Complete Summary

GUIDELINE TITLE

Postradical prostatectomy irradiation in prostate cancer.

BIBLIOGRAPHIC SOURCE(S)

Pollack A, Hayes S, Roach M III, Merrick G, Anscher MS, Beyer DC, Lawton CA, Lee WR, Michalski JM, Rosenthal SA, Vijayakumar S, Carroll PR, Higano CS, Expert Panel on Radiation Oncology-Prostate. Postradical prostatectomy irradiation in prostate cancer. [online publication]. Reston (VA): American College of Radiology (ACR); 2006. 18 p. [116 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Perez CA, Beyer DC, Blasko JC, Forman JD, Hussey DH, Lee WR, Paryani SB, Pollack A, Potters L, Roach M, Scardino P, Schellhammer P, Leibel S. Postradical prostatectomy irradiation in carcinoma of the prostate. American College of Radiology. ACR Appropriateness Criteria. Radiology 2000 Jun;215(Suppl):1419-39.

The appropriateness criteria are reviewed annually and updated by the panels as needed, depending on introduction of new and highly significant scientific evidence.

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Prostate cancer

GUIDELINE CATEGORY

Risk Assessment
Treatment

CLINICAL SPECIALTY

Internal Medicine
Oncology
Radiation Oncology
Radiology
Surgery

INTENDED USERS

Health Plans
Hospitals
Managed Care Organizations
Physicians
Utilization Management

GUIDELINE OBJECTIVE(S)

To evaluate the appropriateness of treatment procedures for prostate cancer patients after radical prostatectomy

TARGET POPULATION

Prostate cancer patients after radical prostatectomy

INTERVENTIONS AND PRACTICES CONSIDERED

1. Treatment planning
2. Radiation therapy (RT), pelvis and prostate bed
3. Hormone therapy (HT)
4. Combination therapy
    - RT plus neoadjuvant and concurrent HT
    - RT plus neoadjuvant, concurrent, and long-term adjuvant HT
5. Observation

MAJOR OUTCOMES CONSIDERED

- Prognostic factors
- Freedom from biochemical failure

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The guideline developer performed literature searches of peer-reviewed medical journals and the major applicable articles were identified and collected.

NUMBER OF SOURCE DOCUMENTS

The total number of source documents identified as the result of the literature search is not known.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Not Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not stated

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

One or two topic leaders within a panel assume the responsibility of developing an evidence table for each clinical condition, based on analysis of the current literature. These tables serve as a basis for developing a narrative specific to each clinical condition.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Delphi)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Since data available from existing scientific studies are usually insufficient for meta-analysis, broad-based consensus techniques are needed for reaching agreement in the formulation of the appropriateness criteria. The American College of Radiology (ACR) Appropriateness Criteria panels use a modified Delphi technique to arrive at consensus. Serial surveys are conducted by distributing questionnaires to consolidate expert opinions within each panel. These questionnaires are distributed to the participants along with the evidence table and narrative as developed by the topic leader(s). Questionnaires are completed by participants in their own professional setting without influence of the other members. Voting is conducted using a scoring system from 1-9, indicating the least to the most appropriate imaging examination or therapeutic procedure. The survey results are collected, tabulated in anonymous fashion, and redistributed after each round. A maximum of three rounds is conducted and opinions are unified to the highest degree possible. Eighty percent agreement is considered a

consensus. This modified Delphi technique enables individual, unbiased expression, is economical, easy to understand, and relatively simple to conduct.

If consensus cannot be reached by the Delphi technique, the panel is convened and group consensus techniques are utilized. The strengths and weaknesses of each test or procedure are discussed and consensus reached whenever possible. If "No consensus" appears in the rating column, reasons for this decision are added to the comment sections.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

ACR Appropriateness Criteria®

Clinical Condition: Postradical Prostatectomy Irradiation in Prostate Cancer

Variant 1: 58-year-old man, stage T1C, Gleason score 5, adenocarcinoma. PSA 6.0 ng/mL. Negative diagnostic workup. Treated with nerve-sparing radical prostatectomy. No extracapsular extension or seminal vesicle invasion. Surgical margins of prostatectomy specimen and nodes negative. Postprostatectomy PSA nondetectable.

