

Original Article

Toxicity and Early Biochemical Outcomes From ¹²⁵Iodine Prostate Brachytherapy in the U.K.

A Prospective Study

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ABSTRACT:

Aims: Transperineal interstitial prostate brachytherapy is increasingly available to patients with early prostate cancer in the U.K., but limited data are available about the toxicity and early results in the U.K. prostate cancer population. We describe our experience and results from prostate brachytherapy to date.

Materials and methods: Two hundred and fifty-five patients were treated at St Luke's Cancer Centre, Guildford, U.K., between March 1999 and November 2002. Of these, over 3 months of follow-up data were available for 216 patients. Patients were assessed at 6 weeks and then at 3, 6, 9 and 12 months after implant, and at 6 monthly intervals thereafter. Prostate-specific antigen (PSA), International Prostate Symptom Score (IPSS) and toxicity, including catheter use, was recorded prospectively.

Results: Median PSA at 1, 2 and 3 years was 0.5, 0.4 and 0.1 ng/ml, respectively. Ninety-five per cent of patients experienced temporary deterioration in their urinary symptoms, which persisted at clinically significant levels (IPSS increase >3 points) for 9 months after implant. The severity of urinary symptoms (IPSS) after implant was most closely related to IPSS at presentation ($P < 0.001$). Acute urinary retention (AUR) occurred in 20 (9.3%) patients, with a further 26 (12.1%) patients using clean intermittent self-catheterisation (CISC) to reduce voiding frequency associated with chronic retention. Median duration of catheter use was 4 weeks. Multivariate analysis revealed that urodynamic status, prostate volume and IPSS score were independently significant ($P < 0.05$) predictors of post-implant catheter use. Twelve patients (5.6%) reported either rectal urgency or mild, self-limiting rectal bleeding.

Conclusion: Brachytherapy was tolerated well, with self-limiting urinary, bowel and sexual toxicity in most patients. Postoperative catheter use in our population is closely linked to pre-implant IPSS score, baseline prostate volume and urodynamic obstruction status. This work confirms the prognostic value of urodynamic assessment, which adds useful prognostic information to assessment of known risk factors such as prostate volume and IPSS. Henderson A. *et al.* (2004). *Clinical Oncology* 16, 95–104

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Key words: Prostate cancer, brachytherapy, prostate-specific antigen, International Prostate Symptom Scores (IPSS), urodynamics, toxicity, urinary symptoms

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Introduction

Transperineal interstitial prostate brachytherapy (TIPB) is increasingly available to patients with early prostate cancer in the U.K., with more than 650 patients receiving seed implants in 2002, and estimates of around 1000 implants planned for 2003 (personal communication, Nycomed, Amersham). This makes up a significant proportion of the estimated cases receiving radical treatment. Analysis of the British Association of Urological Surgeons minimum dataset from January to December 2000 reveals surgery was used as a curative treatment in

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1128 patients, and radiation therapy in 1807 patients [1]. Although these data are incomplete, a postal survey of U.K. consultant urologists revealed that an estimated 1417 radical prostatectomy operations had been performed in 1999 and 2000 [2]. It is likely that, as patients seek what is often perceived as low toxicity and convenient treatment, the number of patients treated with prostate brachytherapy will rise in the U.K. as it has in the U.S.A.

The volume of TIPB carried out in the U.K. is increasing, although little outcome data are available, with only two studies addressing early urinary toxicity in the U.K. population [3,4]. Compared with academic centres in the U.S.A., the U.K. experience of radical prostatectomy has been disappointing, with a higher

incidence of incontinence and erectile dysfunction in carefully conducted U.K. series [5] than in the U.S.A. [6]. This might be because of the demographics of patients diagnosed with, or selected for, treatment of prostate cancer in the U.K., or the delivery of cancer services in the N.H.S. It is important that series of patients with good follow-up in the U.K. are reported to allow an accurate assessment of the role of brachytherapy, and to compare these results with results from the U.S.A., where follow-up periods of up to 12 years have been reported [7–10]. Our centre has used ^{125}I as RapidstrandTM (Oncara, UK) since March 1999. We use ^{125}I TIPB as monotherapy for low-risk disease or as a boost after a course of external beam radiotherapy in high-risk disease (45 Gy in 25 fractions) according to the Seattle protocol [7].

It is clear that the technique of TIPB continues to evolve, with improvements in case selection and delivery of treatment. Non-randomised data increasingly suggest that differences in outcome between surgery, radiotherapy and TIPB, at least in the short term [11,12], are likely to be small for cancer control; however, recommendations about the suitability of a patient with early stage disease for radical treatment may be shaped by factors that can influence symptomatic outcome. Prostate volume, urinary symptoms and symptom scores, general health status, previous radiation exposure, erectile function and history of previous surgery may influence recommendations as much as stage, Gleason grade and prostate-specific antigen (PSA). We report early outcome in a U.K. brachytherapy series with good follow-up for urinary function, complications and PSA, and relate outcome to patient characteristics at presentation. In our most recent cohort of patients, erectile function has been assessed using the International Index of Erectile Function (IIEF), and potency data are reported.

