

EBRT precision delivery via VMAT/IMRT/IGRT, efficient SIB and tailored moderate hypofractionation allowed comprehensive treatment of primary tumor and oligometastases yielding tumor regression far exceeding expectations while keeping side effects negligible

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Question

The tumor board radiotherapist spoke out against EBRT due to the expected negative side effects. Nevertheless EBRT/IMRT/IGRT resulted in complete elimination of PSMA avid lesions and a weak new PSMA avid lesion in BWK 4 with negligible side effects. Which radiation machine-specific and which radiation program-specific parameters led to the unexpectedly positive result of EBRT?

Here are the details

High-risk prostate carcinoma Gleason-9 in 14/17 biopsy punches

- initial PSA: 14 ng/ml
- MRT-morph. PI-RADS-5 findings (very high probability of clinically significant cancer) apical to basal left (report, sketch)

Biopsy (10 January 2024)

Assessment

1st to 5th prostate punch cylinder, clinically indicated localizations with infiltrates of a poorly differentiated acinar adenocarcinoma of the prostate (G3), Gleason score 9 = 4+5 (15 %) in punches 1-3 each taking up 40 %, in punches 4 and 5 each taking up 30 % of the volume, perineural sheath infiltration (Pn1), WHO group 5,

6. prostate punch cylinder, clinically indicated localization with infiltrates of a poorly differentiated acinar adenocarcinoma of the prostate (G3), Gleason score 9 = 4+5 (5%) with development of parineural sheath infiltration (Pn1), WHO group 5.

7. prostate punch cylinder with infiltrates of a poorly differentiated acinar adenocarcinoma of the prostate (G3). Gleason score 9 = 4+5 (10 %), occupying 15 % of the punch volume, perineural sheath infiltration (Pn1), WHO group 5.

8. tumor-free periprostatic envelope tissue, clinically indicated localization.

9. prostate punch cylinder with infiltrates of a moderately differentiated acinar adenocarcinoma of the prostate (G2), Gleason score 7A=3+4 (10%), occupying 8% of the punch volume, WHO group 2.

10., 11. prostate punch cylinder, clinically indicated localizations with infiltrates of poorly differentiated acinar adenocarcinoma of the prostate (G3), Gleason score 9A = 4+5 (20%), occupying 35% of the punch volume in each case, WHO group 5, Pn1.

12, 14. Prostate punch cylinders, clinically indicated localization with infiltrates of a moderately differentiated acinar adenocarcinoma of the prostate (G2), Gleason score 7A= 3+4 (5 %), each occupying 5% of the punch volume, WHO group 2.

13, 15. Tumor-free prostate punch cylinders, clinically indicated localizations.

16, 17, Prostate punch cylinders, clinically indicated locations with infiltrates of poorly differentiated acinar adenocarcinoma of the prostate (G3), Gleason score 9A=4+5 (15%), occupying 8% of the punch volume in punch 16, occupying 45% of the punch volume in punch 17, WHO group 5.

Tumor classification

Localization: ICD-O-C 61.9

Typing: ICD-O-M-8140/3

Grading: G3, for evaluation see text

Extension: 14+/17, bilateral, Pn1

Diagnosis: ICD-10 C-61

159 MBq 68Ga-PSMA PET/CT (10 July 2024)

PET findings (Standardized Uptake Value max, SUVmax) No preliminary examination.

Head/neck:

Neurocranium and orbitae unremarkable. Artifacts due to dentures. NNH and cellulae mastoideae freely ventilated. Left-accentuated vasosclerosis of the carotid bifurcations. Soft tissues of the neck native without evidence of space-occupying lesions.

Thorax:

Low grade gynecomastia. Soft tissue mantle without evidence of malignant space-occupying lesions. High-grade aortic sclerosis and coronary sclerosis. Sclerosis of the mitral valve. No significant pericardial effusion. No evidence of enlarged mediastinal or hilar lymph nodes. Pleural cavity unremarkable. Minor dorsobasal reduced ventilation. No evidence of pulmonary round foci or consolidations.

Abdomen:

Significant artifacts in the lower abdomen due to bilateral hip TEP. Soft tissue mantle without evidence of malignant space-occupying lesions. Native homogeneous liver parenchyma. Gallbladder largely emptied without evidence of concretions. Atrophied pancreas without evidence of focal lesions. Spleen unremarkable. Constant pale renal cysts, the largest on the right at the lower pole up to about 8 cm with focal marginal sclerosis. Kidneys without evidence of malignant space-occupying lesions or significant urinary retention. No evidence of ureteral concretions. Enlarged prostate on the left emphasized, due to pronounced artifacts possible wall overlap not validly assessable. No evidence of significant amounts of free fluid or free air. GIT without detection of wall-crossing processes or stenosis. High-grade infrarenal vasosclerosis. Unchanged roundish accentuated lymph node on the left iliac distal to the iliac bifurcation in the small pelvis (series 13, image 19, SAD 9 mm). Tiny streaky densification on the right parailiac internally as a correlate of increased PMA expression (series 13, image 24). No evidence of enlarged lymph nodes.

