Complete Summary

GUIDELINE TITLE

Best practice policy statement on cryosurgery for the treatment of localized prostate cancer.

BIBLIOGRAPHIC SOURCE(S)

American Urological Association Education and Research, Inc. Best practice policy statement on cryosurgery for the treatment of localized prostate cancer. Linthicum (MD): American Urological Association Education and Research, Inc.; 2008. 50 p. [93 references]

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

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

SCOPE

DISEASE/CONDITION(S)

Locally confined prostate cancer

GUIDELINE CATEGORY

Evaluation
Management
Treatment

CLINICAL SPECIALTY

Oncology
Surgery
Urology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To provide medical practitioners with a current understanding of the principles and strategies for the cryosurgical treatment of localized prostate cancer

TARGET POPULATION

Men with localized prostate cancer

INTERVENTIONS AND PRACTICES CONSIDERED

1. Primary cryosurgery
    - Patient selection
        - Assessment of prostate gland volume and configuration
        - Assessment of need for lymph node dissection
        - Assessment of prostate-specific antigen (PSA) level and calculation of Gleason score
    - Posttreatment biopsy
2. Salvage cryosurgery
    - Patient selection
        - Assessment of PSA level
        - Prostate biopsy
        - Metastatic work-up
        - Assessment of prostate gland size
    - Technical considerations

Note: Subtotal prostate cryosurgery was considered but not recommended.

MAJOR OUTCOMES CONSIDERED

- Posttreatment prostate-specific antigen (PSA) level
- Five-year biochemical disease-free survival rate
- Posttreatment biopsy status
- Physician reported complications (e.g., urinary retention, fistula formation, incontinence, erectile dysfunction, urethral sloughing)
- Health-related quality of life

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

A Medline search was performed using the Medical Subject Headings (MeSH) index headings "prostate cancer," and "cryosurgery," "cryotherapy," and "cryoablation," from 2000 through 2008. Publications were selected for review by the Panel members.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

I Evidence obtained from at least one properly randomized controlled trial.

II–1 Evidence obtained from well-designed controlled trials without randomization.

II–2 Evidence obtained from well-designed cohort or case control analytic studies, preferably from more than one center or research group.

II–3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.

III Opinions of respected authorities, based on clinical experience, descriptive studies and case reports, or reports of expert committees.

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

As noted in the American Urological Association (AUA) *Guideline for the Management of Clinically Localized Prostate Cancer: 2007 Update*, insufficient information was available to include cryosurgery in data meta-analyses. As such, the Panel was charged with developing a Best Practice Policy Statement, which uses published data in concert with expert opinion, but does not employ formal meta-analysis of the literature.

Levels of evidence were assigned based on the recommendations of the U.S. Preventive Services Task Force (see the "Rating Scheme for the Strength of the Evidence" field).

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The American Urological Association (AUA) convened a Panel to develop a Best Practice Statement addressing the use of cryosurgery for the treatment of localized prostate cancer. The Panel formulated recommendations based on review of all material and the Panel members' expert opinions and experience which includes the treatment of several thousands of patients. Recommendations were achieved through a consensus process and may not reflect a unanimous decision by the Panel members.

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

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

This document was submitted for peer review, and comments from all 19 responding physicians and researchers were considered by the Panel in making revisions. The revised document was submitted for a second peer review, and responses from all 21 responding physicians and researchers were considered by the Panel when making final revisions to the document. The final document was submitted to the American Urological Association (AUA) Practice Guideline Committee and Board of Directors for approval.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions of the strength of the evidence (I, II-1, II-2, II-3, and III) are defined at the end of the "Major Recommendations" field.

Scientific Background

To both maximize the destructive effects of cryosurgery and to permit comparisons of outcomes among treatment centers, specific procedural requisites should be followed.