Patients and Methods

Between March 1999 and November 2002, St Luke's Cancer Centre carried out 255 brachytherapy implants for primary prostate cancer. A prospective analysis of toxicity and complications was carried out for the first 216 consecutively treated patients who had more than 3 months of follow-up available after brachytherapy. Demographics of our patients are shown in Table 1. EAU/ESTRO Guidelines for selection and treatment of patients were used after their publication in 2000 (Table 2) [13].

All patients were assessed using history, physical examination, transrectal ultrasound, International Prostate Symptom Score (IPSS), uroflowmetry and post-void residual urine volume determination. Patients with post-void residual urine volumes above 200 ml were offered alternative treatment. Previous transurethral resection of the prostate (TURP) was considered a contraindication to brachytherapy if there was a residual

Table 1 – Patient demographics at presentation

Mean age	64 years
Median presenting PSA (range)	7.9 ng/ml (1.2–26 ng/ml)
Gleason sum	
2–4	45 (21%)
5–6	130 (60%)
7–10	41 (19%)
TNM stage	
T ₁ N ₀ M ₀	76 (35%)
T ₂ N ₀ M ₀	133 (62%)
T ₃ N ₀ M ₀	7 (3%)
Mean initial prostate volume	38 cm ³ (16–91)
Mean presenting IPSS (range)	6.7 (0–26)
Presenting complaint	
Screen detected	90 (42%)
Lower urinary tract symptoms	107 (49%)
Other (e.g. haematuria, UTI)	19 (9%)
Brachytherapy boost after EBRT	49 (23%)
Neoadjuvant androgen deprivation	154 (72%)
Urodynamic evidence of obstruction on ICS nomogram	
Obstructed	60
Equivocal	33
Unobstructed	43
Urodynamic assessment of bladder stability	
Stable bladder	110
Unstable bladder	26

EBRT, external beam radiotherapy; IPSS, International Prostate Symptom Score; ICS, International Continence Society; UTI, urinary tract infection.

TURP defect on transrectal ultrasound scanning. In our series, one patient had undergone bladder neck incision, one patient had a previous TURP and one patient with a prominent middle lobe had this resected before treatment. Patients who had prostate volumes in excess of 50 cc received cytoreductive androgen deprivation (AD). Significant pubic arch interference preventing anterior needle placement on the planning ultrasound (after cytoreduction if necessary) was considered a contraindication to brachytherapy.

All patients were treated with ^{125}I sources, and doses were prescribed to an isodose that encapsulated the prostate. A prescribed dose of 145 Gy was used for patients treated with brachytherapy as monotherapy. Patients with TNM stage >T2a, PSA >10 or Gleason sum >6 were treated with a 3-month course of neoadjuvant AD using lutenising hormone releasing hormone analogues or bicalutamide 150 mg once daily followed by ^{125}I monotherapy. Patients with T3 disease or more than one unfavourable factor (PSA >10 ng/ml, Gleason sum >6, clinical stage >T2a) made up 23% of our series and received external beam radiotherapy (EBRT) at a

Table 2 – EAU/ESTRO guidelines for selection and treatment of patients [13]

Brachytherapy outcome	Recommended/do well	Optional/fair	Investigational/do poorly
Presenting PSA (ng/ml)	<10	10–20	>20
Gleason sum	5–6	7	8–10
TNM stage	T1c–T2a	T2b–T2c	T3
IPSS	0–8	9–19	>20
Prostate volume (cc)	<40	40–60	>60
Q-max (ml/s)	>15	15–10	<10
Post-void residual urine volume (ml)			>200
Previous TURP			+

PSA, prostate-specific antigen. TNM, tumour, nodal and metastatic. IPSS, International Prostate Symptom Score. TURP, transurethral resection of the prostate.

dose of 45 Gy in 25 daily fractions followed by a 110 Gy brachytherapy boost to the prostate. All of these patients received neoadjuvant AD. Two patients were rejected after the planning ultrasound scan, one because of unsuitable prostate conformation and one because of inadequate cytoreduction to allow implantation without pelvic arch interference.

Urodynamic studies (a 20-min test available in most outpatient urology clinics) have been suggested as a useful predictor of risk of acute urinary retention (AUR) after implant [4]. Formal urodynamic studies were carried out in an unselected group of 136 patients, comprising filling cystometry and a pressure/flow study. Obstruction status was classified according to the International Continence Society nomogram [14], and detrusor instability determined as an unprovoked rise of greater than 15 cm of water in detrusor pressure.

Preoperative alpha-blockers (alfuzosin 10 mg once a day or tamsulosin 400 mcg once a day) were used in patients with IPSS >15. After brachytherapy, alpha-blockers were prescribed to all patients for 3 months or until bothersome symptoms resolved. In the event of urinary retention, patients were taught clean intermittent self-catheterisation (CISC) in preference to using an indwelling catheter in order to avoid bacterial colonisation of the bladder [15]. CISC was ceased when post-void residual volumes of urine had fallen to less than 200 ml per catheterisation. CISC was also used to improve symptoms in patients who, although able to void, suffered troublesome lower urinary tract symptoms (LUTS) owing to mild chronic urinary retention. Analgesia and anticholinergics were prescribed as needed. The median follow-up was 16.5 months (range 4.6–46 months) and comprised prospective IPSS questionnaires at 6 weeks, and then at 3, 6, 9 and 12 months. Thereafter, follow-up was at 6-monthly intervals. Because CISC was used by patients who were often able to void urethrally, but with a significant post-void residual urine volume, these patients completed IPSS scores as usual. Although the IPSS has not been validated in patients who use intermittent self-catheterisation to manage chronic subacute retention, it is likely that these scores will more accurately reflect morbidity than either excluding patients who have experienced retention from analysis or allocating a surrogate score (e.g. of maximum

35/35 to patients who are unable to manage without CISC). Patients who were unable to void urethrally did not complete an IPSS score. Significant complications, such as rectal discomfort or bleeding, were recorded prospectively during clinic visits. PSA levels were measured at 3-monthly intervals for 1 year and at 6-monthly intervals thereafter. Ninety-two patients completed pre-implant and at least one post-implant IIEF score. The five questions relating to erectile function were used to define patients as potent if their score was greater than 11/25 [16,17].

