

National Imaging Associates, Inc.*	
Clinical guideline PROSTATE CANCER	Original Date: March 2011
Radiation Oncology	Last Revised Date: January 2022
Guideline Number: NIA_CG_124	Implementation Date: January 2023

MEDICALLY NECESSARY INDICATIONS FOR RADIATION THERAPY^{1, 2}

EBRT/IMRT hypofractionation of 20-28 fractions are recommended to treat localized prostate cancer when pelvic nodes are not treated. Other treatment regimens require physician review and clinical documentation that supports medical necessity.

Very Low Recurrence Risk (Primary Tumor Stage [T] is T1c, PSA <10 ng/ml, and Gleason score ≤ 6, PSA density <0.15ng/nl per g, < 3 biopsy cores positive with ≤ 50% cancer in each)

- Active surveillance (discussed with patient as treatment option)
- External Beam Radiation
 - Highly conformal radiation therapy technique (3D-CRT/IMRT with IGRT). Hypofractionation 20-28 fractions
 - SBRT delivered at five fractions or less at 6.5 Gy per fraction or greater. Appropriate as a standalone radiation modality and not as a boost to other conventional methods of radiation treatment
- LDR (low dose-rate) or HDR (high dose-rate) Brachytherapy

Low Recurrence Risk (Primary Tumor Stage [T] is T1-T2a, PSA <10 ng/ml, and Gleason score ≤ 6)

- Active surveillance (discussed with patient as treatment option)
- External Beam Radiation Therapy
 - Highly conformal radiation therapy technique (3D-CRT/IMRT with IGRT). Hypofractionation 20-28 fractions
 - SBRT delivered at five fractions or less at 6.5 Gy per fraction or greater. Appropriate as a standalone radiation modality and not as a boost to other conventional methods of radiation treatment.
- LDR (low dose-rate) or HDR (high dose-rate) Brachytherapy

Intermediate Recurrence Risk (Primary Tumor Stage [T] T2b-T2c or PSA 10-20 ng/ml or Gleason score 7)

- External Beam Radiation Therapy

* National Imaging Associates, Inc. (NIA) is a subsidiary of Magellan Healthcare, Inc.

- Highly conformal radiation therapy technique (3D-CRT/IMRTwith IGRT). Hypofractionation-20-28 fractions.
- SBRT delivered at five fractions or less at 6.5 Gy per fraction or greater. Appropriate as a standalone radiation modality and NOT as a boost to other conventional methods of radiation treatment.
- Brachytherapy (LDR/HDR) boost combined with EBRT after 20-28 fractions

High Recurrence Risk (Primary Tumor Stage [T] T3a or PSA > 20 ng/ml or Gleason score 8 -10 , or two or more intermediate risk factors)

- External Beam Radiation Therapy
 - Highly conformal radiation therapy technique (3D-CRT/IMRTwith IGRT). Hypofractionation-20-28 fractions.
 - SBRT delivered at five fractions or less at 6.5 Gy per fraction or greater. Appropriate as a standalone radiation modality and NOT as a boost to other conventional methods of radiation treatment.
- Brachytherapy (LDR/HDR) boost combined with EBRT after 20-28 fractions.

Very High Recurrence Risk (Primary Tumor Stage [T] T3b-T4) with Gleason score 8-10 without Metastasis

- External Beam Radiation Therapy
 - Highly conformal radiation therapy technique (3D-CRT/IMRT with IGRT). Hypofractionation-20-28 fractions.
 - SBRT delivered at five fractions or less at 6.5 Gy per fraction or greater. Appropriate as a standalone radiation modality and NOT as a boost to other conventional methods of radiation treatment.
- Brachytherapy (LDR/HDR) boost combined with EBRT after 20-28 fractions

Radiation Therapy for Patients with Locally Advanced or N1 Prostate (T3b – T4, or any T and N1, M0 disease)

- External Beam Radiation Therapy
 - Highly conformal radiation therapy technique (3D-CRT/IMRT with IGRT). Up to 45 fractions are medically necessary for localized or locally recurrent prostate cancer when pelvic nodes are treated.
- Brachytherapy (LDR/HDR) boost combined with EBRT after 20-28 fractions

Palliative Radiotherapy:

