Radiotherapy and Oncology 214 (2026) 111276

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Original Article

Impact of target volume and dose concepts on the outcomes of prostate cancer patients treated with stereotactic body radiotherapy for spinal metastases – a European multicenter cohort study

Isabell Seiler [a,b,1], Sebastian Schäfer [a,b,1], Camilla von Wachter [c], Panagiotis Balermpas [c], Marek Slavik [d], Petr Burkon [d], Johannes Meents [e], Lena Kästner [e,f], Fabian Lohaus [g,h,i,j], Jochen Willner [k], Anna Sabrina Schunn [l], Sophia Drabke [l], Kenneth Klischies [m], Olaf Wittenstein [m], Priska Bank [n], Richard Partl [o], Jörg-Andreas Müller [p], Ahmed Gawish [q], Arne Grün [r], Andrea Baehr [s], Maike Trommer [t,u], Andrea Glasmacher [t], Thomas Mader [v], Richard Holy [w], Yvonne Dzierma [x], Felix Ehret [r,y,z], Alexander Rühle [a,b], Matthias Guckenberger [c], Christos Moustakis [a,b], Thomas Brunner [o], Oliver Blanck [m], Judit Boda-Heggemann [e,f], Nils H. Nicolay [a,b], Franziska Nägler [a,b,*]

[a] *Department of Radiotherapy, University Hospital Leipzig, Stephanstraße 9a, Leipzig, Germany*
[b] *Comprehensive Cancer Center Central Germany, Partner Site Leipzig, Leipzig, Germany*
[c] *Department of Radiation Oncology, University Hospital Zurich, Rämistr. 100, Zurich CH-8091, Switzerland*
[d] *Department of Radiation Oncology, Masaryk Memorial Cancer Institute and Medical Faculty, Masaryk University, Brno, Czech Republic*
[e] *Department of Radiation Oncology, University Medicine Mannheim, Medical Faculty Mannheim, Heidelberg University, Theodor-Kutzer-Ufer 1-3, Mannheim, Germany*
[f] *DKFZ Hector Cancer Institute at the University Medical Center Mannheim, Mannheim, Germany*
[g] *Department of Radiotherapy and Radiation Oncology, Faculty of Medicine and University Hospital Carl Gustav Carus, TUD Dresden University of Technology, Fetscherstraße 74, Dresden, Germany*
[h] *National Center for Tumor Diseases (NCT), NCT/UCC Dresden, a Partnership Between DKFZ, Faculty of Medicine and University Hospital Carl Gustav Carus, TUD Dresden University of Technology, and Helmholtz-Zentrum Dresden-Rossendorf (HZDR), Germany*
[i] *OncoRay – National Center for Radiation Research in Oncology, Faculty of Medicine and University Hospital Carl Gustav Carus, TUD Dresden University of Technology, Helmholtz-Zentrum Dresden-Rossendorf, Dresden, Germany*
[j] *German Cancer Consortium (DKTK), Partner Site Dresden, and German Cancer Research Center (DKFZ), Heidelberg, Germany*
[k] *Department of Radiotherapy, Klinikum Bayreuth GmbH, Preuschwitzer Str. 101, 95445 Bayreuth, Germany*
[l] *Department of Radiation Oncology and Radiotherapy, University Medical Center Mainz, Langenbeckstraße 1, 55131 Mainz, Germany*
[m] *Department of Radiotherapy and Radiation Oncology, University Hospital Schleswig-Holstein, Kiel, Germany*
[n] *Clinic for Radiation Therapy and Radio-Oncology Gera, Waldklinikum Gera, Germany*
[o] *Department of Therapeutic Radiology and Oncology, Comprehensive Cancer Center, Medical University of Graz 8036, Graz, Austria*
[p] *Department of Radiation Oncology, University Hospital Halle (Saale), Ernst-Grube-Str. 40, 06120 Halle (Saale), Germany*
[q] *Department of Radiotherapy and Radiation Oncology, Philipp Marburg University Hospital, Marburg, Germany*
[r] *Charité – Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Department of Radiation Oncology, Berlin, Germany*
[s] *Department of Radiation Oncology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany*
[t] *Department of Radiation Oncology, Faculty of Medicine and University Hospital Bonn, Bonn, Germany*
[u] *Center for Integrated Oncology CIO Aachen Bonn Cologne Duesseldorf, Department of Internal Medicine, Faculty of Medicine and University Hospital Cologne, Germany*
[v] *Department of Radiation Oncology, Kantonsspital Graubünden, Chur, Switzerland*
[w] *Radiotherapy Med 360 Grad in Aachen, Viehhofstraße 43, 52066 Aachen, Germany*
[x] *Department of Radiotherapy, Rostock University Medical Center, Rostock, Germany*
[y] *European Radiosurgery Center Munich, Munich, Germany*
[z] *German Cancer Consortium (DKTK), Partner Site Berlin, a Partnership Between DKFZ and Charité – Universitätsmedizin Berlin, Germany*

* Corresponding author at: Department of Radiotherapy, University Hospital Leipzig, Stephanstraße 9a, Leipzig, Germany.
E-mail address: franziska.naegler@medizin.uni-leipzig.de (F. Nägler).
[1] Both authors contributed equally.

https://doi.org/10.1016/j.radonc.2025.111276
Received 23 September 2025; Received in revised form 3 November 2025; Accepted 4 November 2025
Available online 8 November 2025

ARTICLE INFO

Keywords:
Bone metastases
Prostate cancer
Stereotactic radiotherapy
Metastasis-directed therapy (MDT)
Spine metastases
Target concept
Dose concept
Stereotactic Body Radiotherapy

ABSTRACT

Background and purpose: The importance of metastasis-directed radiotherapy is increasing in the management of oligometastatic prostate cancer. We evaluated different target volume and dose concepts for stereotactic body radiotherapy (SBRT) of spine bone metastases (BoM) from prostate cancer in a large European cohort.
Material and methods: Data of prostate cancer patients receiving SBRT for spine BoM between 2010 and 2024 at 19 European cancer centers were retrospectively collected. Treatment volumes and dose concepts were analyzed regarding their impact on overall survival (OS), freedom from local recurrence (FFLR), biochemical recurrence-free survival (BRFS), and progression-free survival (PFS).
Results: With a median follow-up of 25.1 months (range: 1.4–77.2), 213 patients with 283 spine BoM were evaluated. 1-/3-year PFS with simultaneously integrated boost (SIB) were 85.7 %/73.9 % (BED_4 [Biologically effective dose with α/β-ratio = 4 Gy] ≥ 100 Gy) and for non-SIB concepts 81.2 %/45.5 % (BED_4 ≥ 100 Gy), respectively. 1-/3-year BRFS for SIB-treated BoM amounted to 81.7 %/68.4 % (BED_4 ≥ 100 Gy) and for non-SIB 78.3 %/43.6 % (BED_4 ≥ 100 Gy). OS was not significantly different for the evaluated dose and target volume concepts. For FFLR a significant difference was observed favoring BED_4 ≥ 100 Gy. In multivariable analysis, following factors were positively associated with both PFS and BRFS: BED_4 for GTV_{mean} dose and SIB concept. Adverse events were very low, with fracture rates of 2.2 %.
Conclusion: This multicenter cohort analysis showed that SBRT of spine BoM from prostate cancer is an effective and well-tolerated treatment. Both BED and usage of a SIB concept were associated with improved PFS and BRFS. Prospective studies are needed to confirm these findings and further standardize SBRT concepts.

Introduction

Globally, prostate cancer ranks as the second most prevalent cancer among men [1]. The increasing detection of metastatic disease at diagnosis is primarily attributable to the enhanced efficacy of screening and imaging [2]. Prostate cancer metastases have a predilection for the skeletal system, mainly presenting as osteoblastic lesions [3]. Bone metastases (BoM) are a significant cause of skeletal-related events (SREs), with approximately one-third of them being complicated lesions, resulting in pain, pathological fractures, and neurological impairments [4]. In addition to systemic treatments, palliative radiotherapy constitutes a guideline-recommended treatment for symptomatic BoM, with effective pain relief and stabilization [5,6]. Recent clinical trials revealed the clinical benefit of stereotactic body radiotherapy (SBRT) regarding local control, progression-free (PFS) and overall survival (OS), in selected cases also for oligometastatic disease [7–11]. These findings led to the publication of practice guidelines for bone SBRT [12–14]. Analysis of the STOMP/ORIOLE trials indicated a benefit of metastasis-directed therapy (MDT) over observation for patients with oligometastatic prostate carcinoma (OMPC) [15]. A recent *meta*-analysis revealed encouraging improvements in PFS by adding SBRT to systemic therapy for different OMPC states, with no excessive toxicities observed. However, the level of evidence was considered low or moderate, and OS comparisons remain inconclusive [16]. Also, the findings of the EXTEND and PCS 9 trials indicated a higher degree of efficacy for the combination of SBRT and androgen deprivation therapy (ADT)-/systemic treatment in comparison to either systemic treatment alone or, as reported in the RADIOSA trial, SBRT alone [17–20]. The recent WOLVERINE *meta*-analysis demonstrated a borderline benefit even for OS [21].

