Radiotherapy as an Adjunct to Surgery in the Management of Adult Soft Tissue Sarcomas of the Hand: The First Case Report Using Stereotactic Technology and a Brief Review of Radiation Effects

Ann. Ital. Chir., 2025 96, 7: 894–904
https://doi.org/10.62713/aic.3970

Valentina Zagardo[1], Gianluca Scalia[2,3], Corrado Fichera[4], Davide Matera[4], Giuseppe Emmanuele Umana[2,5], Gianluca Ferini[1,2]

[1]Department of Radiation Oncology, REM Radioterapia srl, 95029 Viagrande, Italy
[2]Department of Medicine and Surgery, Kore University of Enna, 94100 Enna, Italy
[3]Neurosurgery Unit, Department of Head and Neck Surgery, Garibaldi Hospital, 95124 Catania, Italy
[4]Oncology Surgery Unit, Istituto Oncologico del Mediterraneo, 95029 Viagrande, Italy
[5]Department of Neurosurgery, Trauma Center, Gamma Knife Center, Cannizzaro Hospital, 95126 Catania, Italy

Adult soft tissue sarcomas of the hand are rare, representing approximately 2% of upper extremity tumors. Their indolent growth often leads to misdiagnosis and treatment delays. While amputation has traditionally been the standard approach, advances in limb-sparing techniques, supplemented by radiotherapy, have improved local control and functional preservation. However, radiotherapy in hand sarcomas carries significant risks, including impaired wound healing, fibrosis, stiffness, edema, fractures, and, in rare cases, necrosis and radiation-induced sarcomas. This case-based narrative review is built around an institutional case: an 81-year-old woman with recurrent leiomyosarcoma of the left hand who developed graft necrosis following radiotherapy after R2 resection. Despite initially favorable outcomes, the patient experienced severe skin graft complications, leading to functional impairment and the need for additional wound management. A comprehensive narrative literature review of hand sarcomas treated with radiotherapy highlights the challenge of balancing effective tumor control with minimizing adverse effects. While radiotherapy provides high local control rates, particularly in cases with residual disease, complications such as graft necrosis, as reported here, can significantly affect functional outcomes. The review emphasizes the importance of achieving clear surgical margins, as even modern radiotherapy techniques like volumetric modulated arc therapy (VMAT) guided by stereotactic equipment may fail to prevent complications. Long-term follow-up remains essential to detect and manage late sequelae, with the aim of restoring any compromised function. This case underscores the need for careful patient management and the difficult benefit/risk trade-off associated with radiotherapy when surgery alone is insufficient.

Keywords: sarcoma; hand; radiotherapy; surgery; skin; graft; necrosis; adverse events; stereotactic

Introduction

Adult soft tissue sarcomas (a-STS) of the hand are exceedingly rare, comprising approximately 2% of all upper extremity tumors [1]. Their low incidence, coupled with often subtle clinical presentations, frequently leads to misdiagnosis as benign lesions, delaying appropriate treatment and resulting in suboptimal outcomes [2].

Radical surgical excision remains the cornerstone of treatment. Historically, amputation was the standard approach due to the challenges in achieving clear surgical margins. These challenges arise from the hand's intricate anatomy, with limited healthy tissue available for resection and the close proximity of critical structures such as joints, tendons, ligaments, and neurovascular bundles [3].

Submitted: 16 January 2025 Revised: 6 March 2025 Accepted: 19 March 2025 Published: 25 April 2025
Correspondence to: Gianluca Ferini, Department of Radiation Oncology, REM Radioterapia srl, 95029 Viagrande, Italy; Department of Medicine and Surgery, Kore University of Enna, 94100 Enna, Italy (e-mail: gianluca.ferini@grupposamed.com).

Given the profound physical and psychological impact of amputation, limb-sparing surgery has become the preferred approach when oncologically and technically feasible. When combined with adjuvant therapies, such as radiotherapy and chemotherapy in high-risk cases, limb-preserving procedures have demonstrated local control rates comparable to those of amputation [4,5].

Despite its efficacy, radiotherapy in the hand remains challenging due to the heightened risk of complications. In the neoadjuvant setting, its primary goal is tumor downstaging to facilitate resection, though delayed wound healing is a frequent concern [6,7]. In the adjuvant setting, side effects such as fibrosis, stiffness, edema, radiation-induced fractures, and, in rare cases, necrosis or secondary malignancies have been reported [8,9].

These risks raise the question of whether radiotherapy is truly well tolerated and to what extent recent advancements in irradiation techniques and treatment verification systems have improved its safety profile. While concerns about functional impairment were historically justified, the extent to which modern innovations have mitigated these risks remains unclear. Addressing this uncertainty is essential, as

treatment-related morbidity continues to impact patient outcomes despite technological progress.

In this context, we present the case of an 81-year-old patient with leiomyosarcoma of the dorsal left hand who developed graft necrosis following postoperative radiotherapy, significantly affecting quality of life and persisting unresolved for over a year. To contextualize this case, we conducted a comprehensive narrative review of the literature on radiotherapy-associated complications in hand sarcomas, examining whether advances in radiotherapy techniques have led to a reduction in adverse effects and, consequently, improved patient outcomes.

A Case-Based Journey Through the Clinical Presentation and Management of Hand Sarcomas

The Clinical Scenario as Illustrated by an Institutional Case

In February 2023, an 81-year-old female patient with a diagnosis of leiomyosarcoma located on the dorsum of her left hand, which was her non-dominant hand, was referred to our department. Informed consent and consent to participate were obtained from the patient. Her medical history included type 2 insulin-treated diabetes mellitus and hypertension.

The patient initially underwent surgical excision of the lesion in 2019. The pathology report revealed cells with characteristic blunt-ended nuclei. Immunohistochemistry showed positivity for smooth muscle actin, caldesmon, and desmin, while S100 was negative, consistent with a grade 2 leiomyosarcoma. Negative surgical margins were not achieved during the initial procedure, yet no adjuvant treatment was offered at that time.

Regular surveillance ensued, with no signs of recurrence observed until March 2022, when a local recurrence was noted on magnetic resonance imaging (MRI) of the left upper extremity. Surgical excision was performed again, but, similarly to the first procedure, clear margins were not obtained, and no adjuvant treatment was provided.

