

NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedures overview of low dose rate brachytherapy for localised prostate cancer

Introduction

This overview has been prepared to assist members of the Interventional Procedures Advisory Committee in making recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in January 2005

Procedure name

Low dose rate brachytherapy for prostate cancer
Interstitial irradiation for prostate cancer

Specialty societies

British Society of Interventional radiologists

British Association of Urological Surgeons

Royal College of Radiologists

Institute of Physics and Engineering in Medicine

Description

Indications:

Prostate cancer is one of the most common cancers in men. It tends to affect older men, with the risk rising with age. It is not a single disease entity but may be indicated from an incidental biopsy finding to presentation with metastatic prostate cancer, which may or may not cause any symptoms or shorten life.

Symptoms when they occur include urinary outflow obstruction and features of metastases, such as bone pain.

Current treatment and alternatives

Prognosis with prostate cancer is variable and depends on the grade of the tumour and stage of the diagnosed cancer. The American Cancer Society estimate that 98%

of men survive at least 5 years, 84% survive at least 10 years, and 56% survive at least 15 years. Comparative figures from Cancer Research UK estimate survival to be 80%, 61%, and 49% at these times respectively. Treatment options depend on the stage of the cancer. Current treatments for localised prostate cancer include watchful waiting, radiotherapy, and radical prostatectomy. Metastatic prostate cancer is usually treated with hormone therapy.

What the procedure involves:

Brachytherapy is a form of radiotherapy in which delivery of radiation is targeted directly to the prostate gland through the implantation of small radioactive pellets (called seeds).

Under a general or spinal anaesthetic and ultrasound control needles are inserted through the skin of the perineum, these needles deliver the seeds which are left in place permanently in low dose rate therapy.

Permanent seed implants involve inserting around 50- 100 radioactive seeds (Iodine-125, Palladium-103, or echnogenic Iodine-125) into the prostate gland. These seeds give off radiation at a low dose over several weeks or months.

Low dose rate brachytherapy may be used as a primary therapy (monotherapy), in combination with external beam radiation (EBRT).

Efficacy:

Evaluation of the effectiveness of brachytherapy is made difficult by the diversity of different techniques used, patients population selection criteria (clinical stage, Gleason score, pre-treatment serum PSA, use of adjuvant therapies such as external beam radiation therapy and androgen deprivation therapy (ADT), and different lengths of follow-up. There were no randomised controlled trials between treatment options found in the literature search, and few studies reported follow up to more than 5 years.

A recent, large cohort study comparing almost 3000 patients undergoing brachytherapy (either as monotherapy or combined with external beam radiotherapy), External beam radiotherapy at less than 72Gy, or radical prostatectomy found no difference between procedures in biochemical relapse free survival at 5 or 7 yrs post treatment(1). In another comparative study with 869 patients undergoing brachytherapy the 0.5ng/ml PSA nadir level was reached in 86% (748/869) patients after therapy. However in this study outcomes for radical prostatectomy patients were not recorded past 2 yrs so no comparison of long term effect could be made(2).

In a third study, overall survival to a median 58 months in patients with T1-T2 cancer undergoing brachytherapy was found to be similar in 93% (679/733), radical prostatectomy 96% (721/746), and EBRT 96% (325/340)(3). Physical function scores in 92 patients treated with brachytherapy and 327 by radical prostatectomy showed no significant changes in either group from baseline to 24 months, scores changed from 80.9 to 81.6 points and from 90.2 to 89.7 points respectively(4).

Safety:

Complications are generally not well reported(2;3), however following brachytherapy these can include urinary irritative/obstructive symptoms, rectal symptoms including

storage and retention symptoms and sexual dysfunction. One study in 869 patients undergoing brachytherapy without urinary radical prostatectomy impotency rates were as high as 15%, and incontinence rates were reported to be 1% with to 3 years follow-up (2).

The incidence of these complications should be compared to those for other treatment options such as external beam radiotherapy, or radical prostatectomy.

The HTA reports on 2 case series that show disease specific QOL to be lower in patients receiving brachytherapy than those undergoing external beam radiation therapy alone and against a healthy population(5)

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to brachytherapy for prostate cancer. Searches were conducted via the following databases, covering the period from their from 01/01/2002 to 14/06/2004 MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and Science Citation Index. Trial registries and the Internet were also searched. No language restriction was applied to the searches.

The following selection criteria (Table 1) were applied to the abstracts identified by the literature search. Where these criteria could not be determined from the abstracts the full paper was retrieved

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising methodology.
Patient	Patients with localised prostate cancer
Intervention/test	Brachytherapy (low dose rate, or studies including cases of either low or high dose rate which is not differentiated in analysis)
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy. Key efficacy outcomes include: <ul style="list-style-type: none"> - PSA relapse free survival - Disease free survival - Overall survival - Quality of life Key safety outcomes include: <ul style="list-style-type: none"> - Short/long term gastrointestinal toxicity - Short/long term genitourinary toxicity - Sexual function
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on a systematic review including 24 studies.

An additional 8 studies published after the date of the systematic review are also included in this overview

Existing reviews on this procedure

One health technology assessment reports were identified relevant to this topic.

HTA Review: HTA NHS R&D HTA Programme: Clinical and cost-effectiveness of new and emerging technologies for early localised prostate cancer: a systematic review.

Literature search date: January 2002 and February 2002

Conclusions

Safety:

The evidence in terms of complications is mixed. Existing systematic reviews suggest that brachytherapy results in rates of complications similar to or lower than standard treatments. The rates of complications reported in these reviews were similar to the level 5 primary studies (descriptive case series) presented in the current review. However two matched case-control series suggest that disease-specific QoL is lower among brachytherapy patients than patients receiving external beam radiation therapy alone, or when compared with a healthy population. General HRQoL has been shown to be comparable in brachytherapy to standard treatments and similar to age-matched health controls. Impotence rates for brachytherapy appear to be better than rates of 50% reported for radical prostatectomy.

Effectiveness

Evaluation of the effectiveness of brachytherapy is hampered by the diversity of different techniques used, patient population selection criteria (clinical stage, Gleason score, pre-treatment serum PSA), use of adjuvant therapies such as external beam radiation and androgen deprivation therapy, and different lengths of follow-up. Despite a very large literature base identified at the outset, few studies met the inclusion criteria of this review and the majority of these were case series of varying quality.

Studies reporting outcomes over 5 years are rare and the majority of studies use proxies for disease free survival based on serum PSA measurements. Comparisons between brachytherapy and standard treatments are rare and find little difference in outcomes.

