TRANSURETHRAL RADIOFREQUENCY THERMAL ABLATION OF PROSTATIC TISSUE: A FEASIBILITY STUDY IN HUMANS


ABSTRACT

Objectives. To evaluate the feasibility and efficacy of ablating prostatic tissue by inducing thermal lesions using radiofrequency (RF) energy delivered transurethrally through electrodes mounted on a Foley-like catheter.

Methods. Twenty male patients, candidates for radical cystoprostatectomy to treat bladder carcinoma, underwent RF prostate ablation 1 to 8 days before surgery (mean 2.8). Stainless steel, internally cooled, 2-cm-long electrodes mounted on a Foley-like catheter were used to deliver RF energy to the prostatic tissue. Semicircular electrodes were used in 10 patients (group A) and circular electrodes were used in the remaining 10 patients (group B). The urethral, rectal, and prostatic tissue temperatures were recorded. Histologic step sections were performed on whole mounts of the prostates to define the volume of the thermal lesions.

Results. The mean RF energy delivered was 36.5 kJ (range 26.4 to 53.1) in group A and 82.3 kJ (range 38 to 149) in group B. The intraprostatic temperatures were between 44°C and 80°C in group A and between 60°C and 119°C in group B. The urethral and rectal temperatures never exceeded 42°C. No major complications occurred. After the RF procedure, 5 patients who received more than 75 kJ of energy could not void and required catheterization. The mean prostate volume was 11.54 cm³ for group A and 24.02 cm³ for group B. The mean volumes of the thermal lesions and their relative percentages in relation to the whole prostate in groups A and B were, respectively, 1.69 cm³ and 15% and 6.91 cm³ and 29% (P = 0.049). Analysis of variance showed a significant correlation between the thermal lesion volume and the energy delivered, regardless of the electrode shape (P = 0.001).

Conclusions. Satisfactory thermal ablation of prostatic tissue can be achieved using RF electrodes mounted on a Foley-like catheter. The procedure is effective, simple, and safe and, therefore, can be used in pilot clinical studies on patients with benign prostatic hyperplasia.

Several new minimally invasive therapies have been proposed for the treatment of symptomatic benign prostatic hyperplasia (BPH) using interstitial hyperthermia induced with different sources of energy such as microwave, laser, high-intensity focused ultrasound, and radiofrequency (RF). RF energy was delivered either through needles inserted into the prostate transurethrally or transperineally in the experimental treatment of prostate carcinoma. Heat is generated by the molecular friction induced by the RF electrical field in the tissue adjacent to the uninsulated electrode tip, causing areas of coagulative necrosis of limited and predictable volume, the so-called thermal lesions. Their size depends on the total energy delivered, the thermal conductivity of the tissue, and the heat lost by convection through blood flow. Lesion size can be increased by injecting hypertonic electrolyte solutions, the so-called virtual electrode. A new RF delivery system, consisting of a stainless steel, cooled electrode mounted on a Foley-like catheter, has been devised. We sought to verify whether this device can produce prostatic thermal lesions of sufficient size, thus simplifying the procedure and obviating the need for needle insertion and anesthesia.
the surgical specimens were sampled in the same manner: the longitu-
dinal, transverse, and anteroposterior diameters of the prostate were measured. The prostate was sectioned sequen-
tially at 5-mm intervals from the apex to the base perpendic-
ular to its longitudinal diameter, and the slices were embedded as whole-mount sections. The remaining prostatic tissue ad-
herent to the bladder neck was cut longitudinally. The follow-
ing features were noted on the hematoxylin-eosin-stained sec-
tions: evidence of necrosis and hemorrhage, acute inflamma-
tion, epithelial cell type, and stromal alteration type. The greatest anteroposterior and transverse diameters of the RF lesion were measured on the whole-mount sections using a graduated eyepiece. The longitudinal diameter was calculated by multiplying by 5 mm the number of samples in which the lesion was present. The prostatic base lesions were noted sepa-
rateley. The volumes of the prostate and the RF thermal le-
sions were calculated using the following formula: longitudinal

diameter \times \text{transverse diameter} \times \text{anteroposterior diameter} \times 0.52. The percentage of the altered tissue in relation
to the whole prostate was also calculated.