- 30Gy/10FX or
- 37.5Gy/15FX

Adjuvant Post-Prostatectomy or Salvage Radiation Therapy

- External Beam Radiation Therapy
 - Highly conformal radiation therapy technique (3D-CRT/IMRT) Doses 64 – 72 Gy (up to 40 fractions) with IGRT

- One of the following must be met:
 - Detectable PSA or initially undetectable PSA, but with recent detectable and rising values on 2 or more measurements with no evidence of metastatic disease
 - Positive margins
 - Seminal vesicle invasion or extracapsular extension.
 - Gleason 8-10
 - Pathological T3 disease

TREATMENT OPTIONS REQUIRING PHYSICIAN REVIEW

The radiation treatment options below require review by a physician reviewer and may include deliberation on whether or not active surveillance and surgery have been considered prior to the decision to request radiation therapy:

- Brachytherapy alone (monotherapy) may be approved for Intermediate Recurrence Risk (Primary Tumor Stage [T] T2b-T2c or PSA 10-20 ng/ml or Gleason score 7) upon review with a physician reviewer. Brachytherapy alone is not considered appropriate if the patient has unfavorable or poor prognostic risk factors intermediate risk factors and is thus higher risk.
- EBRT/IMRT hypofractionation of 20-28 fractions are recommended to treat localized prostate cancer when pelvic nodes are not treated. Other treatment regimens require physician review and clinical documentation that supports medical necessity.

DOSAGE GUIDELINES

- Moderate Hypofractionation (preferred, for all but low-volume M1, including N1):
 - 3Gy x 20 fractions
 - 2.7Gy x 26 fractions
 - 2.5 x 28 fractions
- Ultra-Hypofractionation (for all but N1 and M1):
 - 7.25-8Gy x 5 fractions & 6.1Gy x 7 fractions
- Ultra-Hypofractionation (for low-volume M1):
 - 6Gy x 6 fractions
- **Low-volume metastatic disease**
 - Per STAMPEDE phase 3 randomized trial,³ 55Gy in 20 fractions (i.e., 2.75Gy x 20) or 6Gy x 6 fractions can be used.
- **High-volume metastatic disease (Visceral met, 4 or more bone mets with at least one metastasis beyond the pelvis vertebral column):**
 - Based on HORRAD⁴ & STAMPEDE trials no RT to prostate would be medically necessary.

- Proton beam is not an approved treatment option for prostate cancer. Studies comparing proton beam therapy alone to 3-D conformal radiation or IMRT are limited. Overall, studies have not shown clinical outcomes to be superior to conventional radiation therapy.^{1, 2, 5-8}

BACKGROUND

Prostate cancer is diagnosed by biopsy and evaluated (staged) to determine extent of disease (local, regional, or distant metastatic). Both surgery and radiation therapy is used to treat prostate cancers that are organ-confined or extend into tissues adjacent to the prostate. Daily prostate localization can be accomplished with imaging modalities, e.g., ultrasound images, computed tomography (CT) images, or implanted fiducial markers, incorporated into an image guided radiation therapy (IGRT) system.

Patients with very low risk disease should be considered for active surveillance if their life expectancy is less than or equal to 20 years. Active surveillance is as well, recommended for patients with favorable intermediate-risk prostate cancer. Observation is the preferred action for men with low-risk prostate cancer with a life expectancy of less than 10 years. Patients with intermediate risk disease may be considered for short course (4-6 months) of neoadjuvant/concomitant/adjuvant ADT. Patients with high risk disease may be considered for pelvic lymph node irradiation and 2-3 years of neoadjuvant/adjuvant ADT.

POLICY HISTORY

Date	Summary
January 2022	<ul style="list-style-type: none"> • Changed “Radiation Therapy for Patients with Locally Advanced or Metastatic Prostate (T3b – T4, or any T and N1, disease)” to “Radiation Therapy for Patients with Locally Advanced or N1 Prostate (T3b – T4, or any T and N1, M0 disease)” • Added Palliative Radiotherapy <ul style="list-style-type: none"> ○ 30Gy/10FX or ○ 37.5Gy/15FX • Added Dosage Guidelines section within Treatment Options Requiring Physician Review
February 2021	<p>Deleted: INDICATIONS FOR RADIATION THERAPY AND TREATMENT OPTIONS Changed to: MEDICALLY NECESSARY INDICATIONS FOR RADIATION THERAPY (NCCN, 2021; Morgan et al, 2018): EBRT/IMRT hypofractionation of 20-28 fractions are recommended to treat localized localized prostate cancer when pelvic nodes are not treated. Other treatment regimens require physician review and clinical documentation that supports medical necessity.</p>

