



# The Role of Radiation Therapy in the Management of Prostate Cancer and Posttreatment Imaging Appearances

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## Abstract

Prostate cancer remains a significant global health concern, necessitating continuous research and innovation in treatment modalities. This review explores the currently employed techniques in radiation dose planning and tumor irradiation in the context of prostate cancer management. In addition, we delve into the nuances of expected posttreatment magnetic resonance imaging (MRI) appearances within the gland or in the prostate bed, postradiation tumor recurrence, and its mimics.

Radiation therapy (RT) has evolved as a cornerstone in prostate cancer treatment, offering both curative and palliative solutions. Recent developments have seen the emergence of advanced techniques such as intensity-modulated radiation therapy (IMRT) and stereotactic body radiation therapy (SBRT), allowing for precise targeting of cancer cells while minimizing damage to surrounding healthy tissue.

The avoidance of normal tissue dose through more conformal dose distribution as in IMRT or proton therapy, improved imaging modalities as in multiparametric magnetic resonance imaging (mpMRI) and prostate positron emission tomography (PET), interventional separation of critical structures from the prostate target, and many other techniques can greatly reduce the side effects of RT. These advancements enhance treatment efficacy and reduce the risk of side effects, promoting improved patient outcomes.

## Keywords

- ▶ prostate cancer
- ▶ external beam radiation therapy
- ▶ brachytherapy
- ▶ proton beam therapy
- ▶ posttreatment imaging appearances
- ▶ post radiation complications

## Introduction: Radiation Therapy and Prostate Cancer

Radiation therapy (RT) targets cancer effectively and specifically due to (1) the higher cytotoxicity of radiation for tumor versus normal tissue and (2) the ability to focus multiple beams on the tumor, thereby concentrating the

effective tumor dose while distributing the entry and exit pathways to reduce the dosage to surrounding normal tissue. Based on these two principles, radiation oncologists determine the total dose (a combination of number of fractions and dose per fraction) and the geometry of the radiation beams to maximize tumor killing while minimizing normal tissue toxicity. Determining the appropriate

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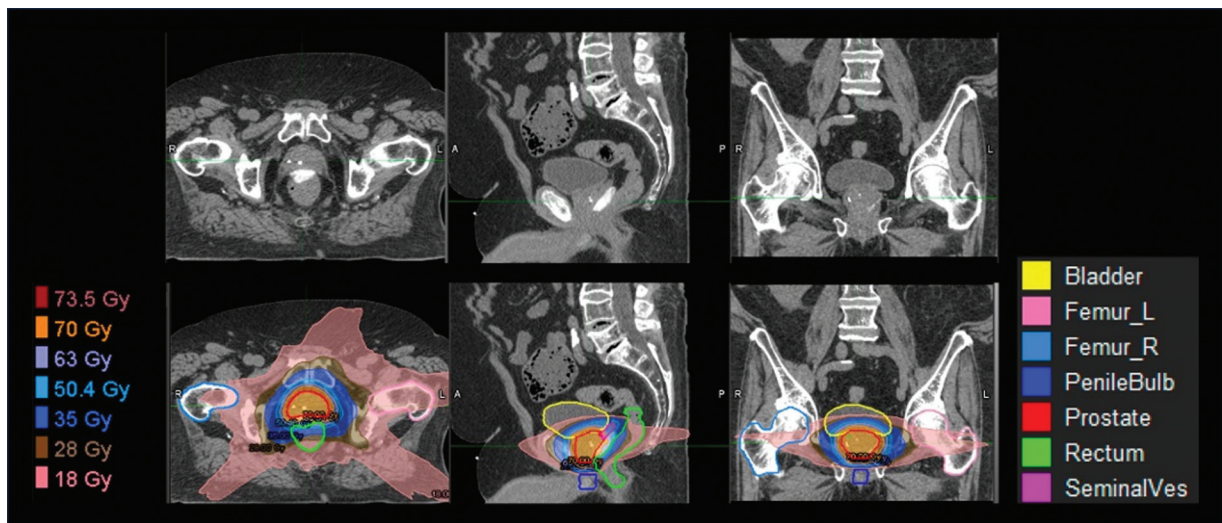
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beam geometry, target delineation, and normal structure avoidance requires accurate radiology studies. Therefore, the necessity and utility of various imaging studies is the focus of this review.

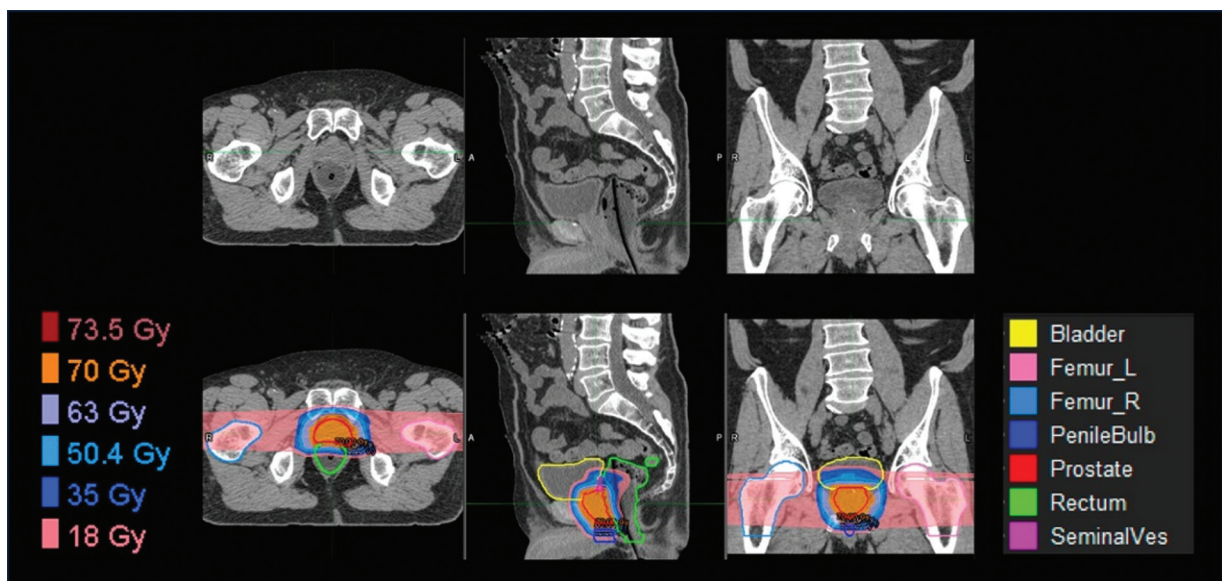
For localized prostate cancer (PCa), treatment options include RT with or without the addition of androgen deprivation therapy (ADT), radical prostatectomy (RP), and, in select cases, active surveillance.<sup>1</sup> The decision to proceed with definitive therapy (i.e., RT or RP) depends on the life expectancy, patient risk stratification, as well as shared decision-making. Within definitive treatment, RT and RP are both appropriate treatments, and the choice of RT is largely dependent on patient preference after discussion of different side effect profiles.

RT may be delivered via external sources, termed external beam radiation therapy (EBRT; ►Fig. 1), or internal sources termed brachytherapy. Additionally, EBRT and brachytherapy may be **combined** for selected patients. EBRT delivers radiation via mega electron volt X-rays (photons) produced by linear accelerators. The advantage of **proton beam therapy** (►Figs. 2 and 3)—another treatment option—theoretically derives from improved dose distribution, although tissue heterogeneity may result in end-range uncertainty.<sup>2,3</sup>

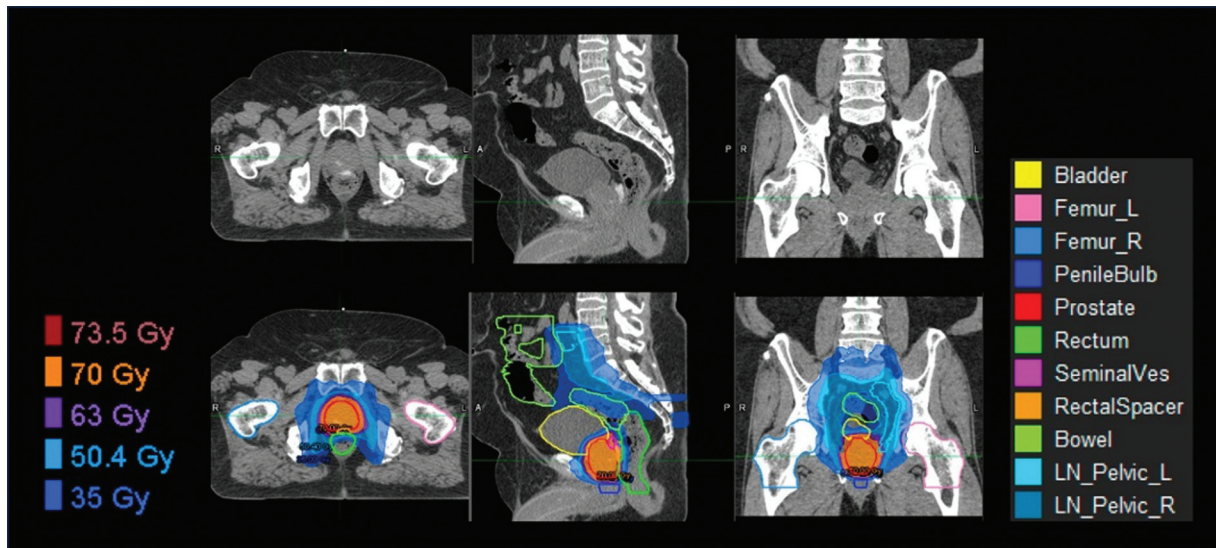
The areas of RT coverage in PCa are guided by risk stratification and extent of detected disease. Due to the multifocal nature of PCa, RT covers the entire prostate gland for localized disease. In higher risk disease, the risk of micrometastatic spread increases and RT may be directed



**Fig. 1** Pretreatment planning computed tomography (CT) for photon beam radiation therapy (RT) targeting localized prostate cancer (PCa). Planning CT simulation (top) and final dosimetric plan (bottom) for localized PCa treated with volumetric modulated arc therapy (VMAT). Total dose of 70 Gy in 28 fractions was delivered to the prostate and seminal vesicles.