Neurohistochemical evaluation of the lesions with antibod-
ies against S100 proteins has also been planned.

STATISTICAL ANALYSIS

Statistical differences were calculated using the JMP soft-
ware package (SAS Institute). The differences between the
treatment groups and the interval variables (diameter, vol-
ume, and percentage) were calculated using the nonparamet-
ric Mann-Whitney U test. When comparing power delivered
to the interval variables (diameter and volume), analysis of
variance on linear fit was used. P values were considered sig-
nificant at 0.05 or less.

RESULTS

CLINICAL ASPECTS

Group A was subjected to RF energy with a power range between 26.4 and 53.1 kJ (mean 36.5) and group B to RF energy with a power range of 38 to 149.6 kJ (mean 82.3) (P = 0.006). The maxi-

mum recorded intraprostatic temperatures for groups A and B were between 40°C and 80°C and
75°C and 119°C; the urethral temperatures were between 33°C and 42°C and 25°C and 34°C; and the rectal temperatures were between 38°C and 42°C and 40°C and 42°C, respectively. RF treat-
ment was usually well tolerated. Discomfort was observed in 6 patients, with mild pain requiring
intravenous pethidine in 9 and severe pain requir-
ing temporary power reduction and additional ad-
ministration of diazepam in 5 patients. No major
complications occurred. After the procedure, all
patients voided spontaneously except for 5 pa-
tients, who received more than 75 kJ RF energy and presented with urinary retention requiring cathetherization.

QUALITATIVE HISTOLOGIC FINDINGS

Macroscopically and on the whole-mount sec-
tions, the thermal lesion often had a butterfly
shape, centered on the urethra, with its largest
“wings” located posteriorly (Fig. 2). Microscopi-
cally, all cases showed damage to the distal urethral
mucosa (epithelial erosion and areas of hemor-
rhage and thrombosis in the lamina propria), and proximal involvement was variable. All cases except for one had lesions to the transitional and peripheral zones. In the transitional zone, collagen condensation was observed, occasionally with nuclear karyolysis of the smooth muscle cells. Glands demonstrated constantly regressive vacuolization of the cytoplasm; lytic necrosis and coagulative necrosis were related to treatment group. Both were present in 4 of 10 patients in group A and in 9 of 10 patients in group B ($P = 0.019$). Lytic necrosis was evident in 3 of 10 patients in group A and in 8 of 10 patients in group B ($P = 0.024$). Areas of interstitial chronic inflammation were evident in most cases, and microabscesses accompanied all cases with neutrophilic glandular exocytosis.

In the peripheral zone, epithelial regressive changes were always seen, and the two types of necrosis followed the same pattern as that of the transitional zone. The external limit of the lesion was not clearly evident and was represented by an irregular rim of stromal edema whose width was unrelated to the treatment group. Base involvement was seen in 3 of 10 patients in group A and in 7 of 9 patients in group B ($P = 0.037$). In 3 of 10 patients in group A and in 9 of 10 patients in group B, a vast hemorrhagic area usually accompanied by tissue clefting posteriorly to the urethra was observed ($P = 0.010$). Only in 1 patient in group A was no measurable lesion evident; in another patient in group A, the whole prostate had diffuse damage. Only 1 patient of group B had extraprostatic hemorrhage and edema also involving the seminal vesicles.

**QUANTITATIVE HISTOLOGIC FINDINGS**

Table I presents the results observed when comparing the differences in the diameters and volumes of the RF lesions in the two treatment groups and the relative percentages of the thermal lesion volumes. Table I also demonstrates that the two groups differed significantly in whole prostate diameters and volumes (group A, mean 11.54 cm$^3$; group B, mean 24.02 cm$^3$).

