Radiofrequency Induced Thermotherapy (RFITT) for BPH: A prospective study with 131 cases during 4-years of clinical experience

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KEY WORDS

prostate ◗ benign prostatic hyperplasia ◗ radiofrequency ablation

ABSTRACT

Introduction. With the objective of improving treatment of benign prostatic hyperplasia (BPH) several therapeutic alternatives have been suggested in recent years. One of the latest is bipolar Radiofrequency-induced Thermotherapy (RFITT®). The aim of the study is to evaluate the efficacy and safety of RFITT for the treatment of symptomatic BPH.

Material and methods. From February 2004 to March 2008 a total number of 131 men at mean age 70.3 yrs with symptomatic BPH underwent transurethral treatment with the Celon*URO* device. All patients were divided into two groups: group I – patients with preoperative spontaneous voiding, and group II – patients with complete urinary retention. Patients underwent a follow-up in 1st, 3rd and every six months and the following parameters were monitored: maximum peak flow (Qmax), postvoid residual urine volume (PVR), international prostate symptoms score (IPSS), and prostate volume. The t-Student test was used to compare the data before and after RFITT.

Results. Average follow-up time was 24.6 months. 108 pts are catheter free with significantly improved maximum peak flow, 16 pts failed, 1 patients died on the 1st postoperative day due to acute cardiovascular disease, 6 pts resigned from the study. Neither serious intra- nor postoperative complications were observed.

Conclusions. Transurethral bipolar radiofrequency induced thermotherapy is a new, safe, and effective treatment for BPH. This minimally invasive method is associated with low risk of complications. It is especially appropriate for elderly unfit patients or those younger men who do not accept the risk of retrograde ejaculation or incontinence.

INTRODUCTION

High-frequency electrical current alternating at a frequency of approximately 400 kHz is the type of electrical energy used in standard operating room electrocautery machines. The aim of using this energy is to produce local heat above 50°C which is an effective means of destroying tissues. Once the tissue has been heated, cell membranes melt and fuse resulting in protein denaturation and irreversible cell death [1].

In 1976 Organ described the electrophysiological principles of destroying tissues with radiofrequency electrical energy [2]. In the early nineties of the 20th century, first attempts of animal tissue ablation with the high-frequency electrical current energy were carried out [3]. In 1995, in Italy the first percutaneous thermoablation of a small hepatic tumor was performed [4]. In the same year Harewood et al. applied the radiofrequency-induced energy in the treatment of benign prostatic hyperplasia [5].

This less invasive method – transurethral needle ablation of the prostate (TUNA) – was performed in relatively numerous centers all over the world as well as a few in Poland [6, 7].

Unlike the TURP, the TUNA technique can be carried out as an in-office procedure under local anesthesia. This allows most patients to resume most activities within a few days. No serious side effects are associated with this therapy. There are some limitations of the method: the difficulties in precise application of the needles into the prostate lobes and a prostate volume greater then 75 ml. Further disadvantages are due to the monopolarity of the system, which requires non-saline irrigation liquid [6, 8].

In 2002, urologists from Berlin, in cooperation with Celon AG, have suggested a newer technique using high-frequency current as the minimally invasive treatment for benign prostatic hyperplasia – the Radiofrequency-induced Thermotherapy (RFITT) for BPH [9].

MATERIAL AND METHODS

From February 2004 to March 2008, a total number of 131 men (average age 70.3 years; range 41 to 89 yrs) with BPH and severe lower urinary tract symptoms (LUTS) underwent transurethral treatment with the Celon*URO* device (Celon AG, Germany). Preoperatively, digital rectal examination (DRE) and transabdominal ultrasonography of the urinary tract were performed as well as postvoid residual volume (PVR), maximum peak flow (Qmax), and International Prostate Symptom Score (IPSS) were measured.

The IPSS and results from the above mentioned diagnostic tests were used to divide patients into stages I-IV according to the commonly described natural history of benign prostatic hyperplasia:

- Stage I – patients with no bothersome symptoms and no significant urine obstruction
- Stage II – patients with bothersome symptoms, but without significant urine obstruction
- Stage III – patients with significant urine obstruction (urine flow less than 10 ml/s and persistent residual urine more than 100 ml)
- Stage IV – patients with possible complications such as chronic retention affecting the upper urinary tract [10, 11, 12].