**Fig. 2** Pretreatment planning computed tomography (CT) for proton beam radiation therapy (RT) targeting localized prostate cancer (PCa). Planning CT simulation (top) and final dosimetric plan (bottom) for localized PCa treated with proton beam therapy. Total dose of 70 Gy (relative biological effectiveness [RBE]) in 28 fractions was delivered to the prostate and seminal vesicles.



**Fig. 3** Pretreatment planning computed tomography (CT) for proton beam radiation therapy (RT) targeting prostate and pelvic nodal field. Planning CT simulation (top) and final dosimetric plan (bottom) for high-risk localized prostate cancer (PCa) treated with volumetric modulated arc therapy (VMAT). Total dose of 70 Gy in 28 fractions was delivered to the prostate and seminal vesicles, and 50.4 Gy in 28 fractions was delivered to the pelvic lymph nodes.

to the draining lymph nodes (LNs; termed whole pelvis RT [WPRT]). The advent of prostate-specific radiotracers (notably prostate-specific membrane antigen [PSMA]) allows the detection of previously occult micrometastatic disease.<sup>4</sup>

For localized PCa not requiring WPRT or to boost the primary disease, brachytherapy—the temporary or permanent placement of sealed radioactive sources (“seeds”)—is an appropriate treatment option. Accurate permanent seed placement in low dose rate (LDR) brachytherapy requires ultrasound guidance, while temporary seed placement in high dose rate (HDR) brachytherapy can be accomplished with ultrasound or computed tomography (CT) guidance.

Finally, the avoidance of normal tissue dose can greatly reduce the side effects of RT. Improved normal tissue avoidance can be accomplished by (1) more conformal dose distribution as in intensity-modulated radiation therapy (IMRT) or **proton therapy**, (2) improved imaging modalities as in multiparametric magnetic resonance imaging (mpMRI) and prostate positron emission tomography (PET), (3) interventional separation of critical structures from the prostate target via *hydrogel spacer*,<sup>5</sup> (4) interfractional daily localization via *fiducial marker* (FM) and *image-guided RT* (IGRT), and (5) intrafractional adaptive planning (i.e., *MR-guided RT delivery* with real-time MR cine tracking<sup>6</sup> or *CT-guided online adaptive RT*).

## Discussion

### What Radiation Oncologists Want to Know from Radiologists

#### The Need for Cross-Sectional Imaging

Advanced cross-sectional imaging techniques like mpMRI and PET prove to be crucial in RT planning of patients with primary PCa for accurate staging of the extraprostatic and

intraprostatic tumor mass, delineation of the intraprostatic gross tumor volume (GTV; allowing for escalating the RT dose targeting the organ-confined tumor, thus reducing the risk of radiation damage to neighboring organs), and in characterization of the biological properties of the PCa.

#### Utility of mpMRI for Upstaging

MpMRI combines the use of anatomical information from T1- and T2-weighted (T2W) imaging with functional information derived from diffusion weighted imaging (DWI) and dynamic contrast-enhanced (DCE) MRI. It is very reliable for the detection and staging of locally advanced PCa,<sup>7</sup> allowing differentiation of intraprostatic tumor and extraprostatic extension, providing guidance for targeted biopsy and intraprostatic boosts.

Both CT and MRI have poor sensitivity and specificity for LN metastases<sup>8</sup> as they both rely on similar properties (shape, size) and anatomical MRI sequences. Up to 80% of PCa LN metastases do not meet the threshold size criteria and are missed at MRI.<sup>9</sup> A meta-analysis reported a pooled sensitivity of 0.39 and a pooled specificity of 0.82 for MRI in LN staging using histology as the gold standard.<sup>10</sup>

DWI-MRI improves the sensitivity and specificity for LN detection.<sup>11</sup> Harisinghani et al showed that MRI with paramagnetic nanoparticles improved the sensitivity from 0.35 to 0.91 compared with conventional MRI.<sup>12</sup> Staging of *bone metastases* with MRI showed a pooled sensitivity of 0.96 and a specificity 0.98<sup>13</sup> in patients with PCa. In summary, mpMRI better identifies high-grade intraprostatic lesions, extraprostatic extension, and LN involvement than standard MRI.

#### Utility of mpMRI in post-RP Patients to Identify Areas of Recurrence for Salvage or Adjuvant RT

Postsurgical anatomy on mpMRI is different due to the open prostatectomy fossa. The functional components of mpMRI



allow the important differentiation between recurrent cancer, residual prostate tissue, inflammatory tissue, and fibrosis (►Figs. 4 and 5).<sup>14</sup>

Locally recurrent PCa in the post-RP patient most commonly occurs at the vesicourethral anastomosis (VUA).<sup>15</sup> Recurrence tends to appear nodular and hyperintense in comparison to pelvic muscle signal intensity on T2W imaging.<sup>16</sup> On DCE, these areas show focal nodular enhancement during the arterial phase with quick washout during the venous phase and typically restricts diffusion.<sup>17</sup> Addition of DCE to T2W for evaluation of post-RP recurrence increases sensitivity and specificity.<sup>18</sup>

Mimics of post-RP recurrent disease such as residual glandular tissue and granulation tissue do not show any signal abnormality on DWI and, except for granulation tissue, should not show early arterial enhancement on DCE.<sup>19</sup> The combinations of T2W + DCE and T2W + DWI + DCE had significantly higher detection rates (82.4%) than T2W alone or T2W + DWI (29.4%), highlighting the importance of DCE.<sup>20</sup>

#### Burden of Metastatic Disease at Presentation and Its Relation to Treatment of the Primary

Bone metastatic burden based on conventional imaging is predictive of overall survival and failure-free survival benefit when prostate RT is added to standard of care in newly diagnosed metastatic PCa (►Figs. 6 and 7). This beneficial

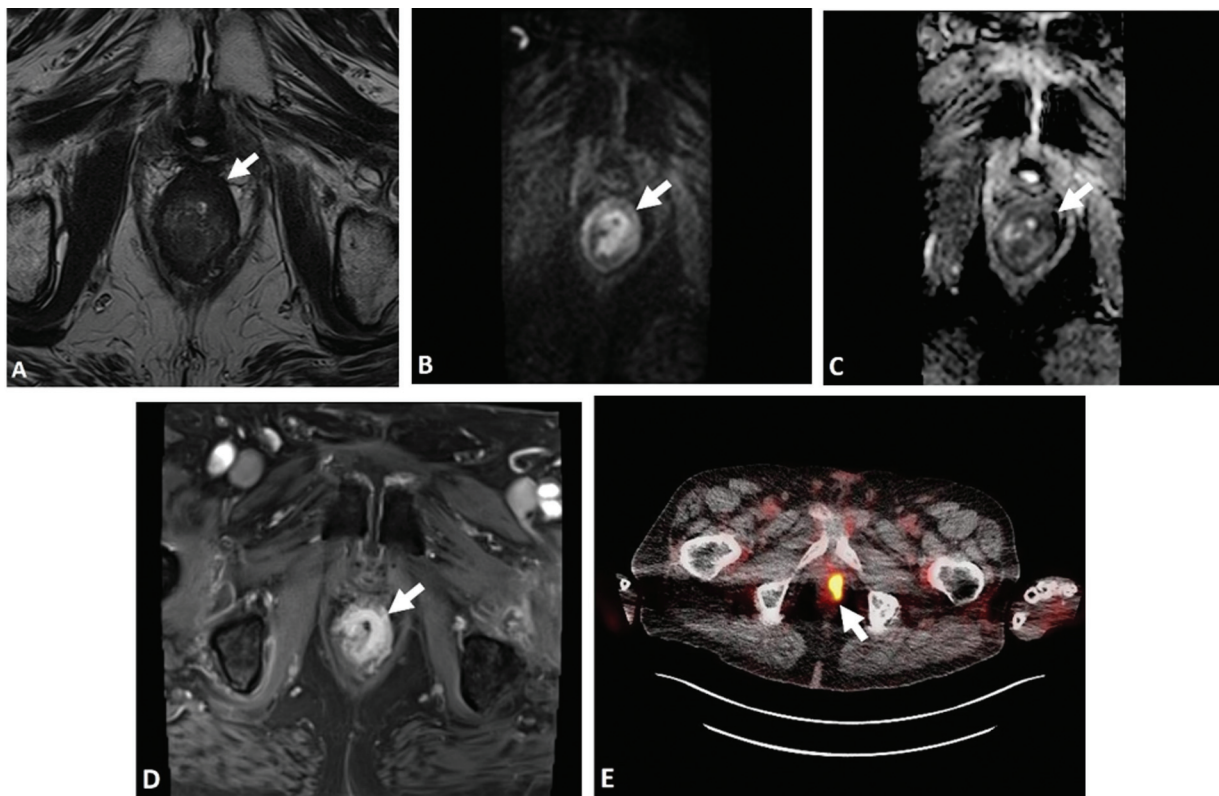
effect is most pronounced in patients with three or fewer bony metastases, in which RT targeting the prostate primary improves survival in patients without visceral or other metastasis.<sup>21</sup> Treating the primary in low burden disease likely disrupts metastatic dissemination from the primary and delays metastatic progression. By contrast, with high burden, metastasis-to-metastasis progression could be the dominant mode of dissemination and treating the primary in this setting has minimal benefit.<sup>21</sup>