Patients in group B had significantly greater lesion volumes than did patients in group A (mean lesion volume 6.91 cm$^3$ for group B versus 1.69 cm$^3$ for group A). Furthermore, the relative percentage of the lesion volume was greater in group B (32% versus 15%), mostly because of a significantly higher proportion of altered prostatic tissue along the anteroposterior and transverse diameters. When compared with the power applied, regardless of the electrode shape, all diameters of the lesions positively and linearly correlated with the amount of power applied (transverse, $P = 0.017$; anteroposterior, $P = 0.011$; and longitudinal, $P = 0.038$). The same feature was seen for volume ($P = 0.001$). The base involvement and the relative percentages of the lesions were unrelated to the amount of power applied.

The interval between the RF treatment and surgery was unrelated to volume of the lesion, relative volume, and base involvement.

**COMMENT**

The thermal lesions induced in prostatic tissue by RF energy delivered by an electrode mounted on a Foley catheter differ significantly in size and morphologic characteristics from those observed with needle-delivered RF. Catheter-mounted electrodes induce a lesion that is not sharply delimited and does not show coagulative necrosis, and its size is related both to the electrode shape and to the amount of energy applied. With needle electrodes, the size of the affected area is confined to a well-defined radius surrounding the needle electrode tip.

The longitudinal extension of the thermal lesions depends on the shape of the catheter-mounted electrode. The circular electrode ensures damage to the proximal portion of the periurethral prostatic tissue and to the prostatic base. Therefore, this solution appears ideal for patients with BPH, for which thermal ablation ought to be preferentially directed to the transitional and central zones of the prostate.

The lesion size also depends on the amount of energy delivered. Some variability with lower levels of energy was observed; however, levels greater than 70 kJ usually ensured a thermal lesion greater than 10 cm$^3$. The total amount of energy delivered with the catheter-mounted electrode is much greater than that applied using interstitial RF, and it approaches the values currently delivered with high-energy microwave thermotherapy. The

![FIGURE 2. Transverse section of the prostate immediately after cystoprostatectomy showing the extent of the thermal lesion induced with a circular electrode.](image-url)
amount of energy delivered is inversely proportional to the electrode surface. Other variables interact in determining the RF lesion size, such as the amount of power applied, application time, and tissue impedance. In this study, amounts of power and time adequate to the electrode surface were used. The RF generator displayed the system impedance in real time, which was maintained at the desired level by regulating the circulation of the electrode-cooling fluid.

The histopathologic evaluation of a small series of patients treated with high-energy microwave thermotherapy who subsequently underwent suprapubic prostatectomy for BPH demonstrated sharply circumscribed intraprostatic thermal lesions consisting of uniform hemorrhagic necrosis and tissue devitalization without significant inflammation. On the other hand, the interval between thermal ablation therapy and surgery was much longer compared with the present series, with a mean of 42 days. A recent report from the same group closely paralleled our experience. In 7 patients with prostate carcinoma, high-energy microwave therapy was applied 4 to 90 hours before radical prostatectomy. Whole-mount sections of the prostate demonstrated hemorrhagic necrosis and tissue devitalization without significant inflammation, mostly centered around the urethra. The mean volume of the necrotic area was 8.8 cm³, and the mean percentage of the prostate involved by necrosis was 22%, without any difference between benign and cancerous tissue.

In the present study, the extent of the thermal lesion correlated with the amount of energy delivered. However, a considerable variability in the lesion size was documented, paralleling the clinical results observed with microwave therapy, and demonstrating that in the prostate, the dispersion of heat depends on tissue conduction and venous blood flow, which may vary considerably from patient to patient. The importance of venous blood flow has also been demonstrated in the size of the RF lesions in the pig liver, whereby occlusion of the portal vein resulted in significantly greater lesions. Therefore, reliable intraprostatic temperature monitoring and feedback on the power output are important features for optimizing treatment results. RF treatment with a catheter-mounted electrode appears to be capable of delivering sufficient energy to compensate for the hemodynamic heat sink effect, which is unpredictable.