Dosimetry data were calculated from computed tomography (CT) scans taken at 0.5 cm intervals using the Varised 6.7 software. As urethral catheters were not *in situ* during CT scanning, a surrogate urethra was used according to the method described and validated by Bucci *et al.* [18]. Dosimetry was calculated from dose volume histograms and expressed as the highest dose to 90% of the prostate (D90) and the percent of the prostate volume receiving 100% and 150% of the prescription dose (V100 and V150). Urethral dose was expressed as the highest dose to 50, 25 and 10% of the urethra (D50, D25, D10).

Prognostic factors for urinary retention were identified from a literature review [4,19,20]. Univariate analyses of data were carried out to assess potentially prognostic factors for urinary retention using non-parametric (Mann–Whitney U/Kruskall–Wallis) or parametric (*t*-test/analysis of variance) methods as appropriate. As all catheterisation events had occurred during the first 3 months of follow-up, unconditional logistic-regression analysis (Stata 7.0 Stata Corp. Texas) was carried out as described by Altman [21]. All factors associated with catheter use at a significance level of 0.10 in the univariate analysis were considered for inclusion in the model. Factors associated with catheter use at a significance level of <0.05 in the multivariate analysis were included in the final model. Changes in IPSS score after implant were compared with paired baseline IPSS score using the sign test.

LUTS were the most common initial presenting complaint, with 49% of our patients presenting to their general practitioner with LUTS. Forty-two per cent of patients had screen-detected prostate cancer. The mean IPSS of 6.7 reflects the higher prevalence of LUTS in the

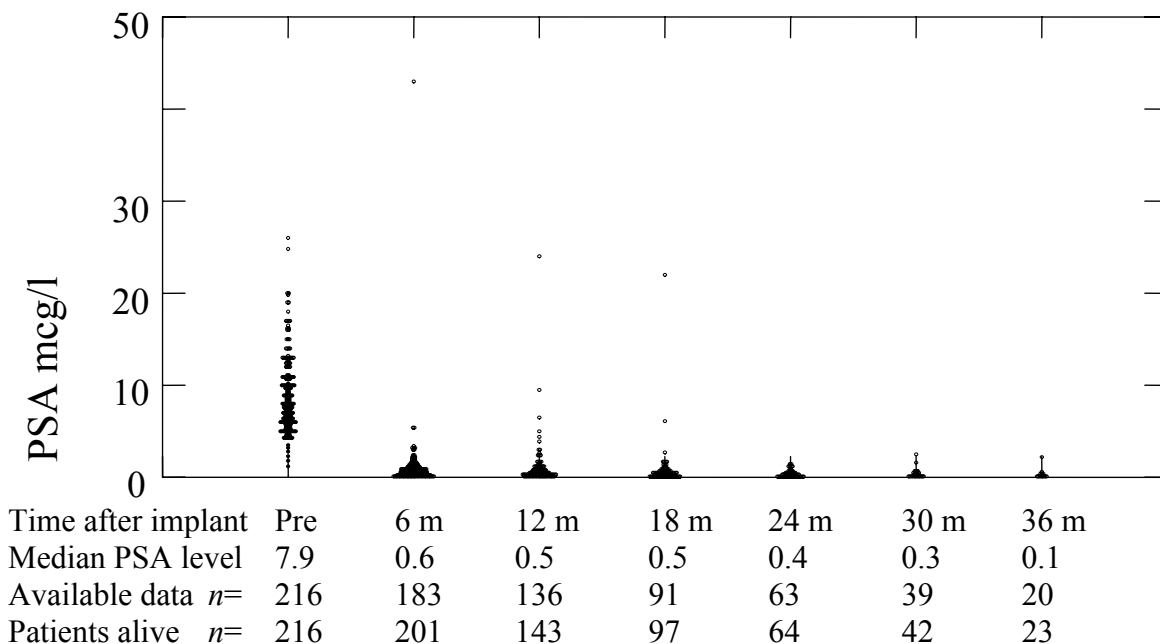


Fig. 1 – PSA outcome vs time after implant (biochemical failures: *n*=6). m, months; PSA, prostate-specific antigen.

unscreened U.K. prostate cancer population compared with series from the U.S.A.

