

## THE ROLE OF PALLIATIVE RADIOTHERAPY IN THE TREATMENT OF METASTATIC MELANOMA

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### Abstract:

To demonstrate the role and effectiveness of palliative radiotherapy in patients with metastatic melanoma, especially in the context of combination therapy with immunotherapy and/or targeted therapy.

**Methodology:** Four patients with metastatic melanoma, treated at the University Clinic for Radiotherapy and Oncology – Skopje are presented. All patients had a performance status (ECOG 0.1) and were treated with palliative radiotherapy due to pain and/or local progression. Different doses and techniques were used according to clinical indication combined with systemic therapy.

**Results:** All patients showed clinical improvement after radiotherapy: pain reduction, regression of local metastases, improvement of functional status and continuation of systemic therapy without interruption. There were no significant side effects of radiotherapy.

**Conclusion:** Palliative radiotherapy is an important tool in the multimodal approach to the management of metastatic melanoma and allows for a rapid palliative effect and potential synergism with immunotherapy and targeted therapy.

**Keywords:** metastatic melanoma, palliative radiotherapy, immunotherapy, targeted therapy, multimodal treatment.

### Introduction

Melanoma is a malignant neoplasm of melanocytic origin with a high potential for metastasis and an unpredictable clinical course. Although early stages of the disease are potentially curable with surgical removal, advanced or metastatic melanoma remains a therapeutic challenge, with limited options for a curative approach. In the last decade, advances in systemic therapy, especially immunotherapy and targeted therapies, have led to a significant improvement in survival in some patients.

However, a significant number of patients continue to develop symptomatic metastases, especially in the brain, bone and soft tissues, which significantly impair quality of life.

Palliative radiotherapy is an important tool in the multidisciplinary treatment of these patients, in order to reduce the tumor burden, alleviate symptoms (pain, bleeding, compression) and improve functional status. Although melanoma has traditionally been considered radioresistant, there is evidence that significant symptomatic control can be achieved with hypofractionated and high doses per fraction.

This paper aims to demonstrate the clinical benefit of palliative radiotherapy in patients with metastatic melanoma through the analysis of four specific cases treated at the University Clinic for Radiotherapy and Oncology in Skopje.

### Methodology

This paper describes a series of four cases of patients diagnosed with metastatic melanoma, who received palliative radiotherapy during the course of the disease.

Each case is documented with anamnesis, systemic therapy used, indication for radiation, radiotherapy regimen and clinical response. Age, ECOG performance status, location of metastases, systemic therapy, doses and techniques of radiation, as well as the response to it were taken into account.

### **CASE 1**

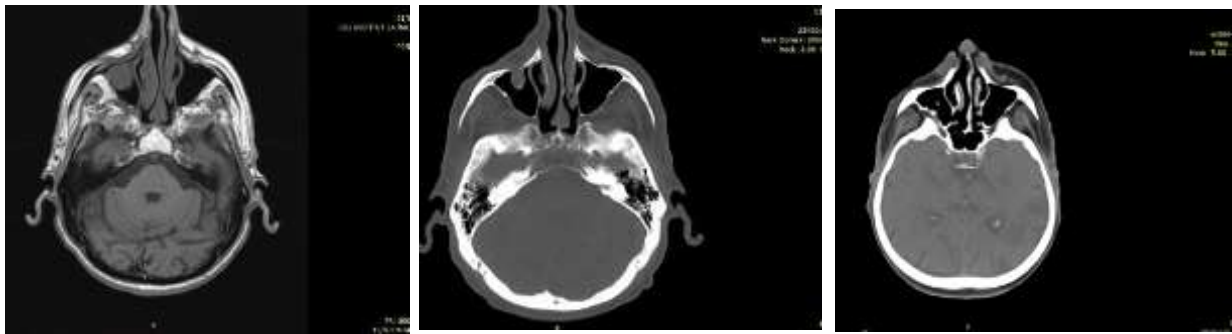
Patient 83 years old, ECOG-0, diagnosed with desmoplastic melanoma of the left facial region, operated on 05.05.2023, with pathohistological finding of T3 tumor but with positive margin, not removed in healthy tissue. BRAF-, PDL-. PET/CT finding from 03.08.2023, without signs of disease.

PET/CT scan from 02.07.2024 with a metabolically active lesion present in the left maxillary sinus.

