

NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedures overview of secondary transperineal cryotherapy for carcinoma of the prostate

Introduction

This overview has been prepared to assist members of the Interventional Procedures Advisory Committee (IPAC) advise on the safety and efficacy of an interventional procedure previously reviewed by SERNIP. It is based on a rapid survey of published literature, review of the procedure by Specialist Advisors and review of the content of the SERNIP file. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared by ASERNIP-S in November 2002 and updated by NICE in February 2004.

Procedure name

- Secondary transperineal cryotherapy for carcinoma of the prostate.

Specialty society

- British Association of Urological Surgeons.

Description

Executive summary

There were no comparative studies, making the quality of the evidence low. Different efficacy outcome measures were used in each paper, making exact comparisons difficult. Nadir PSA¹ 0.3ng/ml was reported for 36% of patients in one paper; Nadir PSA <0.5 ng/ml was reported in 97% of patients in another; Nadir PSA < 0.4 ng/ml was reported in 37% of patients in another; two other papers did not report Nadir PSA. Biochemical-recurrence-free survival was another efficacy measure used, and was reported in one paper as 79% at 6 months and 66% at 12 months, and in another paper as 86% at 12 months and 74% at 24 months. Biomechanical failure

¹ Prostate specific antigen (PSA) is a protein produced by both normal and cancerous cells in the prostate gland. Changes in the PSA level may be used to monitor response to treatment.

was reported in 58% of patients in one paper. Only one paper reported one surgical death, from pulmonary embolism. Other morbidities were reported at high rates: the most common being incontinence, urinary retention, impotence, hydronephrosis, and perineal and rectal pain.

Indications

Carcinoma of the prostate that has been unsuccessfully treated via another method, most typically radiation or hormones.

Summary of procedure

Secondary transperineal cryotherapy may be performed under general or spinal anaesthesia. A warming catheter is initially inserted into the urethra, to prevent it being damaged by the cold. Saline is injected into Denonvilliers' fascia, which temporarily increases the space between the rectum and prostate. Cryoprobes are inserted into the prostate percutaneously through the perineum, using transrectal ultrasound for guidance. Temperature monitor probes may also be placed percutaneously through the perineum. One or two freeze–thaw cycles are then carried out, involving a distinct freezing event in which the entire prostate gland is enclosed in an iceball, followed by a period of complete thawing. After the procedure, a suprapubic catheter is inserted and left in place for 1 to 2 weeks, depending on the postvoid residual-urine volume.

Therapeutic options with curative intent for patients with locally recurrent prostate cancer after radiotherapy treatment are somewhat limited and include salvage radical prostatectomy, salvage cryotherapy and salvage brachytherapy. Salvage cryotherapy is less invasive than salvage radical prostatectomy and recent advances in the technique have helped to decrease the morbidity of the procedure by sparing the surrounding structures such as the rectum.

Literature reviews

A systematic search of MEDLINE, PREMEDLINE, EMBASE, Current Contents, PubMed, Cochrane Library and Science Citation Index was conducted using Boolean search terms, from the inception of the databases until November 2002. The York Centre for Reviews and Dissemination, Clinicaltrials.gov, National Research Register, SIGLE, Grey Literature Reports, relevant online journals and the Internet were also searched in November 2002. Searches were conducted without language restriction.

Articles were obtained on the basis of the abstract containing safety and efficacy data in the form of randomised controlled trials (RCTs), other controlled or comparative studies, case series and case reports. Conference abstracts and manufacturers' information were included if they contained relevant safety and efficacy data. Foreign language papers were included if they contained safety and efficacy data and were considered to add substantively to the English-language evidence base. In the case of duplicate publications, the latest, most complete study was included. All identified studies were included.

List of studies found

Randomised controlled trials	0
Non-randomised comparative studies	0

Case series	13
Case reports	1

Papers were rejected for reporting no clinical outcomes, being review articles without data, involving techniques other than secondary cryotherapy of the prostate, or for reporting data that is included in later papers. Data for five papers are tabulated below. Case series were chosen for tabulation firstly if they reported on both safety and efficacy outcomes, and then by recency. Studies that mixed outcomes for different prostate procedures were rated lowest for tabulation. Studies for which data were not tabulated are listed in the Appendix following the reference list.