For Very Low/Low, Intermediate and High/Very High Recurrence Prostate Cancer. The following was deleted:

- *Various fractionation and dose regimens can be considered based on medical necessity.*
- Highly conformal radiation therapy technique 3D-CRT/IMRT with IGRT up to 45 fractions

For Very Low/Low, Intermediate and High/Very High Recurrence Prostate Cancer. The following was updated :

- Highly conformal radiation therapy technique (3D-CRT/IMRT with IGRT). Hypofractionation 20-28 fractions

For Intermediate and High/Very High Recurrence Prostate Cancer. The following was deleted:

- Brachytherapy (LDR/HDR) boost combined with EBRT after 40-50 Gy

For Intermediate and High/Very High Recurrence Prostate Cancer. The following was updated :

- Brachytherapy (LDR/HDR) boost combined with EBRT after 20-28 Fx

Radiation Therapy for Patients with Locally Advanced or Metastatic Prostate (T3b – T4, or any T and N1, M0 disease)

- Deleted: Various fractionation and dose regimens can be considered based on medical necessity.
- Deleted: Highly conformal radiation therapy technique (3D-CRT/IMRT with IGRT). Up to 45 fractions
- Updated: Highly conformal radiation therapy technique (3D-CRT/IMRT with IGRT). Up to 45 fractions are medically necessary for localized or locally recurrent prostate cancer when pelvic nodes are treated.
- Deleted: Brachytherapy (LDR/HDR) boost combined with EBRT after 40-50 Gy
- Updated : Brachytherapy (LDR/HDR) boost combined with EBRT after 20-28 fractions

High Recurrence Risk (Primary Tumor Stage [T] T3a or PSA > 20 ng/ml or Gleason score 8 -10 , or two or more intermediate risk factors) and

Very High Recurrence Risk (Primary Tumor Stage [T] T3b-T4) with Gleason score 8-10 without Metastasis

Under the above sections added update:

- SBRT delivered at five fractions or less at 6.5 Gy per fraction or greater. Appropriate as a standalone radiation modality and NOT as a boost to other conventional methods of radiation treatment.

	<p>Post-Prostatectomy guideline heading changed to “Adjuvant Post-Prostatectomy or Salvage Radiation Therapy” to include criteria for Salvage Therapy. Guideline also updated to include extracapsular extension. Updated guideline to: Seminal vesicle invasion or extracapsular extension.</p> <p>TREATMENT OPTIONS REQUIRING PHYSICIAN REVIEW Added</p> <ul style="list-style-type: none"> • EBRT/IMRT hypofractionation of 20-28 fractions are recommended to treat localized prostate cancer when pelvic nodes are not treated. Other treatment regimens require physician review and clinical documentation that supports medical necessity. <p>Added and Updated References</p>
February 2020	<ul style="list-style-type: none"> • Proton Beam: Clarification of Proton Beam Guideline whereby the term <i>localized</i> was removed from the following statement: Proton Beam is not an approved treatment option for localized prostate cancer. • Added and updated References
February 2019	<ul style="list-style-type: none"> • External Beam Radiation Therapy: Added: ‘SBRT delivered at five fractions or less at 6.5 Gy per fraction or greater. Appropriate as a standalone radiation modality and not as a boost to other conventional methods of radiation treatment’ • Added and updated references