SBRT enables the delivery of ablative doses to metastatic lesions with high precision, achieving superior and more durable pain control compared to conventional radiotherapy [22–24]. Nevertheless, significant uncertainties concerning the most appropriate choice between locally ablative and palliative bone radiotherapy, as well as treatment volume and dose concepts remain [12,25–28].

Target volume definition in spine SBRT is critical for treatment planning. Approaches range from contouring only the metastatic gross tumor volume (GTV) with small margins to account for setup uncertainties (expanded GTV concept), to encompassing adjacent osseous compartments or the entire involved vertebral body as a clinical target volume (CTV) [29–33]. There are two different concepts for compartmental treatments, either high-dose volumes for the BoM including the adjacent compartments (compartment concept), or high-dose volume covering only the BoM, with the entire vertebral body receiving a lower, homogeneous dose as part of a simultaneous integrated boost (SIB concept) [34,35]. In Fig. 1, schematic dose distributions are presented to illustrate the aforementioned different target volume concepts. However, in clinical practice, considerable variability in treatment patterns is observed [36–38].

This heterogeneity extends to dose-fractionation regimes as well. International consensus guidelines recommend a prescribed dose exceeding BED_{10} = 50 Gy for local ablative SBRT of spine metastases, with variable fractionation schedules [12].

As SBRT becomes increasingly integrated into the multidisciplinary management of OMPC, continued efforts are needed to harmonize practice patterns with the best available evidence.

Thus, the objective of our European multicenter cohort study on SBRT for spine BoM from prostate cancer was to evaluate routinely used SBRT concepts regarding oncological outcomes and safety, depending on applied dose and target volume concepts.

Material and methods

Patient selection

As a project of the working group on radiosurgery and stereotactic radiotherapy of the German Society for Radiation Oncology (DEGRO), we performed a retrospective multicenter cohort analysis on SBRT of BoM. Individual clinical and treatment data of patients with OMPC receiving SBRT for spine BoM between 2010 and 2024 at 19 European cancer centers in Germany, Austria, Switzerland, and the Czech Republic were retrospectively collected and evaluated. The diagnosis of BoM was determined on the basis of radiographic findings revealed by computed tomography (CT), magnetic resonance imaging (MRI), prostate-specific membrane antigen positron emission tomography (PSMA PET/CT), or bone scintigraphy. According to the established European consensus criteria, the initial classification of oligometastatic disease was followed by further subclassification [39]. SBRT parameters, including target volumes, doses, and plan parameters according to the International Commission on Radiation Units and Measurements (ICRU) report 91, were analyzed [40–42]. Previous treatments, concomitant/sequential systemic therapies, and necessary salvage therapies after SBRT were recorded. Biologically effective dose (BED) was calculated with the formula $BED = n \times d \times (1 + d/(\alpha/\beta))$ with n = number of fractions, d = dose per fraction, based on an $\alpha/\beta = 10$ Gy (BED_{10}) as commonly used for tumor tissue and $\alpha/\beta = 4$ Gy (BED_4) for prostate cancer, assuming that BoM occur more frequently in high-grade prostate carcinomas [43]. BED_{10} of at least 48 Gy for the target volume

in a maximum of 10 fractions was requested as the minimal dose for bone SBRT.

This study was approved by the institutional ethics board (127/24-ek) and followed the STROBE guidelines for reporting observational studies (Supplementary Data 2) [44].

Response assessment

OS was calculated from the end of SBRT until death from any cause. PFS was defined as the time interval from completion of SBRT until death or the development of any type of imaging-confirmed cancer progression. Findings of routinely administered pre- and post-SBRT imaging examinations were analyzed retrospectively regarding local recurrence, and fractures, with local recurrence specified as imaging-confirmed progression. When patients received SBRT for multiple BoM, freedom from local recurrence (FFLR) analysis was conducted independently for each lesion. To calculate FFLR following SBRT, the occurrence of lesions was considered to be censored at the time of the most recent imaging. Given that imaging was not routinely performed during follow-up for OMPC with stable prostate-specific antigen (PSA) levels, participating centers conducted a secondary assessment of rising PSA levels after SBRT to determine biochemical recurrence and thus calculate biochemical recurrence-free survival (BRFS). Both acute ($\leq$90 days post SBRT) and chronic (>90 days post SBRT) treatment-related adverse events were documented according to Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 [45].

Statistical analysis

All analyses were performed in Python 3.12.7 using custom scripts. Data preparation and preprocessing relied on pandas (v2.2.3) and NumPy (v2.2.1); statistical inference and survival modeling used SciPy (v1.14.1) and lifelines (v0.30.0); visualization was carried out with Matplotlib (v3.10.0). Descriptive analyses of patient demographics and clinical characteristics were performed. Median values were given as either the 95 % range or the range of the provided values, where applicable. Subgroup analyses compared cohorts defined by treatment technique and mean BED_4/BED_{10} delivered to the GTV. The BED_4/BED_{10} threshold for subgrouping was explored iteratively by increasing the cutoff in 1 Gy steps and recording log-rank test p-values for PFS. Time-to-event outcomes were analyzed with Kaplan–Meier estimators and multivariable Cox proportional hazards models. Patient age, target volume concept, GTV_{mean} BED_4, and tumor volume were preselected as covariates in the Cox proportional hazards model. The proportional hazards assumption test was non-significant. Multivariable models were fitted on complete cases only. Model assumptions were assessed at $\alpha = 0.05$. Kaplan–Meier curves were compared across subgroups using log-rank tests, and survival probabilities at prespecified time points were interpolated and reported with 95 %-confidence intervals (95 %-CI).

Results

Data of 283 lesions from 213 patients treated with bone SBRT for spine BoM from OMPC were included. Detailed patient characteristics are presented in Table 1.

Target volume definition was based on multimodal imaging with PET-CT (235/283; 83 %) and/or MRI (94/283; 33 %) according to institutional standards of each center and national recommendations [46].

Target volumes were predominantly defined with the SIB concept (135/260 evaluable lesions; 51.9 %). The expanded GTV concept (BoM plus safety margins) was used in 38.5 % (100/260) of spine lesions. The minority of 25/260 spine BoM (9.6 %) was delineated as the metastasis plus adjacent osseous compartments and a small safety margin to PTV (compartment concept).

Prescribed dose for the SIB (high-dose PTV) was median 44.0 Gy (range: 35.0 Gy–48.5 Gy) in median 10 (range: 3–10) fractions, and for the expanded GTV concept 35.0 Gy (range: 18.0 Gy–40.0 Gy) in median 5 (range: 1–10) fractions, and for the compartment concept 27.0 Gy (range: 22.5 Gy–34.0 Gy) in median 3 (range: 3–5) fractions. Dose-volume parameters for the target volume and treatment parameters are shown in Table 2.

Concomitant/sequential ADT was administered in 167 of 283 lesions (59 %), whereas 101 of 283 lesions (36 %) received no additional therapy. ADT was evenly distributed among SIB (ADT: 83/283 lesions; 29.3 %; no ADT: 49/283; 17.3 %) and non-SIB (ADT: 84/283; 29.7 %; no ADT: 52/283; 18.4 %) groups.

Median follow-up time was 25.1 months (range: 1.4–77.2). A total of 30 patients died, and 19 local recurrences were reported during the follow-up period.