According to this finding, the patient underwent 3D conformal radiotherapy in the area of the left maxillary sinus with TTD 30 Gy, administered in 10 fractions, 3 Gy DTD. No acute adverse reactions due to the administered radiotherapy were observed. Radiotherapy was administered from 05.08.2024 to 16.08.2024. From 20.08.2024, the patient began receiving mono immunotherapy - Nivolumab 480mg at 4 weekly intervals.

Control scans performed on 27.11.2024 with a finding of complete remission of the previously described metastatic changes without the appearance of new lesions.

The patient is in complete remission and was last evaluated on 15.07.2025, when he received the 13<sup>th</sup> cycle of Nivolumab.



### **CASE 2**

Patient 77 years old, ECOG-0. On 26.01.2024, the patient underwent surgery for a skin lesion in the right maxillary region with a pathohistological finding of nodular type of melanoma with the following characteristics – pTNM=pT4B pNx pMx R1 L1 V1 Stage IIC BRAF-, C-KIT-, NRAS-.

Due to the positive resection margin, the patient was referred to maxillofacial surgery for re-excision, but the clinic did not make a decision to perform it. CT scan of the head and neck and lungs from 13.08.2024 in addition to an oval soft tissue formation in the right maxilla with dimensions of 17x16mm. KTM on the neck from 21.08.2024 in addition to a tumor substrate on the right supraclavicular right with dimensions 95x96mm.

On 04.09.2024, extirpation of the neck metastasis was performed. On 24.10.2024, the patient began specific oncological treatment with immunotherapy - Pemprolizumab 200 mg at a 3-week interval.

On inspection, a mass on the neck was seen again, on 20.11.2024, after which a new KTM finding on the head and neck was performed in addition to new metastatic changes on the right side of the neck.

The patient continues with immunotherapy until 29.01.2025 due to disease progression and worsening general condition. The patient persists with visible tumor masses on the right side of the neck with severe pain and impaired neck movements.

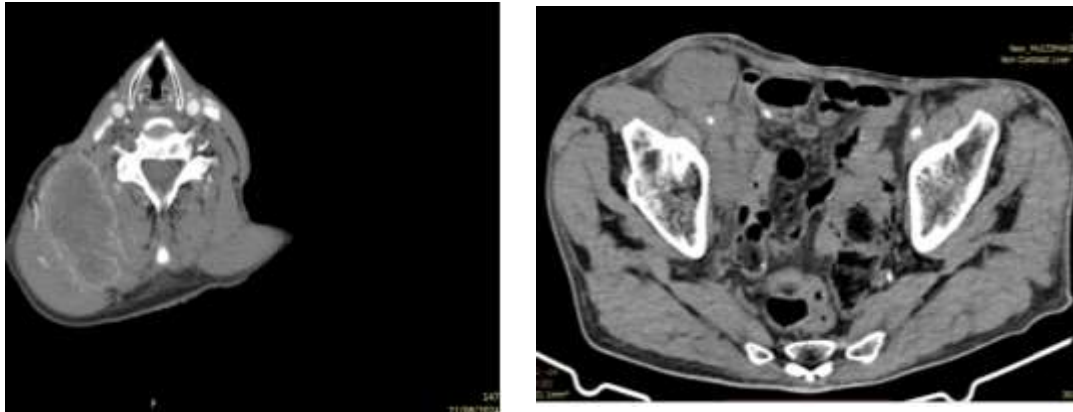
The same is confirmed by the CT findings from 08.01.2025 in support of the progression of metastases in the neck as well as new parenchymal metastatic deposits in the lungs and the first three ribs on the right.

Due to severe pain in the neck region, the patient underwent palliative radiotherapy of the metastatic changes in the right neck region. Radiotherapy was applied with a 3D conformal technique

with a total dose of 30 Gy, conducted in 10 fractions with a 3 Gy daily tumor dose from 17.02.2025 to 28.02.2025.

The radiation treatment was well tolerated without adverse acute reactions and a visibly reduced tumor mass in the right neck region as well as an improved overall general condition.

The patient also underwent a change in specific oncological treatment, so from 30.01.2025, he began receiving palliative chemotherapy with Temozolomide 300mg daily dose in a five-day cycle.



### **CASE 3**

Patient 77 years old, ECOG-0. The patient underwent surgery on 07.07.2023 for melanoma on the right lower leg with the following pathohistological findings- pTNM= pT4A, pNx, pMx, R0,L0,V0, Stage IIB, BRAF+, PDL-.

He was presented to our clinic 4 months after the surgery with CT scan of the thorax and abdomen in addition to metastatic disease in the lungs, and lymph nodes in the right inguinal region.