In December 2022, the patient presented with a second recurrence (Fig. 1A). An MRI of the left hand revealed a nodule measuring 21 × 18 × 45 mm, located on the dorsal aspect of the hand (Fig. 2A,B). This mass showed infiltration into the adjacent muscle structures, extensor tendons, and the overlying skin. It was also in contact with the head of the third metacarpal, although no cortical bone disruption was observed. Additionally, a subcutaneous nodule with a diameter of 6 mm was identified at the level of the head of the fourth metacarpal. A contrast-enhanced total body computed tomography (CT) scan revealed a 5-mm lesion in the lower lobe of the left lung. To further assess staging, an 18F-Fluorodeoxyglucose (FDG) positron emission tomography (PET) scan was performed, which showed increased fluorodeoxyglucose uptake in the dorsum of the left hand, while the lesion in the left lung exhibited no pathological uptake.

Given the persistent recurrence, amputation was initially recommended; however, the patient strongly declined this option, due to its significant impact on her quality of life and autonomy. Consequently, a wide resection surgery was performed (Fig. 1B). The pathology report confirmed the presence of multiple lesions with high mitotic activity, evidence of lymphovascular invasion, and neoplastic infiltration of the skin, consistent with recurrent leiomyosarcoma. No clear margins were obtained.

At the time of admission, the patient reported only mild pain. A dermo-epidermal graft was necessary for wound closure following surgery (Fig. 1C,D). The Musculoskeletal Tumor Society Score (MSTS) was 35/35. Following detailed discussion with the patient, salvage radiotherapy was initiated.

Radiotherapy Treatment Details

In February 2023, radiotherapy was administered using a Novalis TrueBeam STx® system (Palo Alto, Santa Clara, CA, USA), equipped with immobilization and verification systems typically employed in stereotactic treatments, to ensure precise and reproducible patient positioning. The patient was positioned prone, with the left arm in slight abduction above the head (Fig. 1E). Although this posture was not the most comfortable, it facilitated consistent reproducibility of the setup. The arm was immobilized using a radio-transparent polyethylene support, with the left forearm and hand placed inside and secured by a stereotactic mask within the frameless extension of the ExacTrac™ system, resembling a stereotactic brain treatment setup as in [10]. A thin metal wire was placed on the scar to enhance radiological visualization.

A simulation CT scan with a slice thickness of 1.5 mm was obtained and merged with pre- and post-surgical MRI scans (Fig. 2A,B) to accurately delineate the gross tumor volume (GTV), representing the residual R2 (macroscopic residual tumor) disease. The GTV was expanded by 4 cm in the cranio-caudal direction and 1.5 cm radially, following American Society for Radiation Oncology (ASTRO) guidelines [11], to define the clinical target volume (CTV), ensuring coverage of the entire operative bed and any potential subclinical disease spread. The CTV was then refined with the assistance of a radiologist specializing in hand anatomy, reducing it over the unaffected bones (radius and ulna) and ensuring it did not extend beyond the palmar aponeurosis, which acts as a barrier to tumor spread [12]. The CTV was symmetrically expanded by 5 mm to form the planning target volume (PTV).

Despite the superficial location, electrons were not considered due to the complex, non-uniform shape of the target, including curved sections, and the varying thicknesses, which could have compromised dose distribution and led to deviations from the intended plan. For this reason, we chose 6 megavolt photons delivered via volumetric modulated arc therapy (VMAT).

Fig. 1. Management of the recurrent hand sarcoma. (A) Local recurrence on the dorsum of the hand. (B) Operative bed after tumor removal. (C,D) Skin graft placement. (E) The hand on the day of computed tomography (CT) simulation, six weeks after graft positioning. (F) First follow-up in September 2023. (G) Appearance of graft necrosis with pus discharge and surrounding erythema. (H) Partial wound healing.

The total dose delivered was 50 Gy in 25 fractions to the surgical bed with wide margins, followed by a boost of 72 Gy in 36 fractions to the residual R2 disease. The prescribed dose covered 95% of the target volume in both the surgical bed and boost phases (Fig. 2D,E). Three coplanar VMAT arcs (clockwise (CW) 181.0°/179.0°-counterclockwise (CWW) 179.0°/181.0°-CW 181.0°/179.0°) were used to irradiate the extended CTV, while two coplanar arcs were employed for the boost plan (181.0°/179.0° CW-179.0°/181.0° CCW). The maximum point dose was 110% for both plans.

To minimize the risk of target miss and correct any pitch, yaw, and roll deviations due to potential hand motion, treatment was delivered with both ExacTrac and cone beam CT guidance. Daily treatment verification included two pairs of orthogonal Kilovolt (KV) X-ray images: the first to identify and correct any setup discrepancies, and the second to confirm that the corrections were successfully implemented. After adjustments with ExacTrac, a cone beam CT was performed to confirm the target remained within the designated treatment volumes (Fig. 3A,B).

Radiotherapy was initiated six weeks after skin graft implantation to ensure optimal vascularization and healing of the graft. At the conclusion of radiation therapy, only grade 2 erythema was observed.

Follow-Up

In September 2023, the patient returned for a follow-up visit. MRI of the left upper limb revealed regression of the residual disease amidst radiation sequelae (Fig. 2C), while a contrast-enhanced total body CT scan showed progression of the nodule in the inferior lobe of the left lung (5 mm to 11 mm) and the appearance of a new lesion in the lower lobe of the right lung, measuring 5.5 mm, with increased 18F-FDG PET uptake suggestive of metastases (Fig. 4).

On physical examination, no signs of radiation-induced damage were observed, and the MSTS score remained 35/35. The patient reported no pain (Fig. 1F). Considering the metastatic disease, she was referred to the oncology department for initiation of chemotherapy.

In February 2024, the patient presented with necrosis of the skin graft, accompanied by erythema and pus discharge (Fig. 1G). Functional impairment was evident, with an MSTS score of 18/35 (poor). The patient reported moderate pain and was referred back to the original surgeon for further evaluation.