REFERENCES

1. 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. *Pract Radiat Oncol*. Nov-Dec 2018;8(6):354-360. doi:10.1016/j.prro.2018.08.002
2. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Prostate Cancer Version 2.2022. National Comprehensive Cancer Network (NCCN). Updated November 30, 2021. Accessed December 7, 2021. https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf
3. Parker CC, James ND, Brawley CD, et al. Radiotherapy to the primary tumour for newly diagnosed, metastatic prostate cancer (STAMPEDE): a randomised controlled phase 3 trial. *Lancet*. Dec 1 2018;392(10162):2353-2366. doi:10.1016/s0140-6736(18)32486-3
4. Boevé LMS, Hulshof M, Vis AN, et al. Effect on Survival of Androgen Deprivation Therapy Alone Compared to Androgen Deprivation Therapy Combined with Concurrent Radiation Therapy to the Prostate in Patients with Primary Bone Metastatic Prostate Cancer in a Prospective Randomised Clinical Trial: Data from the HORRAD Trial. *Eur Urol*. Mar 2019;75(3):410-418. doi:10.1016/j.eururo.2018.09.008
5. Dutz A, Agolli L, Baumann M, et al. Early and late side effects, dosimetric parameters and quality of life after proton beam therapy and IMRT for prostate cancer: a matched-pair analysis. *Acta Oncol*. Jun 2019;58(6):916-925. doi:10.1080/0284186x.2019.1581373
6. Fang P, Mick R, Deville C, et al. A case-matched study of toxicity outcomes after proton therapy and intensity-modulated radiation therapy for prostate cancer. *Cancer*. Apr 1 2015;121(7):1118-27. doi:10.1002/cncr.29148
7. Santos PMG, Barsky AR, Hwang WT, et al. Comparative toxicity outcomes of proton-beam therapy versus intensity-modulated radiotherapy for prostate cancer in the postoperative setting. *Cancer*. Dec 1 2019;125(23):4278-4293. doi:10.1002/cncr.32457
8. 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*. Mar 2019;201(3):528-534. doi:10.1097/ju.0000000000000071

ADDITIONAL RESOURCES

1. Abdel-Wahab M, Mahmoud O, Merrick G, et al. ACR Appropriateness Criteria® external-beam radiation therapy treatment planning for clinically localized prostate cancer. *J Am Coll Radiol*. Apr 2012;9(4):233-8. doi:10.1016/j.jacr.2011.12.030
2. American Society for Radiation Oncology. Ten Things Physicians and Patients Should Question. ABIM Foundation. Updated 2019. Accessed December 7, 2021. <https://www.choosingwisely.org/societies/american-society-for-radiation-oncology/>
3. American Society for Radiation Oncology. Model Policies: Proton Beam Therapy. Updated June 2017. Accessed December 8, 2021. https://www.astro.org/uploadedFiles/MAIN_SITE/Daily_Practice/Reimbursement/Model_Policies/Content_Pieces/ASTROPBTModelPolicy.pdf
4. Clark E, Thielke A, Kriz H. *Intensity modulated radiation therapy. Final Evidence Report*. Prepared by the Oregon Health & Science University. Center for Evidence-based Policy for the Washington State

Health Care Authority, Health Technology Assessment Program Olympia, WA: Washington State Health Care Authority, Health Technology Assessment Program. 2012;