Treatment	Appropriateness Rating	Comments
Observation	9	
Radiation therapy (RT) alone	1	

Treatment	Appropriateness Rating	Comments
Hormone therapy (HT) alone	1	
RT plus neoadjuvant and concurrent HT	1	
RT plus neoadjuvant, concurrent, and long-term adjuvant HT	1	
Radiation Therapy		
Pelvis and prostate bed	1	
Prostate bed	1	
Pelvic Irradiation, if given		
4000 cGy/20 fractions	1	
4500 cGy/25 fractions	1	
5040 cGy/28 fractions	1	
5400 cGy/30 fractions	1	
Dose to Prostate Bed (may include dose to pelvis)		
4500 cGy/25 fractions	1	
5040 cGy/28 fractions	1	
5400 cGy/30 fractions	1	
5940 cGy/33 fractions	1	
6660 cGy/37 fractions	1	
7020 cGy/39 fractions	1	
7200 cGy/40 fractions	1	
Treatment Plan		
IMRT	1	
3D-CT-based plan	1	
2D-CT-based plan	1	
Non-CT-based plan	1	
Appropriateness Criteria Scale		

Treatment	Appropriateness Rating	Comments
1 2 3 4 5 6 7 8 9 1 = Least appropriate 9 = Most appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 2: 65-year-old man, stage T2A, Gleason score 5, adenocarcinoma. PSA 14.5 ng/mL. Negative diagnostic workup. Treated with nerve-sparing radical prostatectomy. Right seminal vesicle involved by tumor, but surgical margins of prostatectomy specimen negative. Negative lymph nodes. Postprostatectomy PSA 0.3 ng/mL.

Treatment	Appropriateness Rating	Comments
Radiation therapy (RT) alone	7	
RT plus neoadjuvant and concurrent hormone therapy (HT)	5	
RT plus neoadjuvant, concurrent, and long-term adjuvant HT	4	
HT alone	3	
Observation	2	
Radiation Therapy		
Pelvis and prostate bed	4	
Prostate bed	7	
Pelvic Irradiation, if given		
4000 cGy/20 fractions	2	
4500 cGy/25 fractions	7	
5040 cGy/28 fractions	6	
5400 cGy/30 fractions	3	
Dose to Prostate Bed (may include dose to pelvis)		
4500 cGy/25 fractions	2	

Treatment	Appropriateness Rating	Comments
5040 cGy/28 fractions	2	
5400 cGy/30 fractions	3	
5940 cGy/33 fractions	4	
6660 cGy/37 fractions	8	
7020 cGy/39 fractions	5	
7200 cGy/40 fractions	4	
Treatment Plan		
IMRT	7	
3D-CT-based plan	7	
2D-CT-based plan	3	
Non-CT-based plan	2	
Appropriateness Criteria Scale **1 2 3 4 5 6 7 8 9** **1 = Least appropriate 9 = Most appropriate**		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 3: 65-year-old man, stage T2A, Gleason score 5, adenocarcinoma. PSA 14.5 ng/mL. Negative diagnostic workup. Treated with nerve-sparing radical prostatectomy. Right seminal vesicle involved by tumor, but surgical margins of prostatectomy specimen negative. Negative lymph nodes. Postprostatectomy PSA nondetectable.

Treatment	Appropriateness Rating	Comments
Radiation therapy (RT) alone	7	
RT plus neoadjuvant and concurrent hormone therapy (HT)	5	
RT plus neoadjuvant, concurrent, and long-term adjuvant HT	4	
Observation	4	

Treatment	Appropriateness Rating	Comments
HT alone	3	
Radiation Therapy		
Pelvis and prostate bed	4	
Prostate bed	7	
Pelvic Irradiation, if given		
4000 cGy/20 fractions	2	
4500 cGy/25 fractions	7	
5040 cGy/28 fractions	6	
5400 cGy/30 fractions	3	
Dose to Prostate Bed (may include dose to pelvis)		
4500 cGy/25 fractions	2	
5040 cGy/28 fractions	2	
5400 cGy/30 fractions	3	
5940 cGy/33 fractions	4	
6660 cGy/37 fractions	8	
7020 cGy/39 fractions	5	
7200 cGy/40 fractions	3	
Treatment Plan		
IMRT	7	
3D-CT-based plan	7	
2D-CT-based plan	3	
Non-CT-based plan	2	
Appropriateness Criteria Scale **1 2 3 4 5 6 7 8 9** **1 = Least appropriate 9 = Most appropriate**		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 4: 58-year-old man, stage T1C, Gleason score 7, adenocarcinoma. PSA 10.5 ng/mL. Negative metastatic workup. Treated with nerve-sparing radical prostatectomy. Negative lymph nodes. Positive margins at prostate apex. Postprostatectomy PSA detectable at 0.3 ng/mL.

