Mira Keyes, MD, FRCPC, James Morris, MD, FRCPC, Tom Pickles, MD, FRCPC, Michael McKenzie, MD, FRCPC

BC Cancer Agency prostate brachytherapy experience: Indications, procedure, and outcomes

The results from a study of men treated in the provincial Prostate Brachytherapy Program are among the best published in the world.

ABSTRACT: Prostate brachytherapy is a standard treatment for early stage, localized prostate cancer. The BC Cancer Agency Prostate Brachytherapy Program was established over 10 years ago. Today, prostate brachytherapy is available in Vancouver, Victoria, Kelowna, and Abbotsford at regional cancer centres. Over 2750 patients have now been treated using uniform patient selection criteria, customized treatment algorithms, and quality control. The program maintains a large prospective database on outcomes and toxicity. Recently published biochemical (PSA) control rates of the first consecutive 1006 patients found a PSA recurrence-free survival rate of 95.6% at median follow-up of 5 years (range 4 to 10 years). Mild to moderate irritative and obstructive urinary symptoms following the procedure are common and subside in the majority of patients by 6 to 12 months. The short-term catheterization rate is 5% to 10%. The transient rectal irritation rate is 20%. Rectal bleeding requiring treatment occurs in 2% to 3% of patients. At 1 year after the implant, 70% to 80% of men retain erectile function; this rate declines to around 50% at 5 years post-implant. Erectile function after the treatment is related to patients' age and pretreatment sexual function.

Dr Keyes is head of the British Columbia Cancer Agency Prostate Brachytherapy Program and associate professor of radiation oncology in the Department of Surgery at the University of British Columbia. Dr Morris is the past program head and an associate professor of radiation oncology in the Department of Surgery at the University of British Columbia. Dr Pickles is a professor of radiation oncology in the Department of Surgery at UBC. Dr McKenzie is a professor of radiation oncology in the Department of Surgery at UBC.

Prostate brachytherapy (PB) is a standard treatment for localized prostate cancer. The procedure uses real-time transrectal ultrasound guidance to place radioactive sources ("seeds" 0.08×4.5 mm in size) directly into the prostate to deliver radiation to the entire prostate plus a margin 3.0 to 5.0 mm beyond the anatomic prostate to account for microscopic extension of tumor. As radiation dose gradients with brachytherapy are very steep, the dose falls off sharply with increasing distance from the source. As a result, the tumor tissue and prostate are treated with very high doses of radiation while the surrounding normal tissues are largely spared from the radiation effect.

A Norwegian group led by Holm pioneered the technique in the late 1970s. Due to technical and imaging limitations at that time and a relatively low radiation dose, the procedure was unable to effect a cure in most cases. A group of Seattle doctors started performing PB in 1987, introducing much higher doses with the help of modern ultrasound and numerous technical refinements. By the mid-1990s, clinical reports from the Seattle group and others demonstrated freedom from recurrence. The conve-

nience of a day-care procedure, fast recovery time, and mild to moderate side effects combined with excellent biochemical and clinical outcomes resulted in a rapid expansion in the use of PB. Today brachytherapy is the primary treatment modality for 30% to 35% of favorable-risk prostate cancer patients in the US (oral communication with Dr Peter Grimm, Seattle Prostate Institute, April 2009), versus 22% in 1999–2001, versus 3% in 1989–1992 (CaPSURE data).[1]

BCCA Prostate Brachytherapy Program

Recognizing the benefits of PB and the need for it to be available within the provincial health care system, radiation oncologists from the BC Cancer Agency (BCCA) established the Prostate Brachytherapy Program in 1997. To date, over 2750 patients have received PB in BC, making it the largest program in Canada and one of the largest in the world. Operating under the BCCA umbrella, 13 radiation oncologists, in conjunction with specially trained medical physicists and radiation therapists, perform implants at BCCA's four regional cancer centres using consistent selection criteria, treatment algorithms, and quality control. The program maintains a large prospective database including patient records that describe disease characteristics (risk stratification), pathology, and technical (dosimetric) details, as well as clinical and biochemical (PSA) data, side effect scores, and complications.

As well as producing this database, the BCCA Prostate Brachytherapy Program has been responsible for 17 peer-reviewed papers and 34 abstracts, numerous oral presentations, many CME lectures, and industry and peer-reviewed funding of $2.5 million for the development of image-guided brachytherapy in collaboration with the Department of Electrical and Computer Engineering at UBC. The program fosters academic thought and teaching, and supports ongoing research, several clinical trials, a fellowship program, and training of radiation oncology residents.