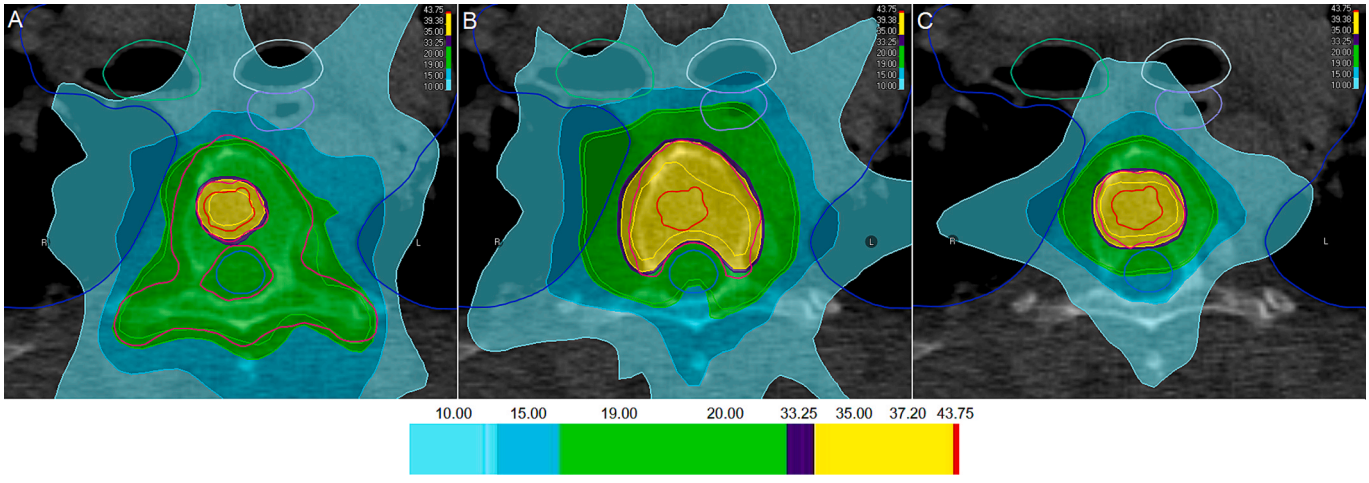

Fig. 1. Schematic dose distributions for the three different target volume concepts A) Simultaneous integrated boost (SIB) with isodoses. GTV (red) includes the metastasis plus a 2 mm margin for the high-dose planning target volume (PTV_{SIB} in pink color), and the conventional-dose PTV (outer pink contour) covers the entire affected vertebral body (CTV in orange) with a small setup safety margin in the same treatment plan. PTV_{SIB}: 5x7Gy prescribed to 80 % (inner yellow isodose), $PTV_{conventional\ dose}$: 5x4Gy (inner green isodose). B) Compartment concept. GTV (red) includes the metastasis, CTV (orange) encompassing adjacent osseous compartments plus small safety margin to the PTV (pink). PTV: 5x7Gy prescribed to 80 % (inner yellow isodose). C) Expanded GTV concept. GTV (red) includes the metastasis, CTV (orange) includes GTV with margin (2–5 mm) plus small safety margin to the PTV (pink). PTV: 5x7Gy prescribed to 80 % (inner yellow isodose). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Table 1
Patient characteristics.

Variable	
Patients (n = total)	213
Bone metastases spine (n = total)	283
Age	
Median in years (range)	72 (48–87)
Karnofsky-Index before SBRT	
Median in % (95 % range)	100 (80–100)
Initial therapy primary tumor (multiple treatment modalities possible)	
Surgery	125 (58.7 %)
Radiotherapy	59 (27.7 %)
Systemic Therapy	32 (15.0 %)
Other	20 (9.4 %)
No information available	47 (16.6 %)
Bone metastases	
Time between initial diagnosis and bone metastasis, median (months)	53.6 (−4.4–177.2)
Synchronous treatment	56
Metachronous treatment	223
Classification according ESTRO/EORTC [39]	
Metachronous oligoprogression	65
Metachronous oligorecurrence	93
Repeat oligoprogression	16
Repeat oligorecurrence	9
Induced oligoprogression	9
Induced oligorecurrence	2
No information available	89
Characteristics of bone metastases	
Radiological osteolytic	45
Radiological osteoblastic	157
Mixed osteolytic/ osteoblastic	10
Soft tissue infiltration yes / no	6 / 233
Spinal canal infiltration yes / no	0 / 226
Symptomatic before SBRT yes / no	33 / 100
PSA before SBRT in ng/ml (95 % range)	7.27 (0.24–87.22)
Systemic therapy	
ADT concomitant / sequential	89 / 78
Cytotoxic chemotherapy	0
No systemic therapy	101
No information available	15
Imaging before treatment planning:	
Diagnostic CT	18
MRI	94
PET (including PSMA-PET)	235
Scintigraphy	26
No information available	9
Number of treated bone metastases per patient median (range)	1 (1–8)
Treatment technique	
LINAC (Photon FF / FFF / unknown)	106 / 112 / 43
Robotic radiosurgery (CyberKnife)	22

Abbreviations: CT: Computed Tomography, MRI: Magnetic Resonance Imaging, PET: Positron Emission Tomography, PSMA: Prostate-Specific Membrane Antigen, LINAC: Linear Accelerator, FF(F): Flattening-Filter(−Free), SBRT: Stereotactic Body Radiotherapy, PSA: Prostate-Specific Antigen, ADT: androgen deprivation therapy.

Oncological outcomes were analyzed across subgroups by target volume concept (SIB vs. non-SIB) and dose concept based on BED_4/BED_{10} for GTV_{mean} dose.

Stratification of FFLR by target volume concept revealed no significant difference in patients treated with SIB or non-SIB. Patients receiving $BED_4 \geq 100$ Gy had significantly improved FFLR compared with those treated with $BED_4 < 100$ Gy ($p = 0.02$). In patients with $BED_4 \geq 100$ Gy, 1-/3-year FFLR was 97.8 % (95 %-CI: 85.3 %-99.7 %)/90.3 % (95 %-CI: 60.5 %-97.9 %) for SIB and 97.7 % (95 %-CI: 84.6 %-99.7 %)/93.8 % (95 %-CI: 76.3 %-98.5 %) for non-SIB (supplementary figure 1).

Table 2
Dose volume parameters according to ICRU91 Parameters presented according to the three treatment concepts.

	SIB concept	Expanded GTV concept	Compartment concept
Number of treatments	135	100	25
Mean target volume (GTV) in cc (range)	2.9 (0.4–17.8)	2.5 (0.5–27.0)	3.9 (0.7–13.7)
Prescribed dose PTV, median in Gy (range)	44.0 (35.0–48.5)	35.0 (18.0–40.0)	27.0 (22.5–34.0)
Number of fractions, median (range)	10 (3–10)	5 (1–10)	3 (3–5)
Median BED_4 PTV (prescribed dose) in Gy (range)	107.3 (80.0–120.0)	96.2 (71.8–120.0)	87.8 (64.7–96.2)
Median BED_{10} PTV (prescribed dose) in Gy (range)	72.0 (56.0–72.0)	59.5 (42.6–72.0)	51.3 (39.4–59.5)
Median PTV $D_{98\%}$ in Gy (range)	39.5 (29.0–47.8)	30.0 (15.9–39.9)	25.7 (21.5–30.1)
Median PTV $D_{2\%}$ in Gy (range)	49.4 (35.8–57.1)	36.0 (22.0–49.9)	32.2 (27.3–42.6)
Median GTV_{mean} in Gy (range)	46.7 (34.8–53.4)	34.6 (22.0–49.2)	29.1 (25.7–41.3)
Median BED_4 GTV_{mean} in Gy (range)	107.4 (80.0–152.6)	104.6 (71.7–171.3)	99.7 (80.9–128.1)
Median BED_{10} GTV_{mean} in Gy (range)	72.0 (55.8–91.1)	60.1 (46.3–89.8)	57.4 (47.8–75.6)
Median BED_4 PTV $D_{2\%}$ in Gy (range)	114.2 (82.7–170.7)	112.2 (75.4–174.3)	118.6 (89.5–136.5)
Median BED_{10} PTV $D_{2\%}$ in Gy (range)	75.7 (57.6–97.8)	64.3 (48.2–99.6)	66.8 (52.2–79.7)

Abbreviations: SIB: Simultaneous Integrated Boost, GTV: Gross Tumor Volume, PTV: Planning Target Volume, BED: Biological Effective Dose.

PFS was positively associated with using a SIB concept compared to non-SIB concepts ($p < 0.002$). Stratification by BED revealed that $BED_4 \geq 100$ Gy as well as $BED_{10} \geq 61$ Gy were significantly associated with improved PFS compared to lower BED ($p < 0.001$). In the $BED_4 \geq 100$ Gy group, a SIB concept was linked to improved PFS compared to non-SIB ($p = 0.012$). The SIB concept reached 1-/3-year PFS of 85.7 % (95 %-CI: 70.7 %-93.3 %)/73.9 % (95 %-CI: 56.5 %-85.2 %) compared to 81.2 % (95 %-CI: 67.0 %-89.8 %)/45.5 % (95 %-CI: 29.1 %-60.5 %) for non-SIB (Figs. 2 and 3, supplementary Fig. 2).

For patients with $BED_4 < 100$ Gy, BRFS was 73.7 % at 1 year (95 %-CI: 44.1 %-89.2 %) for SIB and 53.7 % (95 %-CI: 35.0 %-69.2 %) for non-SIB. The 3-year BRFS in this group decreased to 54.6 % (95 %-CI: 23.8 %-77.4 %) and 0 % (95 %-CI: 0 %-0%). $BED_4 \geq 100$ Gy led to a 1-/3-year BRFS of 81.7 % (95 %-CI: 65.1 %-90.9 %)/68.4 % (95 %-CI: 49.7 %-81.3 %) in the SIB group and 78.3 % (95 %-CI: 63.3 %-87.7 %)/43.6 % (95 %-CI: 23.0 %-62.5 %) in the non-SIB group, respectively. Considering only the administered dose, a significantly better BRFS was shown for $BED_4 \geq 100$ Gy compared to $BED_4 < 100$ Gy ($p < 0.001$). In patients treated with $BED_4 < 100$ Gy, SIB resulted in improved BRFS compared to non-SIB ($p = 0.001$) (Figs. 2 and 3, supplementary Fig. 2). Due to the small sample size of some subgroups, wide confidence intervals were evident, notably in Fig. 3.