#### Radiation Dose Planning

Biologically effective dose (BED) for radiation treatment is a calculation combining the dose per fraction and number of fractions. The principle of *fractionation* in RT is to allow for differential recovery between tumor and normal tissues, thereby maximizing efficacy while minimizing toxicity. For RT in PCa, the dose with conventional fractionation is usually 1.8 to 2 Gy given over 38 to 45 daily fractions for a cumulative dose greater than 76 Gy (as higher doses have proven more effective).<sup>22</sup>

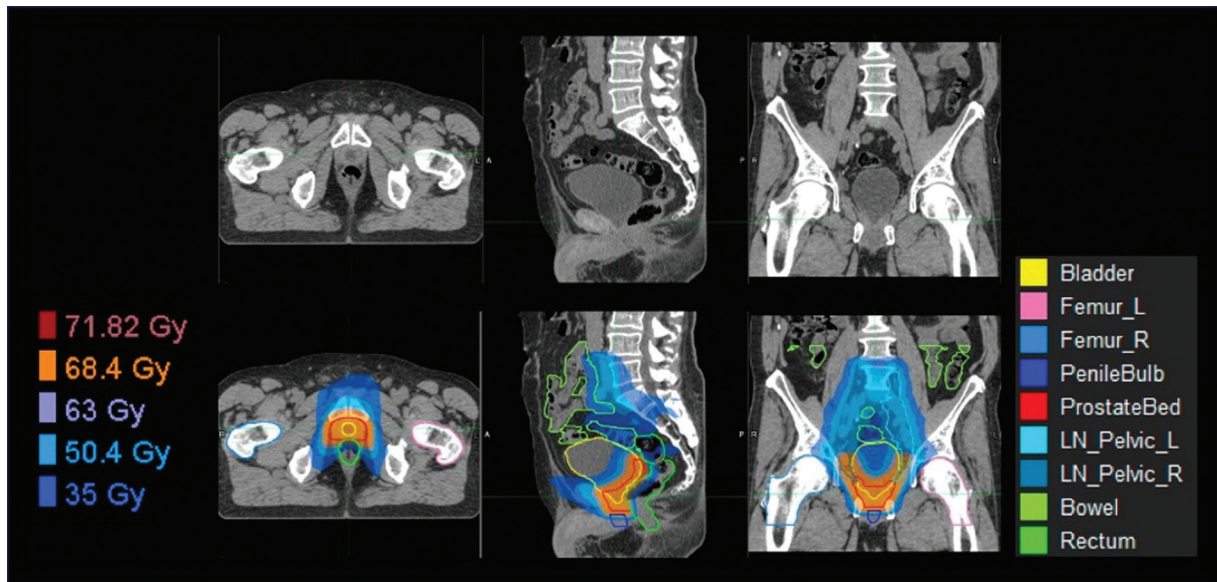
Due to a lower alpha-to-beta ratio (a component of BED calculations), thought to reflect slower tumor proliferation, PCa was hypothesized to benefit from *hypofractionated schedules*.<sup>23,24</sup>

Multiple randomized trials have evaluated *moderate hypofractionation* (2.4–3.4 Gy in ~20–28 daily fractions) in

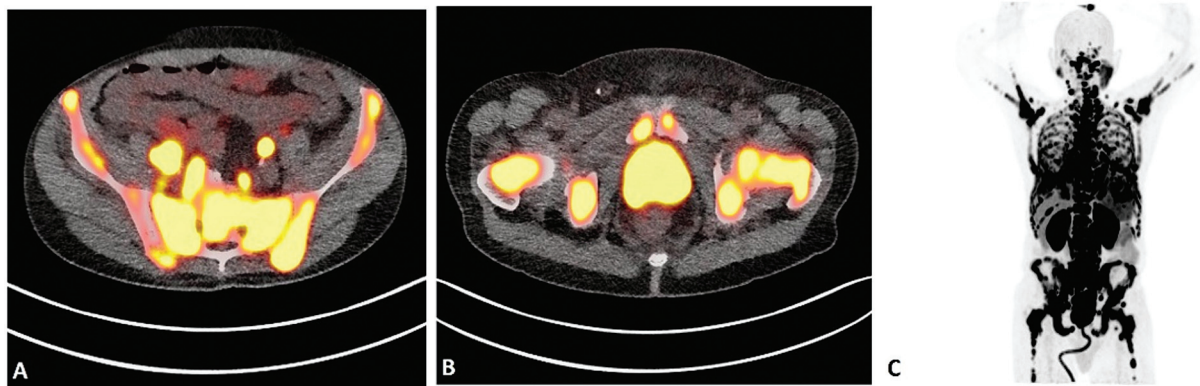


**Fig. 4** Targeting post-radical prostatectomy (RP) recurrence with salvage or adjuvant radiation therapy (RT). Multiparametric magnetic resonance imaging (mpMRI) identifying the area of recurrence (arrows) for salvage or adjuvant RT: mpMRI in a patient with biochemical recurrence (prostate-specific antigen [PSA] 6.28 ng/mL) 7 years after radical prostatectomy (negative margins) for Gleason pattern 4 + 3 prostate cancer showing (A) T2 hypointense soft-tissue thickening along the left anterolateral wall of the lower one-third of the rectum. It (B,C) restricts diffusion and (D) shows early enhancement on dynamic contrast enhanced (DCE). (E) Prostate-specific membrane antigen (PSMA) positron emission tomography (PET) shows avid uptake in the same location.





**Fig. 5** Pretreatment planning computed tomography (CT) for salvage radiation therapy (RT) targeting post-radical prostatectomy (post-RP) recurrence in the prostate bed. Planning CT simulation (top) and final dosimetric plan (bottom) for biochemically recurrent prostate cancer (PCa) salvage RT treated with volumetric modulated arc therapy (VMAT). Total dose of 68.4 Gy in 38 fractions was delivered to the prostate bed and 50.4 Gy in 28 fractions was delivered to the pelvic lymph nodes.



**Fig. 6** Prostate-specific membrane antigen (PSMA) positron emission tomography (PET) in metastatic prostate cancer (PCa).  $^{69}\text{Ga}$ -PSMA PET scan in a patient with metastatic prostate cancer showing diffuse avid radiotracer uptake involving the (A) prostate and (B) pelvic bones. (C) Whole body PET image showing the overall metastatic burden.

localized PCa and most of the evidence supports that it is noninferior concerning tumor control but with a possible increased toxicity. This approach is recommended by professional societies for patients who do not require nodal irradiation (although conventional fractionation to the nodes may be given concurrently).<sup>25</sup>

*Ultra-hypofractionated regimens*, as in stereotactic body radiation therapy (SBRT), where RT is delivered in five or fewer fractions, are also an option for carefully selected patients.<sup>25,26</sup> It should be noted that as moderate and ultra-hypofractionation are newer techniques, fewer long-term data, especially regarding toxicity, are available.