Patient selection

Uniform patient selection criteria were established at the inception of the program and have been followed for the last 10 years. Eligible patients include those meeting all of the Canadian consensus criteria[2] for low-risk disease: clinical stage (CS) ≤ T2a (disease palpable in one prostate lobe), initial PSA ≤ 10 ng/mL, and Gleason score (GS) ≤ 6. In contrast to many Canadian centres, the program includes a subgroup of intermediate-risk patients: CS ≤ T2c (disease palpable in one or both prostate lobes), initial PSA 10 to 15 ng/mL with GS ≤ 6, or GS = 7 with initial PSA ≤ 10 ng/mL.

Androgen suppression (AS) was initially used for those with prostate volume greater than 40 to 45 cc to decrease the prostate size prior to implant or for intermediate-risk features. Today AS is reserved for prostate size greater than 60 to 65 cc and for selected patients with more than 50% of the biopsy cores positive. Recently we have expanded the eligibility criteria to include all patients with intermediate-risk disease: CS ≤ T2c, initial PSA 10 to 20 ng/mL, and GS ≤ 7. Prostate brachytherapy is also used in patients with high-risk disease: CS ≥ T3a (disease palpable outside the prostate), initial PSA > 20 ng/mL, and GS ≥ 8. However, the use of PB in these patients is restricted to those enrolled in a BCCA-led multicentre randomized trial known by the acronym ASCENDE-RT, comparing a brachytherapy boost to an external beam conformal boost after pelvic external beam radiation with neoadjuvant androgen suppression.

The tumor tissue and prostate are treated with very high doses of radiation while the surrounding normal tissues are largely spared from the radiation effect.

Implant procedure and follow-up

The prostate brachytherapy implant is a surgical day-care procedure taking about 1 hour. Patients are discharged home 2 to 3 hours later. The radiation oncologist places the radioactive seeds into the prostate through the perineum, using between 20 and 28 needles, each carrying 2 to 6 seeds

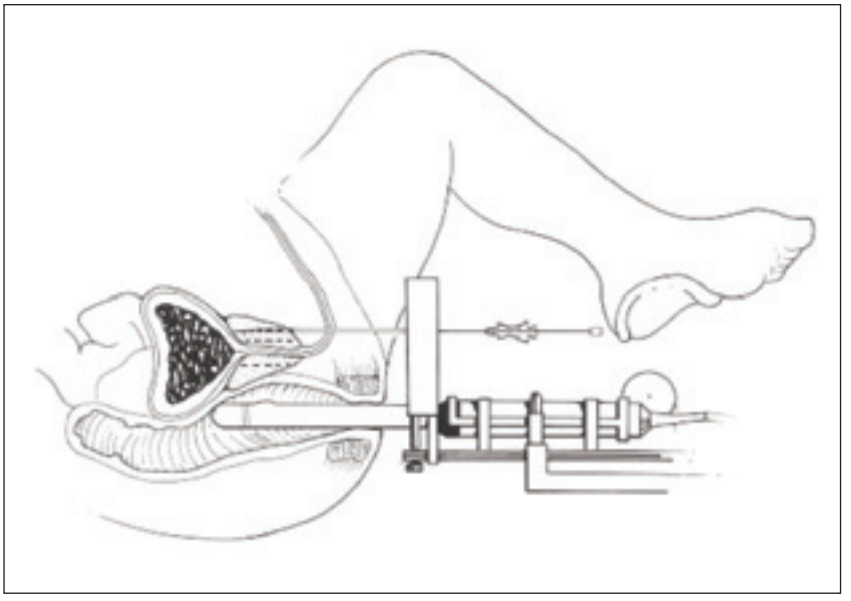

Figure 1. Prostate brachytherapy patient and procedure set-up. Patient in dorsal lithotomy position with ultrasound probe in the rectum, template in front of the perineum, needle and seeds in the prostate.

(**Figure 1**). The seeds are 0.5-cm titanium shells that contain Iodine^{125} (I-125) radioactive silver iodide salt. The half-life of I-125 is 60 days. As radioactive decay is an exponential function, 50% of the radioactivity is released by 2 months, 88% by 6 months, and 99% by 12 months. Steep dose gradients and sharp dose fall around the iodine seeds produce very high radiation dose in the prostate itself and minimal dose in the surrounding normal tissues (**Figure 2**).