Further details of this report are outlined in Table 1

Table 1 Summary of key efficacy and safety findings on brachytherapy (permanent implant)

Abbreviations used: RP – radical prostatectomy; EBRT / XRT – external beam radiation; CRT – conformal radiotherapy; bRFS - Biochemical relapse free survival; bDFS - Biochemical disease free survival; HRQoL – health related quality of life; TURP – transurethral urinary radical prostatectomy

Study Details	Key efficacy findings	Key safety findings	Comments
<p>Hummel et al (2003) (5)</p> <p>Systematic review Literature date: January and February 2002.</p> <p>Systematic reviews (n=4 studies) Crook et al (2001) (Lit search to 1999)</p> <p>Vicini et al (1999) (Lit search to 1988)</p> <p>Vicini et al (1998) (Lit search unclear)</p> <p>Wills & Hailey (1999) (Lit search to 1999)</p> <p>Level 1 evidence (n=2 studies) Merrick et al (2001) 34 patients Wallner et al (2000) 182 patients</p> <p>Level 3 evidence (n=4 studies) Brandeis et al (2000) 256 patients Cha et al (1999) 648 patients Joly et al (1998) 142 patients Wei et al (2002) 1014 patients</p> <p>Level 4 evidence (n=1 study) Schellhammer (2000) 252 patients</p>	<p>Outcomes reported: disease free survival, survival</p> <p>Biochemical disease free survival (bDFS) at 5 years ranged from 57% - 94% and at a 10 years 66% - 92%.</p> <p>One study reported bDFS at 15 years (78%) and two studies reported overall actuarial survival at 5 years (77% and 90%).</p>	<p>Complications: Nine studies reported on morbidity.</p> <p>Brandeis et al – compared brachytherapy and RP. No overall difference in general HRQoL. Urinary symptoms, bowel function, sexual function were worse in brachytherapy group.</p> <p>Two other comparative studies looked at disease specific quality of life.</p> <p>Treatment related complications reported in four case series studies (Level 5)</p> <ul style="list-style-type: none"> - 3 studies reported sexual complications - 3 studies reported genitourinary complications - 2 studies reported gastrointestinal complications <p>Most complications (mainly urinary and bowel) were short-term. Impotence ranged from 15% - 29% of those who were sexually active before treatment.</p>	<p>Primary or secondary cancer not stated.</p> <p>Mix mono and combined therapy, not stated where other treatments failed.</p> <p>The report excludes all level 5 studies with fewer than 100 patients and with follow-up of less than 5 years.</p> <p>Studies were included that evaluated brachytherapy as a monotherapy, in combination with EBRT and with or without androgen deprivation.</p> <p>Many of the studies reported results for patient subgroups and almost all studies commented on the effect of risk factors on prognosis.</p> <p>The in text discussion does not report all the results of the individual studies (these are reported in the data extraction tables)</p> <p>Levels quoted in HTA report: Level1 = RCT's Level2 = Non randomised controlled trials Level3 = Cohort / case control Level4 = Spatial or historically controlled studies Level5 = opinion, descriptive studies, committee reports</p>

Table 1 Summary of key efficacy and safety findings on brachytherapy (permanent implant)

Abbreviations used: RP – radical prostatectomy; EBRT / XRT – external beam radiation; CRT – conformal radiotherapy; bRFS - Biochemical relapse free survival; bDFS - Biochemical disease free survival; HRQoL – health related quality of life; TURP – transurethral urinary radical prostatectomy

Study Details	Key efficacy findings	Key safety findings	Comments
Level 5 evidence (n=13 studies) Blank (2000) 102 patients Blaski et al (2000) 230 patients Brachman et al (2000) 2222 patients Critz et al (1999) 489 patients Galalae et al (1999) 189 patients Grimm et al (2001) 125 patients Percarpio et al (2000) 100 patients Puthawala et al (2001) 536 patients Ragde et al (2001) 769 patients Ragde et al (2000) 229 patients Ragde and Korb (2000) 152 patients Sharkey et al (2000) 780 patients Stokes et al (2000) 540 patients		No long-term gastrointestinal complications were reported. I Incontinence (4%-5%) was associated with patients undergoing TURP before treatment.	Some studies also compared different isotopes.

Table 1 Summary of key efficacy and safety findings on brachytherapy (permanent implant)

Abbreviations used: RP – radical prostatectomy; EBRT / XRT – external beam radiation; CRT – conformal radiotherapy; bRFS - Biochemical relapse free survival; bDFS - Biochemical disease free survival; HRQoL – health related quality of life; TURP – transurethral urinary radical prostatectomy

Study Details	Key efficacy findings	Key safety findings	Comments																		
<p>Kupelian et al (2004) (1)</p> <p>USA</p> <p>2991 consecutive patients</p> <p>1990 - 1998</p> <p>Patients had Stage T1 and T2 adenocarcinoma of the prostate</p> <p>Median follow-up: 56 months (12-145 months)</p>	<p>Outcomes reported: biochemical relapse-free survival</p> <p>Biochemical relapse-free survival</p> <table border="1" data-bbox="562 375 1041 542"> <thead> <tr> <th></th> <th>5 years</th> <th>7 years</th> </tr> </thead> <tbody> <tr> <td>RP</td> <td>81%</td> <td>76%</td> </tr> <tr> <td>EBRT < 72</td> <td>51%</td> <td>47%</td> </tr> <tr> <td>EBRT > 72</td> <td>81%</td> <td>82%</td> </tr> <tr> <td>BT</td> <td>83%</td> <td>76%</td> </tr> <tr> <td>BTRT</td> <td>77%</td> <td>77%</td> </tr> </tbody> </table> <p>Authors report when EBRT < 72 group was removed no difference in biochemical relapse free survival was found between the groups.</p> <p>Multivariate analysis showed pretreatment PSA levels (p<0.001), biopsy Gleason scores (p<0.001) and year of therapy (p<0.001) to be independent predictors of relapse.</p>		5 years	7 years	RP	81%	76%	EBRT < 72	51%	47%	EBRT > 72	81%	82%	BT	83%	76%	BTRT	77%	77%	<p>Complications:</p> <p>Not aim of the paper: authors make no mention of complications.</p>	<p>Primary or secondary cancer not stated.</p> <p>Previous therapy not stated</p> <p>Consecutive patients, selection criteria are not stated.</p> <ul style="list-style-type: none"> - Radical prostatectomy (RP) 1034 patients - External beam radiotherapy (EBRT) < 72 Gy 484 patients - External beam radiotherapy (EBRT) 72 Gy 301 patients - Permanent seed implantation (BT) 950 patients - Combined seeds/EBRT (BTRT) 222 patients <p>None of the patients received adjuvant androgen deprivation for > 6 months.</p> <p>Patients receiving brachytherapy received ¹⁰³Pd and ¹²⁵I.</p> <p>Biochemical relapse free survival (bRFS) was defined as three consecutive rising PSA levels after a nadir for patients receiving brachytherapy and or EBRT (defined differently for RP group).</p> <p>For RP patients biochemical disease</p>
	5 years	7 years																			
RP	81%	76%																			
EBRT < 72	51%	47%																			
EBRT > 72	81%	82%																			
BT	83%	76%																			
BTRT	77%	77%																			

Table 1 Summary of key efficacy and safety findings on brachytherapy (permanent implant)

Abbreviations used: RP – radical prostatectomy; EBRT / XRT – external beam radiation; CRT – conformal radiotherapy; bRFS - Biochemical relapse free survival; bDFS - Biochemical disease free survival; HRQoL – health related quality of life; TURP – transurethral urinary radical prostatectomy