Bacterial cultures identified Staphylococcus aureus and Klebsiella species. Oral antibiotic therapy was initiated, along with gentle warming applied several times daily to enhance perfusion. This was followed by debridement to remove devitalized tissue. Since then, the patient has contin-

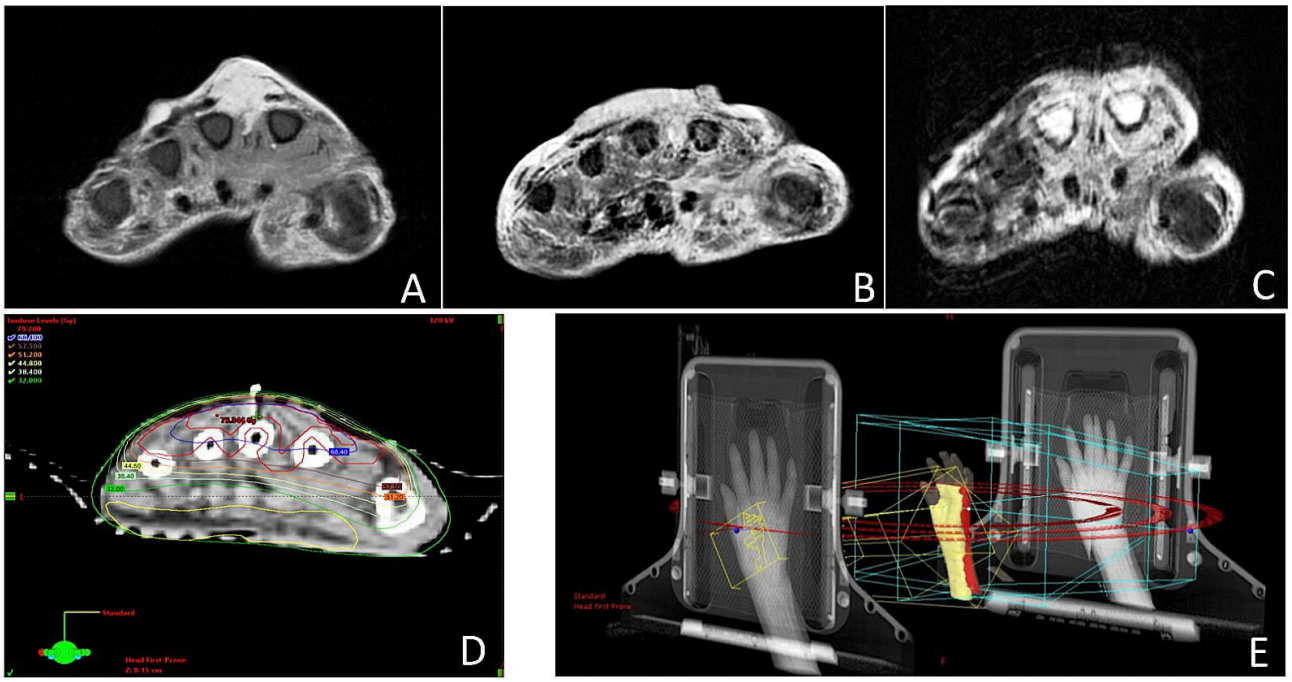

Fig. 2. Comprehensive multimodal imaging and dosimetric evaluation. (A,B) Pre- and post-surgical magnetic resonance imaging (MRI). (C) MRI six months after the completion of radiotherapy showed no signs of recurrence. (D) Isodose levels of the treatment plan, with each color representing a different isodose: green corresponds to 32 Gy, light green to 38.40 Gy, light yellow to 44.80 Gy, orange to 51.20 Gy, brown to 57.50 Gy, and blue to 68.40 Gy. The 68.40 Gy isodose, corresponding to 95% of the prescribed dose for the boost, is shown. The gross tumor volume (GTV) is depicted in pink, while the plantar skin is shown in yellow. (E) Digitally reconstructed radiography (DRR), with the plantar skin outlined in yellow and the target surface in red.

ued with local wound care, demonstrating clinical improvement, though complete healing has not yet been achieved. As of now, she has regained greater mobility in her hand, with an MSTS score of 24/35 (fair), reports minimal pain, and continues gemcitabine-based chemotherapy (Fig. 1H). Fig. 5 provides an overview of the patient's treatment timeline.

Database Search Strategy for a Narrative Literature Review

A comprehensive literature search was conducted using PubMed and Scopus, covering publications from the inception of these electronic databases up to November 2024, to identify studies on the use of radiotherapy in patients with sarcoma of the hand. The search utilized the following English terms: "sarcoma of the hand," "hand sarcoma," "soft tissue sarcoma of the hand," "wrist," "radiotherapy," and "radiation therapy".

Due to the rarity of this clinical scenario, both case reports and case series were included. Exclusion criteria comprised non-English studies, patients aged <18 years, and cases where hand-specific outcome data could not be extracted due to mixed cohorts, such as those involving tumors in other anatomical regions or where the use of radiotherapy could not be distinguished from that of surgery alone.

Table 1 (Ref. [5,9,13–19]) summarizes the nine reviewed studies, with our case included in the final row.

Discussion

Adult soft tissue sarcoma (a-STS) of the hand is a rare but challenging malignancy, primarily due to the functional impairment that may result from surgical and/or radiation treatments [20].

STS comprises various histological subtypes, with epithelioid sarcoma and synovial sarcoma being the most common in adults. In contrast, Ewing's sarcoma and rhabdomyosarcoma predominate in children but may also occur in adults [21–23]. Leiomyosarcoma, as diagnosed in our patient, is typically found in the pelvis and visceral organs, with less frequent involvement of the extremities [21].

Clinically, a-STS of the hand often presents as a slowly growing, painless mass [24]. This indolent course frequently leads to misdiagnosis as a benign condition, delaying appropriate treatment [25]. Patel *et al.* [13] reported a case initially misdiagnosed as carpal tunnel syndrome, while our patient was incorrectly treated under the assumption of a benign cyst, resulting in inadequate initial management.

Once diagnosed, radical surgery remains the cornerstone of treatment. Clear surgical margins are essential for optimal oncologic outcomes, as positive margins increase the risk of local recurrence and worsen prognosis [2]. Historically, amputation was often required due to the challenge of achieving adequate margins in an area where uninvolved, non-functional tissue is inherently limited and fur-