The procedure is done using a real-time ultrasound guidance and fluoroscopy. Seeds are placed according to three-dimensional coordinates predetermined by a customized planning algorithm using computer modelling. From 90 to 150 seeds are left permanently in the prostate. Most implants are done with general or spinal anesthesia; occasionally local anesthesia is used. After the implant, a CT scan of the prostate is performed to ensure accurate placement of the seeds and adequate radiation dose distribution within the prostate. This rigorous quality-assurance procedure was built into our program as standard practice from the outset. Very rarely, patients may be asked to undergo a second procedure to have additional seeds placed in the prostate (1 in 200 men).

Patients are seen 6 weeks after the implant, then every 6 months for 2 to 3 years, and then annually. On each visit PSA and testosterone levels are recorded along with toxicity scores, including physician-assessed urinary and rectal toxicity scores based on Radiation Therapy Oncology Group criteria, and patient-assessed urinary (IPSS) and erectile (SHIM) standardized scores.

Patients are advised to refrain from prolonged close contact (< 2 m) with pregnant women and young infants for 3 to 4 months after brachytherapy. Brief contact (sitting at the same dinner table, giving a child a brief cuddle), does not represent a risk. Regarding the general public, there are no restrictions required after the procedure. The radiation exposure to other people is very low; for example, the total dose of radiation that would be received by a man's sleeping partner (assuming an average separation of 1 m for an average of 8 hours per day) is about the same dose that would be received from cosmic radiation exposure during a single round-trip plane ride from New York to Japan.

Side effects

The recovery time after the procedure is short. Most men return to their usual daily activity within days of the procedure. Although severe long-term side effects are rare, patients may experience short-term urinary symptoms, rectal irritation, and sexual dysfunction.

Urinary symptoms

The hallmark of PB toxicity is urinary side effects. Most men will experience some urinary symptoms after the procedure. About 50% will have moderate obstructive and/or irritative urinary symptoms lasting several months. By 12 months, the urinary symptoms of most patients (90%) will return to baseline.[3] At 7 years after PB, 92.5% of patients will have very little or no urinary symptoms at all. Patients with larger prostate volume, worse baseline urinary function, and those given hormone therapy are more likely to have irritative and obstructive urinary symptoms after PB. Patients treated in more recent years have fewer urinary symptoms after PB compared with patients who received implants earlier on in the program, suggesting that greater technical experience in PB is associated with less urinary toxicity.[3]

Five to ten percent of patients will require a Foley catheter for urinary obstruction (most for less than 1 week, 3% of all patients for several weeks or months).[4] Obstruction is seen more often in patients with poorer baseline

urinary function and those with larger prostate volume before implant. Again, patients treated in more recent years have fewer problems with urinary obstruction compared with patients who received implants earlier in the program. For example, the temporary urinary retention rate decreased from 17% in the first 2 years of the program to 6% in subsequent years.[3,4] With greater experience in the program, the overall rate of urinary side effects has declined. Long-term, less than 3% of men can be expected to require urethral dilatation or a transurethral resection of the prostate to relieve obstructive urinary symptoms.

Rectal symptoms

Mild self-limiting rectal irritation affects 20% of patients. Serious rectal injury requiring a major surgical intervention such as colostomy has occurred in only four patients out of more than 2500 treated with brachytherapy at BCCA. It is important for patients to seek advice from BCCA before any procedure (such as a biopsy) in the rectum because high-dose radiation to the rectum can mean that even a relatively small tissue trauma such as rectal biopsy will precipitate development of rectal fistulae. Similarly, laser photocoagulation is only undertaken when conservative measures have failed. One to three percent of patients will have rectal bleeding requiring a laser photocoagulation procedure.[5]

Sexual function

All curative treatments for prostate cancer have a major potential impact on sexual function. Erectile dysfunction (ED) rates in our experience mirror that of elsewhere: at 1 year after the implant, 70% to 80% of men retain erectile function; this rate declines to around 50% at 5 years post-implant. Younger patients and those with better pretreatment erectile function are likely to do better after the treatment.[6] Many patients will have improvement in their function with oral phosphodiesterase5 (PDE-5) inhibitors: sildenafil, vardenafil, tadalafil. Some patients may need to use medication permanently but some only temporarily. Our study has shown that in some men it may take 1 to 2 years to recover sexual function. This is related to the recovery of testosterone levels after any androgen suppression, and may also be related to recovery from needle trauma to erectile tissue. There are no comparative data based on local surgical outcomes for use when advising patients, but most surgical series cite potency preservation rates of 20% to 50%.