No patients were lost to follow-up from our series. Three patients died of cardiovascular disease unrelated to their treatment 6 months or more after implant, with no biochemical evidence of disease. Although PSA outcomes are currently immature, the early results are encouraging (Fig. 1). Two patients were continued on bicalutamide for 2 years as adjuvant treatment for high-risk disease after implant, and one of these patients experienced biochemical failure after completing the adjuvant treatment. In total, six patients (2.8%) experienced biochemical failure. Five patients commenced hormonal therapy and one patient who had viable tumour on repeat prostate biopsy, which appeared organ confined, underwent salvage radical prostatectomy with clear surgical margins and undetectable post-operative PSA at 1 year. Two patients had distant metastasis and three patients had no site of recurrence identified on digital rectal examination, prostate biopsy, bone-scan or magnetic resonance imaging.

Toxicity is summarised in Table 3. None of the patients treated with brachytherapy alone have suffered permanent urinary incontinence to date. Four (1.9%) patients have needed TURP or bladder-neck incision for bladder-outflow obstruction, and one of these patients had transient stress incontinence after TURP; however, continence returned after pelvic-floor exercises. This patient was the fifth treated in our series and would have been excluded by current guidelines [13] (patient 4: presenting IPSS=21, Qmax=9 ml/s, initial prostate volume 68 cc). The patient treated by salvage radical prostatectomy experienced bothersome postoperative

Table 3 – Outcome summary for first 216 patients

Outcome	Number of patients affected	Patients affected (%)
Catheterised for any reason	46	21.3
Acute urinary retention	20	9.3
Surgery for bladder outflow obstruction	4	1.9
Rectal bleeding/proctitis	12	5.6

incontinence and has been treated by implantation of an artificial urinary sphincter.

Ninety-five per cent of patients experienced temporary deterioration in their urinary symptoms (Fig. 2), with the worst symptoms at 6 weeks after implant. The temporary deterioration in IPSS persisted at clinically significant levels (mean IPSS increase >3 points is clinically significant [22]) for 9 months after implant and continued to improve throughout the follow-up period (Figs. 2 and 3). It is clear from examining the change in IPSS (Fig. 3) that, by 2 years, most patients had no more symptoms than before treatment and, on average, symptom scores improved compared with baseline.

The severity of urinary symptoms (IPSS) after implant was most closely related to IPSS at presentation (Fig. 4). Patients presenting with mild urinary symptoms (IPSS score 0–7) had significantly lower IPSS at all points of follow-up (Mann–Whitney $P<0.05$). No statistically significant differences in IPSS score or IPSS score change were observed in patients who were treated with brachytherapy alone vs EBRT plus brachytherapy

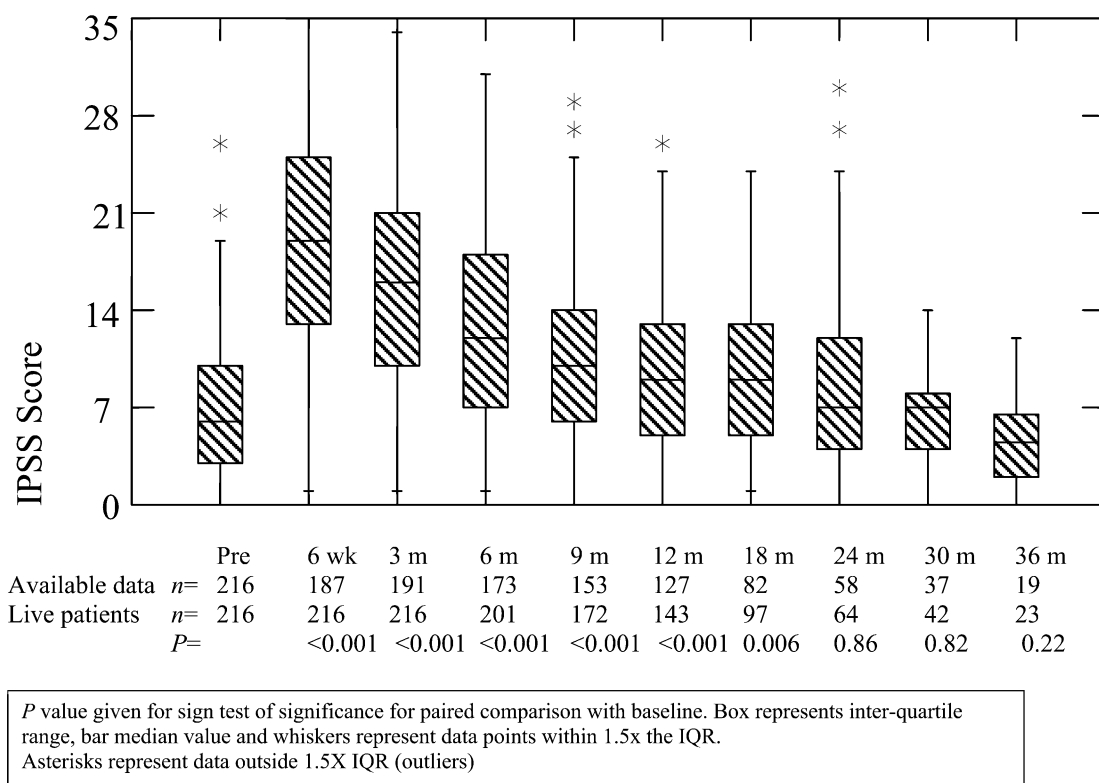


Fig. 2 – IPSS score vs time after implant. m, months; wk, weeks. IPSS, International Prostate Symptom Score.

boost (Fig. 5). Dosimetry parameters were also related to acute postoperative urinary toxicity. As it is difficult to define radiobiologically equivalent doses between patients treated with seeds alone compared with combined EBRT and seeds, only patients receiving ¹²⁵I monotherapy were assessed. Table 4 illustrates the dosimetry in the series to date: no significant differences in acute urinary toxicity as assessed by IPSS scores were found between patients with prostate D90 of either greater or less than 90% of the prescribed dose (whole group) or in patients with urethral dosimetry (D10, D25, D50) in the high- medium- and low-dose tertiles.