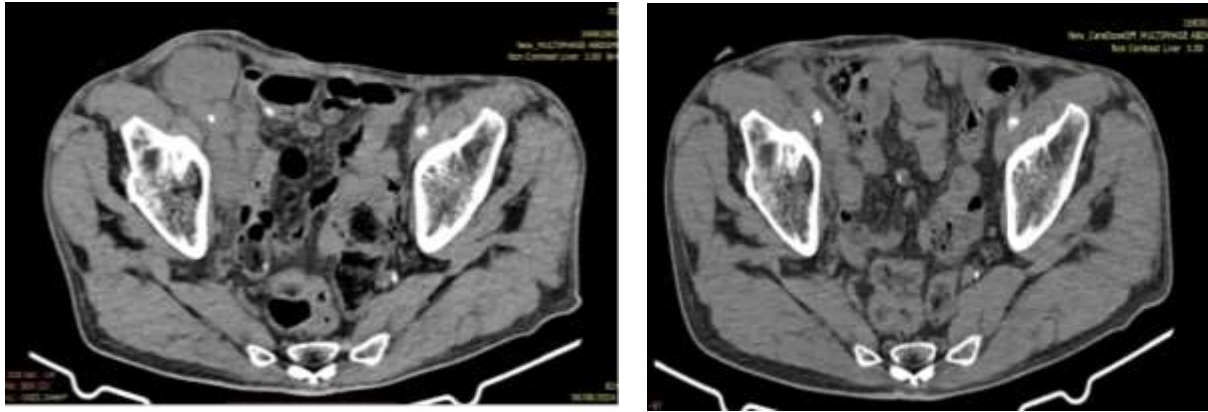
On 24.01.2024, targeted therapy with BRAF/MEK inhibition with the drugs vemurafenib/cobimetinib was initiated, however due to adverse reactions and disease progression - (CT scan from 30.08.2024 new lung lesions as well as volume progression of the right inguinal lymph node, present iliac and para-aortic metastatic deposits), the therapy was discontinued on 07.10.2024.

On 09.10.2024, a new line of therapy was started, namely immunotherapy, Pembrolizumab 200mg at a three-week interval.

Control CT scan on 18.02.2025 in addition to significant regression of metastatic deposits, but due to persistence of metastases and pain in the inguinal region, radiation therapy was added to the patient.

Radiation therapy was performed from 26.05.2025 to 06.06.2025 in 3D conformal technique with a total dose of 25 Gy, 2.5 Gy daily tumor dose. CT findings after the radiotherapy indicated regression of the tumor formation in the right inguinal region, on inspection it was visibly reduced and the patient had no pain in the same region.

The patient continued with immunotherapy and is in good general condition.



#### **CASE 4**

A 60-year-old female patient, ECOG-0. The patient underwent surgery for melanoma in the pubic region with metastases in the right inguinal lymph nodes on 25.11.2021 with the following pathohistological characteristics – pTNM - pT4B, pN2b, pL1, pV0, pR0 Stage IIIC, BRAF+

The patient was first presented to our clinic four months after the surgery, so due to the time period she was not included in adjuvant treatment and was left for follow-up.

Lung CT scan from 03.04.2024 in addition to two nodal clearly limited metastatic changes. Abdominal CT scan with normal findings. On 09.06.2023, surgical intervention for lung metastases was performed.

On 13.07.2023, new control CT scans of the lungs were submitted in addition to new metastatic deposits in the lungs. The patient started on 20.07.2023 with first-line therapy, targeted therapy, BRAF/MEK Inhibition, Vemurafenib/cobimetinib.

Control CT scans of the thorax and abdomen from 02.11.2023 in addition to complete remission of the previously described metastatic changes.

However, due to intense dorsal pain, the patient also underwent a skeletal scan on 20.12.2023 in addition to pathological accumulation in the sternoclavicular joint and eleventh thoracic vertebra.

On 17.01.2025, a single radiation treatment of the thoracic vertebra was performed with a total tumor dose of 8 Gy with 3D conformal radiation technique.

The treatment was well tolerated without adverse reactions and the pain in the dorsal region has completely resolved.

The following control CT scans were performed on 21.05.2024 without signs of disease. The patient is still in complete remission, targeted therapy is still ongoing, the last evaluation was performed on 17.07.2025.