Regarding additional ADT, we observed a positive effect on BRFS. Especially in patients with a lower $BED_4 < 100$ Gy administration of ADT was positively associated with BRFS ($p = 0.01$), while no significant difference was detected for $BED_4 \geq 100$ Gy (supplementary Fig. 3).

There was no significant difference for OS, depending on BED or target volume concept. For $BED_4 < 100$ Gy, 1-/3-year OS reached 100 %

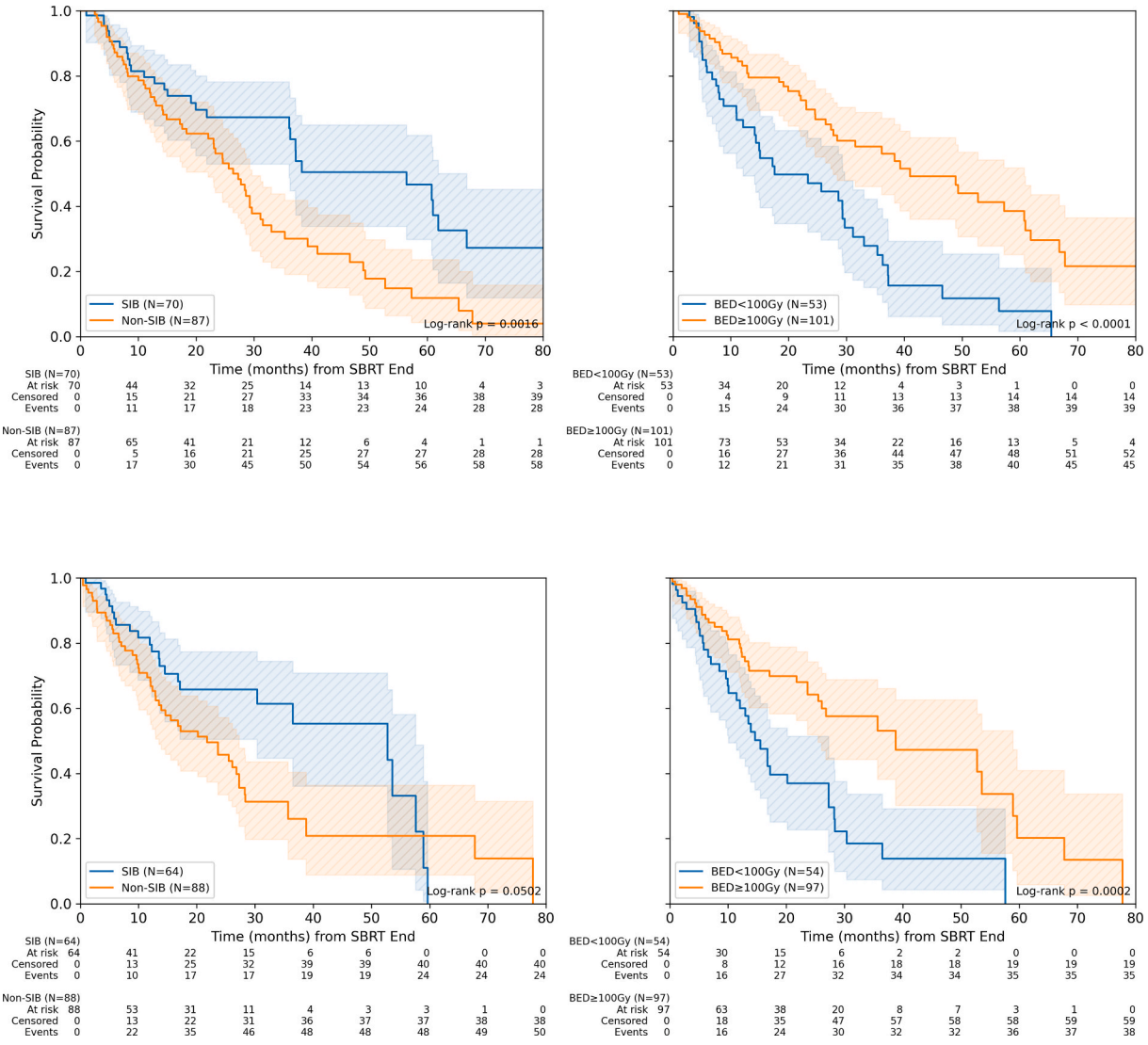

Fig. 2. Oncological outcome depending on treatment concept for SBRT of spine bone metastasis A) Comparison of PFS for simultaneously integrated boost (SIB) concept vs. non-SIB concepts B) Comparison of PFS depending on the BED_4 ($\alpha/\beta = 4$ Gy) in gross tumor volume (GTV_{mean}) C) Comparison of BRFS for SIB vs. non-SIB concepts D) Comparison of BRFS depending on the BED_4 in GTV_{mean}.

(95 %-CI: 100.0 %-100.0 %)/81.5 % (95 %-CI: 43.5 %-95.1 %) for SIB and 94.9 % (95 %-CI: 80.9 %-98.7 %)/91.8 % (95 %-CI: 76.5 %-97.3 %) for non-SIB, respectively. For $BED_4 \geq 100$ Gy, 1-year OS was 96.1 % (95 %-CI: 85.2 %-99.0 %) for SIB and 98.1 % (95 %-CI: 87.6 %-99.7 %) for non-SIB, whereas 3-year OS amounted to 79.1 % (95 %-CI: 59.6 %-90.0 %) for SIB and 87.8 % (95 %-CI: 68.3 %-95.7 %) for non-SIB (supplementary Fig. 4).

In multivariable analysis, higher age was associated with worse OS (HR [hazard ratio] 1.09; 95 %-CI, 1.02–1.17; $p = 0.01$). A higher BED_4 GTV_{mean} was associated with improved PFS (HR 0.99; 95 %-CI: 0.98–0.99, $p < 0.01$) and BRFS (HR 0.98; 95 %-CI: 0.97–0.99, $p < 0.001$). Usage of a SIB concept was linked to improved PFS (HR 0.42; 95 %-CI: 0.26–0.69, $p < 0.001$). Additional administration of ADT was associated with improved BRFS (HR 0.51; 95 %-CI: 0.31–0.83, $p < 0.01$). Details are shown in Table 3.

The overall rate of adverse events was low (20.8 %, 59/283), predominantly grade 1–2 events, with fatigue grade 1 being most frequent (8.1 %, 23/283). Only 0.8 % grade 3 adverse events (2/283, 1x pain and 1x dysphagia) and no grade 4 or 5 adverse events were reported (supplementary Table 1). Fracture rates related to SBRT, without tumor progression, were 0.4 % (1/283, SIB concept) for acute and 1.8 % (5/283: 3x compartment concept, 2x expanded GTV concept) for delayed fractures.

Discussion

To the best of our knowledge, this is the first large multicenter real-world cohort analysis investigating the impact of different treatment concepts of SBRT for spine BoM in patients with prostate cancer with a particular focus on the efficacy and safety of commonly used European practice patterns.

We found that escalation of GTV_{mean} dose to a $BED_4 \geq 100$ Gy was associated with significantly improved PFS and BRFS. Additionally, our data suggest that SIB concept in our retrospective cohort had an impact on PFS and BRFS. No dependency was observed regarding OS, irrespective of target volume or dose concept. The high efficacy was accompanied by excellent tolerability and favorable safety profile with especially low fracture rates.