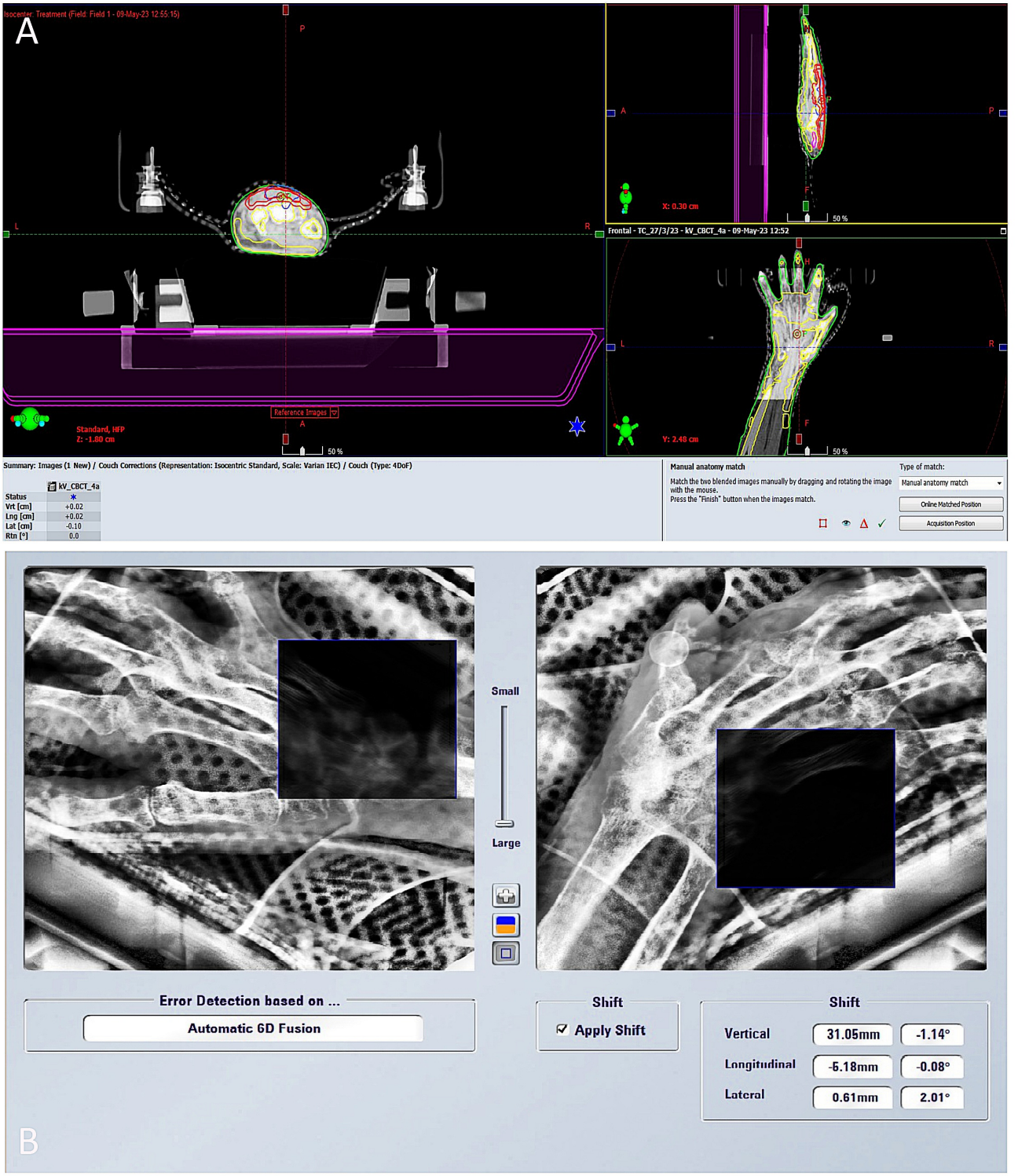

Fig. 3. Verification of treatment setup using cone-beam CT and ExacTrac imaging systems. (A) Treatment setup verification using cone-beam CT. (B) Treatment setup verification using ExacTrac.

ther constrained by critical structures requiring preservation [2]. However, wide resection—when feasible—offers high local control rates, while amputation does not provide superior oncological outcomes and may be reserved for recurrences [26].

Even non-demolitive surgery carries risks such as graft necrosis and infection [27]. Thus, specialized high-volume centers are recommended to optimize management, as evidenced by the inadequate initial treatment in our case. In high-risk scenarios, adjuvant radiotherapy and/or chemotherapy are considered [28]. While chemotherapy remains controversial, it is generally recommended for high-grade tumors, select histologies, or tumors >5 cm [29]. Importantly, chemotherapy does not impair reconstructive

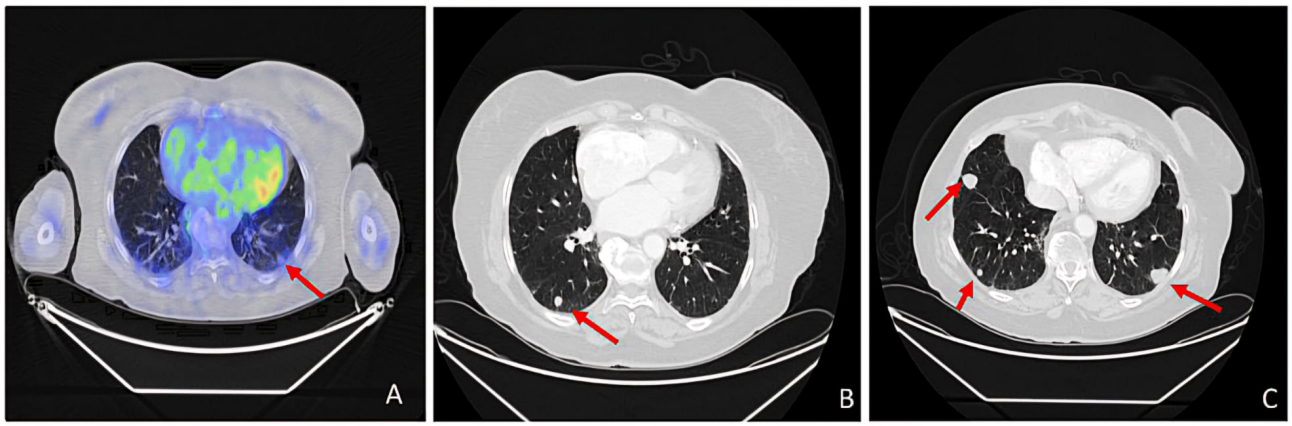

Fig. 4. Multimodal imaging assessment with 18F-Fluorodeoxyglucose (FDG) positron emission tomography (PET) and CT. (A) 18F-FDG-PET scan showing no increased FDG uptake in the lesion located in the lower lobe of the left lung, as indicated by the red arrow. (B,C) Progressive lung disease detected on total body CT scan. The red arrows indicate the progression of the pulmonary nodule in the left lung lobe, as well as the appearance of new pulmonary nodules.