AUR occurred in 20 (9.3%) patients with a further 26 (12.1%) patients using CISC to reduce voiding frequency associated with chronic retention. Median duration of catheter use was 4 weeks, although patients often elected to continue using CISC to reduce nocturnal frequency, despite being able to void urethrally. The results of logistic regression analysis of factors associated with urinary retention are presented in Table 5. No significant relationship between urethral D10, D25 or D50 and catheter use after implant was observed (Table 6). Prostate D90, V100 or V150 were not associated with increased risk of catheter use after implant (Table 6). Dosimetry was therefore excluded from the logistic regression analysis.

Twelve patients (5.6%) reported either rectal urgency or mild rectal bleeding; this was universally self-limiting

and responded to either topical corticosteroid or conservative treatment.

Ninety-two patients were assessed using the IIEF at baseline, and 32 (35%) were potent (IIEF-5 = 11/25) at baseline. As the measurement of IIEF was only available for the most recent patients, median follow-up was 14 weeks and potency was preserved at last follow-up in 59%. Although the numbers are too small for meaningful analysis, potency preservation was encouraging, and only seven of these men required pharmacotherapy (sildenafil 25–100 mg).

Discussion

AUR represents the most significant short-term toxicity for patients, and has the advantage of being a hard end point that can be scored in all patients. This contrasts with the IPSS, which is meaningless in patients who are catheterised, and of questionable clinical relevance in patients who perform intermittent self-catheterisation. Data on catheter use were available on all of our patients, and this is important as there is evidence from other cohorts with comprehensive follow-up in the post-hospital phase that only half of catheterisation events happen in the first week after implant [20]. In our study, less than half (43%) of all ISC events were due to AUR, with the remaining patients using ISC to manage urinary symptoms due to transient subacute retention.

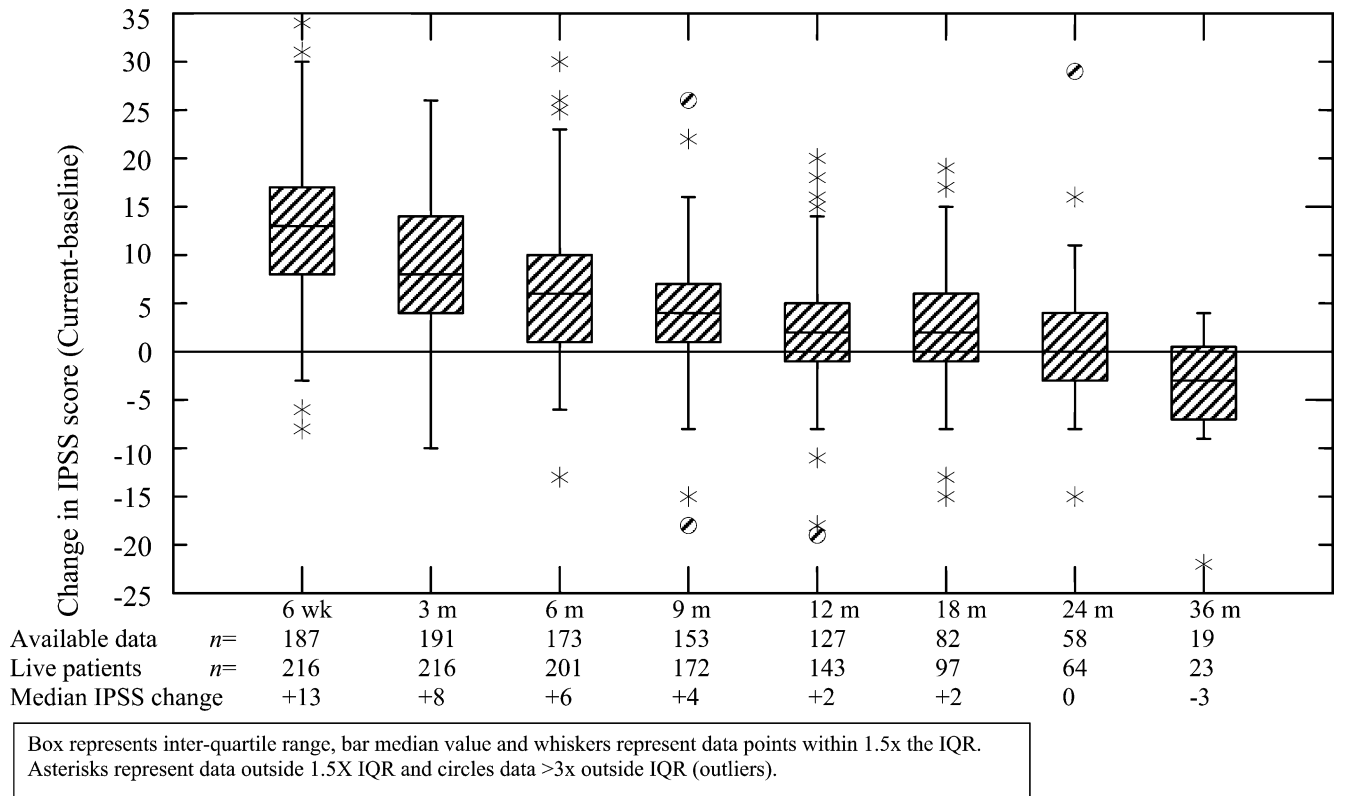


Fig. 3 – Change in IPSS score compared with baseline vs time after implant. IPSS, International Prostate Symptom Score. m, months; wk, weeks.