5. Freeman DE, King CR. Stereotactic body radiotherapy for low-risk prostate cancer: five-year outcomes. *Radiat Oncol*. Jan 10 2011;6:3. doi:10.1186/1748-717x-6-3
6. Hummel S, Simpson EL, Hemingway P, Stevenson MD, Rees A. Intensity-modulated radiotherapy for the treatment of prostate cancer: a systematic review and economic evaluation. *Health Technol Assess*. Oct 2010;14(47):1-108, iii-iv. doi:10.3310/hta14470
7. Institute of Cancer Research (ICR) UK. Intensity-Modulated Radiation Therapy in Treating Patients with Localized Prostate Cancer. Updated February 27, 2019. Accessed October 25, 2021. <https://clinicaltrials.gov/ct2/show/study/NCT00392535>
8. Kang JK, Cho CK, Choi CW, et al. Image-guided stereotactic body radiation therapy for localized prostate cancer. *Tumori*. Jan-Feb 2011;97(1):43-8.
9. Katz A, Santoro M. Quality of life and efficacy for stereotactic body radiotherapy for treatment of organ confined prostate cancer. *International Journal of Radiation Oncology, Biology, Physics*. 2010;78(3):S58.
10. King C. Stereotactic body radiotherapy for prostate cancer: current results of a phase II trial. *Front Radiat Ther Oncol*. 2011;43:428-437. doi:10.1159/000322507
11. King CR, Brooks JD, Gill H, Presti JC, Jr. Long-term outcomes from a prospective trial of stereotactic body radiotherapy for low-risk prostate cancer. *Int J Radiat Oncol Biol Phys*. Feb 1 2012;82(2):877-82. doi:10.1016/j.ijrobp.2010.11.054
12. Michalski JM, Lawton C, El Naqa I, et al. Development of RTOG consensus guidelines for the definition of the clinical target volume for postoperative conformal radiation therapy for prostate cancer. *Int J Radiat Oncol Biol Phys*. Feb 1 2010;76(2):361-8. doi:10.1016/j.ijrobp.2009.02.006
13. Muacevic A, Kufeld M, Rist C, Wowra B, Stief C, Staehler M. Safety and feasibility of image-guided robotic radiosurgery for patients with limited bone metastases of prostate cancer. *Urol Oncol*. May 2013;31(4):455-60. doi:10.1016/j.urolonc.2011.02.023
14. Oermann EK, Suy S, Hanscom HN, et al. Low incidence of new biochemical and clinical hypogonadism following hypofractionated stereotactic body radiation therapy (SBRT) monotherapy for low- to intermediate-risk prostate cancer. *J Hematol Oncol*. Mar 27 2011;4:12. doi:10.1186/1756-8722-4-12
15. Parker CC, Clarke NW, Cook AD, et al. Timing of radiotherapy after radical prostatectomy (RADICALS-RT): a randomised, controlled phase 3 trial. *Lancet*. Oct 31 2020;396(10260):1413-1421. doi:10.1016/s0140-6736(20)31553-1
16. Thompson IM, Valicenti RK, Albertsen P, et al. Adjuvant and salvage radiotherapy after prostatectomy: AUA/ASTRO Guideline. *J Urol*. Aug 2013;190(2):441-9. doi:10.1016/j.juro.2013.05.032
17. Tilki D, D'Amico AV. Timing of radiotherapy after radical prostatectomy. *Lancet*. Oct 31 2020;396(10260):1374-1375. doi:10.1016/s0140-6736(20)31957-7
18. Vale CL, Fisher D, Kneebone A, et al. Adjuvant or early salvage radiotherapy for the treatment of localised and locally advanced prostate cancer: a prospectively planned systematic review and meta-analysis of aggregate data. *Lancet*. Oct 31 2020;396(10260):1422-1431. doi:10.1016/s0140-6736(20)31952-8
19. Yu JB, Soulos PR, Herrin J, et al. Proton versus intensity-modulated radiotherapy for prostate cancer: patterns of care and early toxicity. *J Natl Cancer Inst*. Jan 2 2013;105(1):25-32. doi:10.1093/jnci/djs463

20. Zaorsky NG, Showalter TN, Ezzell GA, et al. ACR Appropriateness Criteria(®) external beam radiation therapy treatment planning for clinically localized prostate cancer, part I of II. *Adv Radiat Oncol*. Jan-Mar 2017;2(1):62-84. doi:10.1016/j.adro.2016.10.002

Reviewed / Approved by NIA Clinical Guideline Committee

GENERAL INFORMATION

It is an expectation that all patients receive care/services from a licensed clinician. All appropriate supporting documentation, including recent pertinent office visit notes, laboratory data, and results of any special testing must be provided. If applicable: All prior relevant imaging results and the reason that alternative imaging cannot be performed must be included in the documentation submitted.

Disclaimer: Magellan Healthcare service authorization policies do not constitute medical advice and are not intended to govern or otherwise influence the practice of medicine. These policies are not meant to supplant your normal procedures, evaluation, diagnosis, treatment and/or care plans for your patients. Your professional judgement must be exercised and followed in all respects with regard to the treatment and care of your patients. These policies apply to all Magellan Healthcare subsidiaries including, but not limited to, National Imaging Associates (“Magellan”). The policies constitute only the reimbursement and coverage guidelines of Magellan. Coverage for services varies for individual members in accordance with the terms and conditions of applicable Certificates of Coverage, Summary Plan Descriptions, or contracts with governing regulatory agencies. Magellan reserves the right to review and update the guidelines at its sole discretion. Notice of such changes, if necessary, shall be provided in accordance with the terms and conditions of provider agreements and any applicable laws or regulations.