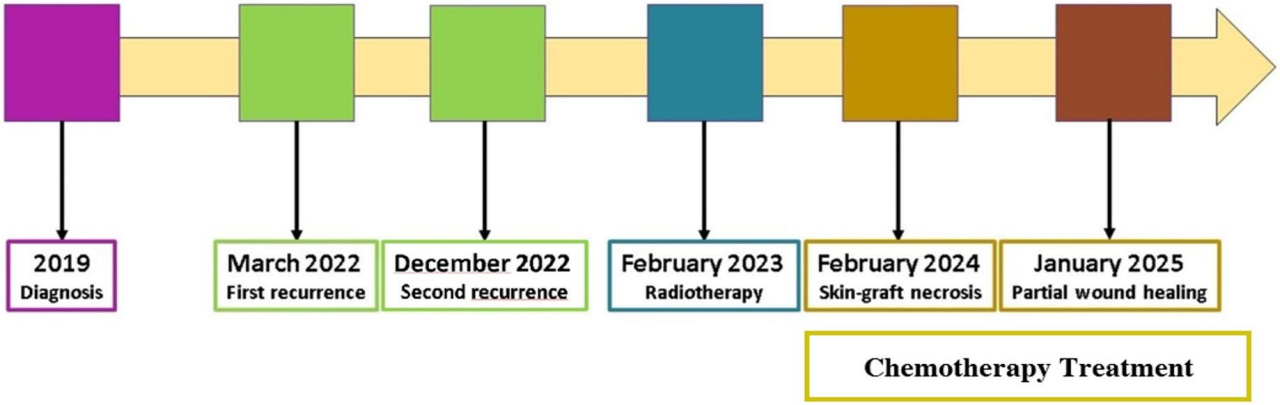

Fig. 5. Timeline of the patient's clinical events. A chronological graphical representation of the key steps from diagnosis to last follow-up.

surgery or compromise hand functionality, even when administered neoadjuvantly [30].

Radiotherapy is increasingly utilized for extremity sarcomas, both in the neoadjuvant and adjuvant settings. Although effective for local control, its long-term tolerability remains uncertain. In our case, radiotherapy, despite its reported safety [31], led to severe late toxicity in the form of skin graft necrosis. Distinguishing between surgical and radiotherapy-induced side effects can be challenging, as both can contribute to complications [27].

Patel *et al*. [13] reported excellent functional outcomes in two patients treated with adjuvant radiotherapy (36 Gy over 3 weeks and 60 Gy over 6 weeks), with no recurrence at 72 and 48 months, respectively. Similarly, Li *et al*. [15] documented favorable outcomes in a 21-year-old patient receiving 45 Gy in 25 fractions, with no lymphedema at 24 months. Anakwenze *et al*. [18] also noted no significant toxicity in two patients treated with concurrent radiochemotherapy. Presumably, the higher dose required in our case contributed to the observed side effects. Kepka *et al*. [32] proposed a 68 Gy threshold to mitigate severe toxicity, which we slightly exceeded (72 Gy) based on our institutional experience and the presence of macroscopic residual disease [33,34].

Notably, our patient had type 2 diabetes mellitus (DM2), which increases susceptibility to radiation-induced complications. Chronic hyperglycemia damages the endothelium, predisposing tissues to necrosis, while DM2-associated immunosuppression—particularly reduced natural killer cell activity—impairs infection control and wound healing [35,36]. Thus, special consideration should be given to diabetic patients undergoing radiotherapy. Nevertheless, the presence of a skin graft alone does not increase complication risk, as demonstrated by Lal *et al*. [37], who found irradiation of skin grafts to be safe.

Reports of severe radiotherapy-associated complications exist. Bray *et al*. [38] described a 72-year-old patient from a series of 26 who developed a pathological fracture one year post-radiotherapy, with an MSTS score of 13 and a Toronto Extremity Salvage Score (TESS) of 75. In the same study,

Table 1. Summary of treatments listed in chronological order.

Authors/years	Type of paper	N° of patients	Sex	Age	Tumor histology	Tumor location	Treatment	Follow-up (months)	LC/DFS/OS	Functional outcomes
Patel *et al.* (1986) [13]	Case series	2	F	20	Epithelioid sarcoma	Between the thenar and hypothenar eminences at the level of the carpal tunnel	S (Marginal excision) + R + C	72	LC: Free of relapse DFS: 1 month OS: alive	She could type a minimum of 100 words. Wrist motion ranged from 30° of extension to 60° of flexion. She was unable to abduct and rotate the first metacarpal, but demonstrated excellent side pinch between the pulp of the thumb and the side of the fingers
			M	70	Epithelioid sarcoma	At the base of the small and ring fingers	S + R	48	LC: Free of relapse DFS: 24 months OS: alive	He had functionally good pulp and key pinch between the thumb and the index finger
Euler *et al.* (1990) [14]	Case report	1	M	22	Ewing's sarcoma	Proximal phalanx of the right long finger	R + C + S (surgical incision)	24	LC: Free of relapse DFS: Free of disease OS: alive	NR
Li *et al.* (1993) [15]	Case report	1	F	21	Rhabdomyosarcoma	Dorsal aspect of the right hand between the thumb and index finger	S (surgical incision) + R + C	24	LC: Free of relapse DFS: Free of disease OS: alive	No functional impairment or lymphedema
Troum and Floyd (1993) [16]	Case report	1	M	28	Alveolar soft part sarcoma	Between the second and third metacarpals, with involvement of the second metacarpal	R + C + S (resection of the second and third rays)	24	LC: Free of relapse DFS: 13 months OS: alive	NR
Ozaki (1995) *et al.* [17]	Case report	1	M	20	Ewing's sarcoma	Long finger of the right hand	R + C + S (wide excision) + a-R	20	LC: Free of relapse DFS: Free of disease OS: alive	NR

Table 1. Continued.

Authors/years	Type of paper	N° of patients	Sex	Age	Tumor histology	Tumor location	Treatment	Follow-up (months)	LC/DFS/OS	Functional outcomes
Anakwenze *et al*. (2009) [18]	Case series	2	M	20	Ewing's sarcoma	Subcutaneous tissue adjacent to the index finger metacarpal	S (wide excision) + R + C	44	LC: Free of relapse DFS: Free of disease OS: alive	The patient is well
			M	18	Ewing's sarcoma	Ring finger-metacarpal bone	S (wide excision) + R + C	78	LC: Free of relapse DFS: Free of disease OS: alive	The patient is well
Puhaindran *et al*. (2014) [9]	Case report	1	F	21	Synovial sarcoma	Dorsal distal aspect of the index metacarpal	S (wide excision) + R + C	90	LC: Local recurrence (amputation) DFS: Free of disease OS: dead	NR
Persitz *et al*. (2021) [19]	Case report	1	M	36	Undifferentiated malignant epithelioid and spindle cell neoplasm	Right hand thenar eminence	S (wide excision) + R	48	LC: Free of relapse DFS: Free of disease OS: alive	NR
Serinelli *et al*. (2021) [5]	Case report	1	F	69	synovial sarcoma	Dorsal ulnar-sided left hand-wrist	S (wide excision) + R	65	LC: Free of relapse DFS: Free of disease OS: alive	NR
Zagardo *et al*. (2025)*	Case report	1	F	81	Leiomyosarcoma	Dorsal hand	S (surgical incision) + R	22	LC: Free of relapse DFS: 7 months for a lung metastasis OS: alive	Impaired hand movement due to graft necrosis. MSTS score (poor)