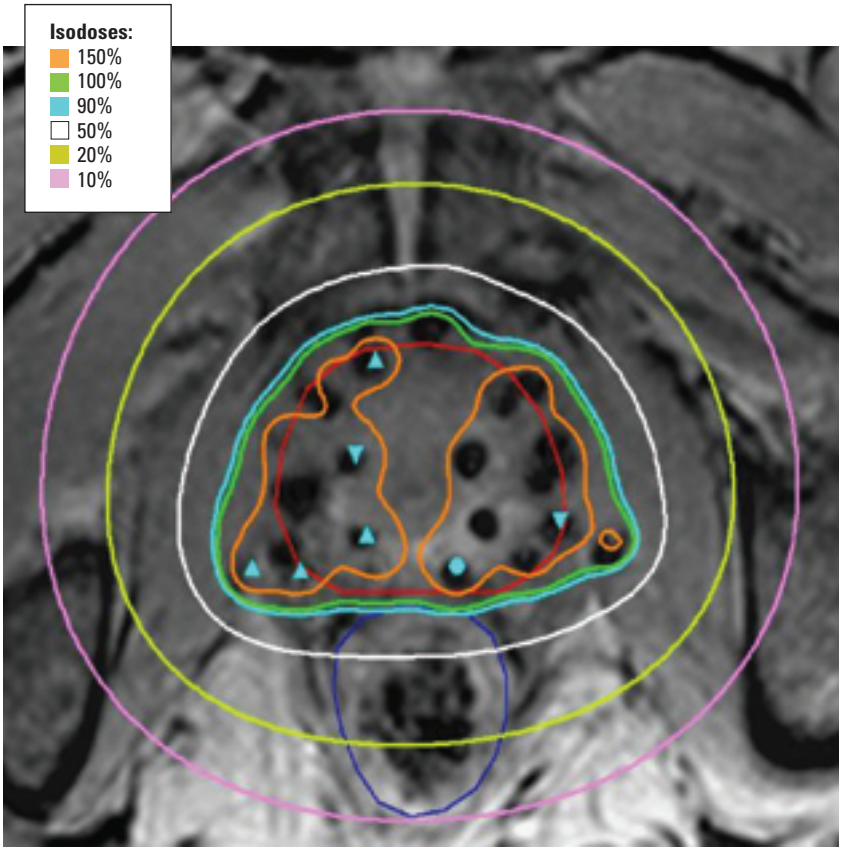

Figure 2. MRI/CT fusion image of the prostate (contours in red), prescription dose 145 Gy (dark green). Rectum outlined in dark blue. The figure illustrates the very steep dose fall-off with prostate brachytherapy and the low radiation dose to surrounding tissues.

PSA outcomes

It is a common practice to inform patients of treatment outcomes using data from other institutions. However, because outcomes in oncology can vary based on experience and expertise, we believe patients should be informed about the predicted outcomes of treatment based on the institutions where they will be treated. The BCCA Prostate Brachytherapy Program has recently published biochemical control rates of the first consecutive 1006 patients; of those, 58% had low-risk and 42% had intermediate-risk disease, and 65% received androgen suppression for 6 months together with the implant (no longer a policy). The results show that after a median follow-up of 5 years (range 4