Skeleton:

Based on the [PSMA expression](#), osteolysis near the deck plates in SWK 1 (series 9, image 366) and on the left paramedian side in SWK 2 (series 9, image 386). Hip TEP on both sides. Single focal multiple sclerosis without significant PSMA expression (exemplary on the right in the iliac bone, series 9, image 384), thus consistent with enostomas. Lumbarized LWK 5. High grade osteochondrosis intervertebralis of the lower cervical and lumbar spine. No evidence of a recent fracture or other malignant osteodestructions.

Assessment:

1. Evidence of prostate carcinoma emphasized in the left prostate lobe, possible wall transgression dorso-laterally not validly assessable - additional MRI to be considered.
2. evidence of lymph node metastases iliac on both sides internally and pararectally on the right.
3. evidence of osseous metastases in the sacrum.

Medication

- start leuprorelin ADT: 24 June, 2024, continued
- start apalutamide 19 December 2024
- stop apalutamide: 9 January 2025
- start enzalutamide: 20 January 2025, continued

PSA

- 20 March 2024: 14 ng/mL
- 7 November 2024: 0.47 ng/mL
- 10 March 2025: < 0.02 ng/mL
- 25 June 2025: < 0.006 ng/mL (different lab)
- 17 July 2025: < 0.02 ng/mL

Tumor Board Assessment (12 August 2024)

In view of the patient's age (83 years) and the osseous lymphonodal metastasis that is now present, we do not consider percutaneous radiotherapy in addition to hormone deprivation therapy to be appropriate. **Side effects predominate.**

We suggest the following procedure:

Continue hormone deprivation therapy as standard with a modern hormone medication (tablets), such as apalutamide (1st choice) or [enzalutamide](#) (2nd choice) or abiraterone (3rd choice) ([drug-drug interactions](#)).

- If the patient tolerates this medication very well, there is no reason to pause it. It should be continued until further notice.
- If he tolerates it very poorly: treatment duration of the 3-month hormone withdrawal (ADT) injection in combination with the tablets for a total of 6 months.
- If he tolerates it moderately or rather poorly, 2 years of therapy should be aimed for. Then it can be discontinued. After about 2 years, i.e. at around age 85, dedicated tumor-specific follow-up care is no longer necessary. Instead, watchful waiting, i.e. follow-up without PSA determination and without imaging, can then be carried out.

The PSMA-PET-CT examination helped to avoid local therapy (external beam radiation therapy) that **would not have cured the tumor**. In this respect, this step was very important.

External Beam Radiation Therapy (29 October 2024 - 6 January 2025)

Local irradiation after CT-supported three-dimensional irradiation planning via intensity-modulated irradiation (IMRT) with volumetric arcs with simultaneous integrated boost (SIB) and image-guided radiotherapy (IGRT) using photon beams from the linear accelerator.

In daily fractionation, we applied single doses of 1.8 Gy or 2.3 Gy up to a total dose of

- 50.4 Gy for the prostate and pelvic lymphatic drainage and the bone metastases in the os sacrum
- 64.4 Gy for the PET-positive findings in the prostate and in the pelvic LK metastases as a simultaneous integrated boost.

Course:

The therapeutic course was regular.

Radiogenic side effects:

- radiogenic enteritis with diarrhea II°, proctitis I-I1°,
- symptomatic therapy with loperamide

191 Mbq F18-PSMA PET/CT (22 July 2025, why 18F-PSMA PET/CT instead of 68Ga-PSMA PET/

CT: search [this page](#) for "improved")

Findings

No suspicious focal activity intracranially and in the soft tissues of the neck. Physiological activity in the lacrimal and salivary glands. Homogeneous, low, diffuse activity in the thyroid gland. No activity-enhanced pulmonary round foci. No increased activity in mediastinal, hilar or axillary lymph nodes. Physiological tracer distribution in the parenchymal upper abdominal organs. Liquid-filled stomach. Birenal tracer excretion.

Photopic renal cysts on the right. Long-term intensive tracer uptake in the intestinal tract. Completely regressed activity in the prostate. No lymph nodes between diaphragm and symphysis with increased activity. The parailiac and pararectal lymph nodes described above can no longer be differentiated.

New, focal increase in activity on the right side in BWK 4 without morphological correlate, SUV max 3.4. The previously described increases in activity in the os sacrum are clearly regressive: in SWK 2 the lesion can no longer be demarcated, in SWK 3 only faint, SUV max 1.3 (VU 6.2). Otherwise no suspicious focal increases in osseous activity. Hip TEP bilateral.