Treatment	Appropriateness Rating	Comments
Radiation therapy (RT) alone	8	
RT plus neoadjuvant and concurrent HT	6	
RT plus neoadjuvant, concurrent, and long-term adjuvant HT	3	
Hormone therapy (HT) alone	2	
Observation	2	
Radiation Therapy		
Pelvis and prostate bed	3	
Prostate bed	8	
Pelvic Irradiation, if given		
4000 cGy/20 fractions	2	
4500 cGy/25 fractions	7	
5040 cGy/28 fractions	5	
5400 cGy/30 fractions	3	
Dose to Prostate Bed (may include dose to pelvis)		
4500 cGy/25 fractions	2	
5040 cGy/28 fractions	2	
5400 cGy/30 fractions	2	
5940 cGy/33 fractions	4	
6660 cGy/37 fractions	8	
7020 cGy/39 fractions	6	
7200 cGy/40 fractions	5	

Treatment	Appropriateness Rating	Comments
Treatment Plan		
IMRT	7	
3D-CT-based plan	7	
2D-CT-based plan	3	
Non-CT-based plan	2	
Appropriateness Criteria Scale **1 2 3 4 5 6 7 8 9** **1 = Least appropriate 9 = Most appropriate**		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 5: 58-year-old man, stage T1C, Gleason score 7, adenocarcinoma. PSA 10.5 ng/mL. Negative metastatic workup. Treated with nerve-sparing radical prostatectomy. Negative lymph nodes. Positive margins at prostate apex. Postprostatectomy PSA nondetectable.

Treatment	Appropriateness Rating	Comments
Radiation therapy (RT) alone	8	
Observation	4	Early salvage treatment should be considered for any rise in PSA.
RT plus neoadjuvant and concurrent hormone therapy (HT)	3	
HT alone	2	
RT plus neoadjuvant, concurrent, and long-term adjuvant HT	2	
Radiation Therapy		
Pelvis and prostate bed	3	
Prostate bed	8	
Pelvic Irradiation, if given		
4000 cGy/20 fractions	2	

Treatment	Appropriateness Rating	Comments
4500 cGy/25 fractions	7	
5040 cGy/28 fractions	6	
5400 cGy/30 fractions	3	
Dose to Prostate Bed (may include dose to pelvis)		
4500 cGy/25 fractions	2	
5040 cGy/28 fractions	2	
5400 cGy/30 fractions	2	
5940 cGy/33 fractions	4	
6660 cGy/37 fractions	8	
7020 cGy/39 fractions	5	
7200 cGy/40 fractions	4	
Treatment Plan		
IMRT	7	
3D-CT-based plan	7	
2D-CT-based plan	3	
Non-CT-based plan	2	
Appropriateness Criteria Scale **1 2 3 4 5 6 7 8 9** **1 = Least appropriate 9 = Most appropriate**		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 6: 64-year-old man, stage T2A, Gleason score 7, adenocarcinoma. PSA 10.5 ng/mL. Negative metastatic workup. Treated with nerve-sparing radical prostatectomy. Prostatectomy margins negative. No seminal vesicle extension. One positive obturator lymph node. Postprostatectomy PSA 0.3 ng/mL.

Treatment	Appropriateness Rating	Comments
Hormone therapy (HT) alone	7	

Treatment	Appropriateness Rating	Comments
Radiation therapy (RT) plus neoadjuvant, concurrent, and long-term adjuvant HT	7	
RT plus neoadjuvant and concurrent HT	4	
RT alone	3	
Observation	2	
Radiation Therapy		
Pelvis and prostate bed	8	
Prostate bed	2	
Pelvic Irradiation, if given		
4000 cGy/20 fractions	2	
4500 cGy/25 fractions	8	
5040 cGy/28 fractions	7	
5400 cGy/30 fractions	4	
Dose to Prostate Bed (may include dose to pelvis)		
4500 cGy/25 fractions	2	
5040 cGy/28 fractions	3	
5400 cGy/30 fractions	3	
5940 cGy/33 fractions	5	
6660 cGy/37 fractions	8	
7020 cGy/39 fractions	5	
7200 cGy/40 fractions	4	
Treatment Plan		
IMRT	8	
3D-CT-based plan	7	
2D-CT-based plan	3	
Non-CT-based plan	2	

Treatment	Appropriateness Rating	Comments
Appropriateness Criteria Scale **1 2 3 4 5 6 7 8 9** **1 = Least appropriate 9 = Most appropriate**		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 7: 64-year-old man, stage T2A, Gleason score 7, adenocarcinoma. PSA 10.5 ng/mL. Negative metastatic workup. Treated with nerve-sparing radical prostatectomy. Prostatectomy margins negative. No seminal vesicle extension. One positive obturator lymph node. Postprostatectomy PSA nondetectable.