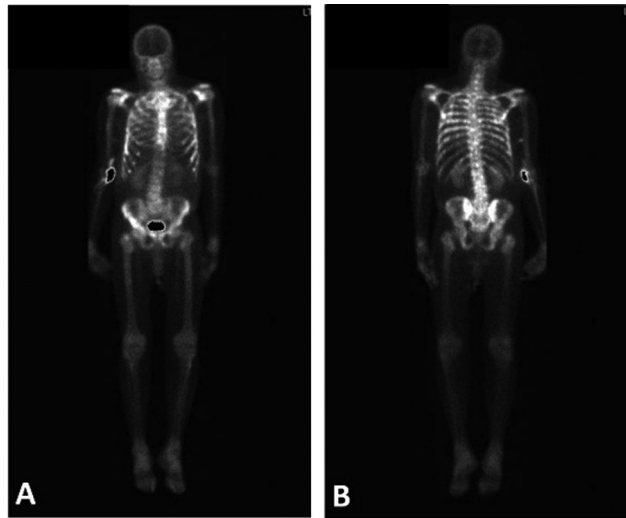
Given the higher doses, especially in ultra-hypofractionated regimens, that is, SBRT, prostate MRI is increasingly

utilized to aid in treatment planning,<sup>6</sup> including novel MR-guided intrafractional and adaptive planning.<sup>6</sup>

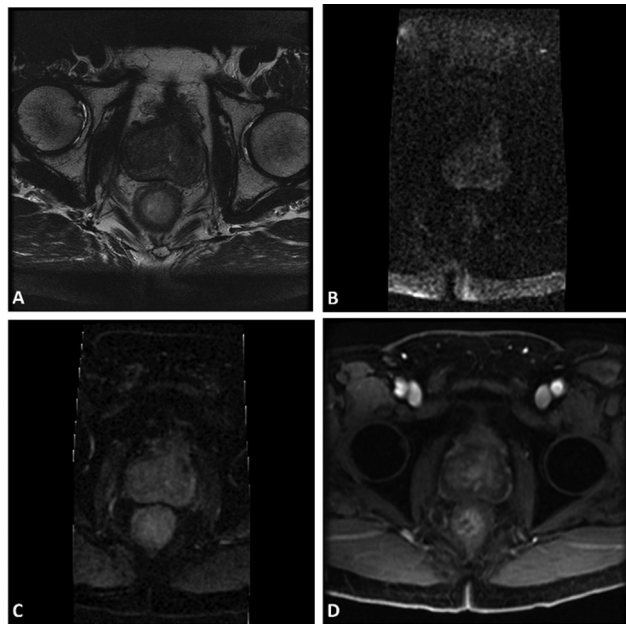
### Post-RT Radiology

#### Normal mpMRI Appearance after RT

The irradiated prostate exhibits a reduced size due to gland atrophy, and the differentiation of zones becomes challenging due to the effacement of prostatic tissue (→ **Fig. 8**). The entire prostate appears hypointense on T2W imaging, posing difficulties in distinguishing between zones and discerning benign from tumor tissue. Postradiation gland fibrosis is characterized by lower cellularity and reduced vascularity compared with pretreatment prostate tissue. Functional



**Fig. 7** Bone scan in metastatic prostate cancer (PCa). (A) Anterior and (B) posterior views of  $^{99m}\text{Tc}$  bone scan in a patient with metastatic PCa showing the extent of osseous metastasis.



**Fig. 8** Normal post-radiation therapy (post-RT) appearance. Multi-parametric magnetic resonance imaging (mpMRI) post-radiotherapy for prostate cancer showing (A) diffuse T2 hypointensity involving the prostate gland with loss of zonal anatomy. No diffusion restriction on (B,C) high  $b$  value diffusion weighted imaging (DWI) or (D) early arterial enhancing lesion on dynamic contrast enhanced (DCE) to suggest recurrence.

sequences (DWI and DCE) are optimal for detecting locally recurrent disease.

Brachytherapy seeds (radioactive metals enclosed in a capsule about the size of a grain of rice) are permanently retained in the prostate after LDR brachytherapy (►Fig. 9). Unlike HDR brachytherapy where the seeds are removed after the procedure, LDR seeds introduce MR susceptibility artifacts that particularly impact DWI, complicating interpretation. These appear as small T2 hypointense ellipsoid structures scattered throughout the prostate gland, gradually

migrating peripherally within the shrinking gland as treatment progresses.<sup>27</sup>

#### Fiducial Markers

FMs, radiopaque seeds placed transperineally prior to RT planning, facilitate the tracking of inter- or intrafraction prostate motions during image-guided radiotherapy (IGRT; ►Fig. 10). The most used markers are made of gold, usually presenting as a local signal void on MR images. Gold FMs are more hyperdense on CT, but they are surrounded by more extensive streak artifacts compared with polymer FMs.<sup>28</sup>

#### Post-RT Recurrence

##### Identifying Recurrence

##### Recurrence Monitoring and Definition

Serial evaluation of serum prostate-specific antigen (PSA) is the mainstay of surveillance testing in males who have undergone definitive therapy for localized PCa. Imaging studies have no role as screening tests for recurrence of localized PCa in the absence of a rising serum PSA or specific symptoms. These tests may be indicated to evaluate a rising PSA after definitive local treatment.<sup>29</sup>

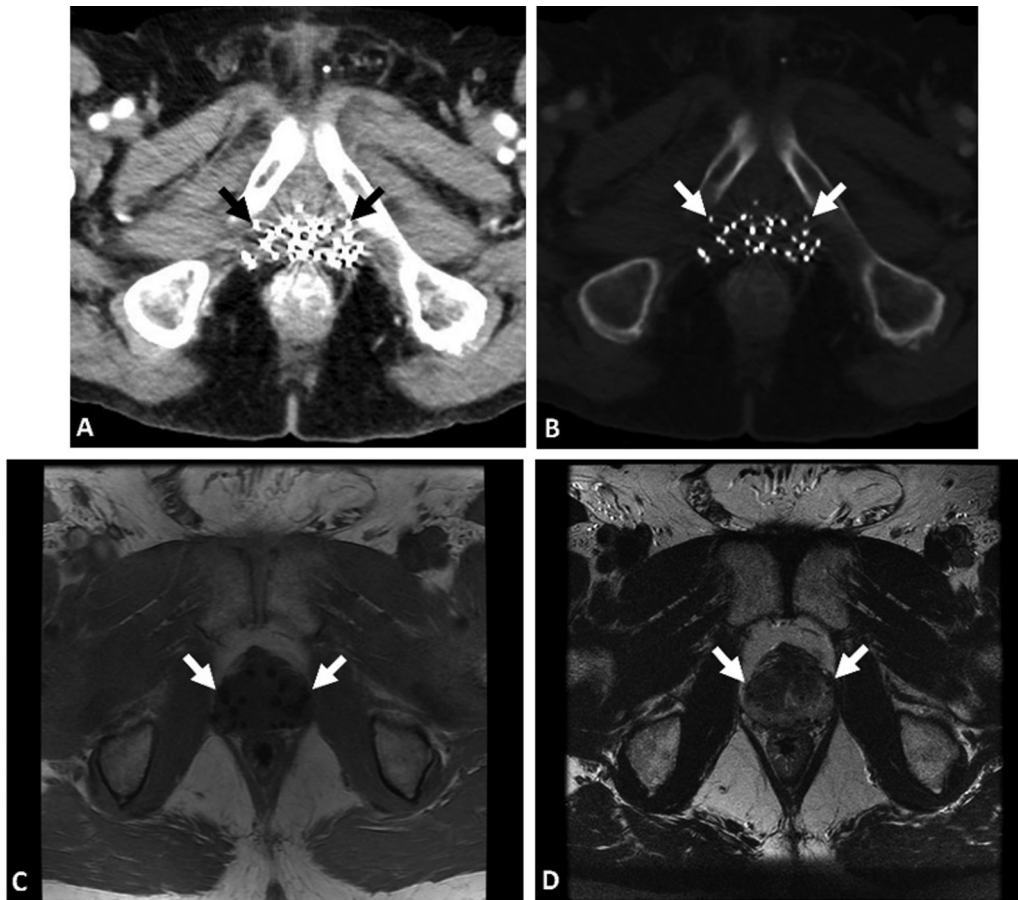
Following RT, achieving a PSA nadir requires a more extended period (~18 months to 3 years) compared with post-RP. The American Society for Therapeutic Radiology and Oncology (ASTRO) utilizes the Phoenix criteria to define post-RP biochemical recurrence (BCR), involving two consecutive measurements indicating a rise in serum PSA of at least 2 ng/mL above the nadir.<sup>30</sup>

Most recurrences after RT (►Fig. 11) are demonstrated to be local, with the prostate being the most common site of recurrence. Consequently, the evaluation of BCR involves an essential role for prostate mpMRI during follow-up,<sup>31</sup> with a baseline mpMRI study of the primary tumor site.

##### Utility of Post-RT Imaging Surveillance

For patients with BCR after RP or RT, PSMA-PET is now the imaging of choice to identify recurrent or residual sites of disease to best guide salvage RT.<sup>32</sup> Although the sensitivity of PSMA-PET is superior to CT or nuclear medicine (NM) bone scan, the detection rates increase with increasing PSA levels<sup>33,34</sup> (►Fig. 12). Although the increased sensitivity has resulted in earlier and more frequent salvage treatments,<sup>35</sup> it remains to be evaluated if PSMA-PET directed salvage results in superior long-term outcomes. Early detection of oligometastatic disease with PSMA-PET also raises the possibility of targeted RT to avoid or prolong progression to systemic therapies such as ADT.<sup>36</sup> To optimize the utility of PSMA PET after definitive treatment, false negatives can be mitigated by repeat, interval imaging (especially at lower, initial PSA levels), but the potential for false positives, especially for bone lesions<sup>37</sup> as well as benign diseases,<sup>38</sup> should be recognized.