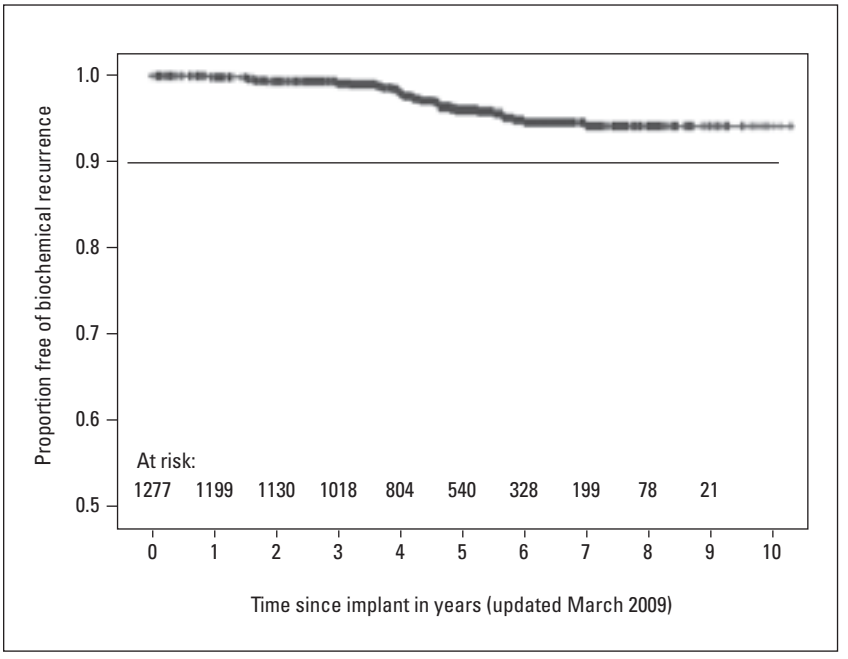

Figure 3. Kaplan-Meier plot of PSA recurrence-free survival as a function of time since implant for all 1277 men treated between 20 July 1998 and 28 February 28, 2005. The 5-year PSA recurrence-free survival rate is 96.0 ± 1.4%; the 8-year rate is 94.1 ± 2.0%.

to 10 years), 95.6% of these patients are PSA recurrence-free using the Phoenix definition of PSA relapse: increase in PSA level by 2 ng/mL or more over the nadir PSA (Figure 3). Median PSA for the entire group was 0.04 ng/mL, which indicates a likely long-term cancer cure in the majority of patients. We have only one patient who has relapsed after the 6-year mark (out of 300 at-risk with follow-up beyond 6 years). Projected 10-year PSA recurrence-free survival is 93.3%. These results confirm the findings from other institutions that PB outcomes are durable. Patients who have PSA levels less than 0.2 ng/mL at 5 years after PB have only a 1% to 2% chance of recurrence.[7] The 7-year actuarial overall survival rate is 93.4%, and only two patients have died of prostate cancer. These results are among the best published in the world.[8,9]

Other treatment options for localized prostate cancer

Treatment choice in prostate cancer is based on the well-established prognostic factors: stage of disease, initial PSA level, and Gleason score. A patient's general condition, comorbidities, and age also play a role in the therapeutic decision. In addition to prostate brachytherapy, other standard treatment options for men with localized prostate cancer include radical prostatectomy, external beam radiation, and active surveillance.

Radical prostatectomy

Radical prostatectomy (RP) is a long-recognized standard treatment option for localized prostate cancer. PSA-based screening has increased the rate of organ-confined disease at the time of diagnosis, increasing the chances for successful outcomes after the surgery. The best candidates for RP are men younger than 70 who have more than 10 years of life expectancy and minor comorbidities. Long-term results of RP for clinically localized disease based upon four large single-institution series indicate PSA recurrence-free survival of 70% to 80%.[10-12] PSA recurrence-free survival rates at 10 to 15 years can be as high as 85% for highly selected men with organ-confined disease seen on surgical specimen in single-institution series from high-volume centres.[13-15] The outcome, however, will depend on the skills and experience of the surgeon.[16,17]

The complications of greatest concern to patients are urinary incontinence and impotence, which are due to operative damage to the urinary sphincter and penile nerves. Nerve-sparing procedure is more likely to preserve sexual function and continence in younger patients. Removal of the prostate, however, may improve urinary symptoms due to benign prostatic hypertrophy, potentially improving quality of life.[17,18] The new, less invasive surgical approaches, such as laparoscopic or robotic radical prostatectomy, offer potentially shorter recovery time but have not been shown to have better cancer-control outcomes.

It is generally believed that results between surgery and PB for patients with localized prostate cancer are comparable. There is only one small randomized control trial published very recently.[19] Two hundred patients were randomized to either radical prostatectomy or prostate brachytherapy. At 5 years follow-up, PSA recurrence free survival was the same in both arms (91%). At 6 months and 1 year follow-up, the prostate brachytherapy group had more irritative urinary symptoms but better sexual function. At 5 years follow-up, there was no detectable difference in quality-of-

life measures between two groups of patients. The US/Canadian ACOSOG-Z0070 trial, which attempted to randomize patients between brachytherapy and surgery, closed due to poor accrual because patients preferred to choose a treatment, rather than be allocated to one. There are no contemporary population-based published surgical outcomes from BC or Canada that we are aware of.

