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Clinical Protocol for IMRT and VMAT radiotherapy in localized prostate cancer: Practical implementation based on institutional guidelines

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Abstract

Background: Radiotherapy represents a cornerstone in the management of localized prostate cancer. The development of modern techniques such as intensity-modulated radiotherapy (IMRT), volumetric modulated arc therapy (VMAT), and image-guided radiotherapy (IGRT) has significantly improved treatment precision while reducing irradiation of surrounding organs at risk. Standardization of treatment planning, target delineation, and dose constraints is essential to optimize tumor control and minimize treatment-related toxicity.

Objective: The aim of this work was to describe and standardize a radiotherapy protocol for the management of localized prostate cancer using modern techniques including IMRT/VMAT and daily image guidance.

Methods: This protocol defines therapeutic decision criteria, target volume delineation, treatment planning procedures, dose prescription, and organ-at-risk constraints for prostate radiotherapy. Risk stratification was based on NCCN classification and predictive nomograms for lymph node involvement [1,4–10]. Target volumes and organs at risk were delineated according to international consensus guidelines [2,3]. Treatment was delivered using IMRT or VMAT techniques with daily cone-beam CT (CBCT) verification. Both conventional and hypofractionated schedules were considered depending on clinical indications.

Results: The proposed protocol provides standardized recommendations for treatment planning, including clinical target volume definition, planning target volume margins, dose prescription strategies, and dose constraints for organs at risk. The integration of IMRT/VMAT techniques with IGRT and CBCT imaging allows improved target coverage while reducing radiation exposure to the rectum, bladder, and other pelvic structures. Hypofractionated schedules may also be safely implemented within this framework.

Conclusion: Modern prostate radiotherapy based on IMRT or VMAT combined with image guidance and standardized planning procedures enables highly conformal treatment delivery with improved therapeutic ratios. The implementation of such structured protocols may enhance treatment consistency, optimize dosimetric outcomes, and contribute to improved clinical results in patients with localized prostate cancer.

Keywords: Prostate cancer; Radiotherapy; IMRT; VMAT; Treatment planning; IGRT

1. Introduction

Prostate cancer is the most frequently diagnosed malignancy among men worldwide and represents a major public health challenge. Radiotherapy plays a central role in the management of localized prostate cancer and is considered an effective alternative to radical prostatectomy for many patients.

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Technological advances in radiation oncology have significantly improved treatment precision. Intensity-modulated radiotherapy (IMRT) and volumetric modulated arc therapy (VMAT) allow highly conformal dose distributions, enabling dose escalation to the prostate while minimizing radiation exposure to adjacent organs such as the rectum, bladder, and femoral heads.

The present work describes a standardized clinical protocol for IMRT and VMAT radiotherapy in localized prostate cancer based on institutional practice and international guidelines.

2. Therapeutic Decision Support

NCCN Risk Classification

Prognostic groups for localized prostate cancer (N0M0) were classified according to NCCN risk stratification as follows:

- Low-risk group: cT1–T2a, Gleason score ≤ 6, and PSA < 10 ng/mL
- Intermediate-risk group: cT2b–c and/or Gleason score = 7 and/or PSA between 10 and 20 ng/mL
- High-risk group: ≥ cT3a and/or Gleason score ≥ 8 and/or PSA > 20 ng/mL

The intermediate-risk group can be further divided into two prognostic subgroups [1]:

- Favorable intermediate risk: one intermediate-risk factor only, Gleason score ≤ 7 (3+4), and <50% positive biopsy cores
- Unfavorable intermediate risk: two or more intermediate-risk factors and/or Gleason score 7 (4+3) and/or ≥50% positive biopsy cores

Since 2014, histological classification has been adapted to the ISUP grading system:

- ISUP Grade 1: former Gleason 3+3, corresponding to well-differentiated tumors
- ISUP Grade 2: former Gleason 3+4, corresponding to well-to-moderately differentiated tumors
- ISUP Grade 3: former Gleason 4+3, corresponding to moderately differentiated tumors
- ISUP Grade 4: former Gleason 4+4, corresponding to poorly differentiated tumors
- ISUP Grade 5: former Gleason 9 or 10, including grade 5 components, corresponding to undifferentiated tumors

2.1. Indications for Pelvic Lymph Node Irradiation

Predictive nomograms for extracapsular extension, lymph node involvement, and seminal vesicle invasion are presented in Appendix A [4–10].