Treatment	Appropriateness Rating	Comments
Hormone therapy (HT) alone	7	
Radiation therapy (RT) plus neoadjuvant, concurrent, and long-term adjuvant HT	7	
RT plus neoadjuvant and concurrent HT	4	
RT alone	3	
Observation	2	
Radiation Therapy		
Pelvis and prostate bed	8	
Prostate bed	2	
Pelvic Irradiation, if given		
4000 cGy/20 fractions	2	
4500 cGy/25 fractions	8	
5040 cGy/28 fractions	7	
5400 cGy/30 fractions	4	
Dose to Prostate Bed (may include dose to pelvis)		
4500 cGy/25 fractions	2	

Treatment	Appropriateness Rating	Comments
5040 cGy/28 fractions	3	
5400 cGy/30 fractions	3	
5940 cGy/33 fractions	5	
6660 cGy/37 fractions	8	
7020 cGy/39 fractions	5	
7200 cGy/40 fractions	4	
Treatment Plan		
IMRT	8	
3D-CT-based plan	7	
2D-CT-based plan	3	
Non-CT-based plan	2	
Appropriateness Criteria Scale **1 2 3 4 5 6 7 8 9** **1 = Least appropriate 9 = Most appropriate**		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 8: 67-year-old man, stage T1C, Gleason score 8, adenocarcinoma. PSA 8.0 ng/mL. Negative metastatic workup. Nerve-sparing radical prostatectomy performed. Margins negative. No seminal vesicle extension. Negative lymph nodes. Postoperative PSA nonmeasurable. Six months postop. PSA rose to 0.6 ng/mL. PSA 3 months later, 0.7 ng/mL. Extent of disease workup, including pelvic MRI, negative.

Treatment	Appropriateness Rating	Comments
Radiotherapy (RT) plus neoadjuvant and concurrent hormone therapy (HT)	7	
RT plus neoadjuvant, concurrent, and long-term adjuvant HT	7	
RT alone	6	
HT alone	5	

Treatment	Appropriateness Rating	Comments
Observation	2	
Radiation Therapy		
Pelvis and prostate bed	6	
Prostate bed	6	
Pelvic Irradiation, if given		
4000 cGy/20 fractions	3	
4500 cGy/25 fractions	8	
5040 cGy/28 fractions	7	
5400 cGy/30 fractions	3	
Dose to Prostate Bed (may include dose to pelvis)		
4500 cGy/25 fractions	2	
5040 cGy/28 fractions	2	
5400 cGy/30 fractions	3	
5940 cGy/33 fractions	6	
6660 cGy/37 fractions	8	
7020 cGy/39 fractions	5	
7200 cGy/40 fractions	4	
Treatment Plan		
IMRT	8	
3D-CT-based plan	7	
2D-CT-based plan	3	
Non-CT-based plan	2	
Appropriateness Criteria Scale **1 2 3 4 5 6 7 8 9** **1 = Least appropriate 9 = Most appropriate**		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 9: 67-year-old man, stage T1C, Gleason score 8, adenocarcinoma. PSA 8.0 ng/mL. Negative metastatic workup. Nerve-sparing radical prostatectomy performed. Margins negative. No seminal vesicle extension. Postoperative PSA nonmeasurable. Six months later PSA rose to 3.5 ng/mL. Extent of disease workup, including pelvic MRI, negative.

Treatment	Appropriateness Rating	Comments
Hormone therapy (HT) alone	8	
Radiation therapy (RT) alone	3	
RT plus neoadjuvant and concurrent HT	3	
RT plus neoadjuvant, concurrent, and long-term adjuvant HT	3	
Observation	2	
Radiation Therapy		Radiation therapy not recommended.
Pelvis and prostate bed	2	
Prostate bed	2	
Pelvic Irradiation		
4000 cGy/20 fractions	2	
4500 cGy/25 fractions	2	
5040 cGy/28 fractions	2	
5400 cGy/30 fractions	2	
Dose to Prostate Bed (may include dose to pelvis)		
4500 cGy/25 fractions	2	
5040 cGy/28 fractions	2	
5400 cGy/30 fractions	2	
5940 cGy/33 fractions	2	
6660 cGy/37 fractions	2	
7020 cGy/39 fractions	2	
7200 cGy/40 fractions	2	

Treatment	Appropriateness Rating	Comments
Treatment Plan		
IMRT	2	
3D-CT-based plan	2	
2D-CT-based plan	2	
Non-CT-based plan	2	
Appropriateness Criteria Scale **1 2 3 4 5 6 7 8 9** **1 = Least appropriate 9 = Most appropriate**		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 10: 67-year-old man, stage T1C, Gleason score 8, adenocarcinoma. PSA 8.0 ng/mL. Negative metastatic workup. Nerve-sparing radical prostatectomy performed. Margins negative. No seminal vesicle extension. Postoperative PSA nonmeasurable. Six months later PSA rose to 9.0 ng/mL. Extent of disease workup, including pelvic MRI, negative.