An automatic intraoperative control mechanism was not available for this feasibility study but will be used in the clinical setting.

The treatment modalities may also influence the thermal lesion shape and extent, since it has been established that an intraprostatic temperature greater than 45°C maintained for 1 hour causes necrosis of prostatic tissue. In the present study, much higher peak temperatures (up to 119°C) were registered, but the treatment duration was considerably shorter, with a mean of 20.9 minutes for group B. We also envisaged a treatment modality that previewed a rather fast initial rise in tem-

| TABLE I. | Diameters and volumes of the whole prostate, RF-induced thermal lesions, and relative percentages of the lesion in the two treatment groups (range [95% confidence interval]) |
|---|---|---|
| Whole prostate | Group A | Group B | P Value |
| Mean diameter (cm) | | | |
| Longitudinal | 2.6 (2–3.5 [2.2–2.9]) | 3.38 (3–4.5 [2.9–3.8]) | 0.008 |
| Transverse | 3.56 (2.5–4.7 [3.1–4.1]) | 3.85 (3–4.6 [3.5–4.2]) | NS |
| Anteroposterior | 2.42 (2–3.4 [2.1–2.7]) | 3.07 (2.5–3.5 [2.8–3.3]) | 0.005 |
| Mean volume (cm³) | 12.42 (5.2–24.7 [7.9–16.8]) | 21.11 (14.1–52.7 [16.4–25.8]) | 0.008 |
| Thermal lesion | | | |
| Mean diameter (cm) | | | |
| Longitudinal | 1.65 (0–2.5 [1.1–2.2]) | 2.45 (1.5–3.06 [2.1–2.8]) | 0.011 |
| Transverse | 1.73 (0–3.36 [1.1–2.4]) | 2.68 (1.83–3.55 [2.3–3]) | 0.007 |
| Anteroposterior | 0.9 (0–2.14 [0.4–1.4]) | 1.89 (0.91–2.75 [1.4–2.3]) | 0.007 |
| Mean volume (cm³) | 1.69 (0–3.5 [0.7–2.7]) | 6.91 (2.53–15.22 [3.9–9.8]) | 0.002 |
| Relative percentage of thermal lesion | | | |
| Mean diameter (cm) | | | |
| Longitudinal | 62 (0–100 [43–81]) | 73 (50–100 [63–84]) | NS |
| Transverse | 49 (0–88 [31–67]) | 70 (46–95 [59–81]) | 0.028 |
| Anteroposterior | 38 (0–85 [16–60]) | 62 (26–91 [47–77]) | 0.082 |
| Mean volume (cm³) | 15 (0–50 [4–26]) | 32 (15–70 [21–43]) | 0.019 |

Key: NS = not significant.
* Semicircular electrode.
† Circular electrode.
‡ Mann-Whitney U test.
perature, which theoretically causes more extensive thermal damage, diminishing the heat-sink effect caused by a compensatory increase in the prostatic blood flow and maintaining maximum temperatures for at least 10 minutes.

CONCLUSIONS

RF thermal lesions of the prostate have been documented using an electrode mounted on a Foley-like catheter. The procedure is simple, relatively well tolerated, and the only complication observed was urinary retention in patients receiving higher energy. A significant cost reduction is possible, compared with other minimally invasive treatments for BPH, since the same RF generator can be shared with interventional radiologists and general surgeons. The combination of a circular electrode and high power settings produced the largest lesions, and the use of electrodes of different length, proportional to the prostate size, is planned. Therefore, we believe that this technique has been sufficiently optimized to begin a clinical study on patients with BPH.

REFERENCES