For patients with N0 disease:

- Low-risk or favorable intermediate-risk patients: no prophylactic pelvic lymph node irradiation
- Unfavorable intermediate-risk or high-risk patients: pelvic lymph node irradiation is recommended when the estimated risk of lymph node involvement is ≥15%, according to the Roach formula [6,7]

For patients with Gleason score 7 (3+4), the risk of lymph node involvement may be further refined using the Kattan and Briganti nomograms [5,8–10].

For patients with N1 disease, pelvic lymph node irradiation combined with a boost to the involved lymph node was indicated.

In cases of very small lymph nodes (<5 mm) or lymph nodes that had completely regressed following androgen deprivation therapy, nodal boost could be omitted and pelvic nodal irradiation alone delivered.

2.2. Indications for Prophylactic Seminal Vesicle Irradiation

Prophylactic seminal vesicle irradiation was performed according to the following rules:

- Low-risk or favorable intermediate-risk patients: irradiation limited to the proximal 1 cm of the seminal vesicles when the MRI index lesion was located at the prostate base or when biopsies were positive at the base

- Unfavorable intermediate-risk or high-risk patients: irradiation of the entire seminal vesicles

If the seminal vesicles were not involved and pelvic nodal irradiation was not indicated, irradiation could be limited to the proximal 1 cm of the seminal vesicles using a hypofractionated schedule of 60 Gy in 20 fractions.

2.3. Indications for Androgen Deprivation Therapy (ADT)

For patients with N0 disease, treatment decisions were based on the NCCN prognostic classification:

- Low-risk patients: external beam radiotherapy (EBRT) alone
- Intermediate-risk patients:
  - Favorable intermediate risk: EBRT alone, with optional short-term ADT for 4–6 months
  - Unfavorable intermediate risk: EBRT combined with short-term ADT (4–6 months)
- High-risk patients: EBRT combined with long-term ADT (18–36 months), depending on the number of high-risk factors
  - If the only high-risk factor was MRI-detected T3a disease with limited extracapsular extension not confirmed on digital rectal examination, ADT for 4–6 months could be considered.

For patients with N1 disease, EBRT combined with long-term ADT for 24–36 months was indicated.

3. Treatment Planning Procedure

3.1. Planning CT Simulation

CT simulation was performed with and without intravenous iodinated contrast agent, with acquisition during the vascular phase.

3.1.1. Acquisition limits:

- Superior limit: L2/L3 vertebral level + 5 cm superiorly in the absence of para-aortic nodal irradiation; if para-aortic irradiation was indicated, acquisition extended to the diaphragmatic domes + 5 cm superiorly
- Inferior limit: ischial tuberosities + 5 cm inferiorly, ensuring complete acquisition of the bladder and rectum

3.1.2. Patient preparation and positioning:

Supine position with knee support to ensure comfort and reproducibility

Rectum emptied of fecal material and gas; the anteroposterior rectal diameter at the level of the prostate should be ≤5 cm. If excessive rectal distension was observed, rectal evacuation using a catheter or enema could be performed

Bladder moderately filled, except in cases of nodal recurrence after prior irradiation of the prostate or prostate bed, where bladder emptying was preferred

3.1.3. Instructions prior to CT simulation:

A rectal enema (Normacol®) was performed the day before and the morning of the simulation

Thirty to forty-five minutes before CT acquisition, patients were instructed to empty their bladder and then drink 3–4 glasses of water, without voiding again before the scan

Administration of iodinated contrast material was performed only after medical validation and under appropriate supervision.