Treatment	Appropriateness Rating	Comments
Hormone therapy (HT) alone	8	
Radiation therapy (RT) alone	3	
RT plus neoadjuvant and concurrent HT	3	
RT plus neoadjuvant, concurrent, and long-term adjuvant HT	3	
Observation	2	
Radiation Therapy		Radiation therapy not recommended.
Pelvis and prostate bed	2	
Prostate bed	2	
Pelvic Irradiation		

Treatment	Appropriateness Rating	Comments
4000 cGy/20 fractions	2	
4500 cGy/25 fractions	2	
5040 cGy/28 fractions	2	
5400 cGy/30 fractions	2	
Dose to Prostate Bed (may include dose to pelvis)		
4500 cGy/25 fractions	2	
5040 cGy/28 fractions	2	
5400 cGy/30 fractions	2	
5940 cGy/33 fractions	2	
6660 cGy/37 fractions	2	
7020 cGy/39 fractions	2	
7200 cGy/40 fractions	2	
Treatment Plan		
IMRT	2	
3D-CT-based plan	2	
2D-CT-based plan	2	
Non-CT-based plan	2	
Appropriateness Criteria Scale **1 2 3 4 5 6 7 8 9** **1 = Least appropriate 9 = Most appropriate**		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 11: 65-year-old man, stage T2B, Gleason score 7, adenocarcinoma PSA 12.0 ng/mL. Negative metastatic workup. Radical prostatectomy performed. Negative margins and lymph nodes. Postoperative PSA nonmeasurable. Four years later, patient found to have PSA of 3.0 ng/mL. 1.5 cm mass palpable in prostatic bed at the level of the apex. Biopsy recurrent adenocarcinoma. Negative diagnostic workup.

Treatment	Appropriateness Rating	Comments

Treatment	Appropriateness Rating	Comments
Radiation therapy (RT) plus neoadjuvant and concurrent hormone therapy (HT)	7	
RT alone	6	
RT plus neoadjuvant, concurrent, and long-term adjuvant HT	6	
HT alone	4	
Observation	2	
Radiation Therapy		
Pelvis and prostate bed	6	
Prostate bed	7	
Pelvic Irradiation, if given		
4000 cGy/20 fractions	3	
4500 cGy/25 fractions	8	
5040 cGy/28 fractions	7	
5400 cGy/30 fractions	3	
Dose to Prostate Bed (may include dose to pelvis)		
4500 cGy/25 fractions	2	
5040 cGy/28 fractions	2	
5400 cGy/30 fractions	2	
5940 cGy/33 fractions	3	
6660 cGy/37 fractions	6	
7020 cGy/39 fractions	7	
7200 cGy/40 fractions	7	
Treatment Plan		
IMRT	7	
3D-CT-based plan	7	

Treatment	Appropriateness Rating	Comments
2D-CT-based plan	3	
Non-CT-based plan	2	
Appropriateness Criteria Scale **1 2 3 4 5 6 7 8 9** **1 = Least appropriate 9 = Most appropriate**		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Introduction

Radical prostatectomy (RP) and radiation therapy (RT) are the primary treatment options for organ-confined prostate cancer (T1-2, stages I or II). Of the two, RP is the most common treatment employed. Eventually, about 40% of patients with high-risk pathologic features, such as a positive margin, extracapsular extension (ECE), or seminal vesicle involvement (SVI) will develop biochemical failure. Thus, RT may play a role either immediately following prostatectomy (based on various known high-risk pathologic features) or at the time of biochemical failure.

There are three main situations in which RT is given after RP: 1) adjuvant radiotherapy (ART) for men with an undetectable or barely detectable prostate-specific antigen (PSA) (<0.2 ng/mL) who have high risk pathologic features; 2) salvage radiotherapy (SRT) for men who have an undetectable or barely detectable PSA (<0.2 ng/mL) immediately postoperatively, but whose PSA rises at some later date -- a delayed rise in PSA (DR-PSA); and 3) SRT for men whose PSA remains at 0.2 ng/mL or above postoperatively -- a persistently detectable PSA (PD-PSA).

The purpose of distinguishing between adjuvant and salvage radiotherapy is rooted in the observation that there are significant differences between the two groups in prognosis after radiotherapy, in dose of RT administered, and in prognostic factors. The further subdivision of salvage patients into two groups, those with a DR-PSA and those with a PD-PSA, is useful because their outcomes after RT appear to be different, with a worse prognosis for those having a PD-PSA. In general, the earlier the rise in PSA after radical prostatectomy, the worse the outcome because of a higher risk of metastatic disease; the PD-PSA group represents the extreme of patients being considered for SRT in this respect.