Summary of key efficacy and safety findings

Study details	Key efficacy findings	Key safety findings	Appraisal/Comments
Case series			
Bales et al. ¹ 1995	Nadir PSA < 0.3 ng/ml = 8/22 (36%)	Urinary retention = 9/22 (41%)	Potential for bias:
USA	Biopsy shows cancer at 3 months = 3/22 (14%)	Urinary stricture = 3/22 (14%)	Small patient numbers. Unknown whether patients were recruited consecutively.
	Biopsy shows benign glands = 10/22 (45%)	Incontinence = 21/22 (96%)	
	TURP shows cancer = 3/12 (25%)	Hydronephrosis = 8/22 (36%)	
Dec 1992–Feb 1994	Developed metastatic disease = 8/22 (36%)	Renal failure = 2/22 (9%)	Outcome measures and their validity:
	PSA < 0.3 ng/ml at 1 year = 3/22 (14%)	Interstitial nephritis = 1/22 (5%)	Conventional outcome measures.
23 patients (24 procedures)		Impotence = 11/11 (100%)	Other comments:
		Urosepsis = 2/22 (9%)	
		Death (from pulmonary embolus) = 1/23 (4%)	
Selection criteria: men previously treated with external beam or interstitial radiation therapy with biopsy-proven recurrent adenocarcinoma of the prostate			
Follow up: up to 23 months			
Chin et al. ² 2001	Positive biopsy cores = 23/745 (3.1%) in 7 patients.	Rectourethral fistula = 4/118 (3%)	Potential for bias:
Canada	PSA nadir < 0.5 ng/ml = 114/118 (97%)	Vesicourethral fistula beyond external sphincter = 1/118 (1%)	Patients recruited consecutively.
Dec 1994–Sept 1999		Incontinence:	Outcome measures and their validity:
		• mild/moderate = 16/118 (14%)	Conventional outcome measures.
118 patients (125 procedures)		• severe = 8/118 (7%)	Other comments:
		Outlet obstruction = 10/118 (9%)	
		Debris sloughing = 6/118 (5%)	
		Bladder neck contracture = 2/118 (2%)	
Selection criteria: increasing serum PSA on 3 specific determinations at least 2 years following radical radiation beam therapy with curative intent			
Follow up: median of 18.6 months			

Study details	Key efficacy findings	Key safety findings	Appraisal/Comments
de la Taille et al. ³ 2000 USA Oct 1994– April 1999 43 patients Selection criteria: localised recurrent prostate cancer after radiation therapy Follow-up: mean 21.9 months	PSA nadir < 0.1 ng/ml = 26/43 (60%). PSA < 4 ng/ml = 16/43 (37%) PSA < 10 ng/ml = 1/43 (3%)# Biochemical recurrence free survival (bRFS) was 79% at 6 months and 66% at 12 months. bRFS of < 0.1 ng/ml group (73%) significantly greater than others (30%), p = 0.0076.	Rectal pain = 11/43 (26%) Perineum swelling/scrotal oedema = 5/43 (12%) Incontinence = 4/43 (9%) Lower tract infection = 4/43 (9%) Haematoma = 2/43 (5%) Obstruction = 2/43 (5%) Urinary urgency = 2/43 (5%) Urethral stricture = 2/43 (5%) Death = 0	Potential for bias: first 25 cases treated with CMS AccuProbe machine; last 18 cases treated with CryoCare Surgical System machine. Patients recruited consecutively. Outcome measures and their validity: Conventional outcome measures. Other comments:
Ghafari et al. ⁴ 2001 USA Oct 1997 – Sept 2000 38 patients Selection criteria: clinically localised, stages T1-T3, radioresistant, recurrent prostate cancer. Follow up: mean 20.7 months	1 distant disease developed in penis bRFS was 86% at 12 months and 74% at 24 months	Incontinence = 3/38 (8%) Urinary tract infection = 1/38 (3%) Haematuria = 3/38 (8%) Perineal, rectal pain = 15/38 (40%) Lower urinary tract symptoms = 6/38 (16%) Swelling = 4/38 (11%) Death = 0	Potential for bias: Small patient numbers. Patients recruited consecutively. Outcome measures and their validity: Conventional outcome measures. Other comments:
Pisters et al. ⁵ 1997 USA July 1992 – March 1995 150 patients	Biochemical failure = 85/146 (58%) Persistently undetectable PSA = 45/146 (31%) Detectable but stable PSA = 16/146 (11%) Negative biopsy = 85/110 (77%) Mean months to biochemical failure = 6.2 (1.4-25.8) Patients with more extensive prior therapy sig. more likely to have biomechanical failure (71%) than group treated only with prior radiation (54%), p = 0.05	Death = 0/150 Fistula = 2/150 (1%) Osteitis pubis = 4/150 (3%) Prostatic abscess = 1/150 (1%) Obstruction requiring transurethral prostatectomy = 25/150 (17%) Obstruction requiring urethral catheterisation = 40/150 (27%) Incontinence = 73%	Potential for bias: Unknown whether patients were recruited consecutively. Outcome measures and their validity: American Urological Association symptom score of unknown validity. Other comments: Patients were analysed in two

Study details	Key efficacy findings	Key safety findings	Appraisal/Comments
Selection criteria: biopsy proved locally recurrent prostate cancer with no clinical evidence of active metastatic disease.		American Urological Association symptom score <10 = 33%; 10 – 20 = 38%; >20 = 29% Perineal pain = 18% Impotence = 72% Any debris = 22%	groups, depending on whether they underwent prior radiation therapy or more extensive prior therapies, including various combinations of radiation, hormonal or chemotherapy.
Follow up: mean 13.5 months			

Specialist Advisor's opinions

Specialist advice was sought from consultants who have been nominated or ratified by their specialist society or Royal College.