**CT:** Pelvic CT is not indicated for routine surveillance of males who have received definitive treatment for localized



**Fig. 9** Brachytherapy seeds. Brachytherapy seeds (arrows) on (A) soft tissue and (B) bone windows of contrast-enhanced computed tomography (CT) appearing as metallic densities in the prostate gland causing streak artifacts due to proton starvation. Brachytherapy seeds in a different patient appearing as signal voids in the prostate gland on (C) T1-weighted and (D) T2-weighted images.

PCa because of the limited sensitivity of CT in detecting low-volume recurrent disease.<sup>39</sup> There is no role for PET scanning using either F-18 fluorodeoxyglucose (FDG) or PSMA to screen for recurrence after definitive local therapy of localized PCa in the absence of a PSA elevation. Use of these imaging studies should be limited to males who are documented to have a rising serum PSA after definitive local therapy.<sup>40</sup>

**MRI:** On T2W imaging, recurrence manifests as a nodular relatively hypointense lesion, often displaying a protrusion of the capsule. Its bulging appearance is likely due to the rapid tumor growth in contrast to the atrophic gland.<sup>41</sup> On DWI, recurrent tumor restricts diffusion and shows early hyperenhancement on DCE MRI corresponding to the nodular area on T2W imaging. In patients experiencing post-RT BCR, the combined T2W + DWI achieved a notably higher area under the curve (AUC) compared with T2W alone.<sup>42</sup> Kim et al discovered that the combination of DWI + DCE achieved a significantly higher AUC (86%) than T2W, DWI, or DCE alone.<sup>43</sup> It is suggested that DCE plays a more crucial role postbrachytherapy than post-EBRT, primarily due to the seed artifact on DWI.<sup>44</sup>

**Bone scan:** In the absence of symptoms, technetium-99 radionuclide bone scan has been replaced by PSA testing for the early detection of an asymptomatic recurrence. The

National Comprehensive Cancer Network (NCCN) guidelines suggest bone imaging for sensitive and reliable detection of skeletal metastases in males who develop symptoms, and bone imaging as often as every 6 to 12 months for those with node-positive disease who are receiving ADT.<sup>45</sup>

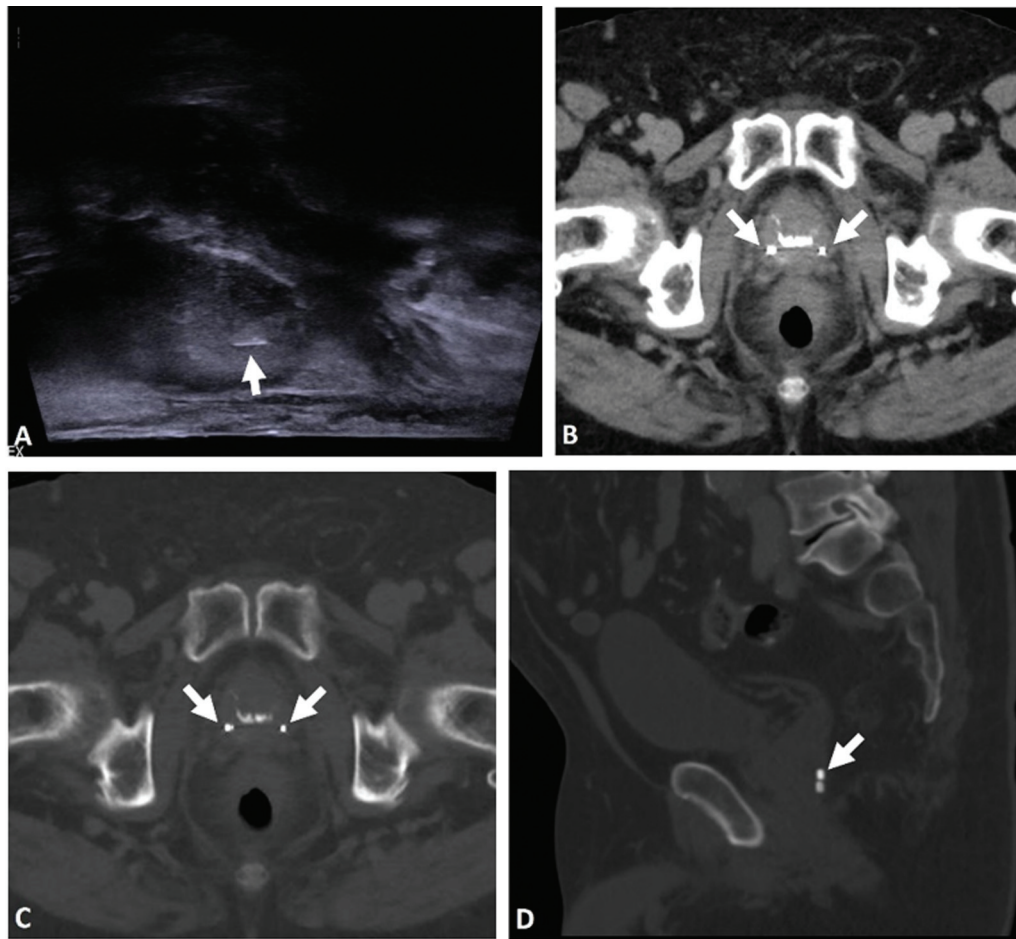
#### *Areas of Research: Posttreatment PSMA Response and Long-Term Outcomes*

Risk factors for recurrence included residual uptake observed after a longer time interval from the end of RT, with prostate lesions having a higher risk compared with bone and LN lesions. Using a cutoff value of greater than 8.6 months after RT, the presence of residual uptake was a diagnostic indicator of recurrence with high sensitivity and specificity, suggesting its potential in identifying recurrence 1 year post-RT.<sup>46</sup>

#### **Radiation Therapy Complications**

Radiation morbidity is proportional to the dose delivered to normal tissue (►Fig. 13). Conformal beam therapy and brachytherapy are able to more specifically target the tumor while excluding dose to nontarget organs. However, due to the physics of radiation delivery, invasion of tumor into normal tissue, and proximity of the prostate to neighboring pelvic structures, some dose spillover to nearby normal





**Fig. 10** Fiducial markers. Transrectal ultrasound in sagittal view showing a fiducial marker (*arrow*) in the prostate apex after insertion via the transperineal route. FM (*arrows*) seen on (B) soft tissue and bone windows (C: axial image; D: sagittal reformation) of contrast-enhanced computed tomography (CT) appearing as metallic densities in the prostate gland.

tissue is unavoidable. Because of this, radiation complications are local, in that nearby tissues are at highest risk of injury.

### Proctitis

The diagnosis of *acute radiation proctitis* should be suspected in patients with diarrhea, mucus discharge, urgency, tenesmus, or bleeding during or within 6 weeks of RT. *Chronic radiation proctitis* should be suspected in patients with a history of pelvic radiation exposure who present with symptoms of constipation, rectal pain, rectal bleeding, or urgency, either as a continuation of acute radiation proctitis or a delayed onset (9–14 months following radiation exposure to 30 years after exposure).

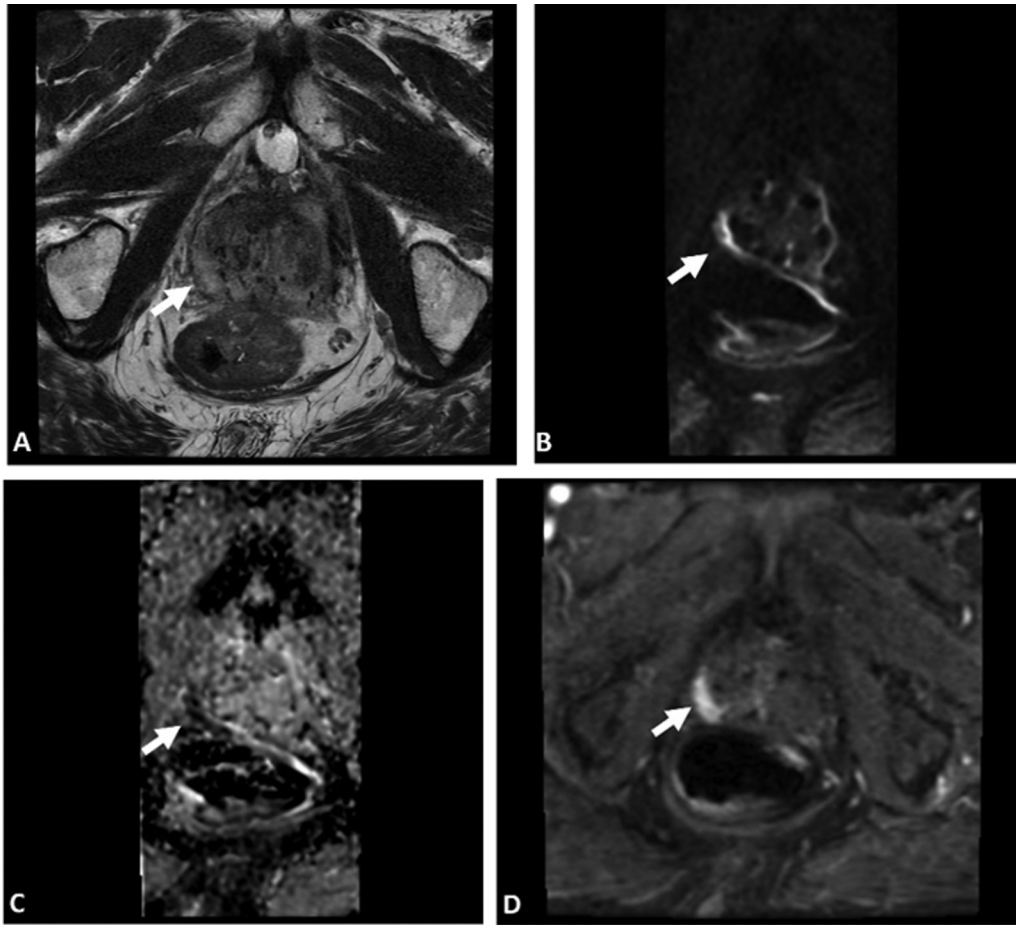
Radiation doses of less than 45 Gy are associated with few long-term radiation side effects. In contrast, doses above 70 Gy cause significant and long-standing injury to the surrounding area.