*, Zagardo *et al*. (2025) refers to the case described in the present review. Abbreviations: S, surgery; R, radiotherapy; C, chemotherapy; M, Male; F, Female; LC, local control; DFS, disease-free survival; OS, overall survival; MSTS, Musculoskeletal Tumor Society Score; NR, not reported.

two other patients treated with neoadjuvant radiotherapy had poor functional outcomes: a 75-year-old with an MSTS score of 14 and a TESS score of 67, and a 60-year-old with an MSTS score of 18 (TESS score unavailable). Radiation dose details were not provided. Puhaindran *et al*. [9] documented a case of radiation-induced sarcoma nine years after adjuvant radiotherapy for a synovial sarcoma. In the cohort of Johnstone *et al*. [39], two patients developed fibrosis and ankylosis after receiving radical radiotherapy at doses of 60 Gy in 30 fractions and 50 Gy in 25 fractions, respectively. Additionally, a 15-year-old developed telangiectasia and mild contracture at rest. Schoenfeld *et al*. [6] reported high complication rates, including fibrosis, telangiectasia, reduced range of motion, and functional impairment of the extremity, though it was unclear whether these were related exclusively to hand sarcomas or also to foot sarcomas.

Radiation-induced sarcomas, though rare, are typically high-grade and carry a poor prognosis [40,41]. Complication rates are higher with brachytherapy [8].

Despite advancements in radiotherapy techniques such as VMAT, which enables more conformal dose delivery, and improved verification systems like cone beam CT and ExacTrac [10], side effects remain difficult to prevent, as demonstrated by our case.

Of note, six of the nine reviewed studies did not report functional outcomes or radiation-related toxicity. Specifically, Euler *et al*. [14] reported the case of a 22-year-old patient with Ewing's sarcoma of the proximal phalanx of the right long finger who underwent neoadjuvant chemoradiotherapy followed by surgical resection, achieving excellent local control. However, the study did not provide details on potential radiation-induced side effects. Similarly, Troum and Floyd [16] presented data on the efficacy of combined radio-chemotherapy followed by surgery, but did not mention any radiation-related toxicities. Excellent local control was also achieved in a 20-year-old patient with Ewing's sarcoma of the hand treated with combined radio-chemotherapy and surgery, again without reference to potential radiotherapy-related adverse effects [17]. Additionally, Persitz *et al*. [19] and Serinelli *et al*. [5] documented the efficacy of combination therapy in hand sarcomas, demonstrating excellent local control in a 36-year-old patient with undifferentiated sarcoma and a 69-year-old patient with synovial sarcoma, respectively. Both underwent surgical resection followed by radiotherapy, with no reported radiation-induced side effects.

Our review suggests that radiotherapy effectively reduces recurrence risk but is associated with significant morbidity. Adverse effects appear to correlate primarily with dose and technique (external beam vs. brachytherapy). However, given the limited available data and heterogeneity in treatment regimens, establishing definitive associations remains challenging. Even with modern planning and verification systems, toxicity remains a concern.

To mitigate radiation-induced necrosis, prophylactic use of pentoxifylline, tocopherols, and vitamin E has been proposed. These agents may reduce inflammation, enhance blood flow, and limit oxidative damage [42,43]. Although they show promise in preventing and treating radiation necrosis, further studies are needed to confirm their efficacy.

At 24 months post-radiotherapy, our patient exhibited no signs of recurrence on 18F-FDG PET and MRI. Our literature review identified only one case of local recurrence requiring amputation [8], supporting the efficacy of radiotherapy in achieving local disease control in high-risk patients.

Regarding treatment-related side effects, early detection and management of radiation-induced complications are critical, highlighting the importance of long-term follow-up. For high-grade sarcomas, we recommend imaging follow-ups every three months for the first two to five years, every six months for the subsequent two years, and then annually [44]. Magnetic resonance should be the primary modality, as it allows prompt detection of recurrences and radiotherapy-induced alterations, including fibrosis and secondary malignancies.

Conclusions

Radiotherapy provides excellent local control in high-risk soft tissue sarcomas of the hand, yet its side effects, such as graft necrosis, pose significant challenges. Despite advancements like VMAT and improved verification systems, these complications remain unavoidable in some cases. Optimizing surgical techniques to achieve adequate oncological margins could reduce the need for radiotherapy, thereby minimizing treatment-related morbidity while maintaining disease control.

Nevertheless, radiotherapy remains essential for cases with macroscopic residual disease or other adverse features. Its contribution to side effects is often intertwined with surgical intervention, making causality difficult to establish. When radiotherapy is indicated, attention must be given to late sequelae—fractures, fibrosis, and radiation-induced sarcomas—that can severely impact quality of life. Long-term follow-up is crucial for early detection and management of these complications.

In conclusion, while radiotherapy ensures high local control rates, its side effects necessitate meticulous patient management. Enhancing surgical practices to minimize non-clear margins—and thus the need for adjuvant radiotherapy—could help preserve functional outcomes and overall patient well-being.

Availability of Data and Materials

Not applicable.

Author Contributions

Conceptualization: VZ, GF and GEU; provision of essential support including access to relevant literature, technical data, and/or institutional resources: GS, CF, and DM; writing—original draft preparation: VZ; writing—review

and editing: GF and GEU; supervision: GF. All authors have been involved in revising it critically for important intellectual content. All authors gave final approval of the version to be published. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring the accuracy and integrity of the manuscript.

Ethics Approval and Consent to Participate

Not applicable.

Acknowledgment

Not applicable.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

References

[1] Nepal P, Songmen S, Alam SI, Gandhi D, Ghimire N, Ojili V. Common Soft Tissue Tumors Involving the Hand with Histopathological Correlation. Journal of Clinical Imaging Science. 2019; 9: 15. https://doi.org/10.25259/JCIS-6-2019.