Adjuvant Radiotherapy

The rationale for administering ART after RP is predicated on the assumption that local disease remains. Local therapy would reduce recurrence in the prostate bed and prevent the residual nidus from disseminating distantly. The decision to administer ART is based on the presence of high-risk pathologic findings in the prostatectomy specimen. The primary high-risk features are ECE, positive margins (prostate cancer at the margin of resection), SVI, and lymph node involvement

(LNI). The frequencies of occurrence are approximately 40% for ECE, 25% for margin positivity, 10% for SVI, and 5% for LNI. Another indication for ART is the presence of residual normal prostate at the inked specimen margin (a cut-through of the prostate), even without conclusive evidence that tumor remains and with an undetectable PSA. The assumption is that a cut-through of the prostate is representative of inadequate surgery and that microscopic disease could be left behind.

The prevalence of persistent local disease following RP is significant and generally under-recognized. Residual disease has been documented in approximately 50% of prostatectomy cases at autopsy and in biopsy specimens of the prostatic fossa and urethrovesical anastomosis. Long-term follow-up has revealed that the risk of biochemical failure following prostatectomy is substantial. Various surgical series have reported that this risk continues to be present between 5 and 10 years post prostatectomy, with an average relative risk of about 2% to 3% per year without reaching a plateau. Late biochemical failures are not insignificant, eventually leading to the development of painful bony metastases in 50% of patients in 7 to 8 years. ART has the potential to reduce failure and ultimately improve quality of life. Patients with a life expectancy of greater than 10 years should benefit from ART.

A powerful predictor of biochemical and local failure after prostatectomy is margin positivity. It is estimated that approximately 40% of men with a positive surgical margin will experience a rise in PSA to detectable levels within 5 to 10 years. Other pathologic features that predict for biochemical failure include extraprostatic extension, Gleason score ≥7, and SVI. Some recent prostatectomy series suggest that positive margins are not very important, but follow-up was short in these studies. The balance of data from available series indicates that margin status is an important determinant of outcome, along with Gleason score and PSA. The extent of margin positivity is another factor shown to influence biochemical failure that has only been examined in retrospective series. ART may have less effect in the case of a small focal positive margin in the absence of other unfavorable pathologic features. In this setting, other factors, such as the degree of extraprostatic extension and/or Gleason score ≥7 disease, appears to contribute to a greater risk of biochemical failure and provide a stronger rationale for ART. Similarly, a focal area of ECE alone is associated with a lower risk of biochemical progression, as compared to more extensive ECE; but, the risk will be higher when accompanied by Gleason score ≥7 disease.

In the setting of negative margins and a rising PSA, a complete biochemical response to SRT is still achieved in the majority of cases, suggesting local disease persistence in the prostatic fossa. A rising PSA after a negative margin has been associated with a worse prognosis in some prostatectomy series; however, one must consider that not every micron of tissue in the prostatectomy specimen is pathologically assessed. The radiotherapy response data suggest that tumor cells were left behind (a focal positive margin) but were not identified on pathologic evaluation. The risk of local disease persistence when there is obvious ECE in addition to Gleason ≥7 disease, even with negative margins, is likely high enough that ART should be considered.

ART Outcome

Many retrospective studies have examined the role of ART. More recently, three prospective randomized trials comparing prostatectomy alone to prostatectomy plus ART have been described. All three have shown an improvement in biochemical control of about 20% with ART, but as yet have not shown a difference in survival. The EORTC 22911 study included 972 patients with pT2-3 prostate cancer with at least one high-risk feature (ECE, positive margins, or SVI). Freedom from biochemical failure (FFBF) at 5 years was 53% in the RP alone group vs 74% in the RP + RT (60 Gy) group. A similar study was conducted by the SWOG and presented at the 2005 meetings of the American Urological Association and American Society of Therapeutic Radiology and Oncology. There were 473 patients with pathologically determined ECE, positive margins, and/or SVI randomized to RT (60-64 Gy) vs. observation. Freedom from biochemical failure was significantly improved by the addition of radiation from 38% to 61% at 5 years and from 23% to 47% at 10 years. This benefit was shared by each of the three pathologic risk groups. ART also prevented the need for androgen deprivation in some patients and delayed use significantly (by 2.5 years) in others. A third study (ARO 96-02) randomized 385 men with pT3 disease after prostatectomy to either RT (60 Gy) or observation. The 4-year FFBF rate was 60% in the RP alone group vs. 81% in the RP + RT group. The results for the three trials are remarkably similar, showing that ART reduces progression.

Salvage Radiotherapy

Radiotherapy is given for salvage after RP in two settings: 1) for a delayed rise in PSA after the PSA has dropped to undetectable immediately post-prostatectomy and 2) for a persistently detectable PSA after surgery. This division may be important because the initial considerations in evaluation may be different and there are reports of a distinction in prognosis. However, many retrospective series were based on small patient numbers and did not separate these patients, making conclusions difficult.