Endoscopy with histology is the mainstay of diagnosis for radiation proctitis. Abdominal imaging should be performed in selected patients with a suspected colovesical fistula and in patients with obstructive symptoms due to a stricture.<sup>47</sup>

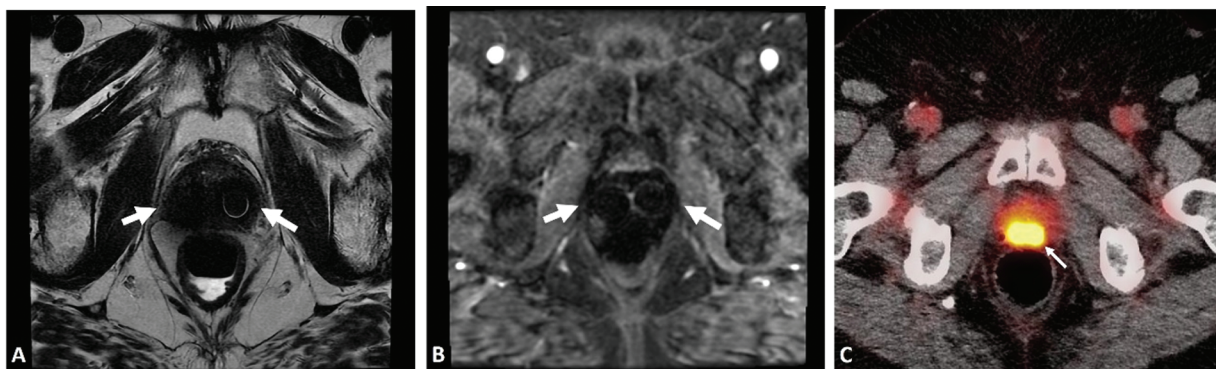
Gastrointestinal (GI) symptoms can be further reduced by using *FM-based position verification* in patients with PCa. With SpaceOAR Hydrogel injection (► **Fig. 14**), Hamstra et al showed improvement in grade 1 and 2 GI toxicity, and grade 1 genitourinary (GU) toxicity, along with patient-reported bowel and urinary quality of life all favoring the use of temporary rectal separation during RT.<sup>5</sup> Rectal complications are much lower with *conformal beam therapy* than with four-box, small-field therapy; however, the incidence of bladder complications is unchanged, probably because of the proximity of the bladder neck and unavoidable exposure to the urethra.<sup>48</sup>

### Cystitis

The 4-year actuarial risk of grade 3 or worse bleeding toxicity from prostate EBRT was 15.5% in the anticoagulation cohort and 3.6% in the control group.<sup>49</sup> *Acute radiation cystitis* is usually self-limiting with patients presenting with urgency, frequency, dysuria, and hematuria and is generally managed with conservative symptomatic therapy or observation. *Chronic radiation cystitis*, which can develop months to years after RT, presents



**Fig. 11** Multiparametric magnetic resonance imaging (mpMRI) in post-radiation therapy (post-RT) recurrence. mpMRI in a 93-year-old patient with biochemical recurrence (prostate-specific antigen [PSA] 9.36 ng/mL) 22 years after brachytherapy for prostate cancer showing (A) a 2.2-cm T2 hyperintense lesion in the right posterior lateral peripheral zone mid-gland, also showing (B,C) diffusion restriction and (D) early arterial enhancement on dynamic contrast enhanced (DCE), suspicious for recurrence (arrows).



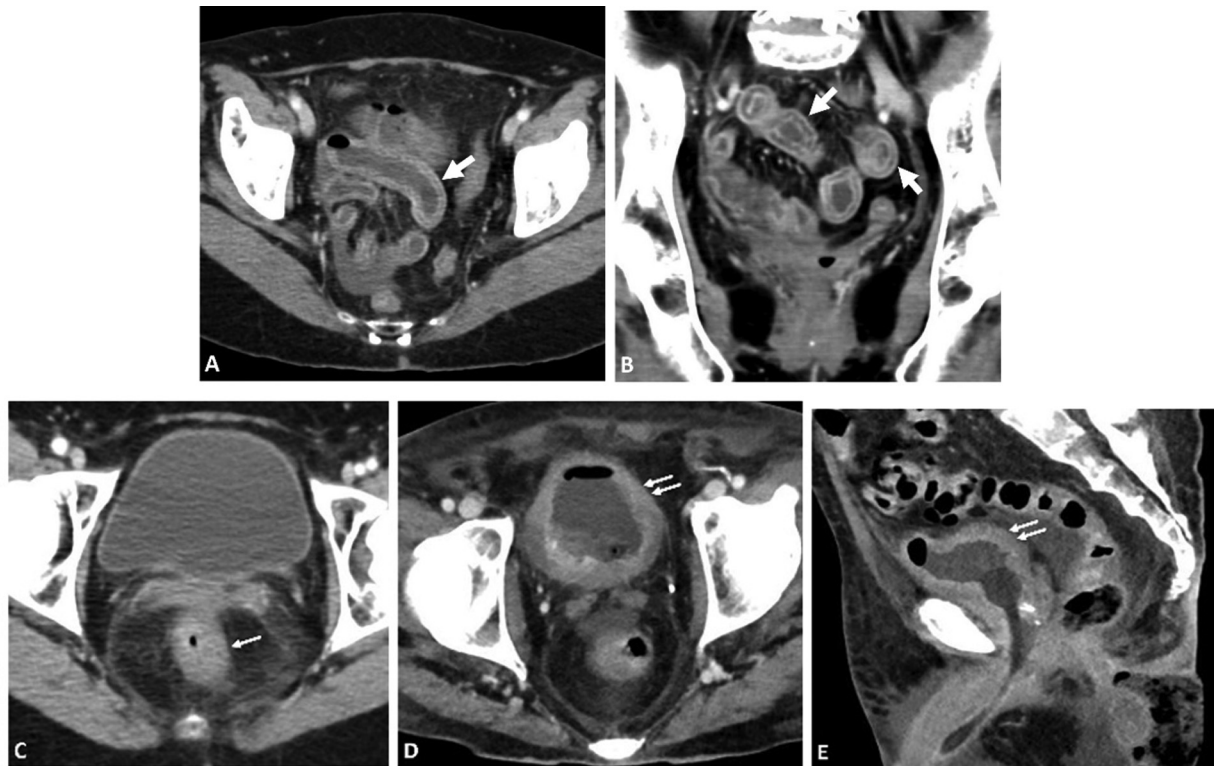
**Fig. 12** Prostate-specific membrane antigen (PSMA) positron emission tomography (PET) in post-radiation therapy (post-RT) recurrence. Magnetic resonance imaging (MRI) performed for biochemical recurrence (prostate-specific antigen [PSA]: 6.84 ng/mL in 2022) shows significant susceptibility artifacts due to fiducial markers (thick arrows) in the prostate gland, precluding optimal assessment on (A) T2 and (B) dynamic contrast enhanced (DCE). (C) Restaging PSMA PET shows avid radiotracer uptake in the posterior midline prostate, suspicious for recurrence (thin arrow).

principally as hematuria, which ranges from mild to life-threatening.