4. Target Volume Delineation

4.1. Clinical Target Volumes (CTV)

4.1.1. CTV_ADP

- N0 patients: no lymph node gross disease volume (CTV_ADP) was defined

- N1 patients: CTV_ADP corresponded to macroscopically involved pelvic lymph nodes identified on CT, MRI, or PET

4.1.2. CTV_PRO

CTV_PRO included the entire prostate gland, with possible inclusion of areas of extracapsular extension and/or seminal vesicle infiltration when present.

Additional rules were applied according to the risk group:

- Low-risk or favorable intermediate-risk patients with an MRI index lesion located at the prostatic base or with positive biopsies at the base: the proximal 1 cm of the seminal vesicles was included in CTV_PRO
- Unfavorable intermediate-risk or high-risk patients without seminal vesicle invasion and not receiving prophylactic pelvic irradiation (60 Gy/20 fractions): the proximal 1 cm of the seminal vesicles was also included in CTV_PRO
- Patients with controlled primary tumor and oligometastatic nodal recurrence (N1 or M1a para-aortic): CTV_PRO was not defined

4.1.3. CTV_VS

Low-risk or favorable intermediate-risk patients: no seminal vesicle CTV was defined

- Unfavorable intermediate-risk or high-risk patients without seminal vesicle invasion and without indication for pelvic nodal irradiation (60 Gy/20 fractions): no CTV_VS was defined
- Unfavorable intermediate-risk or high-risk patients with seminal vesicle invasion and/or indication for pelvic nodal irradiation (70 Gy/28 fractions): CTV_VS included the entire seminal vesicles
- Patients with controlled primary tumor and oligometastatic recurrence (N1 or M1a para-aortic): no CTV_VS was defined

4.1.4. CTV_PELV

- Low-risk or favorable intermediate-risk patients: no pelvic nodal irradiation
- Unfavorable intermediate-risk or high-risk patients with lymph node risk <15%: no pelvic nodal irradiation
- Unfavorable intermediate-risk or high-risk patients with lymph node risk ≥15%: CTV_PELV included the obturator, internal iliac, external iliac, common iliac, and presacral lymph node regions
- N1 patients: CTV_PELV included the obturator, internal iliac, external iliac, common iliac, and presacral nodal regions, with the superior limit at least 1 cm above CTV_ADP
- Patients with controlled primary tumor and oligometastatic recurrence (N1 and/or para-aortic M1a): CTV_PELV included obturator, internal iliac, external iliac, common iliac, presacral, and optionally para-aortic lymph nodes. The superior limit was defined 1 cm above CTV_ADP, and the inferior limit avoided overlap with previously irradiated pelvic fields

Guidelines for lymph node delineation followed the NRG/RTOG consensus atlases [2].

4.2. Planning Target Volumes (PTV)

Margins were applied to the clinical target volumes as follows:

- PTV_ADP = CTV_ADP + 8 mm
- PTV_PRO = CTV_PRO + 5 mm
- PTV_VS = CTV_VS + 8 mm
- PTV_PELV = CTV_PELV + 8 mm

4.3. Organs at Risk (OARs)

Pelvic OAR delineation followed RTOG/NRG contouring atlases [3]. Dose constraints were applied directly to OAR contours without planning risk volume margins.

- Bladder: outer wall contoured along the entire height of the organ.
- Rectum: contoured from the anal verge to the rectosigmoid junction.

- Sigmoid colon: contoured from the rectosigmoid junction to the left colic flexure.
- Small bowel: included the peritoneal cavity within the abdominal wall muscles, encompassing both colons and all small bowel loops from the first slice above the rectum to 2 cm above the superior limit of the CTV, unless bowel loops extended anterior or lateral to the bladder or mesorectum.
- Femoral heads: contoured from the superior border to the level of the lesser trochanter.
- Additional OARs in para-aortic irradiation: kidneys, liver, and spinal canal.

5. Dose Prescription

For each planning target volume (PTV), the prescribed dose was normalized either to the median dose (D50% = 100% of the prescribed dose) or to the mean dose (Dmean = 100% of the prescribed dose).