The time to a rising PSA after prostatectomy, the prostatectomy Gleason score, and the PSA doubling time are independent predictors of distant metastasis and mortality. When the time to biochemical failure (BF) is <3 years (the PD-PSA patients would be included in this group), Gleason score is ≥8, and PSA doubling time is <9 months, the risk of death due to prostate cancer at 5 years is ≥19%. This risk increases to ≥74% at 10 years. PSA doubling time (PSADT) has taken on much more importance over the last 5 years. If the above parameters included a postoperative PSADT of <3 months, nearly 50% will die within 5 years. Even the PSA kinetics prior to prostatectomy may be an independent determinant of mortality. A rapidly rising PSA prior to radical prostatectomy or prior to RT connotes a poor prognosis, suggestive of occult metastatic disease even if the metastatic workup is negative. Although our ability to predict progression after SRT has improved, we are a long way from making conclusive judgments on whether SRT would benefit most men. There is a need to optimize treatment selection with the goal of prolonging survival without unnecessary toxicity, particularly in the setting rapid PSA kinetics.

Factors indicating that post-prostatectomy RT for a PD-PSA might be beneficial include extensive extraprostatic extension (particularly in those with high-grade disease) or positive margins. Other indicators that there may be disease in the prostatic fossa are SVI, a cut-through of the prostate (a partial prostatectomy

when there is palpable, biopsy or imaging evidence of prostate remaining), or incomplete removal of the seminal vesicles in the setting of T3 disease (especially with ECE at the base or with SVI). In the absence of these features and with a PSA that is rising quickly (doubling time <6 months), the probability of distant metastasis is high, and SRT is discouraged.

The results of SRT have been relatively poor, with 5-year FFBF rates in most series ranging from 10% to 66%. The following factors have been correlated with worse FFBF rates: Gleason score >7, SVI, high pre-RT PSA (>1 to >2.5 ng/ml), short PSA doubling time, negative prostatectomy margins, treatment for a PD-PSA (vs. a DR-PSA), a palpable prostatic fossa mass, and RT dose <65 Gy.

SRT Outcome

In general, when the PSA remains detectable after RP, the risk of distant metastasis is greater than when the PSA goes to undetectable and then rises later. Thus, outcomes of SRT in most series have been worse for patients with a PD-PSA compared with a DR-PSA. However, some series have not found a significant difference in FFBF rates between the two groups. While distinguishing between the groups seems to be the most objective way of evaluating the utility of SRT, most of the studies reporting SRT outcomes do not separately analyze the DR-PSA and the PD-PSA patients. In addition, all of these studies are retrospective, and most include small numbers of patients.

As described above, the PSADT time is an important predictor of SRT outcome. The shorter it is, the greater the risk of death due to prostate cancer. A doubling time of ≤10 months in the setting of a DR-PSA or a PD-PSA, indicates a higher likelihood of occult metastatic disease, thus rendering postoperative RT much less effective. Another study showed a PSADT of ≥5 months predicted a response to SRT (a response was defined as a PSA nadir of ≤0.1 ng/ml). One caveat concerning the PSADT as a reliable predictor of distant metastasis is that when the PSA is below 1 ng/mL the estimates may be inaccurate. In reports of postoperative radiotherapy, few have identified PSADT as a predictor of FFBF. In a preliminary recursive partitioning analysis of about 1200 men in a pooled multi-institutional database, PSADT was not independently related to outcome, while pre-RT PSA, Gleason score, and margin status were. Standards are needed for when the PSADT calculation begins (from the PSA just prior to when an accelerated rise occurs or from the time of the first detectable PSA) and the minimum number of PSA values required to accurately calculate a PSADT.

The pre-RT PSA has been found to be the most consistent predictor of FFBF in both univariate and multivariate analyses of SRT. While a clear pre-RT PSA cutpoint has not yet been defined, evidence suggests that lower pre-RT PSAs are associated with higher FFBF rates. The best results have been seen when the pre-RT PSA is ≤1 ng/mL. A significant decline in FFBF is seen when the pre-RT PSA increases from ≤1 ng/mL to 2, and then to >2 ng/mL.

Other important prognostic factors include the Gleason score, margin status, and seminal vesicle invasion. Gleason scores of ≤7 predict for a better prognosis compared with scores of 8 to 10. A positive margin often indicates residual disease in the prostate bed, for which SRT is effective, and FFBF rates are higher when this is the case. Seminal vesicle invasion has been found to be a

determinant of outcome in multivariate analysis in many series as well, with worse FFBF rates when the seminal vesicles were involved.

Androgen Deprivation Therapy

The use of concurrent androgen deprivation therapy (ADT) with adjuvant and salvage RT could impact the course of the disease hypothetically by three principal mechanisms: 1) better disease eradication locally (recurrence in a hypoxic scar may be radioresistant), 2) improved disease control distantly (cells in microscopic metastatic deposits might retain sensitivity to ADT), and 3) the combination of ADT and RT may alter the PSA kinetics in patients who eventually relapse. The mechanism of the effect on the kinetics of BF and the delayed appearance of distant metastasis (DM) is unknown. However, any improvement upon the current results of ART and SRT is potentially worthwhile. In some reports androgen deprivation had positive results in patients at high risk of experiencing a rising PSA after SRT (e.g., a pre-RT PSA >1 ng/mL). Randomized trials are needed and will be forthcoming.