- *Tissue Freeze Rate* – Rapid freezing is recognized as being more destructive than slow freezing. Cancer cells have the opportunity to "adapt" under conditions of slow freezing by losing water to the extracellular milieux, thereby reducing the probability of intracellular ice formation.
- *Temperature Monitoring* – The Panel strongly advises the use of thermocouples when performing cryosurgery despite the lack of supporting evidence-based documentation. The real-time measurement of tissue temperature at critical locations within and proximal to the prostate provides the urologist with an important indication of the status of the freezing process as well as protecting key vital structures such as the rectum and external urethral sphincter. Temperature monitoring is also facilitated by the ultrasound image. The advancing freeze zone is visualized as a hyperechoic rim (white line) on the ultrasound image. The distal edge of the hyperechoic rim represents the transition zone between frozen and unfrozen tissue. This transition occurs at -0.6 degrees C. The inner edge of this rim (closest to cryoneedle/cryoprobe [CN/P]) has been reported to be approximately -15 degrees C to -20 degrees C, the temperature of intracellular ice formation and maximum freeze concentration of solutes.
- *Nadir Temperature* – Throughout much of the history of cryosurgery, -40 degrees C has been used as the end-temperature goal. Anecdotal evidence from both *in vivo* and *in vitro* studies as well as knowledge of the physics of water all point to -40 degrees C as being the lowest nominal temperature at which active human cells can survive. It is recognized that prostate cancer is comparatively temperature labile with a lower lethal temperature near -20 degrees C.
- *Thaw Rate – In vitro* studies confirm that prostate cancer ablation is improved with slow (passive) thawing. Activation of the heating mode in the CN/P does not affect the thaw rate of the distal edges of the gland. Probe heating affects only the frozen tissue mass juxtaposed to the CN/P and not the distally frozen tissue.
- *Freeze Cycles* – The Panel recommends the use of a double freeze-thaw cycle. Clinical experience, along with *in vivo* and *in vitro* studies, demonstrates that a clear benefit accrues with the use of a dual cycle. Those cancer cells not killed by the first freezing are sufficiently stressed so that a second cycle is lethal. In addition, damage to tumor vascularity permits the second freeze to occur more rapidly and extends the -40 degrees C isotherm further from the CN/P.

Primary Cryosurgery ***(Evidence Level II-2/3)***

The consensus opinion of the Panel is that primary cryosurgery is an option, when treatment is appropriate, to men who have clinically organ-confined disease of any grade with a negative metastatic evaluation. High-risk patients may require multi-modal therapy. There are even more limited data regarding the outcomes for clinical T3 disease, and the role of cryosurgery in this setting is currently undetermined.

Patient Selection

Cryosurgery of the prostate is a locally ablative treatment option for the management of prostate cancer. Suitable candidates should have documented prostate cancer that is clinically confined to the prostate. Although cryosurgery is an option for low-, intermediate-, and high-risk patients, gland volume is a factor; the larger the prostate, the more difficult to achieve a uniformly cold temperature throughout the gland. After assessment of volume and gland configuration, technical considerations will need to be made followed by appropriate technical modifications. In some larger glands, neoadjuvant cytoreduction can be considered to overcome the technical limitations of treating a large gland. Neoadjuvant or concomitant hormonal therapy, however, has not been shown to have a positive impact on subsequent cryosurgical outcomes.

The role of lymph node dissection in patients being considered for cryosurgery is similar to that in patients receiving radiation therapy. Elevated prostate-specific antigen (PSA) levels (>20 ng/mL) or Gleason scores of 8 to 10 are associated with an increased incidence of lymph-node involvement. Men with a >25% risk based on established nomograms or some other published criteria may warrant lymph node dissection prior to or concurrent with cryosurgery (see Appendix 4, Partin table in the original guideline document). A prior history of transurethral resection of the prostate (TURP) is a relative contraindication for cryosurgery, especially if there is a large transurethral resection (TUR) defect present. These patients are at increased risk for urethral necrosis leading to sloughing and urinary retention due to failure of the urethral warming device to coapt to the mucosa. While many patients with elevated PSA levels have been treated with cryosurgery, the best results are achieved in patients with PSA levels <10 ng/mL.

Cryosurgery is a minimally invasive option when treatment is appropriate for men who either do not want or are not good candidates for radical prostatectomy because of comorbidities, including obesity or a prior history of pelvic surgery. The latter is based on the opinion and experience of the Panel. Cryosurgery may also be a reasonable option in men with a narrow pelvis or who cannot tolerate external beam radiotherapy, including those with previous nonprostatic pelvic radiation, inflammatory bowel disease, or rectal disorders. As cryosurgery is an outpatient procedure or may only require an overnight stay, it is an option for patients seeking shorter duration treatment of clinically organ-confined prostate cancer. For patients who desire minimally invasive therapy for their intermediate disease, defined as Gleason score 7 and/or Gleason score <8 with a PSA level >10 ng/mL but <20 ng/mL and/or clinical stage T2b, cryosurgery is also an option.

Salvage Cryosurgery ***(Evidence Level II-3)***

It is the opinion of the expert Panel that salvage cryosurgery can be considered as a treatment option for curative intent in men who have failed radiation therapy. The most appropriate candidates have biopsy proven persistent organ-confined prostate cancer, a PSA <10 ng/mL, and a negative metastatic evaluation as determined by standard assessment tools such as imaging modalities.