External beam radiation therapy

External beam radiation therapy (EBRT) is a well-established treatment modality for men with localized prostate cancer. EBRT in combination with androgen suppression is a standard treatment for intermediate, high-risk, or locally advanced prostate cancer. Multiple randomized studies have demonstrated a clinical benefit with the addition of androgen suppression to EBRT[20,21] including improvement in disease-free and overall survival. Substantial evidence has shown that greater radiation doses, which can be safely delivered with three-dimensional conformal radiotherapy and intensity modulated radiotherapy, are critical to achieving optimal tumor control. Recent advances in technology have significantly increased the precision of radiation delivery and enable us to safely deliver the higher doses of radiation needed for overall better outcome.[22] There are very few contraindications for treatment with EBRT. Men not suitable for PB because they cannot undergo general or spinal anesthetic, or because they have various significant comorbidities, large prostate volume (> 70 cc), or higher-risk disease, are all eligible for EBRT. While there are very few studies comparing the side effects of EBRT versus PB, we have published that patients treated with EBRT have significantly fewer urinary side effects but somewhat greater rectal toxicities after the treatment.[23] EBRT is commonly delivered over a period of 6 to 7 weeks of daily treatments.

A recent BCCA matched-pair analysis shows that men treated with PB have superior outcomes for PSA control when compared with men treated with EBRT. Five-year PSA recurrence-free rates are 95% for PB and 85% for EBRT. After 7 years, the PB result was unchanged, but the EBRT had fallen to 75%. Median posttreatment nadir PSA levels are 0.04 ng/mL for PB and 0.62 ng/mL for EBRT groups, suggesting higher failure rates are likely for EBRT with longer follow-up.[23]

It could be argued that striving for high cure rates in all patients is unnecessary, as most patients with localized prostate cancer will die of other causes. However, younger patients with long life expectancy are those most likely to benefit from curative treatment, avoiding difficult issues with disease recurrence and the need for secondary intervention with lifelong androgen suppression.

Active surveillance

Active surveillance (AS) is a novel approach where patients with minimal disease are followed closely and offered curative treatment only if their disease progresses. A small chance of lost opportunity for cure or challenges with ongoing anxiety may be issues in some patients with this approach. However, since about 20% to 40% of all men with cancer detected by PSA screening will be "over diagnosed" (that is, they will never develop any signs or symptoms of prostate cancer before dying of old age or another cause), patients with minimal disease should be encouraged to consider AS.[24] Patients suitable for AS include those with clinically localized prostate cancer as determined by digital rectal exam, an initial PSA < 10 ng/mL, two or fewer positive cores on biopsy, and a GS 6 or less. Repeated periodic biopsy is part of regular follow-up. Two international studies using this approach are actively accruing patients in BC. START (Standard Treatment Against Restricted Treatment) is a

Substantial evidence has shown that greater radiation doses, which can be safely delivered with three-dimensional conformal radiotherapy and intensity modulated radiotherapy, are critical to achieving optimal tumor control.

multigroup trial led by the National Cancer Institute of Canada. Patients are randomly assigned to immediate treatment (radical prostatectomy, external beam radiotherapy, and/or brachytherapy, based on patient and physician preference) or active surveillance. Patients assigned to active surveillance are treated with surgery or radiation therapy according to predetermined criteria (biochemical, histologic, or clinical progression). PRIAS is an international multicentre active surveillance registry trial led by investigators in the Netherlands. Patients who are eligible for active surveillance are enrolled in this trial and participate in a carefully scheduled follow-up program. Watchful waiting is another observational approach for patients with localized prostate cancer. It is reserved for those who are elderly or with a significant comorbidity. Both active surveillance and watchful waiting offer patients the advantage of avoiding treatment toxicity. Two other options—high intensity focused ultrasound (HIFU) and cryotherapy—are not considered standard treatments for early-stage prostate cancer. HIFU in particular has high recurrence rates and is not covered by the BC Medical Plan.[25,26]

Quality of life following PB

Several well-designed quality-of-life studies for localized prostate cancer were published recently. The largest study prospectively measured outcomes reported at multiple centres before and after radical prostatectomy, brachytherapy, or external beam radiotherapy. The study included 1201 patients and 625 spouses.[27] Patients treated with brachytherapy experienced fewer bowel and sexual symptoms than patients undergoing surgery, but found urinary irritation was more common. Each prostate cancer treatment was associated with a distinct pattern of change in quality-of-life domains related to urinary, sexual, bowel, and hormonal function. These changes influenced satisfaction with treatment outcomes among patients and their spouses. Adjuvant hormone therapy was associated with worse outcomes across multiple quality-of-life domains.