These findings underline the importance of high BED even for SBRT of spine BoM of prostate carcinoma, as has already been demonstrated for other metastases and primary tumors [47–51]. Our results also augment the mounting evidence that treating metastatic lesions with

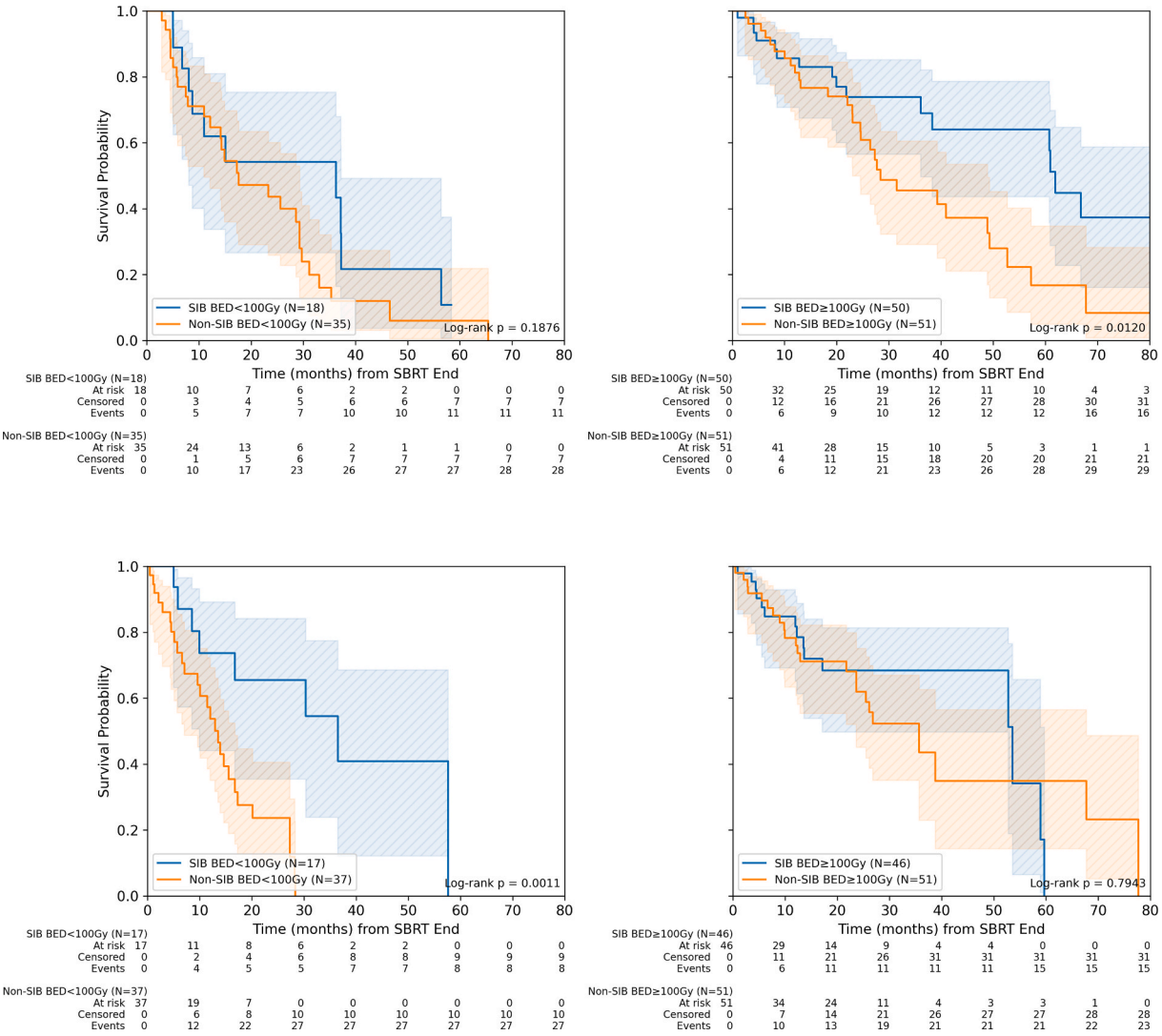

Fig. 3. Comparison of oncological outcome depending on BED_4 for different target volume concepts A) PFS for SIB vs non-SIB concept for $BED_4 < 100$ Gy and B) for $BED_4 \geq 100$ Gy C) BRFS for SIB vs non-SIB concept for $BED_4 < 100$ Gy and D) for $BED_4 \geq 100$ Gy.

SBRT results in a prolonged PFS in patients with OMPC [16,52,53]. A recent systematic review in OMPC reported pooled OS rates of 90.6 % and 80.1 %, and pooled PFS rates of 52.7 % and 28.4 % at 2 and 4 years, respectively [54]. In our retrospective cohort, higher $BED_4 \geq 100$ Gy was associated with improved PFS, and within this high-dose-group, SIB was significantly associated with an improvement of PFS (1-/3-year: 85.7 %/ 73.9 %). PFS was worse in patients treated with $BED_4 < 100$ Gy, whereas the target volume concept itself did not influence PFS within this subgroup. However, underreporting of local recurrence or distant progression is a concern, as patients with OMPC often do not undergo regular imaging in the absence of PSA elevation.

Although FFLR was excellent, PFS and BRFS decreased during follow-up period, underlining the systemic nature of metastatic disease, and the need for systemic therapies [19,55]. Approximately 60 % of BoM in our cohort were treated with additional ADT, which was associated with an improvement in BRFS in the multivariable analysis. In patients who had been treated with a lower $BED_4 < 100$ Gy, the addition of ADT was associated with a positive effect on BRFS. At a $BED_4 \geq 100$ Gy, no significant difference was observed with ADT in terms of either PFS or BRFS. In the PCS 9 trial, the addition of MDT to standard systemic therapy (ADT and enzalutamide) for patients with OMPC also improved PFS and prolonged the interval to the next line of systemic therapy [20]. As demonstrated by the EXTEND trial, the combination of MDT and ADT improves PFS and even causes stronger activation of the systemic immune system, represented by T-cell receptor expansion and contraction [19]. This might also partly contribute to the positive effect observed in our study regarding the SIB concept with two different dose levels and the combination with systemic therapies, thus emphasizing the need for further improvements of systemic therapies as well as integration of standardized SBRT concepts within multimodal treatments.

The optimal dose for SBRT of spinal BoM is still not clearly defined and may depend on treatment indication as well as localization and underlying histology. Also, it has been indicated by a recent *meta*-analysis that higher SBRT doses should be used for (non)-spinal BoM to improve local control. An increase of 1 Gy in BED_{10} was associated with a 1 % decrease in the risk of local failure [56]. According to the European Society for Radiotherapy and Oncology (ESTRO) clinical practice guideline for spinal SBRT, for de novo spine metastases, high dose SBRT practice includes 1x20-24 Gy, 2x12Gy, 3x10Gy, and 5x7Gy ($BED_{10} \geq 50$ Gy_{10}) [12]. We observed a clear dose dependency for BoM of prostate cancer, demonstrating that an escalation of GTV_{mean} dose up to $BED_4 \geq 100$ Gy was associated with improved PFS, BRFS, and FFLR. For FFLR, this could not be confirmed in the multivariable analysis, suggesting that the required dose value could also be even higher. In another retrospective single-institution series for SBRT (24–28 Gy in 2 fractions) of spine metastases from prostate cancer with quarterly radiographic

Table 3
Uni- and multivariable Cox proportional hazard regression analysis for overall survival, progression-free survival, biochemical recurrence-free survival and freedom from local recurrence.

Univariable	**OS**		**PFS**		**BRFS**		**FFLR**	
Variable	**p**	**HR (95 %CI)**	**p**	**HR (95 %CI)**	**p**	**HR (95 %CI)**	**p**	**HR (95 %CI)**
Age	0.08	1.03 (1.00–1.07)	0.80	1.00 (0.98–1.03)	0.07	1.03 (1.00–1.06)	0.26	1.04 (0.97–1.11)
GTV volume	0.56	1.01 (0.98–1.04)	0.17	1.01 (1.00–1.03)	0.65	1.00 (0.97–1.02)	0.33	1.02 (0.98–1.05)
BED_4 GTV_{Mean}	<0.01	0.98 (0.97–0.99)	<0.001	0.99 (0.98–0.99)	<0.001	0.98 (0.97–0.99)	0.22	0.98 (0.95–1.01)
SIB concept	0.78	0.91 (0.52–1.64)	<0.001	0.51 (0.35–0.75)	0.01	0.59 (0.40–0.88)	0.66	0.81 (0.31–2.11)
ADT	0.80	0.93 (0.52–1.65)	0.18	0.79 (0.55–1.12)	<0.01	0.50 (0.33–0.77)	0.86	1.08 (0.43–2.74)
Multivariable								
Age	0.01	1.09 (1.02–1.17)	0.77	1.00 (0.98–1.03)	0.11	1.02 (0.99–1.05)	0.29	1.04 (0.97–1.12)
GTV volume	0.72	1.01 (0.97–1.04)	0.57	1.00 (0.99–1.02)	0.32	0.99 (0.97–1.01)	0.47	1.01 (0.98–1.04)
BED_4 GTV_{Mean}	0.12	0.99 (0.97–1.00)	<0.01	0.99 (0.98–0.99)	<0.001	0.98 (0.97–0.99)	0.36	0.98 (0.95–1.02)
SIB concept	0.71	1.16 (0.52–2.60)	<0.001	0.42 (0.26–0.69)	0.02	0.60 (0.39–0.94)	0.72	1.23 (0.39–3.80)
ADT	0.73	1.21 (0.42–3.42)	0.25	0.77 (0.50–1.20)	<0.01	0.51 (0.31–0.83)	0.81	0.87 (0.30–2.56)

Abbreviations: OS: overall survival, PFS: progression-free survival, BRFS: biochemical recurrence-free survival, and FFLR: freedom from local recurrence, HR: hazard ratio, CI: confidence interval, BED: Biological Effective Dose, SIB: Simultaneous Integrated Boost, GTV: Gross Tumor Volume, ADT: androgen deprivation therapy.

follow-up, local 2-year control rates up to 95 % were reported with a cumulative fracture risk of 10 % [57].