Postoperative catheter use in our population is closely linked to pre-implant IPSS, baseline prostate volume and urodynamic obstruction status. Although previous investigators have correlated a number of factors, including pre-implant IPSS [23], baseline prostate volume and use of neoadjuvant AD [19] with risk of urinary retention, other centres have not identified measures of voiding function, such as flow rate or urodynamic obstruction status, as important when assessed using a multivariate model to predict AUR. This may reflect the relative difficulty of assessing bladder function using uroflowmetry alone, which was not a significant predictor of outcome in our series, and good urinary flow rates may mask urodynamic obstruction in a bladder with good detrusor function but significant obstruction.

Another important difference in our study group is that patients had been selected according to the EAU guidelines, which recommended brachytherapy as most suitable for treating patients with lower IPSS. Since publication of the EAU guidelines, we have not treated patients with IPSS >20, and most of our patients had an IPSS ≤16. Selection of patients with fewer urinary symptoms may have allowed us to assess the importance of other factors, such as prostate volume and urodynamic status, which had a more measurable effect in our population. In the study by Crook *et al.* [19],

patients were advised not to undergo brachytherapy if their pre-brachytherapy flow rate was less than 10 ml/s. Crook *et al.* suggested IPSS was not a significant predictor of AUR on multivariate analysis because patients at the highest risk of bladder outflow obstruction were excluded from their study. In our study, urodynamic assessment of high-risk patients (IPSS >16, prostate volume >35 cc) showed that obstructed patients who received treatment needed to use intermittent self-catheterisation, whereas unobstructed patients did not.

Urethral dosimetry was found to be a significant predictor of urinary morbidity by Wallner *et al.* [24] in 1995, who recommended central urethral doses be kept to less than 400 Gy (250% of prescription dose). Other measures such as D10 have not been found to correlate better with urinary morbidity than maximal urethral dose, although they are perhaps more likely to represent the true extremes of dose than a point dose on a single CT slice. Our limited data (n=60) did not reveal a relationship between D10, D25 or D50 and either IPSS or rates of AUR. This suggests that the current guidelines used (urethral dose 150–250% of prescription dose) seem to protect patients from the severe symptoms associated with urethral necrosis. Further work using longer follow-up and larger sample size might reveal clinically important short- and long-term toxicity resulting from high doses to the urethra.

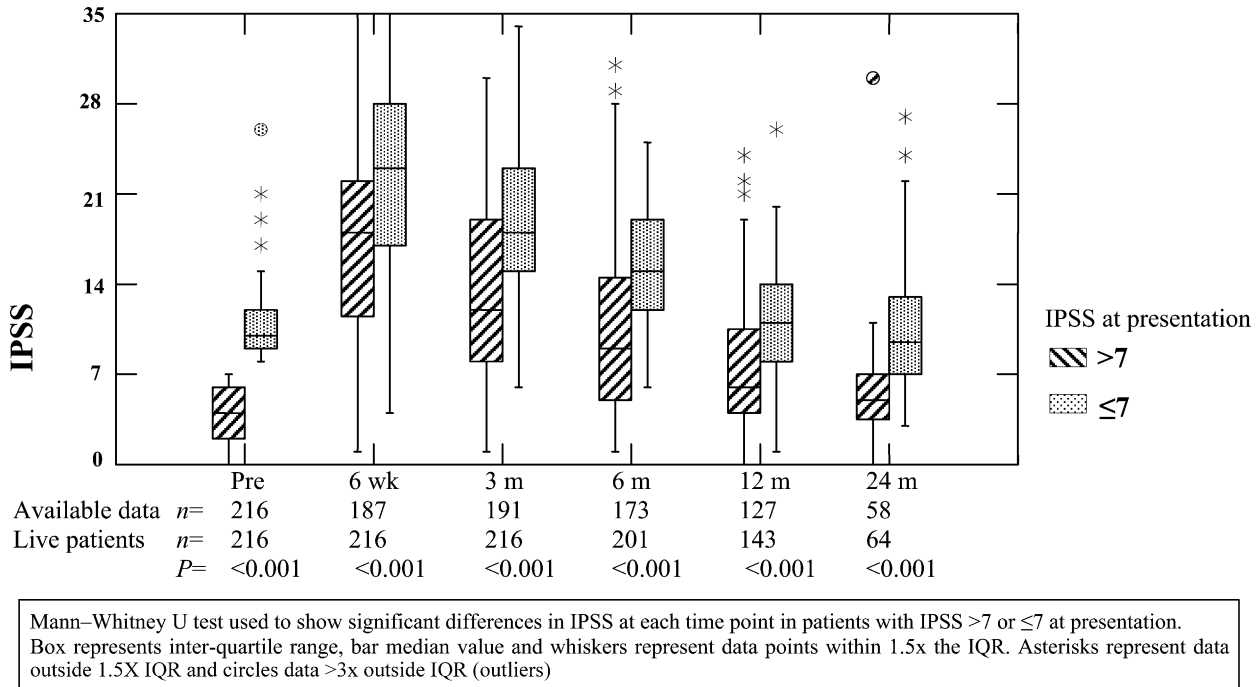


Fig. 4 – IPSS scores for patients with IPSS score >7 vs =7 before implant. IPSS, International Prostate Symptom Score; m, months; wk, weeks.