Other studies have found that patients who received PB showed a trend toward lower functional-scale and symptom-scale scores in the first year after their PB and higher scores and better functional outcome for any subsequent year of follow-up.[28] The quality-of-life studies substantiate the conclusion from our publications related to PB toxicity. Patients treated with PB have initial mild to moderate symptoms (mostly urinary), while they experience very few long-term symptoms, and severe complications are exceedingly rare.

Conclusions

Prostate brachytherapy is a standard treatment option for men with organ-confined prostate cancer. Recently published provincial outcomes indicate that 95% of 1006 men were PSA recurrence-free 5 years after treatment. Obstructive and irritative urinary symptoms were common after the procedure, but transient. Long-term side effects were rare. Potency preservation rate was favorable, particularly in younger men and those with good erectile function before treatment. Other treatment options for men with localized prostate cancer include radical prostatectomy, EBRT, and active surveillance. The optimal treatment modality for each patient will depend on various factors, including disease characteristics, comorbidities, and patient wishes. Patients with localized prostate cancer should be informed of all treatment options available and be assessed by both a urologist and a radiation oncologist before deciding on treatment.[29]

Acknowledgments

The authors wish to thank the BC Cancer Agency Prostate Brachytherapy Program, including Drs Alexander Agranovich, Eric Berthelet, Howard Pai, Winkle Kwan, Mitchell Liu, Jonn Wu, and Ross Halperin. The authors also wish to thank staff in the medical physics department—Dr Ingrid Spadinger (physics head), Mr Robert Harrison, Mr William Kwa, Mr Vincent Lapointe—and Ms Barb Baerg (data analyst) and Ms Veronika Morvan (statistician).

Competing interests

In the last 5 years authors have received unrestricted educational grants from Oncura (makers of the seeds): Dr Morris received funds to conduct two BCCA-lead clinical trials; Dr Pickles received honoraria and meeting support; Dr Keyes received meeting support and unrestricted educational grants to organize program quality assurance meetings.

References

1. Cooperberg MR, Lubeck DP, Meng MV, et al. The changing face of low-risk prostate cancer: Trends in clinical presentation and primary management. J Clin Oncol 2004;22:2141-2149.
2. Lukka H, Warde P, Pickles T, et al.; Canadian GU Radiation Oncologist Group. Controversies in prostate cancer radiotherapy: Consensus development. Can J Urol 2001;8:1314-1322.
3. Keyes M, Miller S, Moravan V, et al. Predictive factors for acute and late urinary toxicity after permanent prostate brachytherapy: Long-term outcome in 712 consecutive patients. Int J Radiat Oncol Biol Phys 2009;73:1023-1032.
4. Keyes M, Schellenberg D, Moravan V, et al. Decline in urinary retention incidence in 805 patients after prostate brachytherapy: The effect of learning curve? Int J Radiat Oncol Biol Phys 2006;64:825-834.
5. Keyes M, Moravan V, Liu M, et al. Rectal

toxicity after I 125 permanent prostate implants in 445 patients: Is rectal and prostate dosimetry related to toxicity? Radiother Oncol 2005;76:S5-S6