Only male patients who presented stages II-IV were qualified

for treatment with radiofrequency-induced thermotherapy. All patients who underwent the RFITT procedure were selected for this nonrandomized prospective study. Patients were informed of the alternative treatment and informed consent was obtained. Inclusion criteria were as follows:

- symptomatic BPH lasting longer than 6 months and failed standard medical therapy with α-blockers or followed by urinary retention
- unsuitability for more invasive therapy due to concomitant diseases
- and/or lack of acceptance of the risk of urinary incontinence or retrograde ejaculation.

Patients with any suspicion of prostatic carcinoma, according to the clinical and laboratory findings, were excluded.

All patients operated on with RFITT were divided into two groups:

Group I – 82 (63%) patients with preoperative spontaneous voiding and severe irritative and obstructive symptoms due to BPH.

Group II – 49 (37%) patients with complete urinary retention.

In patients with follow-up time longer than 6 months, the mean results from the last three visits were calculated and included into the study.

The overall patient characteristics are listed in tables 1-4 and Fig. 1.

All procedures were performed under spinal anesthesia. The bipolar RFITT® (Celon AG, Berlin, Germany) device and a standard 21-22F cystoscope with 6F working channel and 30° optic were applied. The irrigation of the bladder was accomplished with dextrose

Table 1. Patient demography – group I.

Age	40–49	50–59	60–69	70–79	≥80
Number of pts	3	10	20	43	6
% pts	3.7	12.2	24.4	52.4	7.3

Table 2. Patient demography – group II.

Age	40–49	50–59	60–69	70–79	≥80
Number of pts	1	3	8	28	9
% pts	2	6.1	16.3	57.2	18.4

Table 3. Baseline patients' characteristics – group I.

	Range	Mean ±SD
IPSS (0-35 points)	7 - 34	21.5 ±5.9
Peak urinary flow (Qmax, ml/s)	4 - 17	11.3 ±4.8
Prostate volume (ml)	18 - 139	57.9 ±24.7
Post-void residual (ml)	0 - 300	82.9 ±70.4

IPSS – International Prostate Symptom Score.

Table 4. Baseline patients' characteristics – group II.

	Range	Mean ±SD
IPSS total score (0-35 points)	–	–
Peak urinary flow (Qmax, ml/s)	–	–
Prostate volume (ml)	21 - 197	69.1 ±28.8
Post-void residual (ml)	–	–

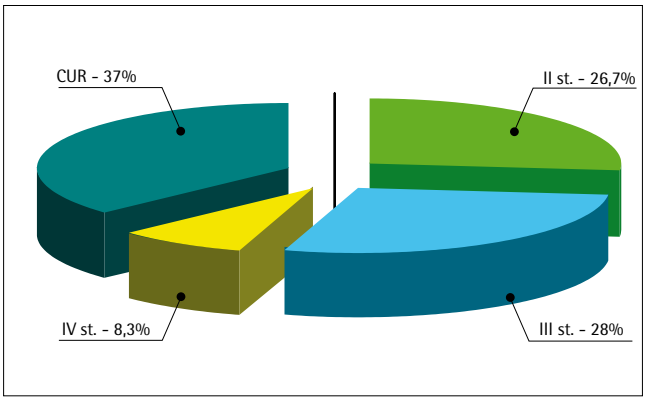

Fig. 1. BPH stages (CUR – complete urinary retention, st. – stage).

5% or normal saline. The flexible applicator Celon-*Uro* was inserted into the lobe of the prostate at a 45° angle. The average depth of puncture was 20 mm and was seen at the level of black marks on the tip of the probe (see figures 2-5).

The tissue of the gland was locally heated up to 120°C and the coagulative effect in the tissue was achieved in about 1 minute. The system's power was set at 6 or 7 W. The lesion size for every puncture was 15 mm x 10 mm. An automatic power control system monitored the temperature at the tip of the probe and an increasing sound signal indicated the end of the coagulation. This excluded an overdose of the energy. Insertion of the probe was repeated several times in each lobe in order to obtain an optimal volume reduction. One puncture was required for approximately every 5 g of prostatic tissue. If the median lobe was present the probe was inserted directly into it and coagulation was carried out. Intravenous antibiotic prophylaxis – amoxicillin and clavulanic acid 1.2 g every 12 hours – was administered immediately after the procedure. An 18F 2-way Foley catheter was placed for ten days in preoperatively voiding patients and for 3 weeks in those with complete urinary retention. Patients were usually discharged on the first postoperative day. Oral fluoroquinolones were prescribed for seven days. Patients underwent a follow-up in 1st, 3rd, and every six months and parameters were monitored.