Little is known about the correlation of target volume concept and oncological outcome of patients with spine BoM. In our large multicenter cohort, SIB concept seems to improve control rates, especially in high-BED settings. It allows dose escalation within the metastatic bone lesion, comparable to the expanded GTV concept. At the same time, it enables additional irradiation of potentially microscopic disease within the whole affected vertebra with a conventional dose, accompanied by reducing risk for skeletal-related events [34,35]. In a recent analysis of SIB concepts for spinal BoM, local control appeared to be influenced by histology. Prostate cancer metastases responded particularly well, which is consistent with the radiosensitivity of prostate lesions and the longer life expectancy of these patients [58]. Multivariable analysis of a further study indicated that non-prostate histologies were associated with higher hazard of local failure and additionally, baseline osteoporosis significantly increased the hazard of post-SBRT fractures [35]. Histology may also have influenced the excellent outcome parameters in our study.

The low fracture rate of 2.2 % observed in our cohort may be explained by the fact that BoM from prostate cancer are mainly osteoblastic and hence less susceptible to fractures [59]. Hypofractionation with median 5 (non-SIB) or 10 (SIB) fractions in our cohort, as well as the median patient age of 72 years, which is younger compared to previous studies, could be other possible reasons for the low rate of vertebral fractures. A large *meta*-analysis, combining data on spinal BoM from different primary cancers, found 9 % total vertebral fracture rate, with 1.7 % requiring surgical stabilization [60]. Chan et al. recently described a vertebral fracture rate of 8.4 % and 12.3 % at one and two years, respectively, for spine SBRT of BoM from different primary sites. Multivariable analysis revealed that a greater BED, baseline fracture, and increasing age were associated with a higher risk of fracture [61].

Due to its retrospective design, the current study has some limitations. The substantial number of 19 participating centers resulted in an increased number of cases and, consequently, an enhancement in the informative value of the analysis. However, this also led to greater variability in SBRT protocols and significant heterogeneity in follow-up procedures across institutions. The retrospective analysis was based on chart review and clinician reports, which may have caused underreporting of events and missing data. In consideration of these potential limitations, this study focused on a specific subgroup characterized by a distinct primary diagnosis and metastasis location in the spine. This methodological decision was made with the objective of averting any potential distortion that might be occasioned by the heterogeneity of histological characteristics of different primary tumors. Nonetheless, discrepancies emerged with regard to treatment techniques, encompassing methodologies such as linear accelerator or robotic radiosurgery, dose prescription, and target or margin definition. Additionally, the reliance on radiological reports for the assessment of local recurrence and the variability in post-SBRT imaging frequency, as this is often guided by PSA kinetics rather than systematic imaging, could have led to a possible underestimation of local recurrences.

Notwithstanding these limitations of a retrospective study with corresponding heterogeneity, our large real-world cohort shows that SBRT of spine BoM from prostate cancer was an effective and well-tolerated treatment. Higher BED was associated with an improvement of PFS and BRFS. Additionally, our data suggest that the target volume concept could influence PFS and BRFS as well. Further prospective studies are needed to confirm these results and determine standardized SBRT concepts and clarify its impact on long-term clinical outcomes such as local control, adverse events, quality of life, and survival.

Data Availability

The dataset generated during the current study is available from the corresponding author on reasonable request.

Disclosure

The authors report no proprietary or commercial interest in any product mentioned or concept discussed in this article.

CRediT authorship contribution statement

Isabell Seiler: Writing – review & editing, Writing – original draft, Investigation, Data curation. **Sebastian Schäfer:** Writing – review &

editing, Writing – original draft, Visualization, Validation, Software, Formal analysis, Data curation. **Camilla von Wachter:** Writing – review & editing, Investigation. **Panagiotis Balermpas:** Writing – review & editing, Investigation. **Marek Slavik:** Writing – review & editing, Investigation. **Petr Burkon:** Writing – review & editing, Investigation. **Johannes Meents:** Writing – review & editing, Investigation. **Lena Kästner:** Writing – review & editing, Investigation. **Fabian Lohaus:** Writing – review & editing, Investigation. **Jochen Willner:** Writing – review & editing, Investigation. **Anna Sabrina Schunn:** Writing – review & editing, Investigation. **Sophia Drabke:** Writing – review & editing, Investigation. **Kenneth Klischies:** Writing – review & editing, Investigation. **Olaf Wittenstein:** Writing – review & editing, Investigation. **Priska Bank:** Writing – review & editing, Investigation. **Richard Partl:** Writing – review & editing, Investigation. **Jörg-Andreas Müller:** Writing – review & editing, Investigation. **Ahmed Gawish:** Writing – review & editing, Investigation. **Arne Grün:** Writing – review & editing, Investigation. **Andrea Baehr:** Writing – review & editing, Investigation. **Maike Trommer:** Writing – review & editing, Investigation. **Andrea Glasmacher:** Writing – review & editing, Investigation. **Thomas Mader:** Writing – review & editing, Investigation. **Richard Holy:** Writing – review & editing, Investigation. **Yvonne Dzierma:** Writing – review & editing, Investigation. **Felix Ehret:** Writing – review & editing, Investigation. **Alexander Rühle:** Writing – review & editing, Project administration. **Matthias Guckenberger:** Writing – review & editing, Conceptualization. **Christos Moustakis:** Writing – review & editing, Project administration. **Thomas Brunner:** Writing – review & editing, Conceptualization. **Oliver Blanck:** Writing – review & editing, Conceptualization. **Judit Boda-Heggemann:** Writing – review & editing, Conceptualization. **Nils H. Nicolay:** Writing – review & editing, Supervision, Project administration, Methodology, Conceptualization. **Franziska Nägler:** Writing – review & editing, Writing – original draft, Project administration, Methodology, Investigation, Data curation, Conceptualization.

Ethics approval

This study was reviewed and approved by the local Ethics Committee (127/24-ek). Informed consent to participate in the study was not required. All methods used in this study were carried out in accordance with relevant guidelines and regulations.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgment

Supported by the Open Access Publishing Fund of Leipzig University.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.radonc.2025.111276.

References

[1] Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2024;74:229–63. https://doi.org/10.3322/caac.21834.

[2] Siegel DA, O'Neil ME, Richards TB, Dowling NF, Weir HK. Prostate cancer incidence and survival, by stage and race/ethnicity - United States, 2001-2017. MMWR Morb Mortal Wkly Rep 2020;69:1473–80. https://doi.org/10.15585/mmwr.mm6941a1.

[3] Macedo F, Ladeira K, Pinho F, Saraiva N, Bonito N, Pinto L, et al. Bone metastases: an overview. Oncol Rev 2017;11:321. https://doi.org/10.4081/oncol.2017.321.

[4] Tiwana MS, Barnes M, Yurkowski E, Roden K, Olson RA. Incidence and treatment patterns of complicated bone metastases in a population-based radiotherapy program. Radiother Oncol 2016;118:552–6. https://doi.org/10.1016/j.radonc.2015.10.015.

[5] van der Velden J, Willmann J, Spałek M, Oldenburger E, Brown S, Kazmierska J, et al. ESTRO ACROP guidelines for external beam radiotherapy of patients with uncomplicated bone metastases. Radiother Oncol 2022;173:197–206. https://doi.org/10.1016/j.radonc.2022.05.024.

[6] Lutz S, Balboni T, Jones J, Lo S, Petit J, Rich SE, et al. Palliative radiation therapy for bone metastases: update of an ASTRO Evidence-based Guideline. Pract Radiat Oncol 2017;7:4–12. https://doi.org/10.1016/j.prro.2016.08.001.

[7] Harrow S, Palma DA, Olson R, Gaede S, Louie AV, Haasbeek C, et al. Stereotactic radiation for the comprehensive treatment of oligometastases (SABR-COMET): extended long-term outcomes. Int J Radiat Oncol Biol Phys 2022;114:611–6. https://doi.org/10.1016/j.ijrobp.2022.05.004.

[8] Giesen A, de Preter N, Fazekas T, de Meerleer G, Gandaglia G, Marra G, et al. Direct treatment of all visible tumour in synchronous oligometastatic prostate cancer: total eradication of tumour or the full Monty treatment. Eur Urol Oncol 2025. https://doi.org/10.1016/j.euo.2025.04.011.