Patient Selection

PSA Levels

Although there is no consensus among urologists or radiation oncologists regarding the timing of salvage therapy, the clinician should consider variables such as stage of disease at presentation, existing comorbidities, patient age, and patient preference. If the PSA level rises acutely and persists above the nadir level or the patient is deemed to have failed clinically based on any currently employed evaluation tool (ASTRO, Phoenix, PSA doubling time/velocity), a prostate biopsy should be performed if there are no contraindications to further therapeutic intervention. The Partin table (see Appendix 4 in the original guideline document) for predicting pathologic stage does not apply to postradiation therapy patients. The patient with a PSA of 10 ng/mL following radiation should not be considered to have the same pathology as a nonradiated patient with a PSA of 10 ng/mL.

Prostate Biopsy

It is the consensus of this panel that a prostate biopsy should be performed when considering salvage cryosurgery and that only men with a positive result should undergo cryosurgery. When a biopsy is undertaken, multiple cores should be obtained, and the pathologists should be informed that the patient has had previous radiation since there are definite pathological changes that can occur postradiation.

Although there is an absence of supporting documentation, biopsy of both seminal vesicles (SVs) is recommended by this panel in addition to a prostate biopsy. Cancer-invaded SVs may appear normal on imaging after radiation therapy. The incidence of SV involvement in a patient status postradiation therapy with a rising PSA is higher than in a nonradiated patient with a similar PSA history.

Metastatic Work-up

If a prostate biopsy reveals recurrent cancer in the gland, a metastatic evaluation including lymph node assessment with imaging of the abdomen and pelvis as well as a bone scan should be performed. Open or laparoscopic biopsy of the pelvic lymph nodes may also be considered for high-risk patients.

Other Factors

Prostate size is less of a problem when considering salvage cryosurgery since the prostate of radiated patients loses volume after radiation therapy. A prior history of transurethral resection of the prostate is a relative contraindication for salvage cryosurgery, especially if there is a large TUR defect present, as these patients are at risk for urethral necrosis leading to sloughing and urinary retention.

Patient Selection Summary

Currently, there are no clearly defined guidelines to aid in the proper selection of patients for salvage cryosurgery. The optimal candidates for the procedure are men who have pathologic evidence of locally recurrent disease without clinical evidence of metastatic disease, a PSA ≤4 ng/mL, a long PSA doubling time, no evidence of SV invasion, and a life expectancy >10 years.

Technical Considerations and Modifications

Salvage cryosurgery can be performed in the patient with recurrent disease following external beam radiation therapy (EBRT) as well as interstitial prostate brachytherapy. Previously placed radioactive seeds can be visualized quite well under transrectal ultrasound (TRUS) and may cause some confusion as their sonographic appearance is similar to the tip of the cryoneedles, especially in the transverse view. Placing the needles in the sagittal plane can overcome this difficulty, since the length of the cryoneedles can be easily followed in this view. Due to previous radiation, the gland may be adherent to the anterior rectal wall, diminishing the thickness of Denonvilliers' fascia. This needs to be assessed by TRUS prior to freezing so the surgeon can determine how to appropriately place the posterior cryoprobes and the Denonvilliers' thermocouple. If the space between the anterior rectal wall and posterior prostatic capsule is <5 mm, it may not be possible to drive the temperatures down to –40°C safely, and freezing should be terminated when the leading edge of the ice ball has extended just beyond the capsule, even if the target temperature of –40°C is not reached. Double freeze-thaw cycles have better outcomes in terms of biochemical failure-free and local recurrence-free survival rates compared to a single freeze-thaw cycle.

When counseling patients for any salvage procedure, the risks of urinary incontinence need to be addressed. Placement of a thermosensor to monitor the temperature of the external sphincter can reduce the potential of thermal injury to this muscle. The thermosensor is introduced through the perineal skin and advanced until the impression of the tip of the thermocouple can be seen in the sphincter. The placement can be documented by TRUS with/without cystoscopy.

Subtotal Prostate Cryosurgery ***(Evidence Level III)***

While this minimally invasive technique of cryosurgery is attractive from a conceptual perspective, clinical experience is limited and long-term results are unavailable. The Panel's consensus is that cases of subtotal prostate cryoablation should be collected prospectively in a database for future analysis.

Overview Conclusions

While there is no Level I evidence from prospective, randomized trials to support the role of cryosurgery over other therapeutic options in the treatment of prostate cancer, the literature contains documentation reporting the seven- to eight-year biochemical disease-free results of cryosurgery. The literature reports that the morbidity profile associated with cryosurgery has improved in all aspects, including continence, rectal/urethral fistula formation, urethral sloughing, and potency in association with the technological advances over the last 10 to 15 years.