Study Details	Key efficacy findings	Key safety findings	Comments												
<p>Sharkey et al (2002) (2)</p> <p>USA</p> <p>1993 – 2002</p> <p>1077 patients with stage T1 and T2 adenocarcinoma of the prostate.</p> <p>869 patients treated with brachytherapy Mean age: 72.3 years (48-93 years) Mean preoperative PSA levels were 7.2ng/ml (0.0-93 ng/ml)</p> <p>208 patients with prostatectomy Mean age: 63.9 years (28 – 79 years) Mean preoperative PSA levels were 6.8ng/ml (0.0-61 ng/ml)</p> <p>Median follow-up: 3 years (1-7 years)</p> <p>229 brachytherapy and 53 prostatectomy patients were followed up for 5 years or more.</p> <p>Transperineal ultrasound-guided palladium-103 TheraSeed implants.</p>	<p>Outcomes reported: biochemical freedom from recurrence</p> <p>Biochemical relapse-free survival</p> <table border="1"> <thead> <tr> <th></th> <th>3 years</th> <th>5 years</th> <th>7 years</th> </tr> </thead> <tbody> <tr> <td>RP</td> <td>86%</td> <td>81%</td> <td>74%</td> </tr> <tr> <td>BT</td> <td>91%</td> <td>87%</td> <td>76%</td> </tr> </tbody> </table> <p>No statistically significant differences observed.</p> <p>Authors undertook a cox regression on possible prognostic factors. The most significant variable was pretreatment PSA level (95 CI 1.02-1.05) p <0.0001.</p> <p>The 0.5 ng/ml PSA level nadir was achieved by a total of 748/869 (86%) brachytherapy patients - 302 (35%) at 3 months, 295 (34%) at 1 year, 79 (9%) at 2 years, 37 (4%) at 3 years, 14 (2%) at 4 years, 10 (1%) at 5 years, 3 (<1%) at 6 years and 3 (<1%) at 7 years – there were no results past 2 years for patients who had undergone prostatectomy.</p>		3 years	5 years	7 years	RP	86%	81%	74%	BT	91%	87%	76%	<p>Complications</p> <p>Complications reported in the discussion section of the paper and were not recorded as 'preliminary estimates'</p> <p>Brachytherapy Less than 1% incontinence (patients not having TURP) Less than 5% with a prior resection Impotence 10-15%</p> <p>Prostatectomy Incidence of incontinence is less than 1% Incidence of impotence is less than 45%</p>	<p>Organ specific disease</p> <p>No details of previous therapy</p> <p>Retrospective</p> <p>Patients in the prostatectomy group were slightly younger and were at higher risk.</p> <p>Different methods of defining recurrence: In the brachytherapy group a PSA level greater than 1.5 and a positive biopsy was considered a recurrence, for the surgery group a PSA level greater than 0.2ng/ml was considered a recurrence.</p> <p>Complications were not reported or described well.</p> <p>62 deaths in the brachytherapy group and none in the prostatectomy group. Patients who died without having recurred were considered censored at the date last seen – all mortalities were due to reasons other than prostate cancer.</p> <p>7 years results only based on a subset of patients with enough follow-up.</p> <p>Authors note that they are currently understanding a prospective analysis.</p>
	3 years	5 years	7 years												
RP	86%	81%	74%												
BT	91%	87%	76%												

Table 1 Summary of key efficacy and safety findings on brachytherapy (permanent implant)

Abbreviations used: RP – radical prostatectomy; EBRT / XRT – external beam radiation; CRT – conformal radiotherapy; bRFS - Biochemical relapse free survival; bDFS - Biochemical disease free survival; HRQoL – health related quality of life; TURP – transurethral urinary radical prostatectomy

Study Details	Key efficacy findings	Key safety findings	Comments																														
<p>Potters et al (2004) (3) USA 1992 – 1998</p> <p>1819 patients with T1 or T2 cancer of the prostate - 733 patients treated with brachytherapy (BT) by either I-125 or Pd-103 implant - 746 patients underwent radical prostatectomy - 340 patients underwent external beam radiation (median dose of 74 Gy)</p> <p>Mean age: 65.9 years</p> <p>Median follow-up: 58 months (range 1-134 months)</p>	<p>Outcomes reported: freedom from biochemical recurrence (FBR), survival</p> <table border="1"> <thead> <tr> <th>Outcome</th> <th>BT</th> <th>RP</th> <th>RT</th> <th>All</th> </tr> </thead> <tbody> <tr> <td>FBR</td> <td>614 (84%)</td> <td>621 (83%)</td> <td>268 (79%)</td> <td>1503 (83%)</td> </tr> <tr> <td>Overall survival</td> <td>679 (93%)</td> <td>721 (96%)</td> <td>325 (96%)</td> <td>1724 (95%)</td> </tr> <tr> <td>Dead – no evidence of disease</td> <td>51 (7%)</td> <td>11 (1.5%)</td> <td>11 (3%)</td> <td>73 (4%)</td> </tr> <tr> <td>Dead of disease</td> <td>2 (0.3%)</td> <td>3 (0.4%)</td> <td>4 (2%)</td> <td>9 (0.7%)</td> </tr> <tr> <td>Dead unknown</td> <td>1 (0.1%)</td> <td>11 (1.5%)</td> <td>0 (0%)</td> <td>12 (0.7%)</td> </tr> </tbody> </table>	Outcome	BT	RP	RT	All	FBR	614 (84%)	621 (83%)	268 (79%)	1503 (83%)	Overall survival	679 (93%)	721 (96%)	325 (96%)	1724 (95%)	Dead – no evidence of disease	51 (7%)	11 (1.5%)	11 (3%)	73 (4%)	Dead of disease	2 (0.3%)	3 (0.4%)	4 (2%)	9 (0.7%)	Dead unknown	1 (0.1%)	11 (1.5%)	0 (0%)	12 (0.7%)	<p>Complications: Authors do not report on complications</p>	<p>Not stated whether primary or secondary cancer</p> <p>No adjuvant therapy allowed</p> <p>Patients were excluded if where there was no data on pre-treatment PSA, Gleason scores and no follow-up. Patients who received neoadjuvant or adjuvant therapy were also excluded from the analysis.</p> <p>Unclear as to how patients were chosen for treatment options.</p> <p>Freedom from biochemical recurrence for patients undergoing BT and RT was defined as three consecutive PSA rises (defined differently for RP group)</p> <p>Authors note that biochemical outcomes is primarily determined by pre-treatment PSA levels and biopsy Gleason score.</p>
Outcome	BT	RP	RT	All																													
FBR	614 (84%)	621 (83%)	268 (79%)	1503 (83%)																													
Overall survival	679 (93%)	721 (96%)	325 (96%)	1724 (95%)																													
Dead – no evidence of disease	51 (7%)	11 (1.5%)	11 (3%)	73 (4%)																													
Dead of disease	2 (0.3%)	3 (0.4%)	4 (2%)	9 (0.7%)																													
Dead unknown	1 (0.1%)	11 (1.5%)	0 (0%)	12 (0.7%)																													
<p>Henderson et al (2004) (6) UK Case series</p> <p>216 patients with primary prostate cancer.</p> <p>49 patients (23%) had brachytherapy boost after EBRT 154 patients (72%) had neoadjuvant androgen deprivation.</p>	<p>Outcomes reported: PSA levels</p> <p>Median PSA levels at 1, 2, and 3 years were 0.5, 0.4 and 0.1 ng/ml respectively</p> <p>No other outcomes reported</p>	<p>Complications:</p> <p>95% (205/216) patients experienced deterioration in urinary symptoms to clinically significant levels for 9 months after implant</p> <p>Catheterised for any reason 21.3% (45/261) Acute urinary retention 9.3% (20/216)</p>	<p>Primary or secondary cancer not stated. T 1 – 3, N0, M0</p> <p>Previous EBRT 23% Androgen deprivation 73%</p> <p>All patients treated with ¹²⁵I. Patients treated with brachytherapy as a monotherapy received a dose of 145 Gy –those with brachytherapy as a boost</p>																														

