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ORIGINAL ARTICLE

Prostate brachytherapy: a three-year experience from the first 116 patients in Greece

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Summary

Purpose: *To present the results from the first 116 patients with localized prostate cancer treated with transperineal ultrasonography-guided permanent brachytherapy, with special emphasis on the complications of this method.*

Patients and methods: *During the last 3 years, 116 patients with localized prostate cancer underwent transperineal ultrasonography-guided permanent implantation with I^{125} seeds. Permanent implantation consisted of 21-82 I^{125} seeds of 0.529 mCi each, for a total implant dose of 145 Gy. The peripheral loading implant was used and a-blockers preimplantation were administered to most of our patients.The follow-up consisted of clinical examination and serum prostate specific antigen (PSA) estimation every 3 months. Three successive rises of PSA with a 3-month interval inbetween constituted a biochemical failure.*

Results: *No patient was incontinent after treatment. Acute urinary retention was developed in 9 (7.7%) patients. During the first 3 months postimplantation approximately 55% of the patients complained of dysuria, urgency, frequency and nocturia, but their urinary complaints disappeared within one year postimplantion. Three (2.5%) patients developed mild proctitis. Sixty-seven percent of the potent patients remained potent at the end of the first year. Biochemical relapse appeared in 5 (4%) of the 116 patients studied.*

Conclusion: *It seems that prostate brachytherapy, a method that is well tolerated and safely administered, can be accomplished with minimal acute and chronic complications. Prostate size is a predictor for acute urinary retention and prophylactic use of a-blockers seems to reduce the incidence of postimplantion acute retention. Also, lower incidence of impotence was found in comparison with the incidence after radical prostatectomy.*

Key words: brachytherapy, complications, I^{125} seeds, prostate cancer, PSA

Introduction

The treatment of localized prostate cancer remains a controversial area in oncology. Although there are many options for treatment, the Prostate Cancer Clinical Guidelines Panel of the American Urologic Association endorses radical prostatectomy, external beam radiation, and interstitial brachytherapy as standard treatment for the localized forms of the disease [1]. The term brachytherapy is derived from the Greek terms "brachys" (short), and "therapy" (treatment). Pasteau and Delgrais attempted the first brachytherapy in 1914 [2] with radium inserted through a urethral catheter. Prostate brachytherapy came into the modern era in 1983 by Holm and associates [3] but Blasko et al. [4] are generally considered to have developed and popularized the current techniques. Prostate brachytherapy has become a popular treatment option for localized prostate cancer and in USA is almost as common as radical prostatectomy. In Greece, our institute is the only center dealing with this technique. The first patient was treated in 2000.

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Patients and methods

From December 2000 to November 2003, 116 patients diagnosed with localized prostate cancer under-

went transperineal ultrasonography-guided permanent implantation with I^{125} seeds. The median patients' age was 69.5 years (range 57-77) and their median follow-up was 27.2 months (range 12-48). The mean prostate volume was 23.7 cm^3 (range 8-48.2). PSA values, stage and Gleason score stratification are shown in Table 1. About 70% of the patients belonged to the low risk group according to the ASTRO and EAU guidelines (PSA < 0 ng/ml, stage T2a, Gleason score < 6). In the second year of this study, hormone therapy (LHRH analogue plus antiandrogen) was given for 3 months preimplantation and for another 3 postimplantation to 3 intermediate risk group patients (if one of the previously described risk factors was increased). Out of the 8 patients of the high risk group (if 2 of the previously described risk factors were increased), hormone therapy (LHRH analogue plus antiandrogen) was given to 4 of them and external beam radiation to the rest. One of our patients had a transurethral prostatectomy (TURP), 15 months before the implantation and another one had a transvesical prostatectomy 10 years ago. Permanent implantation consisted of 21-82 (median 51) I^{125} seeds (Rapid-strand) with an activity of 0.529 mCi required for a total implanted dose of 145 Gy.

Dose distribution was performed with the Plato brachytherapy Planning System V14.1, Nucletron, dedicated for seeds brachytherapy. The dose delivered to the target volume was ≥ 90% of the prescribed dose, based on Dose Volume Histogram (DVH). Over 65% of the patients subjected to brachytherapy had postimplant dosimetry showing that in 90% of them a dose ≥ 90% of the prescribed dose had been delivered, whereas the remaining 10% of the patients treated had received a dose varying between 80 and 90% of the prescribed dose.

Three to 4 weeks before implantation, all patients underwent a transrectal ultrasound (TRUS) for estimation of the prostate volume, which in turn determined the number of the seeds needed. After that, each patient was admitted for the implantation, which was performed under general anaesthesia. In the first cases this procedure took as long as 3 hours, but it has now been reduced to 1.5 hours. The urethral catheter was removed 3-4 hours after the completion of the procedure and the patient was able to leave the hospital next morning, after a mean hospital stay of 24 hours. Postimplantation, we routinely gave antibiotics for one week and α-blockers for one month. In the second year of this technique, α-blockers were given one week before the implantation. Postimplantation, physical examination and serum PSA estimation were employed for patient monitoring every 3 months. Three successive rises of PSA within a 3-month interval constituted a biochemical failure. A PSA bounce was defined as >15% elevation in PSA compared with the most recent value, followed by a decline to a level of less than or equal to the prebounce value.

Table 1. *PSA, stage and Gleason score stratification*

PSA (ng/ml)	*Patients n (%)*	*Cleason score*	*Patients n (%)*	*Stage*	*Patients n (%)*
<10	79 (68)	<6	78 (67)	T1c	39 (34)
10-20	29 (25)	7	30 (26)	T2a	44 (38)
>20	8 (7)	>7	8 (7)	T2b	33 (28)
Total	116		116		116

Results

Eight (7%) patients developed ecchymosis and 2 (1%) a small haematoma in the perineum that required simple symptomatic treatment (Table 2). Seven of the first 30 (6%) patients had urinary bleeding that disappeared a few hours later without any specific treatment. Acute urinary retention was developed in 9 (7.7%) patients within 1-8 days after implantation (Table 2).