The efficacy of the treatment was assessed with the following measurements:

- Maximum peak flow improvement
- Postvoid residual urine volume decrease
- Improvement of LUTS measured in IPSS
- Prostate volume decrease measured transabdominally with Bruel&Kjaer Falcon 2101 sonography unit

The safety of the procedure was assessed based on:

- Intra- and postoperative complications related to the operation
- Appearance of urinary incontinence
- Appearance of retrograde ejaculation

The following parameters were also assessed:

- Operation time
- Coagulation time
- Number of probe insertions (punctures)
- Hospitalization time
- Volume of irrigation fluid

Continuous variables are shown as average ± standard deviation (SD), and the t-Student test was used to compare them before and after RFITT. A value for p less than 0.05 was considered significant.

Fig. 2. Probe application scheme.

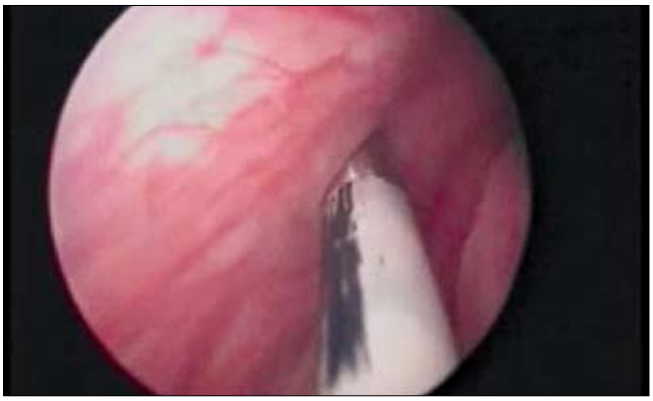

Fig. 4. The probe inserted into the prostate gland.

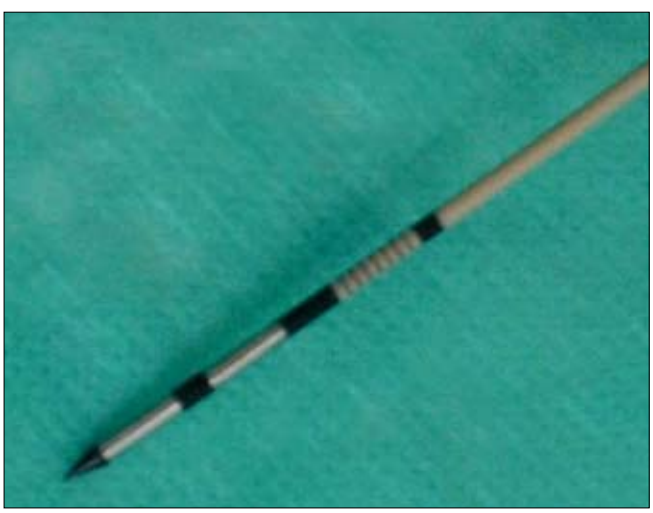

Fig. 3. Bipolar flexible applicator Celon-*UroProbe*.

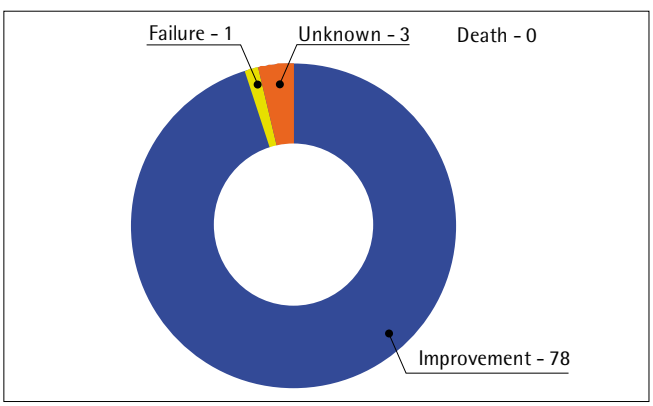

Fig. 5. Overall outcomes – group I.