Table 1 Summary of key efficacy and safety findings on brachytherapy (permanent implant)

Abbreviations used: RP – radical prostatectomy; EBRT / XRT – external beam radiation; CRT – conformal radiotherapy; bRFS - Biochemical relapse free survival; bDFS - Biochemical disease free survival; HRQoL – health related quality of life; TURP – transurethral urinary radical prostatectomy

Study Details	Key efficacy findings	Key safety findings	Comments
Mean age:64 years Median presenting PSA 7.9ng/ml (1.2-26ng/ml) Minimum 3 month Follow-up		Rectal bleeding / proctitis 5.6% (12/216)	

Study Details	Key efficacy findings	Key safety findings	Comments																																																																	
<p>Downs et al (2003) (4)</p> <p>USA</p> <p>Patients had undergone primary therapy for prostate cancer from June 1995-January 2001</p> <p>92 patients with brachytherapy as monotherapy</p> <p>327 patients treated with radical prostatectomy</p> <p>Technique: Transperineal approach using TRUS. Several different types of implants were used.</p> <p>Mean follow-up:18.0 months in the Brachytherapy group and 20.7 months in the radical prostatectomy group.</p>	<p>Outcomes reported: health related quality of life (SF-36), disease specific health related quality of life (UCLA Prostate Cancer Index).</p> <p>Health related quality of life looked at physical function, role physical, role emotional, vitality, mental health, social function, bodily pain, general health, health 1 year ago.</p> <table border="1" data-bbox="584 411 1272 997"> <thead> <tr> <th>Outcome</th> <th>Prior BT/RP</th> <th>6-12 months</th> <th>12-18 months</th> <th>18-24 months</th> </tr> </thead> <tbody> <tr> <td>Physical function</td> <td>80.9/90.2</td> <td>77.4/88.8</td> <td>79.3/89.8</td> <td>81.3/89.7</td> </tr> <tr> <td>Role physical</td> <td>74.7/82.4</td> <td>67.6/81.3</td> <td>68.8/82.2</td> <td>72.0/81.3</td> </tr> <tr> <td>Emotional</td> <td>86.0/78.9</td> <td>85.7/87.2</td> <td>87.9/86.9</td> <td>87.9/85.6</td> </tr> <tr> <td>Vitality</td> <td>67.0/67.9</td> <td>63.4/67.9</td> <td>62.9/67.0</td> <td>64.4/67.2</td> </tr> <tr> <td>Mental health</td> <td>78.3/76.1</td> <td>80.8/79.7</td> <td>80.5/81.1</td> <td>81.3/78.6</td> </tr> <tr> <td>Social function</td> <td>89.8/87.3</td> <td>89.1/89.3</td> <td>85.8/89.6</td> <td>90.4/87.9</td> </tr> <tr> <td>Bodily pain</td> <td>84.1/86.8</td> <td>78.9/86.3</td> <td>81.7/84.8</td> <td>80.1/85.3</td> </tr> <tr> <td>General health</td> <td>89.8/87.3</td> <td>68.8/75.5</td> <td>67.1/75.2</td> <td>71.1/74.1</td> </tr> <tr> <td>Health 1 year ago</td> <td>84.1/86.8</td> <td>57.0/60.2</td> <td>64.3/69.7</td> <td>61.8/61.3</td> </tr> <tr> <td>MCS</td> <td>53.5/50.1</td> <td>54.3/52.6</td> <td>53.5/52.8</td> <td>54.3/51.8</td> </tr> <tr> <td>PCS</td> <td>48.9/53.1</td> <td>46.7/51.8</td> <td>46.7/51.8</td> <td>47.7/52.0</td> </tr> </tbody> </table> <p>Authors state that patients treated with BT or RP did not differ greatly in general HRQOL after treatment. Both treatment groups showed early functional impairment in most general domains with scores returned to or approaching baseline in most domains 18-24 months after treatment.</p> <p>Disease specific health related quality of life looked at urinary function, urinary bother, bowel function, bowel bother, sexual function, and sexual bother.</p> <table border="1" data-bbox="584 1385 1272 1436"> <thead> <tr> <th>Outcome</th> <th>Prior BT/RP</th> <th>6-12 months</th> <th>12-18 months</th> <th>18-24 months</th> </tr> </thead> </table>	Outcome	Prior BT/RP	6-12 months	12-18 months	18-24 months	Physical function	80.9/90.2	77.4/88.8	79.3/89.8	81.3/89.7	Role physical	74.7/82.4	67.6/81.3	68.8/82.2	72.0/81.3	Emotional	86.0/78.9	85.7/87.2	87.9/86.9	87.9/85.6	Vitality	67.0/67.9	63.4/67.9	62.9/67.0	64.4/67.2	Mental health	78.3/76.1	80.8/79.7	80.5/81.1	81.3/78.6	Social function	89.8/87.3	89.1/89.3	85.8/89.6	90.4/87.9	Bodily pain	84.1/86.8	78.9/86.3	81.7/84.8	80.1/85.3	General health	89.8/87.3	68.8/75.5	67.1/75.2	71.1/74.1	Health 1 year ago	84.1/86.8	57.0/60.2	64.3/69.7	61.8/61.3	MCS	53.5/50.1	54.3/52.6	53.5/52.8	54.3/51.8	PCS	48.9/53.1	46.7/51.8	46.7/51.8	47.7/52.0	Outcome	Prior BT/RP	6-12 months	12-18 months	18-24 months	<p>Complications: (see efficacy section)</p>	<p>Primary cancer not stated, T1-3.</p> <p>Primary mono-therapy.</p> <p>Study population was 4,141 men from the CaPSURE database.</p> <p>Unclear how the got final number in analysis.</p> <p>Patients treated with neoadjuvant hormonal therapy or brachytherapy in combination with external beam radiotherapy were excluded from the study.</p> <p>Total number of questionnaires completed were used to develop mean as such the number of patients surveyed at each time point may represent different patients as well.</p>
Outcome	Prior BT/RP	6-12 months	12-18 months	18-24 months																																																																
Physical function	80.9/90.2	77.4/88.8	79.3/89.8	81.3/89.7																																																																
Role physical	74.7/82.4	67.6/81.3	68.8/82.2	72.0/81.3																																																																
Emotional	86.0/78.9	85.7/87.2	87.9/86.9	87.9/85.6																																																																
Vitality	67.0/67.9	63.4/67.9	62.9/67.0	64.4/67.2																																																																
Mental health	78.3/76.1	80.8/79.7	80.5/81.1	81.3/78.6																																																																
Social function	89.8/87.3	89.1/89.3	85.8/89.6	90.4/87.9																																																																
Bodily pain	84.1/86.8	78.9/86.3	81.7/84.8	80.1/85.3																																																																
General health	89.8/87.3	68.8/75.5	67.1/75.2	71.1/74.1																																																																
Health 1 year ago	84.1/86.8	57.0/60.2	64.3/69.7	61.8/61.3																																																																
MCS	53.5/50.1	54.3/52.6	53.5/52.8	54.3/51.8																																																																
PCS	48.9/53.1	46.7/51.8	46.7/51.8	47.7/52.0																																																																
Outcome	Prior BT/RP	6-12 months	12-18 months	18-24 months																																																																