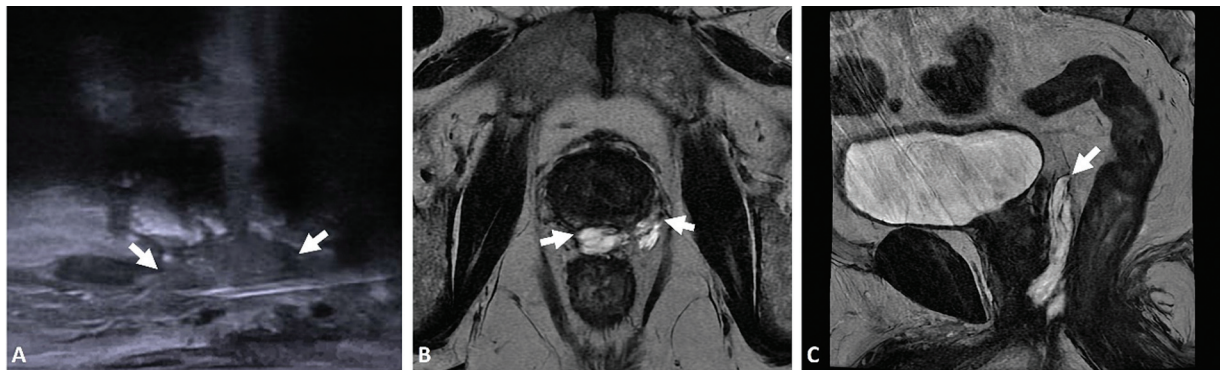
Cystoscopy is used to confirm the diagnosis and to rule out other conditions, such as bladder cancer or other recurrent metastatic tumors. Intravenous pyelography (IVP) is useful

to evaluate anatomical abnormalities of the GU tract. If hematuria is present, IVP or CT urography is needed to rule out other causes of bleeding, such as calculus disease and neoplasia. CT scanning may also help in the diagnosis of bladder fistulas.





**Fig. 13** Post-radiation therapy (post-RT) complications. Contrast-enhanced computed tomography (CECT) in patients following external beam radiation therapy (EBRT) for prostate cancer showing a few complications. (A) Axial and (B) coronal reformatted images of radiation enteritis (*thick arrows*) with mural thickening and water halo sign involving the pelvic small bowel loops confined to the field of radiation. (C) Axial image of radiation proctitis (*thin arrow*) with rectal wall thickening and perirectal fat stranding. (D) Axial and (E) sagittal reformatted images of radiation cystitis (*double arrows*) with diffuse urinary bladder wall thickening.



**Fig. 14** SpaceOAR. (A) Transrectal ultrasound in axial view showing transperineal injection of hydrogel (SpaceOAR). (B) Axial and (C) sagittal T2-weighted images showing rectoprostatic separation due to hydrogel injection (*arrows*).

Fewer grade 2 bladder complications occur with *IMRT*, but the rates of grade 3 complications are similar.<sup>48</sup>

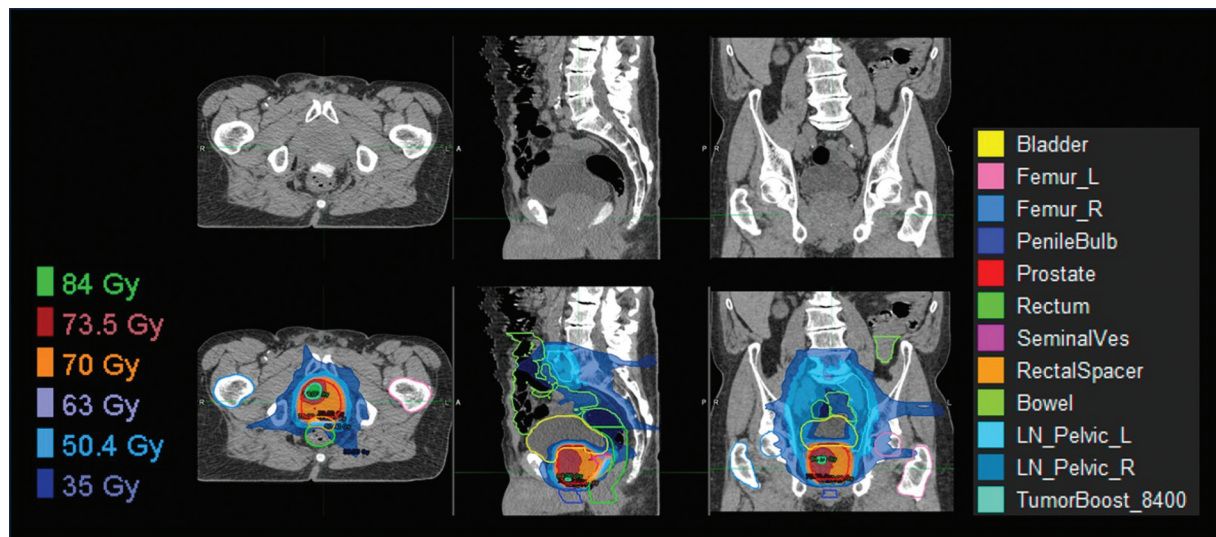
### Reducing Post-RT Toxicity with EBRT and Intraprostatic Boost

The incorporation of an intraprostatic boost to EBRT involves an additional concentrated dose of radiation delivered directly to the organ-confined tumor within the prostate and improved disease-free survival for patients with localized intermediate- and high-risk PCa without impacting toxicity and quality of life (– **Fig. 15**).<sup>50</sup>

### Summary

This review provides an overview of the available techniques including recent advancements in RT in the context of PCa management. Advanced radiation techniques, such as *IMRT* and *SBRT*, enhance treatment precision, minimizing damage to surrounding tissue. In addition, radiologists must be aware of expected posttreatment appearances and complications in the appropriate clinical and biochemical context. Knowledge of mpMRI sequences and their advantages and limitations plays a key role in the





**Fig. 15** External beam radiation therapy (EBRT) with intraprostatic boost in a patient with localized prostate cancer (PCa). Planning computed tomography (CT) simulation (top) and final dosimetric plan (bottom) for localized, high-risk PCa with a targetable intraprostatic lesion treated with volumetric modulated arc therapy (VMAT). Total dose of 70 Gy in 28 fractions was delivered to the prostate and seminal vesicles, 50.4 Gy in 28 fractions was delivered to the pelvic lymph nodes, and 84 Gy in 28 fractions was delivered to the intraprostatic lesion visualized on multiparametric magnetic resonance imaging (mpMRI).

differentiation of postradiation recurrence from its mimics.

#### Funding

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#### Conflict of Interest

None declared.

#### References

- Schaeffer EM, Srinivas S, Adra N, et al. Prostate cancer, version 4.2023. NCCN clinical practice guidelines in oncology. *J Natl Compr Canc Netw* 2023;21(10):1067–1096
- Kamran SC, Light JO, Efstathiou JA. Proton versus photon-based radiation therapy for prostate cancer: emerging evidence and considerations in the era of value-based cancer care. *Prostate Cancer Prostatic Dis* 2019;22(04):509–521
- Efstathiou JA, Kamran SC, Spratt DE. Protons versus photons for prostate cancer: an answer that is long overdue and coming. *Int J Radiat Oncol Biol Phys* 2021;110(04):1098–1100
- Combes AD, Palma CA, Calopedos R, et al. PSMA PET-CT in the diagnosis and staging of prostate cancer. *Diagnostics (Basel)* 2022;12(11):2594
- Hamstra DA, Mariados N, Sylvester J, et al. Continued benefit to rectal separation for prostate radiation therapy: final results of a phase III trial. *Int J Radiat Oncol Biol Phys* 2017;97(05):976–985
- Leeman JE, Cagney DN, Mak RH, et al. Magnetic resonance-guided prostate stereotactic body radiation therapy with daily online plan adaptation: results of a prospective phase 1 trial and supplemental cohort. *Adv Radiat Oncol* 2022;7(05):100934
- de Rooij M, Hamoen EHJ, Witjes JA, Barentsz JO, Rovers MM. Accuracy of magnetic resonance imaging for local staging of prostate cancer: a diagnostic meta-analysis. *Eur Urol* 2016;70(02):233–245
- Lebastchi AH, Gupta N, DiBianco JM, et al. Comparison of cross-sectional imaging techniques for the detection of prostate cancer lymph node metastasis: a critical review. *Transl Androl Urol* 2020;9(03):1415–1427
- Heesakkers RA, Hövels AM, Jager GJ, et al. MRI with a lymph-node-specific contrast agent as an alternative to CT scan and lymph-node dissection in patients with prostate cancer: a prospective multicohort study. *Lancet Oncol* 2008;9(09):850–856
- Hövels AM, Heesakkers RAM, Adang EM, et al. The diagnostic accuracy of CT and MRI in the staging of pelvic lymph nodes in patients with prostate cancer: a meta-analysis. *Clin Radiol* 2008;63(04):387–395
- Vallini V, Ortori S, Boraschi P, et al. Staging of pelvic lymph nodes in patients with prostate cancer: Usefulness of multiple b value SE-EPI diffusion-weighted imaging on a 3.0 T MR system. *Eur J Radiol Open* 2015;3:16–21
- Harisinghani MG, Barentsz J, Hahn PF, et al. Noninvasive detection of clinically occult lymph-node metastases in prostate cancer. *N Engl J Med* 2003;348(25):2491–2499
- Woo S, Suh CH, Kim SY, Cho JY, Kim SH. Diagnostic performance of magnetic resonance imaging for the detection of bone metastasis in prostate cancer: a systematic review and meta-analysis. *Eur Urol* 2018;73(01):81–91
- Allen SD, Thompson A, Sohaib SA. The normal post-surgical anatomy of the male pelvis following radical prostatectomy as assessed by magnetic resonance imaging. *Eur Radiol* 2008;18(06):1281–1291
- Lopes Dias J, Lucas R, Magalhães Pina J, et al. Post-treated prostate cancer: normal findings and signs of local relapse on multiparametric magnetic resonance imaging. *Abdom Imaging* 2015;40(07):2814–2838
- Grant K, Lindenberg ML, Shebel H, et al. Functional and molecular imaging of localized and recurrent prostate cancer. *Eur J Nucl Med Mol Imaging* 2013;40(Suppl 1):S48–S59
- Sella T, Schwartz LH, Swindle PW, et al. Suspected local recurrence after radical prostatectomy: endorectal coil MR imaging. *Radiology* 2004;231(02):379–385
- Casciani E, Poletti E, Carmenini E, et al. Endorectal and dynamic contrast-enhanced MRI for detection of local recurrence after radical prostatectomy. *AJR Am J Roentgenol* 2008;190(05):1187–1192
- Panebianco V, Barchetti F, Sciarra A, et al. Prostate cancer recurrence after radical prostatectomy: the role of 3-T diffusion imaging in multi-parametric magnetic resonance imaging. *Eur Radiol* 2013;23(06):1745–1752