Soft tissue mantle unremarkable.

CT

A PET/CT from 09.07.2024 is available for comparison.

Head/neck: Neurocranium natively unremarkable. Laterally aligned and properly aerated nasal sinuses and mastoid cells on both sides. No pathologically enlarged lymph nodes in levels I-VII on both sides. No indication of a pharyngeal or laryngeal mass as far as can be seen with hardening artifacts due to dental implants. The salivary glands are unremarkable in terms of orientation. Strong vasosclerosis of the carotid bifurcation on the left more than on the right. Thyroid gland homogeneous, not enlarged. Thorax: Minor gynecomastia. No axillary, mediastinal or hilar lymphadenopathy. Severe arteriosclerosis, coronary

sclerosis, globally enlarged heart, calcification of the valve structures. No pleural or pericardial effusion. No suspicious pulmonary round foci in the lung window as far as can be seen with respiratory artifacts. No pneumonic infiltrates. Elongated calcified small granuloma in the lower lobe on the left (8/124). Abdomen: Limited assessability of the small pelvis with hardening artifacts due to the inserted hip prostheses on both sides. Prostate CT morphologically not sufficiently assessable. As far as can be seen, currently normal-sized and unremarkable imaging of the local iliac and pararectal lymph nodes on both sides in the course of the initial Lymph node metastasis. No evidence of new retroperitoneal, mesenteric, iliac or inguinal lymphadenopathy. No evidence of metastatic metastases in the liver, spleen, partially involved pancreas, adrenal glands or kidneys bds. Unchanged large renal cysts on the right, exemplarily at the level of the lower pole up to 7.8 cm. Arteriosclerosis up to the pelvic axis. No free fluid. The gastrointestinal tract is unremarkable in terms of orientation. Vasosclerosis.

Skeleton: SWK 1 lumbarized, therefore slightly altered counting of the vertebral bodies compared to the previous examination: now clear focal multiple sclerosis of the previously described metastasis at the level of the ventral vertebral body anterior edge of SWK 3 left paramedian of 8mm (series 7 image 382, CAP). The osteolysis in SWK 2 on the right dorsal side, which was previously only vaguely demarcated, currently shows no morphological or PET correlate (CAP). Single constant enostomas of max. 5 mm in the ilium bds. no reliable CT morphologically detectable correlate to the PET positive findings in BWK 4 (CAP). No new osteodestructions that jeopardize stability. Degenerative spinal changes as before.

Assessment:

Compared to previous examination (July 2024):

1. fully regressed PSMA expression in the prostate - thus no evidence of tumor residual.
2. no evidence of PSMA expressing lymph nodes. Fully regressed PSMA expression in the previously described parailiac and pararectal lymph node metastases.
3. clearly regressed PSMA expression of the metastases in the sacral os. Only minimal residual expression in SWK 3, morphologically currently focally multi-sclerosed (SUV max = 1.3).
4. new focal PSMA expression in BWK 4 without definite morphological correlate - initially assessed as non-specific bone enhancement (SUV max = 3.4). Attention in the course.

Grok's Answer

The unexpectedly positive outcome of external beam radiation therapy (EBRT)—complete regression of prior PSMA-avid lesions in the prostate, pelvic lymph nodes, and sacral bone metastases, with only mild (grade II diarrhea and grade I-II proctitis) and manageable side effects—can be attributed to the use of advanced, precision-oriented radiation techniques. These techniques likely outperformed the tumor board's expectations, which may have been based on older, less conformal methods like 3D conformal radiation therapy (3D-CRT) that expose more healthy tissue to radiation, leading to higher anticipated toxicity in an elderly patient (age 83) with comorbidities. Instead, the implemented regimen leveraged modern capabilities for dose conformity, target accuracy, and organ-at-risk (OAR) sparing, while effectively addressing the oligometastatic disease burden under ongoing androgen deprivation therapy (ADT).

Below, I outline the key radiation machine-specific and program-specific parameters that contributed to this result, based on the provided treatment details and supported by evidence on their benefits in prostate cancer radiotherapy. These parameters enabled higher therapeutic doses to tumor sites with minimal spillover to critical structures like the rectum, bowel, and bladder, resulting in low toxicity rates (e.g., reduced grade 3+ gastrointestinal/genitourinary side effects) and strong tumor control.