Table 1 Dose prescription

Clinical group	PTV_PRO	PTV_VS	PTV_PELV	PTV_ADP
Low Favorable / Intermediate	60 Gy / 20 fx	—	—	—
	a80 Gy / 40 fx	—	—	—
	b78 Gy / 39 fx	—	—	—
	c76 Gy / 38 fx	—	—	—
Unfavorable Intermediate / High	With pelvic irradiation			
	70 Gy / 28 fx	56 Gy / 28 fx	50.4 Gy / 28 fx	—
	Option (sequential)			
	a80 Gy / 40 fx	56 Gy / 28 fx	50.4 Gy / 28 fx	—
	b78 Gy / 39 fx	56 Gy / 28 fx	50.4 Gy / 28 fx	—
	c76 Gy / 38 fx	56 Gy / 28 fx	50.4 Gy / 28 fx	—
	Without pelvic irradiation			
	60 Gy / 20 fx	—	—	—
	Option (sequential)			
	a80 Gy / 40 fx	—	—	—
	b78 Gy / 39 fx	—	—	—
	c76 Gy / 38 fx	—	—	—
N1d	70 Gy / 28 fx	56 Gy / 28 fx	50.4 Gy / 28 fx	61.6 Gy / 28 fx
Brachy boost	46 Gy / 23 fx	56 Gy / 28 fx	50.4 Gy / 28 fx	—
Brachy boost	46 Gy / 23 fx	46 Gy / 23 fx	46 Gy / 23 fx	57.5 Gy / 23 fx
Recurrence N1/M1a – Controlled primary	46 Gy / 23 fx	46 Gy / 23 fx	46 Gy / 23 fx	57.5 Gy / 23 fx

a T3b–T4
b If anticoagulants or irradiating the whole dose of a VS tumor
c Salvage radiotherapy for intraprostatic recurrence after ablation; d In the exceptional case of prophylactic extension to paraaortic with boost to paraaortic lymph node ADP = favor 25 sessions:
PTV_PRO = 67.5 Gy (2.7 Gy/fx);
PTV_VS = 52.1 Gy (2.1 Gy/fx); PTV_PELV (including LA region) = 46 Gy (1.8 Gy/fx);
PTV_ADP = 57.5 Gy/fx.

6. Dosimetric Objectives

For each CTV/PTV pair associated with a specific prescribed dose, the following constraints were considered mandatory:

- CTV
  - D98% ≥ 98% of the prescribed dose
- PTV
  - D95% ≥ 95% of the prescribed dose
  - Hot spot within the highest-dose PTV
  - D1cc ≤ 107% of the prescribed dose

Table 2 Dosimetric objectives

Volume	Prescription	Coverage objective
CTV_PRO / PTV_PRO	80 Gy / 40 fx	CTV_80: D98% ≥ 78.4 Gy
		PTV_80: D95% ≥ 76 Gy
	78 Gy / 39 fx	CTV_78: D98% ≥ 76.4 Gy
		PTV_78: D95% ≥ 74.1 Gy
	76 Gy / 38 fx	CTV_76: D98% ≥ 74.5 Gy
		PTV_76: D95% ≥ 72.2 Gy
	70 Gy / 28 fx	CTV_70: D98% ≥ 68.6 Gy
		PTV_70: D95% ≥ 66.5 Gy
	60 Gy / 20 fx	CTV_60: D98% ≥ 58.8 Gy
		PTV_60: D95% ≥ 57 Gy
	46 Gy / 23 fx	CTV_46: D98% ≥ 45.1 Gy
		PTV_46: D95% ≥ 43.7 Gy
CTV_VS / PTV_VS	56 Gy / 28 fx	CTV_56: D98% ≥ 54.9 Gy
		PTV_56: D95% ≥ 53.2 Gy
	54 Gy / 27 fx	CTV_54: D98% ≥ 52.9 Gy
		PTV_54: D95% ≥ 51.3 Gy
	46 Gy / 23 fx	CTV_46: D98% ≥ 45.1 Gy
		PTV_46: D95% ≥ 43.7 Gy
CTV_PELV / PTV_PELV	50.4 Gy / 28 fx	CTV_50.4: D98% ≥ 49.4 Gy
		PTV_50.4: D95% ≥ 47.9 Gy
	50 Gy / 25 fx	CTV_50: D98% ≥ 49 Gy
		PTV_50: D95% ≥ 47.5 Gy
	46 Gy / 23 fx	CTV_46: D98% ≥ 45.1 Gy
		PTV_46: D95% ≥ 43.7 Gy

7. Dose Constraints for Organs at Risk

Ideal constraints were defined as recommended whenever achievable but allowed to be exceeded if necessary to ensure adequate target coverage. Limiting constraints were defined as upper limits that should not be exceeded unless clinically justified.