- 20 Kitajima K, Hartman RP, Froemming AT, Hagen CE, Takahashi N, Kawashima A. Detection of local recurrence of prostate cancer after radical prostatectomy using endorectal coil MRI at 3 T: addition of DWI and dynamic contrast enhancement to T2-weighted MRI. *AJR Am J Roentgenol* 2015;205(04):807–816
- 21 Ali A, Hoyle A, Haran AM, et al. Association of bone metastatic burden with survival benefit from prostate radiotherapy in patients with newly diagnosed metastatic prostate cancer: a secondary analysis of a randomized clinical trial. *JAMA Oncol* 2021;7(04):555–563
- 22 Zietman AL, Bae K, Slater JD, et al. Randomized trial comparing conventional-dose with high-dose conformal radiation therapy in early-stage adenocarcinoma of the prostate: long-term results from proton radiation oncology group/american college of radiology 95-09. *J Clin Oncol* 2010;28(07):1106–1111
- 23 Ritter M. Rationale, conduct, and outcome using hypofractionated radiotherapy in prostate cancer. *Semin Radiat Oncol* 2008;18(04):249–256
- 24 Brand DH, Kirby AM, Yarnold JR, Somaiah N. How low can you go? The radiobiology of hypofractionation. *Clin Oncol (R Coll Radiol)* 2022;34(05):280–287
- 25 Morgan SC, Hoffman K, Loblaw DA, et al. Hypofractionated radiation therapy for localized prostate cancer: executive summary of an ASTRO, ASCO and AUA evidence-based guideline. *J Urol* 2019;201(03):528–534
- 26 Jackson WC, Silva J, Hartman HE, et al. Stereotactic body radiation therapy for localized prostate cancer: a systematic review and meta-analysis of over 6,000 patients treated on prospective studies. *Int J Radiat Oncol Biol Phys* 2019;104(04):778–789
- 27 Gaur S, Turkbey B. Prostate MR imaging for posttreatment evaluation and recurrence. *Radiol Clin North Am* 2018;56(02):263–275
- 28 Chan MF, Cohen GN, Deasy JO. Qualitative evaluation of fiducial markers for radiotherapy imaging. *Technol Cancer Res Treat* 2015;14(03):298–304
- 29 Penson DF. Follow-up surveillance after definitive local treatment for prostate cancer - UpToDate. Accessed December 14, 2023 at: <https://www.uptodate.com/contents/follow-up-surveillance-after-definitive-local-treatment-for-prostate-cancer>
- 30 Roach M III, Hanks G, Thames H Jr, et al. Defining biochemical failure following radiotherapy with or without hormonal therapy in men with clinically localized prostate cancer: recommendations of the RTOG-ASTRO Phoenix Consensus conference. *Int J Radiat Oncol Biol Phys* 2006;65(04):965–974
- 31 Zumsteg ZS, Spratt DE, Romesser PB, et al. Anatomical patterns of recurrence following biochemical relapse in the dose escalation era of external beam radiotherapy for prostate cancer. *J Urol* 2015;194(06):1624–1630
- 32 Mottet N, Bellmunt J, Bolla M, et al. EAU-ESTRO-SIOG guidelines on prostate cancer. Part 1: screening, diagnosis, and local treatment with curative intent. *Eur Urol* 2017;71(04):618–629
- 33 Tan N, Bavadian N, Calais J, et al. Imaging of prostate specific membrane antigen targeted radiotracers for the detection of prostate cancer biochemical recurrence after definitive therapy: a systematic review and meta-analysis. *J Urol* 2019;202(02):231–240
- 34 Perera M, Papa N, Roberts M, et al. Gallium-68 prostate-specific membrane antigen positron emission tomography in advanced prostate cancer—updated diagnostic utility, sensitivity, specificity, and distribution of prostate-specific membrane antigen-avid lesions: a systematic review and meta-analysis. *Eur Urol* 2020;77(04):403–417
- 35 Perera M, Papa N, Christidis D, et al. Sensitivity, specificity, and predictors of positive <sup>68</sup>Ga-prostate-specific membrane antigen positron emission tomography in advanced prostate cancer: a systematic review and meta-analysis. *Eur Urol* 2016;70(06):926–937
- 36 Mohan R, Kneebone A, Eade T, et al. Long-term outcomes of SBRT for PSMA PET detected oligometastatic prostate cancer. *Radiat Oncol* 2023;18(01):127
- 37 Seifert R, Telli T, Opitz M, et al. Unspecific <sup>18</sup>F-PSMA-1007 bone uptake evaluated through PSMA-11 PET, bone scanning, and MRI triple validation in patients with biochemical recurrence of prostate cancer. *J Nucl Med* 2023;64(05):738–743
- 38 de Galiza Barbosa F, Queiroz MA, Nunes RF, et al. Nonprostatic diseases on PSMA PET imaging: a spectrum of benign and malignant findings. *Cancer Imaging* 2020;20(01):23
- 39 Krämer S, Görlich J, Gottfried HW, et al. Sensitivity of computed tomography in detecting local recurrence of prostatic carcinoma following radical prostatectomy. *Br J Radiol* 1997;70(838):995–999
- 40 Crawford ED, Koo PJ, Shore N, et al; RADAR III Group. A clinician's guide to next generation imaging in patients with advanced prostate cancer (RADAR III). *J Urol* 2019;201(04):682–692
- 41 McCammack KC, Raman SS, Margolis DJA. Imaging of local recurrence in prostate cancer. *Future Oncol* 2016;12(21):2401–2415
- 42 Kim CK, Park BK, Lee HM. Prediction of locally recurrent prostate cancer after radiation therapy: incremental value of 3T diffusion-weighted MRI. *J Magn Reson Imaging* 2009;29(02):391–397
- 43 Kim CK, Park BK, Park W, Kim SS. Prostate MR imaging at 3T using a phased-arrayed coil in predicting locally recurrent prostate cancer after radiation therapy: preliminary experience. *Abdom Imaging* 2010;35(02):246–252
- 44 Rouvière O, Vitry T, Lyonnet D. Imaging of prostate cancer local recurrences: why and how? *Eur Radiol* 2010;20(05):1254–1266
- 45 Dwyer M. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic. 2024. Accessed December 14, 2023 at: <https://www.nccn.org/home/member->
- 46 Hotta M, Nguyen K, Thin P, et al. Kinetics of PSMA PET uptake in prostate cancer lesions after radiation therapy: a single-center retrospective study. *J Clin Oncol* 2022;40(06):36
- 47 Friedman LS, Hong TS. Radiation proctitis: clinical manifestations, diagnosis, and management. UpToDate. Accessed December 14, 2023 at: <https://www.uptodate.com/contents/radiation-proctitis-clinical-manifestations-diagnosis-and-management>
- 48 Lips IM, Dehnad H, van Gils CH, Boeken Kruger AE, van der Heide UA, van Vulpen M. High-dose intensity-modulated radiotherapy for prostate cancer using daily fiducial marker-based position verification: acute and late toxicity in 331 patients. *Radiat Oncol* 2008;3(01):15
- 49 Choe KS, Jani AB, Liauw SL. External beam radiotherapy for prostate cancer patients on anticoagulation therapy: how significant is the bleeding toxicity? *Int J Radiat Oncol Biol Phys* 2010;76(03):755–760
- 50 Kerkmeijer LGW, Groen VH, Pos FJ, et al. Focal boost to the intraprostatic tumor in external beam radiotherapy for patients with localized prostate cancer: results from the FLAME randomized phase III trial. *J Clin Oncol* 2021;39(07):787–796