[2] Lin PP, Guzel VB, Pisters PWT, Zagars GK, Weber KL, Feig BW, *et al*. Surgical management of soft tissue sarcomas of the hand and foot. Cancer. 2002; 95: 852–861. https://doi.org/10.1002/cncr.10750.

[3] Collin CF, Friedrich C, Godbold J, Hajdu S, Brennan MF. Prognostic factors for local recurrence and survival in patients with localized extremity soft-tissue sarcoma. Seminars in Surgical Oncology. 1988; 4: 30–37. https://doi.org/10.1002/ssu.2980040108.

[4] Gerrand CH, Wunder JS, Kandel RA, O'Sullivan B, Catton CN, Bell RS, *et al*. Classification of positive margins after resection of soft-tissue sarcoma of the limb predicts the risk of local recurrence. The Journal of Bone and Joint Surgery. British Volume. 2001; 83: 1149–1155. https://doi.org/10.1302/0301-620x.83b8.12028.

[5] Serinelli S, Gitto L, Zaccarini DJ. Synovial sarcoma of the hand-wrist: a case report and review of the literature. Journal of Medical Case Reports. 2021; 15: 12. https://doi.org/10.1186/s13256-020-02613-4.

[6] Schoenfeld GS, Morris CG, Scarborough MT, Zlotecki RA. Adjuvant radiotherapy in the management of soft tissue sarcoma involving the distal extremities. American Journal of Clinical Oncology. 2006; 29: 62–65. https://doi.org/10.1097/01.coc.0000197660.23734.24.

[7] Bedi M, King DM, DeVries J, Hackbarth DA, Neilson JC. Does Vacuum-assisted Closure Reduce the Risk of Wound Complications in Patients With Lower Extremity Sarcomas Treated With Preoperative Radiation? Clinical Orthopaedics and Related Research. 2019; 477: 768–774. https://doi.org/10.1097/CORR.0000000000000371.

[8] Rohde RS, Puhaindran ME, Morris CD, Alektiar KM, Schupak KD, Healey JH, *et al*. Complications of radiation therapy to the hand after soft tissue sarcoma surgery. The Journal of Hand Surgery. 2010; 35: 1858–1863. https://doi.org/10.1016/j.jhsa.2010.08.030.

[9] Puhaindran ME, Hamilton K, Schlumbohm S, Rich M, Mitchell D, Steensma M. Radiation-induced osteosarcoma of the hand: case report. The Journal of Hand Surgery. 2014; 39: 1151–1154. https://doi.org/10.1016/j.jhsa.2014.03.010.

[10] Ferini G, Zagardo V, Viola A, Aiello MM, Harikar MM, Venkataram T, *et al*. Considerations on surgery invasiveness and response and toxicity patterns in classic palliative radiotherapy for acrometastases of the hand: a hint for a potential role of stereotactic body radiation therapy? A case report and literature review. Frontiers in Oncology. 2023; 13: 1146041. https://doi.org/10.3389/fonc.2023.1146041.

[11] Salerno KE, Alektiar KM, Baldini EH, Bedi M, Bishop AJ, Bradfield L, *et al*. Radiation Therapy for Treatment of Soft Tissue Sarcoma in Adults: Executive Summary of an ASTRO Clinical Practice Guideline. Practical Radiation Oncology. 2021; 11: 339–351. https://doi.org/10.1016/j.prro.2021.04.005.

[12] Watson HK, Paul H, Jr. Pathologic anatomy. Hand Clinics. 1991; 7: 661–668.

[13] Patel MR, Desai SS, Gordon SL. Functional limb salvage with multimodality treatment in epithelioid sarcoma of the hand: a report of two cases. The Journal of Hand Surgery. 1986; 11: 265–269. https://doi.org/10.1016/s0363-5023(86)80067-3.

[14] Euler E, Wilhelm K, Permanetter W, Kreusser T. Ewing's sarcoma of the hand: localization and treatment. The Journal of Hand Surgery. 1990; 15: 659–662. https://doi.org/10.1016/s0363-5023(09)90033-8.

[15] Li C, Crawford S, Mundt AJ, Vijayakumar S. Computer-aided treatment design of a distal upper extremity soft tissue tumor with electron beam radiotherapy. Medical Dosimetry: Official Journal of the American Association of Medical Dosimetrists. 1993; 18: 143–148. https://doi.org/10.1016/s0958-3947(06)80009-9.

[16] Troum S, Floyd WE, 3rd. Alveolar soft-part sarcoma of the hand. The Journal of Hand Surgery. 1993; 18: 1016–1018. https://doi.org/10.1016/0363-5023(93)90394-I.

[17] Ozaki T, Hashizume H, Kawai A, Inoue H. Ewing's sarcoma of the hand: magnetic resonance images and treatment. The Journal of Hand Surgery. 1995; 20: 441–444. https://doi.org/10.1016/S0363-5023(05)80103-0.

[18] Anakwenze OA, Parker WL, Wold LE, Amrami KK, Amadio PC. Ewing's sarcoma of the hand. The Journal of Hand Surgery, European Volume. 2009; 34: 35–39. https://doi.org/10.1177/1753193408094922.

[19] Persitz J, Beit Ner E, Chechik I, Keren T, Avisar E. Epithelioid sarcoma of the hand: a wolf in sheep's clothing. Journal of Plastic Surgery and Hand Surgery. 2021; 55: 96–104. https://doi.org/10.1080/2000656X.2020.1838914.

[20] Pang K, Guo X, Liu T, Wang L, Chen R, Zhang Z, *et al*. The Role of a Multidisciplinary Team in the Diagnosis and Treatment of Bone and Soft Tissue Sarcomas: A Single-Center Experience. Journal of Personalized Medicine. 2022; 12: 2079. https://doi.org/10.3390/jpm12122079.

[21] Husain N, Verma N. Curent concepts in pathology of soft tissue sarcoma. Indian Journal of Surgical Oncology. 2011; 2: 302–308. https://doi.org/10.1007/s13193-012-0134-6.

[22] Ducimetière F, Lurkin A, Ranchère-Vince D, Decouvelaere AV, Péoc'h M, Istier L, *et al*. Incidence of sarcoma histotypes and molecular subtypes in a prospective epidemiological study with central pathology review and molecular testing. PloS One. 2011; 6: e20294. https://doi.org/10.1371/journal.pone.0020294.

[23] Mavrogenis AF, Panagopoulos GN, Angelini A, Lesenský J, Vottis C, Megaloikonomos PD, *et al*. Tumors of the hand. European Journal of Orthopaedic Surgery & Traumatology: Orthopedie Traumatologie. 2017; 27: 747–762. https://doi.org/10.1007/s00590-017-1984-y.