Placing a catheter for 1-12 days and administering α-blockers and antibiotics relieved all patients except three. These 3 patients, after 3 attempts to remove the catheter, were unable to void and 7 months later a TURP was performed. Care was taken to preserve the bladder neck at 5 and 7 o'clock position, as well as the apex of the prostate. Two of them are continent and one has stress incontinence. Most of the retentions occurred in the first year. From the second year onward, α-blockers were routinely administered one week before implantation. During the first 3 months, 51% of

Table 2. Complications

Complications	*Patients, n*	*%*
Ecchymosis	8	6.9
Haematoma	2	1.2
Acute retention	9	7.7
Dysuria	59	51
Nocturia	57	49
Frequency	62	53
Urgency	48	41
Incontinence	0	0
Proctitis	3	2.5
Haematuria	7	6

the patients complained of dysuria (grade 1 in 27% and grade 2 in 24%), 41% of urgency, 53% of frequency and 49% of nocturia (20% grade 1 and 29% grade 2) (Table 2). Six months postimplantation, only 12% of the patients complained of some degree of urinary symptoms. All patients except 9 had normalized their urinary complaints by 1 year postimplantation. No patient complained of incontinence. Three (2.5%) patients complained of proctitis (grade 1), 2-3 weeks after the implantation. However, they recovered 1-2 months later without medical intervention. One patient had 2 episodes of mild rectal bleeding one month postimplantation; however, bleeding disappeared 2 days later without any specific treatment. Twenty-five percent of the patients were impotent before treatment. From the patients who were potent but received no hormone therapy, 70% were in the same condition 6 months later, 67% after one year and 65% at the end of the second year.

All patients returned to normal activities within 10 days after brachytherapy. At 9 months, 75% of the patients had reached a PSA nadir of < 0.5 ng/ml, whereas 92% of the patients had reached their lowest PSA value within 1 year. PSA bounce was seen in 6 patients at 15 months and in 3 at 18 months. Although the follow-up period is short (median 27.2 months), our results are encouraging since only 5 patients showed biochemical relapse at 18, 21, 25, 32, and 41 months postimplantation. Three of them belonged to the intermediate risk group and 2 to the high risk group, since they had undergone implantation in the first year of our study and received no hormone therapy.

Discussion

In patients with localized prostate cancer, radical prostatectomy still is the first choice treatment in our hospital. Coexisting disease and patient's denial dictate an alternative choice of curative treatment [5,6] with minimal complications [7,8] such as transperineal ultrasound-guided radioactive I^{125} seeds implantation.

Complications after brachytherapy are divided in acute and chronic. In general, acute complications are those that occur within the first year caused by the acute effects of radiation as well as those as a result of trauma. On the contrary, chronic complications occur after the first year and represent solely the effects of radiation [9]. According to our results, it seems that acute urinary complications are common, while chronic are rare. Other investigators [10,11] also support this finding. About 55% of our patients complained of dysuria, urgency and nocturia during the first 3 months. In 75% of our patients with acute urinary retention, the size of the prostate was more than 37cc, which is in agreement with other reports [12,13] stating that the size of the prostate is an important predictor of urinary retention. Another observation was that 65% of retention cases occur in the first year.

Patients operated during the second year since this method started were given α-blockers about 10 days before the implantation. This resulted in reduced acute retention, which has also been found in the literature [14]. It is well known that incontinence is rare in patients without a prior TURP, while it is as high as 85% in men with prior TURP [15]. In 2 of our patients with prior prostatectomy, implantation was performed and 13 months later both of them were continent. It seems that when using the peripheral loading implant the incidence of incontinence is lower [16].

Proctitis ranges between 1-21% [17,18]. Rectal damage can be mild and self-limited, or severe enough to cause a prostatorectal fistula. Three (2.5%) of our patients developed proctitis (two grade 1 and one grade 2). More severe rectal complications such as ulcer or fistula have been reported in patients who had their rectal bleeding treated by some sort of caustic therapy [19]. It is therefore crucial to inform the patients that they have to avoid any rectal procedures before consulting the physician who had performed the implantation.

One of the patient's reasons to prefer brachytherapy to surgery is the adequate erectile function. The likelihood of erectile function 1-6 years following implantation ranges between 62-86% [20,21]. Although the follow-up of our patients is short, 65% of them, who were potent before brachytherapy and received no hormone therapy, remained potent 18 months later.

Our results do not allow firm conclusions on the overall outcome of patients treated with this technique, but they are encouraging since, so far, only 5 out of 116 patients have shown biochemical failure. This is very promising and we expect to have good biochemical control 5 years after treatment, as described by others [22-24].

Our results show that prostate brachytherapy can be accomplished with minimal acute and chronic complications. The incidence of incontinence in patients with prior prostatectomy may be lower if the peripheral loading implant is used. The size of the prostate is a rather good predictor for acute urinary retention after brachytherapy. Prophylactic use of α-blockers seems to reduce the incidence of postimplant retention. It seems that administration of antiandrogens for 6 or more months may protect the intermediate and high-

risk group patients from biochemical relapse. Since no randomized data are available, the role of antiandrogens prior to brachytherapy has yet to be established [25]. Another advantage of brachytherapy is the lower incidence of impotence. Prostate brachytherapy is well tolerated and safely delivered to patients with localized prostate cancer.

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