Study Details	Key efficacy findings	Key safety findings	Comments																														
	<table border="0"> <tr> <td>Urinary function</td> <td>91.7/92.4</td> <td>85.9/75.1</td> <td>84.3/76.0</td> <td>88.1/75.5</td> </tr> <tr> <td>Urinary bother</td> <td>86.5/85.3</td> <td>78.2/79.8</td> <td>78.0/81.8</td> <td>85.6/83.6</td> </tr> <tr> <td>Bowel function</td> <td>89.0/87.9</td> <td>86.2/88.6</td> <td>90.2/88.6</td> <td>89.5/88.3</td> </tr> <tr> <td>Bowel bother</td> <td>90.6/89.5</td> <td>83.1/89.6</td> <td>88.0/89.1</td> <td>87.1/90.6</td> </tr> <tr> <td>Sexual function</td> <td>51.2/59.9</td> <td>38.5/24.2</td> <td>35.6/28.3</td> <td>33.8/28.0</td> </tr> <tr> <td>Sexual bother</td> <td>60.3/67.7</td> <td>44.1/32.4</td> <td>43.9/35.4</td> <td>44.5/38.8</td> </tr> </table> <p>Authors state that by 18 months after treatment no significant change scores differences were detected in patients treated with Brachytherapy.</p>	Urinary function	91.7/92.4	85.9/75.1	84.3/76.0	88.1/75.5	Urinary bother	86.5/85.3	78.2/79.8	78.0/81.8	85.6/83.6	Bowel function	89.0/87.9	86.2/88.6	90.2/88.6	89.5/88.3	Bowel bother	90.6/89.5	83.1/89.6	88.0/89.1	87.1/90.6	Sexual function	51.2/59.9	38.5/24.2	35.6/28.3	33.8/28.0	Sexual bother	60.3/67.7	44.1/32.4	43.9/35.4	44.5/38.8		
Urinary function	91.7/92.4	85.9/75.1	84.3/76.0	88.1/75.5																													
Urinary bother	86.5/85.3	78.2/79.8	78.0/81.8	85.6/83.6																													
Bowel function	89.0/87.9	86.2/88.6	90.2/88.6	89.5/88.3																													
Bowel bother	90.6/89.5	83.1/89.6	88.0/89.1	87.1/90.6																													
Sexual function	51.2/59.9	38.5/24.2	35.6/28.3	33.8/28.0																													
Sexual bother	60.3/67.7	44.1/32.4	43.9/35.4	44.5/38.8																													
<p>Merrick et al (2003) (7)</p> <p>Cross sectional study</p> <p>USA 1995-1998</p> <p>205 patients with T1c-T3 prostate cancer. Mean age at implant: 66.4 years</p> <p>51 patients with newly diagnosed prostate cancer served as controls</p> <p>Mean follow-up: 66.3 months (range 51-89 months)</p> <p>Technology: ¹⁰³ Pd or ¹²⁵ I</p>	<p>Outcomes reported: late urinary morbidity</p> <p>Response rate to questionnaire 95.1% (195/205)</p> <table border="0"> <thead> <tr> <th>Outcomes</th> <th>BT (n=195)</th> <th>Control (n=51)</th> <th>P value</th> </tr> </thead> <tbody> <tr> <td>Function</td> <td>91.5 ± 14.0</td> <td>90.2 ± 13.4</td> <td>0.546</td> </tr> <tr> <td>Bother</td> <td>81.2±14.3</td> <td>82.0±15.4</td> <td>0.756</td> </tr> <tr> <td>Incontinence</td> <td>89.4±18.1</td> <td>86.2±18.1</td> <td>0.269</td> </tr> <tr> <td>Irritation/obstruction</td> <td>84.4±12.2</td> <td>85.7±12.7</td> <td>0.503</td> </tr> <tr> <td>Urinary EPIC average</td> <td>85.5±12.5</td> <td>85.4±13.2</td> <td>0.960</td> </tr> <tr> <td>IPSS</td> <td>7.0±5.0</td> <td>7.2±5.9</td> <td>0.970</td> </tr> </tbody> </table> <p>There were no statistically significant differences found between the two groups in terms of urinary morbidity.</p>	Outcomes	BT (n=195)	Control (n=51)	P value	Function	91.5 ± 14.0	90.2 ± 13.4	0.546	Bother	81.2±14.3	82.0±15.4	0.756	Incontinence	89.4±18.1	86.2±18.1	0.269	Irritation/obstruction	84.4±12.2	85.7±12.7	0.503	Urinary EPIC average	85.5±12.5	85.4±13.2	0.960	IPSS	7.0±5.0	7.2±5.9	0.970	<p>Complications (see efficacy section)</p>	<p>Primary cancer not stated T1-3.</p> <p>Previous therapy not stated</p> <p>High PSA level patients also received EBRT. Hormonal manipulation for cases with poor prognosis</p> <p>Tools used: Expanded Prostate Cancer Index Composite (EPIC), International Prostate Symptom Score (IPSS).</p> <p>Some patients also received supplemental EBRT.</p> <p>Questionnaire was mailed and patients were called if not returned within 4 weeks.</p> <p>Controls were used as no baseline urinary function details were available.</p> <p>Controls were significantly</p>		
Outcomes	BT (n=195)	Control (n=51)	P value																														
Function	91.5 ± 14.0	90.2 ± 13.4	0.546																														
Bother	81.2±14.3	82.0±15.4	0.756																														
Incontinence	89.4±18.1	86.2±18.1	0.269																														
Irritation/obstruction	84.4±12.2	85.7±12.7	0.503																														
Urinary EPIC average	85.5±12.5	85.4±13.2	0.960																														
IPSS	7.0±5.0	7.2±5.9	0.970																														