[24] Brien EW, Terek RM, Geer RJ, Caldwell G, Brennan MF, Healey JH. Treatment of soft-tissue sarcomas of the hand. The Journal of Bone and Joint Surgery. American Volume. 1995; 77: 564–571. https://doi.org/10.2106/00004623-199504000-00009.

[25] Larios F, Gonzalez MR, Ruiz-Arellanos K, Aquilino E Silva G, Pretell-Mazzini J. Is Unplanned Excision of Soft Tissue Sarcomas Associated with Worse Oncological Outcomes?-A Systematic Review and Meta-Analysis. Cancers. 2024; 16: 443. https://doi.org/10.3390/cancers16020443.

[26] Duran-Moreno J, Kontogeorgakos V, Koumarianou A. Soft tissue

sarcomas of the upper extremities: Maximizing treatment opportunities and outcomes. Oncology Letters. 2019; 18: 2179–2191. https://doi.org/10.3892/ol.2019.10575.

[27] Ferguson PC. Surgical considerations for management of distal extremity soft tissue sarcomas. Current Opinion in Oncology. 2005; 17: 366–369. https://doi.org/10.1097/01.cco.0000166651.38417.c8.

[28] Nakayama R, Mori T, Okita Y, Shiraishi Y, Endo M. A multidisciplinary approach to soft-tissue sarcoma of the extremities. Expert Review of Anticancer Therapy. 2020; 20: 893–900. https://doi.org/10.1080/14737140.2020.1814150.

[29] Potkrajcic V, Kolbenschlag J, Sachsenmaier S, Daigeler A, Ladurner R, Golf A, *et al*. Postoperative complications and oncologic outcomes after multimodal therapy of localized high risk soft tissue sarcoma. Radiation Oncology (London, England). 2022; 17: 210. https://doi.org/10.1186/s13014-022-02166-4.

[30] Rivard JD, Puloski SS, Temple WJ, Fyfe A, Kwan M, Schachar N, *et al*. Quality of life, functional outcomes, and wound complications in patients with soft tissue sarcomas treated with preoperative chemoradiation: a prospective study. Annals of Surgical Oncology. 2015; 22: 2869–2875. https://doi.org/10.1245/s10434-015-4490-7.

[31] Munaretto NF, Logli AL, Rose PS, Petersen IA, Ahmed SK, Bakri K, *et al*. Radiotherapy Does Not Impact Long-term Function Following Resection of Soft-tissue Sarcomas of the Hand. Anticancer Research. 2020; 40: 1463–1466. https://doi.org/10.21873/anticanres.14089.

[32] Kepka L, DeLaney TF, Suit HD, Goldberg SI. Results of radiation therapy for unresected soft-tissue sarcomas. International Journal of Radiation Oncology, Biology, Physics. 2005; 63: 852–859. https://doi.org/10.1016/j.ijrobp.2005.03.004.

[33] Ferini G, Palmisciano P, Zagardo V, Viola A, Illari SI, Marchese V, *et al*. Combining a Customized Immobilization System with an Innovative Use of the ExacTrac System for Precise Volumetric Modulated Arc Therapy of Challenging Forearm Sarcomas. Practical Radiation Oncology. 2023; 13: 148–152. https://doi.org/10.1016/j.prro.2022.10.005.

[34] Harikar MM, Ferini G, Palmisciano P, Shakir M, Amico P, Ferraresi S, *et al*. Case Report: Adjuvant image-guided radiation therapy reduces surgical invasiveness in malignant peripheral nerve sheath tumors. Frontiers in Oncology. 2023; 13: 1129537. https://doi.org/10.3389/fonc.2023.1129537.

[35] Dong G, Li Y, Zhao Q, Pang B, Qi X, Wei J, *et al*. Effects of diabetes on the development of radiation pneumonitis. Respiratory Research. 2021; 22: 160. https://doi.org/10.1186/s12931-021-01754-4.

[36] Zagardo V, Pergolizzi S, Ferini G. Extensive necrosis of the tongue as a very early adverse event of head and neck radiotherapy. Oral Oncology. 2024; 155: 106880. https://doi.org/10.1016/j.oraloncology.2024.106880.

[37] Lal ST, Banipal RPS, Bhatti DJ. Tolerance of skin grafts to postoperative radiotherapy. International Journal of Applied & Basic Medical Research. 2015; 5: 187–189. https://doi.org/10.4103/2229-516X.165382.

[38] Bray PW, Bell RS, Bowen CV, Davis A, O'Sullivan B. Limb salvage surgery and adjuvant radiotherapy for soft tissue sarcomas of the forearm and hand. The Journal of Hand Surgery. 1997; 22: 495–503. https://doi.org/10.1016/S0363-5023(97)80019-6.

[39] Johnstone PA, Wexler LH, Venzon DJ, Jacobson J, Yang JC, Horowitz ME, *et al*. Sarcomas of the hand and foot: analysis of local control and functional result with combined modality therapy in extremity preservation. International Journal of Radiation Oncology, Biology, Physics. 1994; 29: 735–745. https://doi.org/10.1016/0360-3016(94)90561-4.

[40] Patel SR. Radiation-induced sarcoma. Current Treatment Options in Oncology. 2000; 1: 258–261. https://doi.org/10.1007/s11864-000-0037-6.

[41] Pitcher ME, Davidson TI, Fisher C, Thomas JM. Post irradiation sarcoma of soft tissue and bone. European Journal of Surgical Oncology: the Journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology. 1994; 20: 53–56.

[42] Otluoglu GD, Yılmaz B, Ekinci G, Bayri Y, Bozkurt SU, Dağçınar A. Pentoxifylline and Vitamin E Can Restrict Radiation Necrosis via Vascular Pathways, Experimental Study in an Animal Model. World Neurosurgery. 2023; 179: e530–e538. https://doi.org/10.1016/j.wneu.2023.08.135.

[43] Nieder C, Zimmermann FB, Adam M, Molls M. The role of pentoxifylline as a modifier of radiation therapy. Cancer Treatment Reviews. 2005; 31: 448–455. https://doi.org/10.1016/j.ctrv.2005.07.007.

[44] Sawamura C, Matsumoto S, Shimoji T, Okawa A, Ae K. How long should we follow patients with soft tissue sarcomas? Clinical Orthopaedics and Related Research. 2014; 472: 842–848. https://doi.org/10.1007/s11999-013-3076-6.