The opinion of the Specialist Advisors was that

- The procedure is novel.
- Performed by a very small number of surgeons at a limited number of centres.
- Would have only minor impact on the NHS as a whole.
- Main potential adverse effects of the procedure are urinary incontinence, impotence and rectal damage/fistulation.
- Cancer control is uncertain.
- The procedure requires a significant degree of expertise in probe placement.
- Because of the lack of expertise in the UK in this procedure, training would have to be conducted overseas, principally in North America.
- The Advisors were unaware of any major trials or registries of the procedure.
- There is no regulation of the initiation of this procedure.
- Not known if the procedure warrants its own code.

Issues for consideration by IPAC

The Alberta Heritage Foundation for Medical Research released a Technote on Cryosurgery for Prostate Cancer in May 2002 (TN 35), which summarises some literature and combines this with expert opinion. While acknowledging that cryosurgery shows promise, the Technote concludes that better quality studies are required. It also notes that the USA FDA approved the technology in 1997, and that a randomised controlled trial is underway at the Tom Baker Centre.

Included studies

1. Bales GT, Williams MJ, Sinner M, Thisted RA, et al. Short-term outcomes after cryosurgical ablation of the prostate in men with recurrent prostate carcinoma following radiation therapy. *Urology* 1995; 46(5):676-80.
2. Chin JL, Pautler SE, Mouraviev V, Touma N, et al. Results of salvage cryoablation of the prostate after radiation: Identifying predictors of treatment failure and complications. *Journal of Urology* 2001; 165(6 Part 1):1937-41.
3. De La Taille A, Hayek O, Benson MC, Bagiella E, et al. Salvage cryotherapy for recurrent prostate cancer after radiation therapy: The Columbia experience. *Urology* 2000; 55(1):79-84.
4. Ghafar MA, Johnson CW, De La TA, Benson MC, et al. Salvage cryotherapy using an argon based system for locally recurrent prostate cancer after radiation therapy: The Columbia experience. *Journal of Urology* 2001; 166(4):1333-7.
5. Pisters LL, Voneschenbach AC, Scott SM, Swanson DA, et al. The efficacy and complications of salvage cryotherapy of the prostate. *Journal of Urology* 1997; 157(3):921-5.

Appendix: Studies that met the inclusion criteria but were not tabulated.

Greene GF, Pisters LL, Scott SM, Voneschenbach AC. Predictive value of prostate specific antigen nadir after salvage cryotherapy. *Journal of Urology* 1998; 160(1):86-90.

Ellis DS. Cryosurgery as primary treatment for localized prostate cancer: A community hospital experience. *Urology* 2002; 60(2A Suppl S):34-9.

Cespedes RD, Pisters LL, von Eschenbach AC, McGuire EJ. Long-term follow up of incontinence and obstruction after salvage cryosurgical ablation of the prostate: results in 143 patients. *Journal of Urology* 1997; 157:237-40.

Pisters LL, Perrotte P, Scott SM, Greene GF, et al. Patient selection for salvage cryotherapy for locally recurrent prostate cancer after radiation therapy. *Journal of Clinical Oncology* 1999; 17:2514-20.

Perrotte P, Litwin MS, McGuire EJ, Scott SM, et al. Quality of life after salvage cryotherapy: The impact of treatment parameters. *Journal of Urology* 1999; 162(2):398-402.

Sesia G, Ferrando U, Fontana G, Laudi M, et al. Palliative cryotherapy in inoperable prostate carcinoma. *Recent Results in Cancer Research* 1977;(60):84-90.

Sesia G, Ferrando U, Fontana G, Favro PG. Long-term results of cryotherapy in the management of inoperable carcinoma of the prostate. *Panminerva Medica* 1975; 17(11-12):390-1.

Watanabe T, Rivas DA, Miettinen M, Gomella L, et al. Total incontinence secondary to sphincter destruction after prostate cryotherapy for recurrent prostatic carcinoma. *International Journal of Urology* 1996; Vol 3(4):324-5.

Zisman A, Pantuck AJ, Cohen JK, Beldegrun AS. Prostate cryoablation using direct transperineal placement of ultrathin probes through a 17-gauge brachytherapy template - Technique and preliminary results. *Urology* 2001; 58(6):988-93.