[9] de Bie KCC, Zuur LG, Meijer D, Meijnen P, Hinnen KA, Oprea-Lager DE, et al. Oncological outcomes in patients with prostate-specific membrane antigen positron emission tomography/computed tomography-detected oligometastatic prostate cancer treated with metastasis-directed radiotherapy as the single treatment modality. Eur Urol Oncol 2025. https://doi.org/10.1016/j.euo.2025.04.002.

[10] Palma DA, Olson R, Harrow S, Gaede S, Louie AV, Haasbeek C, et al. Stereotactic ablative radiotherapy for the comprehensive treatment of oligometastatic cancers: long-term results of the SABR-COMET phase II randomized trial. J Clin Oncol 2020;38:2830–8. https://doi.org/10.1200/JCO.20.00818.

[11] Miszczyk M, Rajwa P, Yanagisawa T, Nowicka Z, Shim SR, Laukhtina E, et al. The efficacy and safety of metastasis-directed therapy in patients with prostate cancer: a systematic review and meta-analysis of prospective studies. Eur Urol 2024;85:125–38. https://doi.org/10.1016/j.eururo.2023.10.012.

[12] Guckenberger M, Andratschke N, Belka C, Bellut D, Cuccia F, Dahele M, et al. ESTRO clinical practice guideline: stereotactic body radiotherapy for spine metastases. Radiother Oncol 2024;190:109966. https://doi.org/10.1016/j.radonc.2023.109966.

[13] Burgess L, Nguyen E, Tseng C-L, Guckenberger M, Lo SS, Zhang B, et al. Practice and principles of stereotactic body radiation therapy for spine and non-spine bone metastases. Clin Trans Radiation Oncol 2024;45:100716. https://doi.org/10.1016/j.ctro.2023.100716.

[14] Nguyen TK, Louie AV, Kotecha R, Saxena A, Zhang Y, Guckenberger M, et al. Stereotactic body radiotherapy for non-spine bone metastases: a meta-analysis and international stereotactic radiosurgery society (ISRS) clinical practice guidelines. Radiother Oncol 2025;205:110717. https://doi.org/10.1016/j.radonc.2025.110717.

[15] Deek MP, van der Eecken K, Sutera P, Deek RA, Fonteyne V, Mendes AA, et al. Long-term outcomes and genetic predictors of response to metastasis-directed therapy versus observation in oligometastatic prostate cancer: analysis of STOMP and ORIOLE trials. J Clin Oncol 2022;40:3377–82. https://doi.org/10.1200/JCO.22.00644.

[16] Persson AE, Hallqvist A, Bjørn Larsen L, Rasmussen M, Scherman J, Nilsson P, et al. Stereotactic body radiotherapy as metastasis-directed therapy in oligometastatic prostate cancer: a systematic review and meta-analysis of randomized controlled trials. Radiat Oncol 2024;19:173. https://doi.org/10.1186/s13014-024-02559-7.

[17] Tang C, Sherry AD, Haymaker C, Bathala T, Liu S, Fellman B, et al. Addition of metastasis-directed therapy to intermittent hormone therapy for oligometastatic prostate cancer: the EXTEND phase 2 randomized clinical trial. J Am Med Assoc Oncol 2023;9:825–34. https://doi.org/10.1001/jamaoncol.2023.0161.

[18] Marvaso G, Corrao G, Zaffaroni M, Vincini MG, Lorubbio C, Gandini S, et al. ADT with SBRT versus SBRT alone for hormone-sensitive oligorecurrent prostate cancer (RADIOSA): a randomised, open-label, phase 2 clinical trial. LancetOncol 2025;26:300–11. https://doi.org/10.1016/S1470-2045(24)00730-7.

[19] Sherry AD, Siddiqui BA, Haymaker C, Fellman BM, Medina-Rosales MN, Bathala TK, et al. Continuous androgen deprivation therapy with or without metastasis-directed therapy for oligometastatic prostate cancer: the multicenter phase 2 randomized EXTEND trial. Eur Urol 2025. https://doi.org/10.1016/j.eururo.2025.07.006.

[20] Niazi T, Saad F, Tisseverasinghe S, Koul R, Thibault I, Chung PWM, et al. Metastases-directed therapy in addition to standard systemic therapy in oligometastatic castration-resistant prostate cancer in Canada (GROUQ-PCS 9): a multicentre, open-label, randomised, phase 2 trial. Lancet Oncol 2025;26:1158–67. https://doi.org/10.1016/S1470-2045(25)00351-1.

[21] Tang C, Sherry AD, Hwang H, Francolini G, Livi L, Tran PT, et al. World-wide oligometastatic prostate cancer (omPC) meta-analysis leveraging individual patient data (IPD) from randomized trials (WOLVERINE): an analysis from the X-MET collaboration. JCO 2025;43:15. https://doi.org/10.1200/JCO.2025.43.5_suppl.15 (5_suppl).

[22] Song X, Wei J, Sun R, Jiang W, Chen Y, Shao Y, et al. Stereotactic body radiation therapy versus conventional radiation therapy in pain relief for bone metastases: a