#### **Results**

This series describes four cases of patients with advanced or metastatic malignant melanoma, in whom palliative radiotherapy was indicated and implemented with the aim of reducing symptoms and local control of the disease.

The patients' age ranged from 60 to 83 years, all with ECOG performance status 0 at the time of inclusion in radiotherapy treatment. All patients had previous systemic treatment (immunotherapy, targeted therapy or combination), with partial or insufficient response to treatment.

Palliative radiotherapy was performed in all patients with 3D conformal techniques.

The applied doses varied depending on the location and size of the lesions, ranging from **8 Gy in one fraction to 30 Gy in 10 fractions**. The most frequently irradiated regions were the **neck, thoracic spine and inguinal region**, where patients had painful and/or growing metastatic masses.

All four patients experienced **significant pain relief** after radiotherapy, as well as **local regression** of the tumor formations confirmed by computed tomography in three of them. One patient also reported significant improvement in neck mobility and ease of daily activities. In another patient, **complete control of pain in the thoracic region** was achieved after a single treatment of 8 Gy.

All patients continued with systemic therapy after completion of radiation.

No patient experienced treatment toxicity higher than grade 2, indicating good tolerability of the therapy. The general condition remained stable, without significant deterioration in the post-radiation period.

### **Discussion**

Palliative radiotherapy remains an important tool in the treatment of metastatic melanoma, especially when there is symptomatic local progression, compression or pain. In the presented series of 4 patients, radiotherapy was effective and well tolerated.

In all patients, radiotherapy led to clinical benefit – in the form of pain reduction, lesion control and improvement in functional status. The acceptable toxicity of the treatment is particularly significant, taking into account the age of the patients and the comorbidities in the patients.

In two cases, radiotherapy was combined with immunotherapy, which may have contributed to more effective systemic and local control. The combination of RT+IO is also supported by current research, which suggests a potential synergistic effect, especially in the context of abscopal effects and enhanced T-cell infiltration.

It is important to emphasize that, although palliative in intention, radiotherapy has led to **complete remission** in some patients, indicating that its role is not only symptomatic but may also be control, especially in oligometastatic disease.

These results are in line with the available literature, where RT has shown efficacy in metastatic melanoma in bone and soft tissues, with minimal toxicity and the potential to improve quality of life.

Lymph nodes are frequently involved in metastatic melanoma, especially in regions such as the axillary, inguinal, and cervical regions. Large or progressive lymphatic metastases may cause pain, edema, compression of vascular or neural structures, or necrosis with secondary infection.

### **Clinical data:**

In a retrospective study published in the Radiation Oncology Journal (2018), patients with lymphatic metastases from melanoma treated with 30 Gy in 10 fractions showed significant symptom reduction and control of local progression in >60% of cases.

EORTC recommendations for palliative RT suggest doses of 20–30 Gy, depending on expected survival and symptoms, with 3D-CRT allowing precise coverage of lymphatic regions and protection of critical organs (e.g. femoral vessels, plexus).

Bone metastases from melanoma, although less common than brain or skin metastases, often cause intense pain, pathological fractures, or spinal compression.

### **Clinical evidence:**

A case review from MD Anderson Cancer Center (2015) showed that RT with 8 Gy in a single fraction or 20 Gy in 5 fractions has a pain-relieving effect in >70% of patients.

According to ASTRO guidelines (2020), short palliative regimens are equally effective as longer ones, but patients with a longer life expectancy may benefit from higher-dose 3D-CRT (30 Gy/10 fractions) for better long-term local control.

Stereotactic bodywork (SBRT) is still used selectively, but 3D-CRT is the gold standard in most cases for symptomatic control.

3D-CRT is a basic technique in palliative radiation oncology.

It uses CT planning, with the ability to precisely model the dose, thus achieving: Precise tumor coverage and minimal radiation to healthy tissues, which is especially important in patients already receiving systemic therapy (immune/targeted)

## Conclusion

Palliative radiotherapy is an effective and safe therapeutic modality for symptomatic relief and local control in patients with metastatic melanoma.

In the presented case series, radiation led to significant pain relief, lesion regression, and improvement in functional status in all patients. Particularly positive results were observed when radiotherapy was administered in combination with immunotherapy, indicating the potential synergy between these modalities.

Although the number of patients is small, the results suggest that timely inclusion of radiotherapy as part of a multimodality approach may contribute to improving quality of life and prolonging disease control in patients with advanced melanoma.

Further studies are needed to investigate in more detail the optimal doses, techniques, and timing of application in this context.

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