancer. The frequency of use of reirradiation varies according to the different series between 6 and 31 % of the reported patients initially treated in a Department of Radiation Oncology, but a rate of around 20 % is closest to the reality of daily practice [3, 17, 18]. The likelihood of reirradiation will be directly related to the primary tumor, being only 3 % in brain tumors but reaching 100 % in some series of multiple myeloma. In patients undergoing whole brain radiotherapy for cerebral metastases, about half of them will have central nervous system progression during their lifetime. However, reported rates of retreatment of patients with brain metastases range from 3.2 to 13.3 % [19, 20].

Similarly, between 9 and 40 % of patients with bone metastases will be candidates for reirradiation during the course of their disease [21]. This is not surprising, given that some of the tumors more susceptible to retreatment are characterized by their tendency to metastasize to bone, such as lung, prostate and multiple myeloma. In our experience, the primary tumor of the 22 patients that were reirradiated with palliative intent corresponded to lung, prostate or breast cancer in 70 % of the cases. The median interval between the first irradiation and retreatment was longer for breast cancer than for lung or prostate cancer, in accordance with the known natural history of these cancers and the potential availability of effective systemic therapies.

The response rates after reirradiation are similar to those observed after the first course of radiotherapy. The group of Jeremic et al. [22] observed that responses to radiation occurred in 84 % of the patients treated for the first time and 87.5 % of the patients reirradiated in a retrospective series of 105 patients. The group of Mithal et al. [7] reported an overall response rate to reirradiation of 73 % (80/109) with a complete response rate of 31 %. These authors noted that there was "no effective patient age, sex, primary tumor-type or site seen on response to re-treatment."

In these studies, complete response is defined as freedom from symptoms, whereas the definition of partial response varies. In addition to defining response, there exists an inherent difficulty of measuring a response when radiotherapy is given as a local treatment, while cancer symptoms can come from multiple sites, often also palliated by other systemic agents, including a variety of analgesics, chemotherapy, hormonal therapy, bisphosphonates, etc.

According to the scale previously described in the "Materials and methods" and currently used in our department, 95.5 % of the patients had "good response" to the first irradiation and 82 % for the second irradiation. Although a comprehensive analysis of overall survival is beyond the scope of this work, the results observed are similar to those observed by other groups. In the univariate analysis, patients with a primary diagnosis of breast cancer had the best survival rates as expected considering the nature, clinical course and available therapeutic options for breast cancer.

We are aware that a major limitation of our study is its retrospective nature, covering the experience of a radiation department over 10 years. This implies certain heterogeneity in the radiation schemes used, a direct consequence of the preferences of oncologists involved in the treatment of these patients. For a long time, the palliative radiotherapy schedules most frequently used in our department have been 10 × 300 or 5 × 400 cGy (Table 2). Usually, shortened treatment regimens (i. e., 5 × 400 cGy, 5 × 300 cGy) were reserved for patients with poor KPS, while more protracted schedules (i. e., 10 × 300 cGy, 10 × 250 cGy,

18 × 180 cGy) were preferred in patients with better performance status. Single-fraction schedules (i. e., 1 × 600 cGy, 1 × 800 cGy) were used occasionally but were not considered as first choice scheme (Table 2). Nevertheless, increasing use of single fractions in last years, not limited only to patients with poor KPS, is related to the growing body of evidence obtained from long-term results of clinical trials published along last decade, contributing to change the daily clinical practice.

Despite the growing body of evidence supporting the retreat of metastatic tumor lesions with palliative intent, many radiation oncologists are reluctant to generalize its use, mainly due to the risk of toxicity secondary to treatment, especially in cases of brain and spinal-cord reirradiation. Although the results obtained by different researchers, including those observed in our analysis, do not support the hypothesis of a significant increase in complications with reirradiation, it is not yet considered a standard practice. The risk of complications depends on the BED delivered to the normal organs at risk (i.e., spinal cord, brain) [2, 9]. BED takes into account both the total dose of radiotherapy and the dose per fraction. In the case of reirradiation, it seems appropriate to calculate also cumulative BED (i.e., BED of the first plus BED of the second course of RT). In our series, despite the wide variety of radiotherapy schedules used, the median cumulative BED for both treatments is 133 Gy_2, in accordance with the recommendations of other authors. Only one patient exceeds this range, reaching a cumulative BED of 210 Gy_2. This patient, with a metastatic melanoma, was treated both times with a scheme of 6 fractions of 500 cGy, given that melanoma is a tumor that responds best to high fractions of radiotherapy.

The risk of serious late complications in the brain includes both the development of demyelinization areas (clinically associated with the somnolence syndrome), necrosis of the white matter or the appearance of areas of leukoencephalopathy or vascular lesions with important clinical consequences with focal neurological symptoms (motor and sensory deficits, seizures), as well as more complex neuropsychological impairment (learning deficits, intellectual decline, personality changes) and cerebrovascular effects (stroke deficits, dementia). These experiences have in common the cumulative radiation dose which did not exceed 60 Gy (equivalent to a BED of 140 Gy with $\alpha/\beta = 2$). [5] Four out of the 22 patients included in our analysis underwent whole brain reirradiation. Median cumulative BED for both irradiations was of 133 Gy_2 (range 112.5–150 Gy_2). Despite the limited follow-up of these patients, no cases of late neurological toxicity were observed.