systematic review and meta-analysis. Int J Radiat Oncol Biol Phys 2023;115:909–21. https://doi.org/10.1016/j.ijrobp.2022.10.017.
[23] Wong HC, Lee SF, Chan AW, Caini S, Hoskin P, Simone CB, et al. Stereotactic body radiation therapy versus conventional external beam radiotherapy for spinal metastases: a systematic review and meta-analysis of randomized controlled trials. Radiother Oncol 2023;189:109914. https://doi.org/10.1016/j.radonc.2023.109914.
[24] Bindels BJJ, Mercier C, Gal R, Verlaan J-J, Verhoeff JJC, Dirix P, et al. Stereotactic body and conventional radiotherapy for painful bone metastases: a systematic review and meta-analysis. J Am Med Assoc Netw Open 2024;7:e2355409. https://doi.org/10.1001/jamanetworkopen.2023.55409.
[25] Grosinger AJ, Alcorn SR. An update on the management of bone metastases. Curr Oncol Rep 2024;26:400–8. https://doi.org/10.1007/s11912-024-01515-8.
[26] Gillespie EF, Yang JC, Mathis NJ, Marine CB, White C, Zhang Z, et al. Prophylactic radiation therapy versus standard of care for patients with high-risk asymptomatic bone metastases: a multicenter, randomized phase II clinical trial. J Clin Oncol 2024;42:38–46. https://doi.org/10.1200/JCO.23.00753.
[27] Mercier C, Billiet C, Ost P, Vandecasteele K, Kerf G de, Claessens M et al. Dose-escalated stereotactic versus conventional radiotherapy for painful bone metastases (ROBOMET): a multicenter, patient-blinded randomized clinical trial. JCO 2025:JCO2401447. doi: 10.1200/JCO-24-01447.
[28] Chmiel E, Guckenberger M, Gillespie EF, Siva S. Sharper focus, greater comfort? Lessons from the ROBOMET trial. JCO 2025:JCO2500659. doi: 10.1200/JCO-25-00659.
[29] Cox BW, Spratt DE, Lovelock M, Bilsky MH, Lis E, Ryu S, et al. International spine radiosurgery consortium consensus guidelines for target volume definition in spinal stereotactic radiosurgery. Int J Radiat Oncol Biol Phys 2012;83:e597–605. https://doi.org/10.1016/j.ijrobp.2012.03.009.
[30] Palma DA, Olson R, Harrow S, Gaede S, Louie AV, Haasbeek C, et al. Stereotactic ablative radiotherapy versus standard of care palliative treatment in patients with oligometastatic cancers (SABR-COMET): a randomised, phase 2, open-label trial. Lancet 2019;393:2051–8. https://doi.org/10.1016/S0140-6736(18)32487-5.
[31] Guckenberger M, Dahele M, Ong WL, Sahgal A. Stereotactic body radiation therapy for spinal metastases: benefits and limitations. Semin Radiat Oncol 2023;33:159–71. https://doi.org/10.1016/j.semradonc.2022.11.006.
[32] Guckenberger M, Wilke L, Billiet C, Rogers S, Franzese C, Schnell D, et al. Dose-intensified SBRT for vertebral oligometastases: results from a prospective clinical trial. Radiother Oncol 2025;208:110940. https://doi.org/10.1016/j.radonc.2025.110940.
[33] Chen Y-L, Lai S-F, Yang W-C, Lu S-L, Chan H-M, Lin W-H, et al. 1989 phase II randomized trial of elective versus involved target irradiation in stereotactic spine radiosurgery (NCT04033536). Radiother Oncol 2025;206:S1503–5. https://doi.org/10.1016/S0167-8140(25)00777-7.
[34] Guckenberger M, Billiet C, Schnell D, Franzese C, Spałek M, Rogers S, et al. Dose-intensified stereotactic body radiotherapy for painful vertebral metastases: a randomized phase 3 trial. Cancer 2024;130:2713–22. https://doi.org/10.1002/cncr.35310.
[35] Waltenberger M, Strick C, Vogel MME, Diehl C, Combs SE. SBRT of spinal metastases using a simultaneous integrated boost concept in oligometastatic cancer patients is safe and effective. Cancers (Basel) 2023;15. https://doi.org/10.3390/cancers15245813.
[36] Waltenberger M, Vogel MME, Bernhardt D, Münch S, Dobiasch S, Redmond KJ, et al. Radiotherapy concepts for spinal metastases-results from an online survey among radiation oncologists of the German Society for Radiation Oncology. Strahlenther Onkol 2024;200:159–74. https://doi.org/10.1007/s00066-023-02082-w.
[37] Nägler F, Gleim N, Seiler I, Rühle A, Hering K, Seidel C, et al. Stereotactic radiotherapy for spinal and non-spinal bone metastases: a patterns-of-care analysis in German-speaking countries as part of a project of the interdisciplinary Radiosurgery and Stereotactic Radiotherapy Working Group of the DEGRO/DGMP. Strahlentherapie und Onkologie 2025. https://doi.org/10.1007/s00066-025-02387-y.
[38] Nägler F, Seiler I, Schäfer S, Meents J, Lohaus F, Grün A et al. Stereotactic body radiotherapy for spine and non-spine bone metastases in prostate carcinoma – a multicenter cohort analysis. J Bone Oncol 2025:100710. doi: 10.1016/j.jbo.2025.100710.
[39] Guckenberger M, Lievens Y, Bouma AB, Collette L, Dekker A, deSouza NM, et al. Characterisation and classification of oligometastatic disease: a European society for radiotherapy and oncology and European organisation for research and treatment of cancer consensus recommendation. Lancet Oncol 2020;21. https://doi.org/10.1016/s1470-2045(19)30718-1. e18-e28.
[40] Brunner TB, Boda-Heggemann J, Bürgy D, Corradini S, Dieckmann UK, Gawish A, et al. Dose prescription for stereotactic body radiotherapy: general and organ-specific consensus statement from the DEGRO/DGMP working group stereotactic radiotherapy and radiosurgery. Strahlentherapie und Onkologie 2024;200:737–50. https://doi.org/10.1007/s00066-024-02254-2.
[41] Wilke L, Andratschke N, Blanck O, Brunner TB, Combs SE, Grosu A-L, et al. ICRU report 91 on prescribing, recording, and reporting of stereotactic treatments with small photon beams. Strahlentherapie und Onkologie 2019;195:193–8. https://doi.org/10.1007/s00066-018-1416-x.
[42] Seuntjens J. ICRU Report 91: prescribing, recording, and reporting of stereotactic treatments with small photon beams. J ICRU 2014..
[43] van Leeuwen CM, Oei AL, Crezee J, Bel A, Franken NAP, Stalpers LJA, et al. The alfa and beta of tumours: a review of parameters of the linear-quadratic model, derived from clinical radiotherapy studies. Radiat Oncol 2018;13:96. https://doi.org/10.1186/s13014-018-1040-z.
[44] von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet 2007;370:1453–7. https://doi.org/10.1016/S0140-6736(07)61602-X.
[45] U.S. Department of Health and Human Services. Common Terminology Criteria for Adverse Events (CTCAE). [April 10, 2025]; Available from: https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/ctcae_v5_quick_reference_5x7.pdf.
[46] Schmitt D, Blanck O, Gauer T, Fix MK, Brunner TB, Fleckenstein J, et al. Technological quality requirements for stereotactic radiotherapy expert review group consensus from the DGMP working group for physics and technology in stereotactic radiotherapy. Strahlenther Onkol 2020;196:421–43. https://doi.org/10.1007/s00066-020-01583-2.
[47] Burkon P, Kazda T, Pospisil P, Slavik M, Kominek L, Selingerova I, et al. Ablative dose stereotactic body radiation therapy for oligometastatic disease: a prospective single institution study. Neoplasma 2019;66:315–25. https://doi.org/10.4149/neo_2018_180731N558.
[48] Csiki E, Simon M, Papp J, Barabás M, Mikáczó J, Gál K, et al. Stereotactic body radiotherapy in lung cancer: a contemporary review. Pathol Oncol Res 2024;30:1611709. https://doi.org/10.3389/pore.2024.1611709.
[49] Nägler F, Vorbach S, Mohamed AA, Thaqi S, Adebahr S, Ehret F, et al. Pulmonary stereotactic body radiation therapy of oligometastatic head-and-neck squamous cell carcinoma: a multicenter retrospective study. Int J Radiat Oncol Biol Phys 2025;122:140–9. https://doi.org/10.1016/j.ijrobp.2024.12.015.
[50] Guckenberger M, Klement RJ, Allgäuer M, Andratschke N, Blanck O, Boda-Heggemann J, et al. Local tumor control probability modeling of primary and secondary lung tumors in stereotactic body radiotherapy. Radiother Oncol 2016;118:485–91. https://doi.org/10.1016/j.radonc.2015.09.008.
[51] Klement RJ, Abbasi-Senger N, Adebahr S, Alheid H, Allgaeuer M, Becker G, et al. The impact of local control on overall survival after stereotactic body radiotherapy for liver and lung metastases from colorectal cancer: a combined analysis of 388 patients with 500 metastases. BMC Cancer 2019;19:173. https://doi.org/10.1186/s12885-019-5362-5.
[52] Yan M, Moideen N, Bratti VF, de Moraes FY. Stereotactic body radiotherapy (SBRT) in metachronous oligometastatic prostate cancer: a systematic review and meta-analysis on the current prospective evidence. Br J Radiol 2020;93:20200496. https://doi.org/10.1259/bjr.20200496.
[53] Rogowski P, Roach M, Schmidt-Hegemann N-S, Trapp C, von Bestenbostel R, Shi R, et al. Radiotherapy of oligometastatic prostate cancer: a systematic review. Radiat Oncol 2021;16:50. https://doi.org/10.1186/s13014-021-01776-8.
[54] Fiorica F, Sava T, Giuliani J, Tebano U, Napoli G, Franceschetto A, et al. Metastasis-directed therapy in oligometastatic prostate cancer: biological rationale and systematic review of published data. Cancers (Basel) 2025;17. https://doi.org/10.3390/cancers17081256.
[55] Deek MP, Taparra K, Phillips R, Velho PI, Gao RW, Deville C, et al. Metastasis-directed therapy prolongs efficacy of systemic therapy and improves clinical outcomes in oligoprogressive castration-resistant prostate cancer. Eur Urol Oncol 2021;4:447–55. https://doi.org/10.1016/j.euo.2020.05.004.
[56] Cao Y, Chen H, Sahgal A, Erler D, Badellino S, Biswas T, et al. An international pooled analysis of SBRT outcomes to oligometastatic spine and non-spine bone metastases. Radiother Oncol 2021;164:98–103. https://doi.org/10.1016/j.radonc.2021.08.011.
[57] Abugharib A, Zeng KL, Tseng C-L, Soliman H, Myrehaug S, Husain Z, et al. Spine stereotactic body radiotherapy for prostate cancer metastases and the impact of hormone sensitivity status on local control. Neurosurgery 2022;90.
[58] Pastorello E, Nicosia L, Allegra AG, De-Colle C, Giaj-Levra N, Ricchetti F, et al. Stereotactic body radiotherapy for spinal oligometastases with or without simultaneous integrated boost: results from a monocentric retrospective analysis. Clin Oncol 2025;46:103918. https://doi.org/10.1016/j.clon.2025.103918.
[59] Bianchi D, Falcinelli C, Molinari L, Gizzi A, Di Martino A. Osteolytic vs. osteoblastic metastatic lesion: computational modeling of the mechanical behavior in the human vertebra after screws fixation procedure. J Clin Med 2022;11. https://doi.org/10.3390/jcm11102850.
[60] Guninski RS, Cuccia F, Alongi F, Andratschke N, Belka C, Bellut D, et al. Efficacy and safety of SBRT for spine metastases: a systematic review and meta-analysis for preparation of an ESTRO practice guideline. Radiother Oncol 2024;190:109969. https://doi.org/10.1016/j.radonc.2023.109969.
[61] Chan AW, Zeng KL, Moore-Palhares D, Atenafu EG, Chen H, Myrehaug S, et al. Spine stereotactic body radiation therapy in geriatric patients: implications of age and dose on iatrogenic vertebral compression fracture risk. Int J Radiat Oncol Biol Phys 2025;121:1185–93. https://doi.org/10.1016/j.ijrobp.2024.11.082.