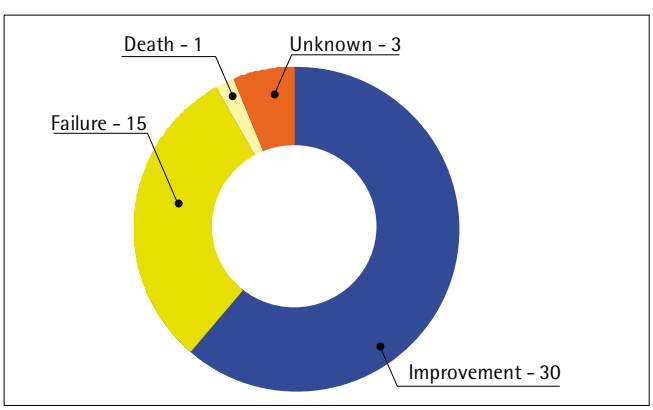

Fig. 6. Overall outcomes – group I.

RESULTS

One hundred and twenty-five (95.4%) patients were assessed in the follow-up period. Six (4.6%) patients resigned from the study. The average follow-up time was 24.6 (range 2-48) months. The operation time was 15 to 45 (average 22) minutes. The coagulation (ablation) time measured automatically in the main unit was 3 to 17 (average 11 ±2.5) minutes. The number of probe insertions for each patient was 7 to 21 (average 12 ±2.7). From 1.2 to 11.5 liters (average 5.8 ±2.3) of irrigation fluid were used during the procedure. The mean hospitalization time was 1.9 days (range 1-4).

One hundred and eight (82%) patients are catheter free with a significantly improved maximum peak flow from 4 ml/s to 43 ml/s (average 14.9 ±5.7), 16 (12%) patients failed (required TURP – 7 pts or adenomectomy – 9 pts), 1 (0.8%) patient died on the 1st postoperative day due to acute cardiovascular disease. All patients treated with open adenomectomy presented large glands (>100 ml). Of the 7 men who underwent TURP, 6 had a permanent catheter before RFITT. The overall outcomes are shown in figures 5 and 6.

Table 5. Measured parameters – group I.

	Range	Mean ±SD	Difference compared with values before RFITT	P
IPSS	3 - 22	9.1 ±5.3	-12.4	1×10^{-14}
Peak urinary flow (ml/s)	8 - 27	15.2 ±5.6	+3.9	4×10^{-6}
Prostate volume (ml)	15 - 95	44 ±18.3	-13.9	8×10^{-8}
Post-void residual (ml)	0 - 150	25.3 ±36.3	-57.6	2×10^{-7}

In group I, the IPSS, maximum peak flow, prostate volume and PVR showed a significant improvement compared with these values before treatment (p respectively 1×10^{-14}, 4×10^{-6}, 8×10^{-8}, 2×10^{-7}) (Table 5).

In group II, 30 (61%) patients were catheter-free during the follow-up. They presented significant prostate volume reduction and satisfactory uroflowmetry. An IPSS of about 7 points and the average PVR of 55 ml are also acceptable (Table 6).

Except one death due to cardiac disease no serious intra- or postoperative complications were observed. Bleeding was not re-

markable although in three cases bladder irrigation was required on the first postoperative day. Retrograde ejaculation and urinary incontinence were not noticed. All complications are listed in the table 7.

DISCUSSION

Transurethral resection of the prostate (TURP) still remains the gold standard in treatment of benign prostatic hyperplasia (BPH). Although TURP is a very effective surgical procedure with excellent objective and subjective success rates, it is associated with significant morbidity and the highest risks for serious complications, including bleeding, impotence and incontinence. With the objective of improving treatment of BPH several less invasive procedures have been suggested in the recent years [6, 13, 14]. Minimally invasive approaches usually use some form of heat to destroy excess prostate tissue. The heat most frequently may be delivered by radiofrequency waves or lasers [7, 15, 16, 17]. Transurethral needle ablation (TUNA) utilizing radiofrequency electric current has gained considerable popularity worldwide particularly after approval by the Food and Drug Administration [17].

The advantages of TUNA are: controlled area of coagulative necrosis, performance under local anesthesia, quick recovery, and few side effects [18, 19, 20]. The limitations of this method are listed in the introduction. The innovative technique developed by Celon – bipolar radiofrequency induced thermotherapy for BPH (RFITT®) seems to eliminate these disadvantages.