Radiation-induced damage to small volume of spinal cord may severely impair normal function, leading to the

serious condition of radiation myelopathy, which is irreversible and can reduce the quality of life of the treated patient [8, 23] Our experience in the specific case of spinal-cord reirradiation is scarce, as only 1 of the 22 patients examined was retreated by a spinal-cord compression. This patient had a long survival after initial diagnosis of breast cancer and presented metastatic spinal-cord compression during follow-up treated with palliative radiotherapy, developing 58 months later a new clinically evident metastatic spinal-cord compression in the same location, undergoing a second radiation treatment. The cumulative BED for both treatments was 135 Gy_2. During the follow-up, we observed no significant late toxicity whereas the patient is currently alive and asymptomatic.

Conclusion

The results we observed after reirradiation of patients with a metastatic tumor in an area previously irradiated with palliative intent are consistent with those previously published by other groups, supporting both the efficacy of palliative reirradiation as its feasibility and good tolerability. We are very conscious about the heterogeneity of metastatic sites and the limited number of patients in our series. However, considering the characteristics of these patients, a second treatment with palliative radiotherapy offers the possibility of symptomatic relief in a high percentage of patients without major complications, as long as the cumulative BED of both treatments were maintained below threshold levels recommended.

Further studies are necessary to properly define the appropriate scheme of radiation therapy in the context of palliative reirradiation.

Conflict of interest None.

References

1. Morris DE (2000) Clinical experience with retreatment for palliation. Semin Radiat Oncol 10(3):210–221
2. Nieder C, Milas L, Ang KK (2000) Tissue tolerance to reirradiation. Semin Radiat Oncol 10(3):200–209
3. Barton MB, Hudson HM, Delaney G, Gruver P, Liu Z (2011) Patterns of retreatment by radiotherapy. Clin Oncol (R Coll Radiol) 23(1):10–18
4. Abusaris H, Storchi PR, Brandwijk RP, Nuyttens JJ (2011) Second re-irradiation: efficacy, dose and toxicity in patients who received three courses of radiotherapy with overlapping fields. Radiother Oncol 99(2):235–239
5. Maranzano E, Trippa F, Pacchiarini D et al (2005) Re-irradiation of brain metastases and metastatic spinal cord compression: clinical practice suggestions. Tumori 91(4):325–330
6. Eisenhauer EA, Therasse P, Bogaerts J et al (2009) New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). Eur J Cancer 45(2):228–247
7. Mithal NP, Needham PR, Hoskin PJ (1994) Retreatment with radiotherapy for painful bone metastases. Int J Radiat Oncol Biol Phys 29(5):1011–1014
8. Cox JD, Stetz J, Pajak TF (1995) Toxicity criteria of the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC). Int J Radiat Oncol Biol Phys 31(5):1341–1346
9. Jones B, Dale RG, Deehan C, Hopkins KI, Morgan DA (2001) The role of biologically effective dose (BED) in clinical oncology. Clin Oncol (R Coll Radiol) 13(2):71–81
10. Rades D, Rudat V, Veninga T, Stalpers LJ, Hoskin PJ, Schild SE (2008) Prognostic factors for functional outcome and survival after reirradiation for in-field recurrences of metastatic spinal cord compression. Cancer 113(5):1090–1096
11. Nieder C, Grosu AL, Andratschke NH, Molls M (2006) Update of human spinal cord reirradiation tolerance based on additional data from 38 patients. Int J Radiat Oncol Biol Phys 66:1446–1449
12. Karnofsky DA, Burchenal JH (1949) The clinical evaluation of chemotherapeutic agents in cancer. In: MacLeod CM (ed) Evaluation of chemotherapeutic agents. Columbia Univ Press, New York, p 196
13. Möller TR, Brorsson B, Ceberg J et al (2003) A prospective survey of radiotherapy practice 2001 in Sweden. Acta Oncol 42:387–410
14. Kong W, Zhang-Salomons J, Hanna TP et al (2007) A population based study of the fractionation of palliative radiotherapy for bone metastasis in Ontario. Int J Radiat Oncol Biol Phys 69:1209–1217
15. Esco R, Palacios A, Pardo J, Biete A, Carceller JA, Veiras C, Vazquez G, Spanish Society of Radiotherapy Oncology (2003) Infrastructure of radiotherapy in Spain: a minimal standard of radiotherapy resources. Int J Radiat Oncol Biol Phys 56(2):319–327
16. Nieder C, Pawinski A, Haukland E, Dokmo R, Phillipi I, Dalhaug A (2010) Estimating need for palliative external beam radiotherapy in adult cancer patients. Int J Radiat Oncol Biol Phys 76(1):207–211
17. Statewide Services Development Branch (2009) 2008 radiotherapy management information system report. NSW Health, Sydney
18. Williams MV, Drinkwater KJ (2009) Radiotherapy in England in 2007: modelled demand and audited activity. Clin Oncol 21:575–590
19. Sadikov E, Bezjak A, Yi QL, Wells W, Dawson L, Millar BA, Laperriere N (2007) Value of whole brain re-irradiation for brain metastases–single centre experience. Clin Oncol (R Coll Radiol) 19(7):532–538 Epub 2007 Jul 26
20. Son CH, Jimenez R, Niemierko A, Loeffler JS, Oh KS, Shih HA (2011) Outcomes alter whole brain reirradiation in patients with brain metastases. Int J Radiat Oncol Biol Phys 82(2):e167–e172
21. Ratanatharathorn V, Powers WE, Moss WT et al (1999) Bone metastasis: review and critical analysis of random allocation trials of local field treatment. Int J Radiat Oncol Biol Plays 44:1–18
22. Jeremic B, Shibamoto Y, Igrutinovic I (1999) Single 4 Gy re-irradiation for painful bone metastases following single fraction radiotherapy. Radiother Oncol 52:123–127
23. Maranzano E, Trippa F, Casale M, Anselmo P, Rossi R (2011) Reirradiation of metastatic spinal cord compression: definitive results of two randomized trials. Radiother Oncol 98(2):234–237