Table 3 OAR dose constraints

- Prostate treated at 2 Gy/fraction (conventional fractionation)

Organ	Indicator	Ideal constraints	Limiting constraints	Ideal constraints (Gy/fraction = 2.5)	Limiting constraints (Gy/fraction = 2.5)
Rectum	D5%	≤80 Gy	≤80 Gy	≤80 Gy	≤70 Gy
	D20%	≤65 Gy	≤70 Gy	≤53 Gy	≤63 Gy
	D30%	≤60 Gy	≤65 Gy	≤59 Gy	≤51 Gy
	D55%	≤55 Gy	≤55 Gy	≤46 Gy	—
Bladder	D5%	≤75 Gy	≤80 Gy	≤69 Gy	≤73 Gy
	D25%	≤65 Gy	≤65 Gy	≤60 Gy	≤64 Gy
	D55%	≤50 Gy	≤55 Gy	≤46 Gy	≤51 Gy
Small bowel	Dmax	≤30 Gy	≤30 Gy	≤30 Gy	≤30 Gy
	V45 Gy	≤200 cc	≤300 cc	≤300 cc	≤300 cc
Femoral heads	D5%	ALLOW AS POSSIBLE	≤55 Gy	Same as rectum	Same as rectum

- Dose constraints for hypofractionated prostate radiotherapy

Organ	Indicator	Ideal constraints	Limiting constraints
Rectum	V60 Gy	≤5%	≤5%
	V57 Gy	≤10%	≤35%
	V50 Gy	≤25%	≤45%
Bladder	V55 Gy	≤5%	≤35%
	V50 Gy	≤15%	≤45%
Femoral heads	D5%	≤5%	Same as rectum

DX% = dose received by X% of the volume
VXGy = volume receiving at least X Gy; *Limiting constraints for the small bowel derive from BED calculation (see Appendix B). Possibility to reach up to 30 cc if paraaortic irradiation.*

8. Treatment Delivery

8.1. Session Frequency

Treatment was delivered once daily, five days per week, from Monday to Friday. All arcs defined during planning were delivered at each fraction.

8.2. Daily Repositioning Procedure

For treatment of the primary tumor without prophylactic pelvic irradiation, CBCT images had to cover the entire PTV_PRO. Bladder or rectal filling was taken into account only if it interfered with adequate repositioning on PTV_PRO.

If necessary, the bladder or rectum was emptied and the patient repositioned. If the bladder was completely empty, the patient was asked to drink and repositioning was repeated.

For treatment of the primary tumor with prophylactic pelvic irradiation, and for pelvic irradiation with or without para-aortic irradiation in the absence of primary tumor treatment, daily image guidance was also required to verify target positioning.

8.3. Medical Monitoring During Treatment

Patients were assessed once weekly during treatment. The minimum data collected included:

- Weight
- Karnofsky performance status
- Acute toxicities according to CTCAE
- Urinary: pollakiuria, dysuria, hematuria, painful urination
- Digestive: diarrhea, rectal bleeding

8.4. Follow-up after Treatment

The first follow-up consultation took place 3 months after treatment with PSA testing, followed by a second consultation 6 months later (9 months after treatment) with PSA testing. If the patient remained clinically stable, annual follow-up was recommended, with PSA monitoring every 6 months.