Definitions:

Levels of Evidence

I Evidence obtained from at least one properly randomized controlled trial.

II–1 Evidence obtained from well-designed controlled trials without randomization.

II–2 Evidence obtained from well-designed cohort or case control analytic studies, preferably from more than one center or research group.

II–3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.

III Opinions of respected authorities, based on clinical experience, descriptive studies and case reports, or reports of expert committees.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for main recommendations (see "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of cryosurgery for the treatment of localized prostate cancer

POTENTIAL HARMS

Primary Cryosurgery

- Urinary retention/obstruction
- Penile and/or scrotal swelling
- Penile paresthesia
- Fistula formation
- Incontinence
- Erectile dysfunction
- Urethral sloughing
- Ureteral stricture
- Perineal pain
- Urinary tract infection/sepsis

Salvage Cryosurgery

- Incontinence
- Rectourethral fistula

- Rectal fistula
- Rectal pain
- Urethral sloughing
- Erectile dysfunction
- Perineal pain
- Obstruction/retention

Refer to Tables 1 and 2 and the sections titled "Treatment Outcomes" in the original guideline document for information on patient outcomes and complication rates after primary and salvage cryosurgery, respectively.

CONTRAINDICATIONS

CONTRAINDICATIONS

A prior history of transurethral resection of the prostate is a relative contraindication for cryosurgery, especially if there is a large transurethral resection defect present as these patients are at increased risk for urethral necrosis leading to sloughing and urinary retention.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This document provides guidance only and does not establish a fixed set of rules or define the legal standard of care. As medical knowledge expands and technology advances, this best practice statement will change. Today they represent not absolute mandates but provisional proposals or recommendations for treatment under the specific conditions described. For all these reasons, this best practice statement does not preempt physician judgment in individual cases. Also, treating physicians must take into account variations in resources and in patient tolerances, needs, and preferences. Conformance with the best practice statement reflected in this document cannot guarantee a successful outcome.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

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)

American Urological Association Education and Research, Inc. Best practice policy statement on cryosurgery for the treatment of localized prostate cancer. Linthicum (MD): American Urological Association Education and Research, Inc.; 2008. 50 p. [93 references]

ADAPTATION

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

DATE RELEASED

2008

GUIDELINE DEVELOPER(S)

American Urological Association Education and Research, Inc. - Medical Specialty Society

SOURCE(S) OF FUNDING

American Urological Association Education and Research, Inc. (AUA)

GUIDELINE COMMITTEE

Cryosurgery for the Treatment of Localized Prostate Cancer
Best Practice Statement Panel

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Panel Members: Richard J. Babaian, MD, (*Chair*); Bryan Donnelly, MD, (*Facilitator*); Duke Bahn, MD; John G. Baust, PhD; Martin Dineen, MD; David Ellis, MD; Aaron Katz, MD; Louis Pisters, MD; Daniel Rukstalis, MD; Katsuto Shinohara, MD; J. Brantley Thrasher, MD

Panel Managers: Kirsten Aquino; Judy Goldfarb

AUA Staff: Heddy Hubbard, PhD; Edith M. Budd; Michael Folmer; Katherine Moore; Kadiatu Kebe

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

All panel members completed Conflict of Interest disclosures. Those marked with (C) indicate that compensation was received; relationships indicated by (U) indicate no compensation was received.

Consultant or Advisor: Richard J. Babaian, Endocare (C); Aaron Katz, Oncura (C), Endocare (C); Louis Pisters, Endocare (C); Martin Dineen, Abbeymoor Medical Inc. (C), Endocare (C); Bryan Donnelly, Endocare (C); Katsuto Shinohara, Nihon Mediphysics (C), Wilex AG (C); Investigator: Louis Pisters, Protox Therapeutics (C); Scientific Study or Trial: Martin Dineen, Oakwood Pharmaceuticals (C), Duramed (C), Amgen (C), National Cancer Institute – Johns Hopkins (C), Mentor (C), Sanofi (C), GlaxoSmith-Kline (C), AstraZeneca (C), Schering Plough (C), GTX (C); Katsuto Shinohara, KineMed (C), GlaxoSmithKlein (U); Meeting Participant or Lecturer: John G. Baust, Galil Medical (C); Other: Richard J. Babaian, Gen-Probe (C); David Ellis, Endocare (C).

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the American Urological Association, Inc. (AUA) Web site.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on January 12, 2009.

COPYRIGHT STATEMENT

DISCLAIMER

NGC DISCLAIMER

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public

or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at http://www.guideline.gov/about/inclusion.aspx .

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

Date Modified: 3/16/2009