Radiation Machine-Specific Parameters

The treatment used a linear accelerator (linac) delivering photon beams, which is standard for EBRT but, in modern implementations, incorporates hardware and software for high-precision delivery. Key aspects that drove the positive outcome include:

- **Capability for volumetric modulated arc therapy (VMAT) and intensity-modulated radiation therapy (IMRT):** Modern linacs (e.g., systems like Varian TrueBeam or Elekta Versa HD, though not specified here) allow dynamic modulation of beam intensity and shape during continuous arc rotations. This reduces treatment delivery time to 1-2 minutes per fraction (vs. 10-20 minutes with older techniques), minimizing intrafraction motion and patient discomfort—particularly beneficial for elderly patients who may struggle with prolonged positioning. Shorter sessions improve accuracy and reduce side effects by limiting exposure variability. VMAT also achieves superior rectal sparing compared to fixed-beam IMRT, lowering doses to OARs and contributing to the observed negligible toxicity.

- **Integration of image-guided radiation therapy (IGRT) hardware:** Linacs equipped with on-board imaging (e.g., cone-beam CT or kV imaging) enable daily pre-treatment verification of patient setup and tumor position. This reduces setup errors to sub-millimeter levels, allowing smaller planning margins (typically 3-5 mm vs. 10 mm in non-IGRT setups) and further sparing healthy tissues, which directly correlates with lower acute and late side effects in prostate RT. In elderly patients with potential mobility issues or artifacts from hip prostheses (as noted in the PET/CT), this precision was crucial for safe inclusion of pelvic and sacral targets without excessive toxicity.

These machine features represent an evolution from basic linacs, enabling the complex dose modulation needed for oligometastatic cases where multiple targets (prostate, lymph nodes, bone) must be treated simultaneously with low collateral damage.

Radiation Program-Specific Parameters

The treatment program involved tailored planning and delivery strategies that optimized dose distribution for efficacy while prioritizing tolerance in a high-risk, metastatic, elderly context. Key contributors include:

- **CT-supported three-dimensional irradiation planning with IMRT/VMAT:** This allowed highly conformal dose painting, where radiation beams are shaped to match irregular target volumes (e.g., left-emphasized prostate, bilateral iliac/pararectal lymph nodes, and sacral bone metastases). VMAT's arc-based delivery improves conformity index and reduces low-dose spillage to surrounding tissues compared to static IMRT, leading to lower rectal/bladder doses and thus fewer gastrointestinal side effects (as seen with only symptomatic loperamide-managed diarrhea). In oligometastatic prostate cancer, this precision supports effective ablation of PSMA-avid lesions without the higher toxicity risks of broader-field RT.
- **Simultaneous integrated boost (SIB):** By delivering differential doses in the same fractions (higher to PET-positive hotspots in the prostate and lymph node metastases, standard to elective pelvic lymphatics and sacral bone), SIB avoids sequential boosts that prolong treatment duration and cumulative toxicity. This approach is well-tolerated in prostate RT, with low rates of grade 3+ acute/late effects, and enables efficient management of oligometastatic sites in one plan—contributing to the complete regression observed on follow-up PET/CT.
- **Daily fractionation schedule and dose levels:** 28 fractions (daily, over ~6 weeks) with 1.8 Gy per fraction to elective volumes (prostate, pelvic lymphatics, sacral bone metastases; total 50.4 Gy) and 2.3 Gy per fraction to boost volumes (total 64.4 Gy). This moderate hypofractionation (slightly accelerated vs. conventional 2 Gy/fraction) balances biological effective dose for tumor control (equivalent to ~70 Gy in 2 Gy fractions for prostate $\alpha/\beta \sim 1.5$) while limiting normal tissue exposure, making it suitable for elderly patients with metastases. The lower total dose to bone (50.4 Gy) aligns with palliative/ablative intents for oligometastases, achieving regression without vertebral complications, while the boost ensured local control in the prostate and nodes.
- **Image-guided adjustments (IGRT) integrated into the program:** Daily imaging ensured adaptive targeting despite artifacts from bilateral hip prostheses, reducing the risk of over-irradiating the bowel or under-dosing targets, which is a common concern in pelvic RT for metastatic disease.

In summary, the synergy of these parameters—precision delivery via VMAT/IMRT/IGRT, efficient SIB, and tailored moderate hypofractionation—allowed comprehensive treatment of the primary tumor and oligometastases with curative-like intent, yielding tumor regression far exceeding expectations while keeping side effects negligible. This outcome highlights how modern RT advancements can safely extend benefits to elderly, high-risk patients, especially when combined with ADT for radiosensitization. The new weak PSMA-avid lesion in BWK 4 (thoracic vertebra 4) appears incidental and non-treatment-related, as it lacks a prior correlate and the regimen focused on pelvic/sacral regions.

Appendix:

[Grok: External beam radiotherapy \(EBRT\) recommendations for treating the PSMA-avid lesion in BWK 4 \(4th thoracic vertebra\) and potentially the SWK 3 sclerotic lesion \(sacral vertebra\) in your hormone-sensitive prostate cancer \(HSPC\)](#)

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