Bowel toxicity was self-limiting in our study. However, the incidence of treatment-related rectal bleeding may continue to rise slightly, as our mean follow-up was less than 2 years.

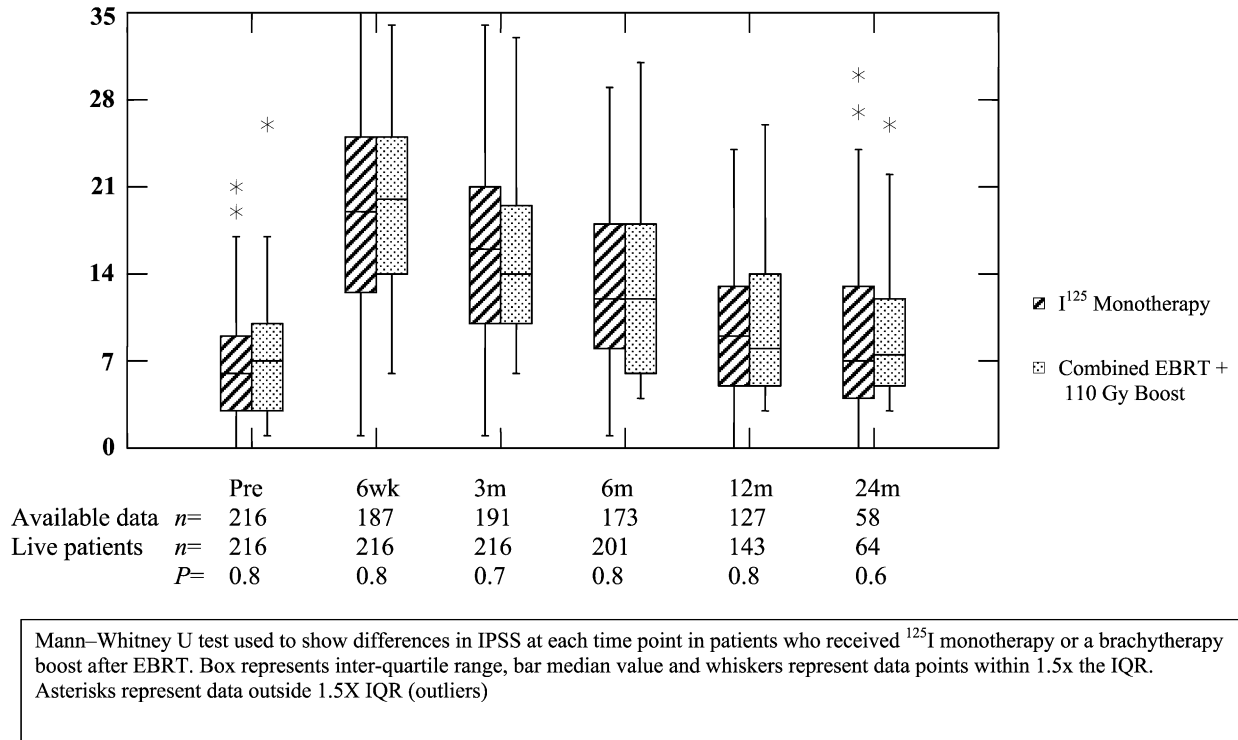
Our erectile function data are currently immature, and spontaneous recovery of erectile function at up to 18 months after brachytherapy has been reported [25]. Other studies have suggested that neo-adjuvant AD [26] and use of supplemental EBRT [17] are important determinants of potency after implant, although we currently lack sufficient data to analyse these factors in our series. Although late (>3 years after brachytherapy), falls in potency [17] are common and would be expected in patients after brachytherapy as monotherapy and as part of combination treatments; our early results are encouraging and mirror early experience in the U.S.A [17].

Preliminary PSA outcome data from our series is encouraging, with 88% of the 20 patients with 3-year PSA data available having nadir PSA levels of <0.5 ng/ml. Previous series have established that PSA levels continue to decrease for at least 48 months after brachytherapy [8], and PSA nadirs of <0.5 ng/ml were associated with a 5-year biochemical relapse-free survival (BRFS) of 93% in previous series after brachytherapy alone. Evidence of the predictive value of nadir PSA is also available from work by Critz *et al.* [27], where nadir of less than <0.5 ng/ml after combined brachytherapy and EBRT was associated with 5-year BRFS of 93% and 10-year BRFS of 83% [27]. There is also strong evidence

from the external beam literature that low PSA nadir predicts more durable biochemical control with PSA levels of less than 1.0 ng/ml associated with 10-year freedom from biochemical relapse rates of 96% [28].