Study Details	Key efficacy findings	Key safety findings	Comments																																																														
<p>Merrick et al (2003) (8)</p> <p>USA April 1995- February 1998</p> <p>187 patients with T1c-T3 prostate cancer. Mean age at implant: 66.6 years</p> <p>Mean follow-up: 68.3 months (range 54-92 months)</p> <p>Technology: ¹⁰³ Pd or ¹²⁵ I</p>	<p>Outcomes reported: late rectal function</p> <table border="1" data-bbox="584 277 1240 724"> <thead> <tr> <th>Outcomes</th> <th>1999 survey</th> <th>2002 survey</th> <th>P value</th> </tr> </thead> <tbody> <tr> <td>Frequency</td> <td>0.74 ± 0.81</td> <td>0.81 ± 0.76</td> <td>0.18</td> </tr> <tr> <td>Consistency</td> <td>90.2 ± 13.4</td> <td>0.59 ± 0.52</td> <td>0.06</td> </tr> <tr> <td>Urgency</td> <td>90.2 ± 13.4</td> <td>0.66 ± 0.71</td> <td>0.41</td> </tr> <tr> <td>Abdominal discomfort</td> <td>90.2 ± 13.4</td> <td>0.27 ± 0.50</td> <td>1.00</td> </tr> <tr> <td>Hemorrhoidal Discomfort</td> <td>90.2 ± 13.4</td> <td>0.28 ± 0.61</td> <td>0.22</td> </tr> <tr> <td>Rectal bleeding</td> <td>90.2 ± 13.4</td> <td>0.29 ± 0.62</td> <td>0.35</td> </tr> <tr> <td>Continence</td> <td>90.2 ± 13.4</td> <td>0.45 ± 0.64</td> <td>0.37</td> </tr> <tr> <td>Nighttime bowel movement</td> <td>90.2 ± 13.4</td> <td>0.04 ± 0.14</td> <td>0.03</td> </tr> <tr> <td>Completeness</td> <td>90.2 ± 13.4</td> <td>0.54 ± 0.63</td> <td>0.21</td> </tr> <tr> <td>Total score</td> <td>90.2 ± 13.4</td> <td>3.92 ± 2.84</td> <td>0.29</td> </tr> </tbody> </table> <p>In the 2002 study, none of the 187 patients developed ulceration, fistula formation, or required blood transfusion.</p> <p>Compared with the individual mean scores for the six questions improved and remained unchanged for one question (abdominal discomfort) whereas non significant deteriorations in the frequency and continence scores were recorded.</p> <p>Specific results: (not presented for all questions)</p> <table border="1" data-bbox="584 999 1211 1110"> <tbody> <tr> <td>Change in bowel function</td> <td>1999</td> <td>2002</td> </tr> <tr> <td>Better</td> <td>12%</td> <td>15%</td> </tr> <tr> <td>Same</td> <td>69%</td> <td>73%</td> </tr> <tr> <td>Worse</td> <td>19%</td> <td>12%</td> </tr> </tbody> </table> <table border="1" data-bbox="584 1139 1211 1193"> <tbody> <tr> <td>Rectal bleeding</td> <td>1999</td> <td>2002</td> </tr> <tr> <td>No bleeding</td> <td>74.3%</td> <td>78.6%</td> </tr> </tbody> </table>	Outcomes	1999 survey	2002 survey	P value	Frequency	0.74 ± 0.81	0.81 ± 0.76	0.18	Consistency	90.2 ± 13.4	0.59 ± 0.52	0.06	Urgency	90.2 ± 13.4	0.66 ± 0.71	0.41	Abdominal discomfort	90.2 ± 13.4	0.27 ± 0.50	1.00	Hemorrhoidal Discomfort	90.2 ± 13.4	0.28 ± 0.61	0.22	Rectal bleeding	90.2 ± 13.4	0.29 ± 0.62	0.35	Continence	90.2 ± 13.4	0.45 ± 0.64	0.37	Nighttime bowel movement	90.2 ± 13.4	0.04 ± 0.14	0.03	Completeness	90.2 ± 13.4	0.54 ± 0.63	0.21	Total score	90.2 ± 13.4	3.92 ± 2.84	0.29	Change in bowel function	1999	2002	Better	12%	15%	Same	69%	73%	Worse	19%	12%	Rectal bleeding	1999	2002	No bleeding	74.3%	78.6%	<p>Complications (see efficacy section)</p>	<p>different in terms of Gleason score and pre-treatment PSA.</p> <p>Primary cancer not stated T1-3.</p> <p>Previous therapy not stated</p> <p>High PSA level patients also received EBRT. Hormonal manipulation for cases with poor prognosis</p> <p>Tools used: rectal function assessment score.</p> <p>Some patients had brachytherapy as a boost.</p> <p>Original patient population (baseline questionnaires was 209) – some patients had subsequently died.</p> <p>Only two questions had specific results described in the text of the paper.</p>
Outcomes	1999 survey	2002 survey	P value																																																														
Frequency	0.74 ± 0.81	0.81 ± 0.76	0.18																																																														
Consistency	90.2 ± 13.4	0.59 ± 0.52	0.06																																																														
Urgency	90.2 ± 13.4	0.66 ± 0.71	0.41																																																														
Abdominal discomfort	90.2 ± 13.4	0.27 ± 0.50	1.00																																																														
Hemorrhoidal Discomfort	90.2 ± 13.4	0.28 ± 0.61	0.22																																																														
Rectal bleeding	90.2 ± 13.4	0.29 ± 0.62	0.35																																																														
Continence	90.2 ± 13.4	0.45 ± 0.64	0.37																																																														
Nighttime bowel movement	90.2 ± 13.4	0.04 ± 0.14	0.03																																																														
Completeness	90.2 ± 13.4	0.54 ± 0.63	0.21																																																														
Total score	90.2 ± 13.4	3.92 ± 2.84	0.29																																																														
Change in bowel function	1999	2002																																																															
Better	12%	15%																																																															
Same	69%	73%																																																															
Worse	19%	12%																																																															
Rectal bleeding	1999	2002																																																															
No bleeding	74.3%	78.6%																																																															
<p>Litwin M S (2004)(9)</p> <p>Cohort study CaPSURE</p> <p>USA</p> <p>31 participating sites,</p>	<p>At baseline, immediately after surgery and every 3 to 6 months participants completed a self-evaluation questionnaire, the validated UCLA prostate cancer index. General QOL was assessed by the SF-36, and co-morbidity with a 12 item medical history checklist</p> <p>Bowel function scores Bowel function is assessed in terms of rectal urgency, loose</p>	<p>(see efficacy section)</p>	<p>Primary (localised) cancer within 6months of diagnosis</p> <p>Previous treatment not stated, but probably none given time constraints.</p> <p>No details of loss to follow up</p>																																																														