Adjuvant versus Salvage Radiotherapy

The optimal timing of ART vs. SRT, for patients with high-risk pathologic features remains controversial. Some have supported watchful waiting before administering SRT. This rationale is based on three points. First, half of men will be treated unnecessarily. Second, salvage rates are fairly good when the pre-RT PSA is low (≤1.0 ng/ml). Third, the progression to distant metastasis after biochemical failure may be long. It is beyond the scope of this article to compare ART to SRT in depth. Without a randomized trial to eliminate selection bias, it is impossible to ascribe an advantage to one strategy over the other based on FFBF outcomes. At least ART has a proven benefit in randomized, prospective studies, supporting first principles that RT treatment should be used if the risk of local failure is >20% and the side effect profile is reasonable. Local persistence leads to distant metastasis in most malignancies, and there is evidence that this is the case for prostate cancer. In younger men with a long life expectancy, ART should be considered.

Irradiation in Patients with Positive Lymph Nodes

LNI portends a very poor prognosis, with a high rate of distant failure. Although there are emerging data indicating that RP or RT should be used along with ADT when LNI is identified, there is no well-established benefit from this approach as yet. ART might be of some value when there is evidence of an appreciable local-regional tumor burden, such as extensive positive margins. There are insufficient data on the subject of pelvic nodal irradiation to make any recommendations, even when LNI has been documented.

Abbreviations

- C, cervical
- CT, computed tomography
- HT, hormone therapy
- IMRT, intensity modulated radiation therapy
- MRI, magnetic resonance imaging

- PSA, prostate-specific antigen
- RT, radiation therapy
- T, thoracic vertebra

CLINICAL ALGORITHM(S)

Algorithms were not developed from criteria guidelines.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are based on analysis of the current literature and expert panel consensus.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Selection of appropriate treatment procedures for prostate cancer patients after radical prostatectomy

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

An American College of Radiology (ACR) Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists, and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those exams generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the U.S. Food and Drug Administration (FDA) have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Personal Digital Assistant (PDA) Downloads

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Pollack A, Hayes S, Roach M III, Merrick G, Anscher MS, Beyer DC, Lawton CA, Lee WR, Michalski JM, Rosenthal SA, Vijayakumar S, Carroll PR, Higano CS, Expert Panel on Radiation Oncology-Prostate. Postradical prostatectomy irradiation in prostate cancer. [online publication]. Reston (VA): American College of Radiology (ACR); 2006. 18 p. [116 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1996 (revised 2006)

GUIDELINE DEVELOPER(S)

American College of Radiology - Medical Specialty Society

SOURCE(S) OF FUNDING

The American College of Radiology (ACR) provided the funding and the resources for these ACR Appropriateness Criteria®.

GUIDELINE COMMITTEE

Committee on Appropriateness Criteria, Expert Panel on Radiation Oncology–Prostate

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Panel Members: Alan Pollack, MD, PhD; Shelly Hayes, MD; Mack Roach III, MD; Gregory Merrick, MD; Mitchell S. Anscher, MD; David C. Beyer, MD; Colleen A. Lawton, MD; W. Robert Lee, MD; Jeff M. Michalski, MD, MBA; Seth A. Rosenthal, MD; Srinivasan Vijayakumar, MD; Peter R. Carroll, MD; Celestia S. Higano, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Perez CA, Beyer DC, Blasko JC, Forman JD, Hussey DH, Lee WR, Paryani SB, Pollack A, Potters L, Roach M, Scardino P, Schellhammer P, Leibel S. Postradical prostatectomy irradiation in carcinoma of the prostate. American College of Radiology. ACR Appropriateness Criteria. Radiology 2000 Jun;215(Suppl):1419-39.

The appropriateness criteria are reviewed annually and updated by the panels as needed, depending on introduction of new and highly significant scientific evidence.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.

ACR Appropriateness Criteria® *Anytime*, *Anywhere*™ (PDA application). Available from the ACR Web site.

Print copies: Available from the American College of Radiology, 1891 Preston White Drive, Reston, VA 20191. Telephone: (703) 648-8900.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- ACR Appropriateness Criteria®. Background and development. Reston (VA): American College of Radiology; 2 p. Electronic copies: Available in Portable

Document Format (PDF) from the American College of Radiology (ACR) Web site.

PATIENT RESOURCES

None available

NGC STATUS

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Date Modified: 11/3/2008