The results from our series are in keeping with recently published series in the U.S.A [9,29]. Although our series contains our first patients, and includes our learning curve experience for this procedure, we believe that the mentoring process has resulted in avoidance of the problem of poor early results that were reported during the discovery curve at some U.S. institutions [7,30], where high implant quality was not verified and may not have been achieved.

Although some centres in the U.K. have only offered brachytherapy as monotherapy for the select group of patients with low-risk disease and low prostate volume at presentation, this may be related to a lack of funding for seed implantation resulting in a pressure to ration care to patients suitable for monotherapy. A recent patterns of care survey in 58 centres in the U.S.A. [31] found that, of the 32% of 36 496 patients diagnosed with prostate cancer who were treated with seed brachytherapy, 46% received supplemental EBRT and 40% received AD. We commonly used neoadjuvant AD in intermediate risk disease or for cytoreduction and combined brachytherapy with supplemental EBRT for high-risk disease. Although in our series the addition of EBRT was well tolerated, randomised studies to establish the additional efficacy, toxicity and optimum delivery of supplemental EBRT are awaited from the current



Mann–Whitney U test used to show differences in IPSS at each time point in patients who received ¹²⁵I monotherapy or a brachytherapy boost after EBRT. Box represents inter-quartile range, bar median value and whiskers represent data points within 1.5x the IQR. Asterisks represent data outside 1.5X IQR (outliers)

Fig. 5 – IPSS scores for patients who received 145 Gy brachytherapy implant alone or 45 Gy EBRT+110 Gy brachytherapy boost to prostate. EBRT, external beam radiotherapy; IPSS, International Prostate Symptom Score.

Table 4 – Dosimetric data in series to date

	Number	Mean	SD
Dosimetric data for ¹²⁵ I monotherapy	167		
D90 (Gy)	167	141	22
V100 (%)	167	87	9
V150 (%)	167	49	14
Urethral D10 (Gy)	60	232	54
Urethral D25 (Gy)	60	208	31
Urethral D50 (Gy)	60	182	23
Dosimetric data based on activity of implant only for EBRT+110 Gy boost	49		
D90 (Gy)	49	105	16
V100 (%)	49	85	9

EBRT, external beam radiotherapy.

Radiation Therapy Oncology Group study. The rationale for using EBRT, in combination with a brachytherapy implant in patients at significant risk of extraprostatic extension, is to ensure that an adequate dose of radiotherapy is delivered to the periprostatic tissues while dose escalating the prostate volume.

The role of neoadjuvant AD before TIPB in improving oncological outcome is not firmly established, although non-randomised studies suggest the possibility of advantage in combining neoadjuvant AD with brachytherapy [32,33]. This survival advantage was, however, confined to patients who received poor-quality implants (D90 <90% of prescribed dose), and the follow-up was shorter in the AD group. Our programme

produced D90 >90% of the prescribed dose in 88% of our last 25 patients, the minimum D90 within these 25 patients was 121 Gy. In light of the most recent literature and our recent results, we are now happy to treat patients with low-intermediate risk disease with seed monotherapy alone. AD is generally used with cytoreductive intent for larger prostates, and we continue to combine EBRT with seed implantation and AD for high-risk disease.

Conclusion

Brachytherapy was tolerated well, with self-limiting urinary, bowel and sexual toxicity in most patients. Early

Table 5 – Risk factors for postoperative catheter use

Risk factors for catheter use	Univariate <i>P</i> value	Multivariate analysis		
		Odds ratio (OR)	OR 95% CI	<i>P</i> value
Patient factors				
Age	0.15			NS
Prostate volume <35 cc (vs >35 cc)	0.001	3.14	1.6–6.3	0.001
Baseline IPSS score >7 (vs ≤7)	0.005	2.5	1.2–5.0	0.011
Uroflowmetry	0.09			NS
Urodynamic Status (unobstructed vs obstructed)	0.008	0.14	0.03–0.64	0.012
Urodynamic status (equivocal vs obstructed)		0.80	0.27–2.34	0.684
Androgen deprivation	0.51			NS
Pre-implant alpha blocker	0.12			NS
EBRT used (vs monotherapy)	0.17			NS

NS, not significant. IPSS, International Prostate Symptom Score. EBRT, external beam radiotherapy.

Table 6 – Dosimetric risk factors for postoperative catheter use

Analysis of dosimetry in I ¹²⁵ monotherapy	Number	Univariate <i>P</i> value
Seed strength	167	0.35
D90	167	0.33
V100	167	0.60
V150	167	0.46
Urethral D10 continuous variable	60	0.71
Urethral D10 analysed by tertile	60	0.15
Urethral D25 continuous variable	60	0.43
Urethral D25 analysed by tertile	60	0.15
Urethral D50 continuous variable	60	0.66
Urethral D50 analysed by tertile	60	0.15

PSA outcomes in the U.K. show encouraging decreases in PSA similar to those observed in series from the U.S.A. with longer follow-up. Current dosimetry guidelines result in relatively few patients receiving very high doses to the urethra, and pre-implant factors, including IPSS, prostate volume and urodynamics seem more important predictors of AUR and urinary symptoms than dosimetric factors in the current era of carefully planned and delivered brachytherapy.

Our awareness of the value of prostate volume measurement, IPSS and pressure flow urodynamics has allowed us to reduce the catheterisation rate in our last 50 patients to <5%.

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