Study Details	Key efficacy findings	Key safety findings	Comments																																
<p>consecutively recruited by participating urologists</p> <p>n=1,584 radical prostatectomy (RP) = 1,276 external beam radiation (XRT) = 99 brachytherapy = 209</p> <p>Patients chose therapy option and were treated according to usual practices</p> <p>Inclusion criteria: clinically localised prostate cancer within 6 months of diagnosis</p> <p>2 years follow up (minimum)</p> <p>Age =64yrs, Male = 100%, White =84%, Tumor stage T1 =42%, T2 =55%, T3 =2%</p> <p>Significant factors in univariate analysis (age, PSA level at diagnosis, and biopsy Gleason score) were entered into multivariate ANOVA model.</p>	<p>stools, cramping pelvic pain, and occasional rectal bleeding. Initial scores post procedure showed a significant advantage with RP over XRT and Brachytherapy (P<0.001), these higher scores persisted at 3 months and through to 24 months.</p> <table border="1" data-bbox="577 300 1279 443"> <thead> <tr> <th></th> <th>RP</th> <th>XRT</th> <th>Brachy</th> </tr> </thead> <tbody> <tr> <td>Quarter 0</td> <td>75±1.2</td> <td>60±2.1</td> <td>68±2.1</td> </tr> <tr> <td>Quarter 1</td> <td>84±1.2</td> <td>73±2.2</td> <td>77±2.0</td> </tr> <tr> <td>Quarter 8</td> <td>84±1.4</td> <td>78±2.8</td> <td>80±3.3</td> </tr> </tbody> </table> <p>(scores 0 to 100 (±SE) higher scores better outcome)</p> <p>Bowel bother scores Bowel bother is defined as distress or annoyance caused by impairments in bowel function. Post-operatively the bowel bother scores for RP were significantly better than for XRT and Brachytherapy (p<0.001). This remained a significant difference Vs XRT but not Vs Brachytherapy through to 24 months</p> <table border="1" data-bbox="577 691 1279 834"> <thead> <tr> <th></th> <th>RP</th> <th>XRT</th> <th>Brachy</th> </tr> </thead> <tbody> <tr> <td>Quarter 0</td> <td>74±1.7</td> <td>50±3.0</td> <td>61±3.0</td> </tr> <tr> <td>Quarter 1</td> <td>83±1.8</td> <td>67±3.2</td> <td>76±2.8</td> </tr> <tr> <td>Quarter 8</td> <td>83±2.0</td> <td>73±3.9</td> <td>80±4.7</td> </tr> </tbody> </table> <p>(scores 0 to 100 (±SE) higher scores better outcome)</p>		RP	XRT	Brachy	Quarter 0	75±1.2	60±2.1	68±2.1	Quarter 1	84±1.2	73±2.2	77±2.0	Quarter 8	84±1.4	78±2.8	80±3.3		RP	XRT	Brachy	Quarter 0	74±1.7	50±3.0	61±3.0	Quarter 1	83±1.8	67±3.2	76±2.8	Quarter 8	83±2.0	73±3.9	80±4.7		<p>Not randomised sample, with potential for clinicians involved to sway treatment option</p> <p>Incomparable baseline demographic and clinical outcomes may not be adjusted for adequately in analysis.</p> <p>RP group were significantly younger mean 61.2 yrs VS XRT group 70.9yrs, VS Brachy group =68.6 yrs (p<0.0001), and had a lower comorbidity count (p<0.0001)</p> <p>The XRT group had a significantly higher Gleason scores than the other two groups (p<0.0001)</p> <p>The demographic homogeneity of the study cohort might limit generalisability of findings</p> <p>Study examined the treatment of early stage prostate cancer only.</p>
	RP	XRT	Brachy																																
Quarter 0	75±1.2	60±2.1	68±2.1																																
Quarter 1	84±1.2	73±2.2	77±2.0																																
Quarter 8	84±1.4	78±2.8	80±3.3																																
	RP	XRT	Brachy																																
Quarter 0	74±1.7	50±3.0	61±3.0																																
Quarter 1	83±1.8	67±3.2	76±2.8																																
Quarter 8	83±2.0	73±3.9	80±4.7																																

Validity and generalisability of the studies

Factors that limit generalisability of evidence.

- One of the major difficulties in assessing the literature on this procedure is the different clinical scenarios for which brachytherapy is used to treat patients with localised prostate cancer.
- The studies use a variety of seeds between trials, and the number of seeds implanted may vary.
- These studies rely on biochemical failure as a surrogate marker rather than metastasis-free or overall survival as an end point.
- Different definitions of biochemical disease free survival (e.g. nadir, ASC)
- Patient selection bias may exist where prognostic features are used to select for treatment modality.
- There is potential variation in efficacy for low risk and high risk patients
- The tumour stage varies from study to study, most patients had early localised prostate cancer T1-T2, although some studies did include a proportion of patients with T3 disease
- Other characteristics such as initial PSA and Gleason score varied among the studies.
- USA data may not be generalisable to UK

Specialist advisors' opinions

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

All the advisors considered the procedure to be an established practice, despite most of them confirming that it is being undertaken by less than 10 % of specialists in their field.

In terms of efficacy it was felt that brachytherapy was the equal of radical prostatectomy or external beam therapy in well selected patients.

Advisors confirmed short term adverse events to include acute retention, and temporary urethritis. Other complications may include incontinence, erectile dysfunction, proctitis, or fistulation of the urinary or GI tract.

Uncertainty remains regarding the comparability of tumour volume reduction and mortality outcomes, potential seed migration to lungs, and the use of adjuvant treatments for patients at increased risk. It was commented that there is a need to consider low and high dose rate therapy separately.

There were concerns of inadequate dosing particularly by clinicians new to the procedure, but this can be improved by the use of software. In addition seed

migration within the prostate to other body sites is also a concern but may be overcome with the introduction of biodegradable catheters.

There were clear signals that well conducted training programmes are required for the development of this procedure. It was anticipated that the procedure would be used in 'a minority of hospitals in the UK, but at least 10'. There is need for inter-speciality collaboration between radiologist, urologist, and oncologist.

Issues for consideration by IPAC

A randomised controlled trial (SPIRIT) was initiated to compare radical prostatectomy versus brachytherapy for patients with T1c or T2a N0 M0 prostate cancer. However despite enthusiasm in the UK for this trial the central administration in the US (ACOSOG) have confirmed that the SPIRIT trial has now closed (www.ncrn.org.uk accessed 26th April 2004). The decision to close was based on extremely slow accrual with only 56 of the necessary 1980 patients currently recruited to date.

NICE Clinical Guideline – Prostate cancer: diagnosis and treatment.

The NICE clinical guideline on prostate cancer is currently in the scoping phase, issues for consideration may include the following

- Low dose versus high dose therapy
- Comparison of available therapies for prostate cancer.