Unlike the TUNA technique, RFITT allows to perform the ablation effectively also in patients with large asymmetric glands. The bipolar flexible applicator Celon-*UroProbe* can be inserted under direct vision into almost any part of the prostate, including the median lobe which is inaccessible for TUNA. Thanks to bipolar RFITT technology, a coagulative effect is confined to the desired area in the prostatic tissue. Also the use of isotonic irrigation fluid makes RFITT safer in comparison to monopolar systems [9, 17].

The RFITT procedure may be carried out with or without cystostomy. Zargar Shoshtari and co-workers established a 14F suprapubic catheter before the operation which was removed after a voiding trial, 10 to 14 days postoperatively. The urethral catheter was removed on the seventh postoperative day. Their patients were all operated on under local anesthesia [17].

In our study the patients were drained postoperatively only with 18F Foley catheter. We did not perform cystostomy before RFITT because of the short operation time, slight bleeding and using relatively small amount of irrigative fluid. We preferred the spinal anesthesia for patients who underwent this procedure. Such anesthesia provided patients with more comfort during the operation and did not result in longer hospitalization.

In group I the IPSS, maximum peak flow, prostate volume and post-void residual urine volume showed a significant improvement compared with these values before RFITT (-12.4 points, +3.9 ml/s, -13.9 ml, -57.6 ml respectively). Only 1 (1.3%) patient failed the treatment.

In group II, 30 (61%) patients were catheter-free within the observation period. They presented significant prostate volume reduction and satisfactory uroflowmetry. The IPSS of around 7 points and the mean PVR of 55 ml are also acceptable. It should be emphasized that this comparatively low success rate was influenced by failures in patients with large adenomas (>100 ml).

There are a few reports concerning radiofrequency-induced thermotherapy for BPH [9, 16, 17]. To the best of our knowledge there are no papers comparing RFITT with TURP, which is considered the "gold standard" for the surgical treatment of BPH. Therefore we refer to authors using the same radiofrequency induced energy for the ablation of prostatic tissue. There are several studies assessing transurethral needle ablation (TUNA) in symptomatic BPH, and some comparing it with other techniques, including TURP [7, 21]. The results to date indicate that needle ablation is safe and effective for relieving symptoms in patients with benign prostatic hyperplasia, and the effect has been shown to be durable for at least 2 years [8]. In our study we obtained similar durability of relevant effects with the use of radiofrequency-induced thermotherapy (RFITT). Using the same technique Zargar Shoshtari et al. had achieved statistically significant improvements in maximum flow rate, prostate volume, IPSS and PVR at 3 and 18 months follow-up [17].

Hill and other authors emphasize that the incidence of erectile dysfunction, incontinence and urethral strictures was greater in patients undergoing TURP than in those treated with TUNA, with significantly fewer adverse events in TUNA group than in those receiving TURP [18, 21]. Likewise, TUNA has fewer anesthetic requirements and results in a shorter hospital stay than TURP (WMD: -1.9 days (-2.75, -1.05)) [7].

No clinically significant complications like bleeding, urinary incontinence, or retrograde ejaculation have been reported by numerous surgeons performing minimally invasive procedures based on radiofrequency induced energy [6, 17, 21].

The important disadvantage of these methods is the lack of prostatic tissue for histological evaluation [8].

To sum up, the bipolar interstitial radiofrequency-induced thermotherapy for BPH (RFITT) is a cost-effective and quick procedure with short hospitalization. In most cases, patients were monitored overnight and discharged home the morning after surgery. Obtaining a significant improvement in relevant BPH parameters makes this technique a valuable alternative to surgical methods and also to other less invasive procedures like TUNA or lasers. We would like to emphasize good results achieved in patients with urinary retention. Almost two thirds of patients presenting preoperatively a permanent catheter started to void spontaneously after RFITT. Most of those who failed had adenomas larger than 100 cm^3. We consider that the improved experience in performing RFITT will allow successful application of this treatment for patients with large glands.

Table 6. Measured parameters – group II.

	Range	Mean ±SD	Difference compared with values before RFITT	P
IPSS	4 - 21	6.9 ±5	–	–
Peak urinary flow (ml/s)	4 - 43	14.7 ±6.7	–	–
Prostate volume (ml)	20 - 180	54 ±29.4	-15	1×10^{-5}
Post-void residual (ml)	0 - 390	54.9 ±87.9	–	–

Table 7. Intra- and postoperative complications.

Complications	Number/%
Death	1/0.8
Minor bleeding	3/2.3
Urinary tract infection	2/1.5
Late bleeding	1/0.8