9. Discussion

The management of localized prostate cancer has evolved considerably with the development of advanced radiotherapy techniques such as IMRT and VMAT. These technologies allow highly conformal dose distributions that improve target coverage while reducing irradiation of surrounding organs at risk, particularly the rectum, bladder, and small bowel. In prostate cancer, where the anatomical proximity of these structures represents a major challenge, IMRT and VMAT have become standard techniques in modern radiotherapy practice.

Compared with conventional three-dimensional conformal radiotherapy, IMRT allows modulation of beam intensity across multiple fields, enabling better dose conformity around complex target volumes. VMAT further improves treatment delivery by using continuous gantry rotation with dynamic modulation of dose rate, multileaf collimator position, and gantry speed. This technique offers several advantages, including improved dose homogeneity, reduced treatment time, and enhanced sparing of organs at risk.

Another critical component of modern prostate radiotherapy is image-guided radiotherapy (IGRT). Daily imaging allows precise verification of patient positioning and internal organ motion before each treatment fraction. The use of cone-beam CT (CBCT) is particularly important in this context. Prostate position can vary significantly from day to day due to changes in bladder filling and rectal distension. CBCT imaging enables visualization of the prostate, bladder, rectum, and surrounding anatomy immediately before treatment delivery, allowing corrections when necessary. This improves treatment accuracy and makes it possible to reduce planning target volume margins while maintaining adequate coverage of the clinical target volume.

The integration of IGRT with IMRT or VMAT has therefore significantly improved the therapeutic ratio in prostate cancer radiotherapy. Smaller margins reduce the dose delivered to adjacent organs at risk, thereby decreasing gastrointestinal and genitourinary toxicities. Standardized contouring of both target volumes and organs at risk, based on international consensus guidelines such as those proposed by NRG Oncology and the Radiation Therapy Oncology Group, further contributes to treatment consistency and safety [2,3].

Dose escalation has also played an important role in improving biochemical control in localized prostate cancer. However, dose escalation must be carefully balanced against the risk of increased toxicity to surrounding organs. Modern IMRT and VMAT techniques enable safe dose escalation by achieving highly conformal dose distributions that limit exposure to critical structures.

In recent years, hypofractionated radiotherapy schedules have gained increasing attention in prostate cancer treatment. The radiobiological characteristics of prostate cancer suggest a relatively low alpha/beta ratio, indicating greater sensitivity to larger doses per fraction. This has led to the development of moderate hypofractionation regimens, such as 60 Gy delivered in 20 fractions, which have demonstrated efficacy comparable to conventional fractionation while significantly reducing overall treatment duration. Hypofractionation offers several advantages, including improved patient convenience, reduced treatment burden, and more efficient use of radiotherapy resources.

The use of hypofractionation also requires careful planning and strict adherence to dose constraints for organs at risk. Dose-volume histogram parameters are essential tools for evaluating treatment plans and ensuring that both target coverage and organ protection objectives are achieved. In the present protocol, dosimetric objectives are defined for both the clinical target volume and the planning target volume, with constraints designed to maintain adequate coverage while minimizing exposure to surrounding normal tissues.

Pelvic lymph node irradiation may be indicated in selected patients with an increased risk of nodal involvement. Predictive models such as the Roach formula or contemporary nomograms can help identify patients who may benefit from nodal irradiation [4–10]. Accurate delineation of pelvic nodal volumes is essential in this context and should follow internationally accepted contouring atlases to ensure consistent treatment planning [2].

Overall, the integration of advanced technologies such as IMRT, VMAT, IGRT, and CBCT has transformed the radiotherapeutic management of localized prostate cancer. These techniques allow the delivery of highly conformal, dose-escalated, and hypofractionated treatment schedules while maintaining acceptable toxicity levels. By combining precise imaging, standardized contouring, and optimized dosimetric planning, modern prostate radiotherapy protocols aim to maximize tumor control while minimizing treatment-related morbidity.

10. Conclusion

IMRT and VMAT represent highly effective radiotherapy techniques for the management of localized prostate cancer. The implementation of standardized treatment protocols including precise target delineation, strict dose constraints, and daily image guidance ensures optimal tumor control while minimizing treatment-related toxicity.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare that they have no conflict of interest.

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