Reference List

- (1) Kupelian PA, Potters L, Khuntia D, Ciezki JP, Reddy CA, Reuther AM et al. Radical prostatectomy, external beam radiotherapy <72 Gy, external beam radiotherapy > or =72 Gy, permanent seed implantation, or combined seeds/external beam radiotherapy for stage T1-T2 prostate cancer. *International Journal of Radiation Oncology, Biology, Physics* 2004; 58(1):25-33.
- (2) Sharkey J, Cantor A, Solc Z, Huff W, Chovnick SD, Behar RJ et al. Brachytherapy versus radical prostatectomy in patients with clinically localized prostate cancer. *Current Urology Reports* 2002; 3(3):250-257.
- (3) Potters L, Klein E, Kattan M, Reddy CA, Ciezki J, Reuther AM et al. Monotherapy for stage T1-T2 prostate cancer: radical prostatectomy, external beam radiotherapy, or permanent seed implantation. *Radiotherapy & Oncology* 2004; 71:29-33.
- (4) Downs TM, Sadetsky N, Pasta DJ, Grossfeld GD, Kane CJ, Mehta SS et al. Health related quality of life patterns in patients treated with interstitial prostate brachytherapy for localized prostate cancer--data from CaPSURE.[see comment]. *Journal of Urology* 2003; 170(5):1822-1827.
- (5) Hummel S, Paisley S, Morgan A, Currie E, Brewer N. Clinical and cost-effectiveness of new and emerging technologies for early localised prostate cancer: a systematic review. [Review] [175 refs]. *Health Technology Assessment (Winchester, England)* 2001; 7(33):iii-ix.
- (6) Henderson A, Ismail AKA, Cunningham M, Aldridge S, Loverock L, Langley SEM et al. Toxicity and Early Biochemical Outcomes From 125Iodine Prostate Brachytherapy in the U.K.: A Prospective Study. *Clinical Oncology* 2004; 16(2):95-104.
- (7) Merrick GS, Butler WM, Wallner KE, Galbreath RW, Lief JH. Long-term urinary quality of life after permanent prostate brachytherapy. *International Journal of Radiation Oncology*Biography*Physics* 2003; 56(2):454-461.
- (8) Merrick GS, Butler WM, Wallner KE, Hines AL, Allen Z. Late rectal function after prostate brachytherapy. *International Journal of Radiation Oncology, Biology, Physics* 2003; 57(1):42-48.
- (9) Litwin MS, Sadetsky N, Pasta DJ, Lubeck DP. Bowel function and bother after treatment for early stage prostate cancer: a longitudinal quality of life analysis from CaPSURE. *J Urol* 2004; 172(2):515-519.

Appendix A: Additional papers on selective international radiation therapy not included in the summary tables

Article title	Number of patients/follow-up	Comments	Direction of conclusions
Merrick GS, Wallner KE, Butler WM. Permanent interstitial brachytherapy for the management of carcinoma of the prostate gland. [Review] [75 refs]. Journal of Urology 2003; 169(5):1643-1652	N/A	Review paper	Refinements of brachytherapy process may improve biochemical and QOL outcomes
Norderhaug I, Dahl O, Hoisaeter PA, Heikkila R, Klepp O, Olsen DR et al. Brachytherapy for Prostate Cancer: A Systematic Review of Clinical and Cost Effectiveness. European Urology 2003; 44(1):40-46	N/A	Review paper	Efficacy of brachytherapy appears to be similar to surgery or EBRT
Potters L, Fearn P, Kattan MW. External radiotherapy and permanent prostate brachytherapy in patients with localized prostate cancer. Brachytherapy 2002; 1(1).	n=1476 6 yrs	Case series	A comparative trial between treatment options is necessary to examine efficacy
Kollmeier MA, Stock RG, Stone N. Biochemical outcomes after prostate brachytherapy with 5-year minimal follow-up: Importance of patient selection and implant quality. International Journal of Radiation Oncology*Biophysics*Physics 2003; 57(3):645-653	n=243 5yrs	Case series	Support the use of brachytherapy in low risk patients
Henderson A, Laing RW, Langley SEM. Quality of Life Following Treatment for Early Prostate Cancer: Does Low Dose Rate (LDR) Brachytherapy Offer a Better Outcome? A Review. European Urology 2004; 45(2):134-141	N/A	Review	Quality of life following brachytherapy compares favourably with other radical treatment options in managing of early prostate cancer
Robinson JW, Moritz S, Fung T. Meta-analysis of rates of erectile function after treatment of localized prostate carcinoma. International Journal of Radiation Oncology, Biology, Physics 2002; 54(4):1063-1068.	54 articles	Meta-analysis	Only looking at outcome of erectile dysfunction after brachytherapy with or without ERBT
Stone NN, Stock RG. Complications following permanent prostate brachytherapy. [Review] [50 refs]. European Urology 2002; 41(4):427-433	N/A	Review	Urinary retention occurred in 1.5-22% of the patients postimplant
Kang SK, Chou RH, Dodge RK, Clough RW, Kang HS, Hahn CA et al. Gastrointestinal toxicity of transperineal interstitial prostate brachytherapy. International Journal of Radiation Oncology, Biology, Physics 2002; 53(1):99-103	n=134	Case series	There is a small risk of severe late toxicity. External beam radiation and higher stage were related to toxicity
Albert M, Tempany CM, Schultz D, Chen MH, Cormack RA, Kumar S et al. Late genitourinary and gastrointestinal toxicity after magnetic resonance image-guided prostate brachytherapy with or without neoadjuvant external beam radiation therapy. Cancer 2003; 98(5):949-954	n=201 median 2.8 yrs	Case series	Rate of rectal bleeding requiring coagulation in Brachytherapy patients compared with patients with additional ERBT

			was 8% versus 30%, respectively (log-rank P value = 0.0001)
--	--	--	---

Appendix B: Literature search for low dose rate brachytherapy for localised prostate cancer

The following search strategy was used to identify papers in Medline. A similar strategy was used to identify papers in EMBASE, Current Contents, PredMedline and all EMB databases.

For all other databases a simple search strategy using the key words in the title was employed. Studies relating to low dose rate brachytherapy were selected by eye.

	Search History	Results	Display
1	exp Prostatic Neoplasms/	20396	Display
2	exp NEOPLASMS/	471646	Display
3	exp CARCINOMA/	103542	Display
4	exp ADENOCARCINOMA/	61255	Display
5	or/2-4	471646	Display
6	exp Prostatic Diseases/	24475	Display
7	exp PROSTATE/	5212	Display
8	or/6-7	26529	Display
9	5 and 8	20685	Display
10	((carcinoma or neoplasia or neoplasm\$ or adenocarcinoma or cancer\$ or tumor\$ or tumour\$ or malignan\$) adj3 prostat\$).tw.	20502	Display
11	1 or 9 or 10	24079	Display
12	exp BRACHYTHERAPY/	4102	Display
13	brachytherap\$.tw.	3328	Display
14	12 or 13	4679	Display
15	11 and 14	1012	Display
16	limit 15 to yr=2002-2004	367	Display
17	limit 16 to (human and english language)	321	Display
18	comment.pt.	151153	Display
19	17 not 18	308	Display
20	from 19 keep 1-308	308	Display