6. Macdonald AG, Keyes M, Kruk A, et al. Predictive factors for erectile dysfunction in men with prostate cancer after brachytherapy: Is dose to the penile bulb important? Int J Radiat Oncol Biol Phys 2005; 63:155-163.
7. Stock RG, Klein TJ, Cesaretti JA, et al. Prognostic significance of 5-year PSA value for predicting prostate cancer recurrence after brachytherapy alone and combined with hormonal therapy and/or external beam radiotherapy. Int J Radiat Oncol Biol Phys 2009;74:753-758.
8. Morris WJ, Keyes M, Palma D, et al. Population-based study of biochemical and survival outcomes after permanent 125I brachytherapy for low- and intermediate-risk prostate cancer. Urology 2009;73: 860-865.
9. Morris WJ, Keyes M, Palma D, et al. Evaluation of dosimetric parameters and disease response after 125 Iodine transperineal brachytherapy for low- and intermediate-risk prostate cancer. Int J Radiat Oncol Biol Phys 2009;73:1432-1438.
10. Walsh PC, Partin AW, Epstein JI. Cancer control and quality of life following anatomical radical retropubic prostatectomy: Results at 10 years. J Urol 1994;152(5 Pt 2):1831-1836.
11. Gerber GS, Thisted RA, Scardino PT, et al. Results of radical prostatectomy in men with clinically localized prostate cancer. JAMA 1996;276:615-619.
12. Pound CR, Partin AW, Eisenberger MA, et al. Natural history of progression after PSA elevation following radical prostatectomy. JAMA 1999;281:1591-1597.
13. Han M, Partin AW, Pound CR, et al. Long-term biochemical disease-free and cancer-specific survival following anatomic radical retropubic prostatectomy. The 15-year Johns Hopkins experience. Urol Clin North Am 2001;28:555-565.
14. Roehl KA, Han M, Ramos CG, et al. Cancer progression and survival rates following anatomical radical retropubic prostatectomy in 3,478 consecutive patients: Long-term results. J Urol 2004; 172:910-914.
15. Bianco FJ Jr, Scardino PT, Eastham JA. Radical prostatectomy: Long-term cancer control and recovery of sexual and urinary function ("trifecta"). Urology 2005;66(5 suppl):83-94.
16. Klein EA, Bianco FJ, Serio AM, et al. Surgeon experience is strongly associated with biochemical recurrence after radical prostatectomy for all preoperative risk categories. J Urol 2008;179:2212-2216; discussion 2216-2217.
17. Bianco FJ Jr, Riedel ER, Begg CB, et al. Variations among high volume surgeons in the rate of complications after radical prostatectomy: Further evidence that technique matters. J Urol 2005;173: 2099-2103.
18. Kundu SD, Roehl KA, Eggener SE, et al. Potency, continence and complications in 3,477 consecutive radical retropubic prostatectomies. J Urol 2004;172(6 Pt 1):2227-2231.
19. Giberti C, Chiono L, Gallo F, et al. Radical retropubic prostatectomy versus brachytherapy for low-risk prostatic cancer: A prospective study. World J Urol. 2009; 27:607-612.
20. Bolla M, Collette L, Blank L, et al. Long-term results with immediate androgen suppression and external irradiation in patients with locally advanced prostate cancer (an EORTC study): A phase III randomised trial. Lancet 2002;360(9327): 103-106.
21. Pilepich MV, Winter K, Lawton CA, et al. Androgen suppression adjuvant to definitive radiotherapy in prostate carcinoma—long-term results of phase III RTOG 85-31. Int J Radiat Oncol Biol Phys 2005; 61:1285-1290.
22. Peeters ST, Heemsbergen WD, Koper PC, et al. Dose-response in radiotherapy for localized prostate cancer: Results of the Dutch multicenter randomized phase III trial comparing 68 Gy of radiotherapy with 78 Gy. J Clin Oncol 2006;24:1990-1996.
23. Pickles T, Keyes M, Morris WJ. Brachytherapy or conformal external RT for prostate cancer: A single-institution matched-pair analysis. Int J Radiat Oncol Biol Phys 2010;76:43-44.
24. Draisma G, Etzioni R, Tsodikov A, et al. Lead time and overdiagnosis in prostate-specific-antigen screening: Importance of methods and context. J Natl Cancer Inst 2009;101:362-363.
25. Misrai V, Roupret M, Chartier-Kastler E, et al. Oncologic control provided by HIFU therapy as single treatment in men with clinically localized prostate cancer. World J Urol 2008;26:481-485.
26. BC Cancer Agency. HIFU. www.bccancer.bc.ca/HPI/CancerManagementGuidelines/Genitourinary/Prostate/HIFU.htm (accessed 11 January 2010).
27. Sanda MG, Dunn RL, Michalski J, et al. Quality of life and satisfaction with outcome among prostate-cancer survivors. N Engl J Med 2008;358:1250-1261.
28. Wyler SF, Engeler DS, Seelentag W, et al. Health-related quality of life after radical prostatectomy and low-dose-rate brachytherapy for localized prostate cancer. Urol Int 2009;82:17-23.
29. BC Cancer Agency. Brachytherapy Guidelines. www.bccancer.bc.ca/HPI/CancerManagementGuidelines/Genitourinary/Prostate/Brachytherapy.htm (accessed 29 January 2009). BCMJ