

# TRANSRECTAL FOCUSED ULTRASOUND COMBINED WITH TRANSURETHRAL RESECTION OF THE PROSTATE FOR THE TREATMENT OF LOCALIZED PROSTATE CANCER: FEASIBILITY STUDY

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## ABSTRACT

**Purpose:** We studied the feasibility of combined treatment with high intensity focused ultrasound (HIFU) and transurethral resection or incision of the prostate for localized prostate cancer to decrease the risk of posttreatment prolonged urinary retention.

**Materials and Methods:** Included in this feasibility study were 30 patients fulfilling certain criteria, namely localized prostate cancer indicated for HIFU, age 60 years or older, prostate volume 45 cc or less, no more than 4 positive samples at sextant biopsy, baseline prostate specific antigen (PSA) 10 ng/ml or less and no evidence of cancer extension. They received the combined treatment under general anesthesia using an Ablatherm HIFU device (EDAP SA, Lyon, France).

**Results:** The enrolled patients were a mean of 72 years old and presented with a median prostate volume of 30 cc. Median Gleason score was 6, median PSA was 7 ng/ml and pretreatment sextant biopsies provided a median of 2 positive samples. Mean operative time was 2 hours 48 minutes, including resection and HIFU. An average of 616 HIFU shots were delivered. The urinary catheter was removed at day 2 after treatment. Median hospital stay was 3 days. Only a few complications were observed. In regard to the oncological aspects at a mean of 20 months of followup 86% of the patients had negative biopsies after HIFU. Median PSA was 0.9 ng/ml. At 1 year of followup the mean International Prostate Symptom Score was 8. Regarding sexual function, 73% of previously potent patients reported preserved sexual activity.

**Conclusions:** The combination of endoscopic resection or incision of the prostate with HIFU treatment decreases urinary catheterization time and improves posttreatment urinary status without additional morbidity.

**KEY WORDS:** prostate; prostatic neoplasms; ultrasonography; surgical procedures, minimally invasive; transurethral resection of prostate

Several treatment options are available today for the management of localized prostate cancer, such as radical surgery, external beam radiation, brachytherapy and cryotherapy. In the 1990s a new option using high intensity focused ultrasound (HIFU) was evaluated<sup>1–5</sup> and its efficacy has been experimentally and clinically established.<sup>6–11</sup> Due to the risk of treatment associated prolonged urinary retention we evaluated the feasibility of combining endoscopic resection of prostate or bladder neck incision in a single operative time to allow removal of the urinary catheter at day 2 or 3 after treatment.

## MATERIAL AND METHODS

From April 1999 to November 2001, 30 patients presenting with localized prostate cancer were included in this feasibility study who fulfilled certain selection criteria, namely age older than 60 years, prostate volume 45 cc or less, a maximum of 4 positive samples on sextant biopsy, prostate specific antigen (PSA) 10 ng/ml or less, and normal abdominal scan and bone scintigraphy. These patients did not receive any hormonal treatment. All 30 patients received combined treatment under general anesthesia, of whom 22 underwent endoscopic transurethral prostate resection (TURP) and 8

who presented with a prostate volume of less than 30 cc underwent bladder neck incision (BNI). A transurethral double flow catheter was placed immediately after resection and the patient was then positioned in the lateral decubitus position to receive transrectal HIFU.

This study was performed using an Ablatherm HIFU device. Among its major components the transrectal probe includes a 7 MHz ultrasound imaging probe, and a 3 MHz piezoelectric treatment transducer. Contiguous HIFU shots are delivered 1.7 mm apart with a 5-second shot duration and another 5-second interval between shots. The volume to be treated is defined by the urologist using the longitudinal and transverse ultrasound imaging system. At the end of treatment the transrectal probe is removed. The patient is hospitalized a mean of 3 days. The bladder tube is removed on day 2 in the morning. Prophylactic antibiotic medication and low molecular weight heparin are administered for 1 week.

During followup PSA was measured at 3, 6, 12, 18 and 24 months, and yearly thereafter. Followup biopsy was performed at 1 year and thereafter in case of rising PSA. Quality of life and urinary symptoms were assessed using health related quality of life and International Prostate Symptom Score questionnaires (I-PSS). Sexual function was assessed through a short questionnaire exploring erection, ejaculation and sexual intercourse capacities.

## RESULTS

*Population and treatment description.* Patient characteristics at inclusion were mean age 72 years (range 61 to 79),

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median prostate volume 30 cc (range 11 to 45) and median initial PSA 7 ng/ml (range 1 to 10). The median number of positive samples at the diagnosis sextant prostate biopsy was 2 of 6 with a median Gleason score of 6 (range 4 to 7).

Mean treatment time was 2 hours 48 minutes, including TURP/BNI and HIFU. Mean HIFU treatment time was 1 hour 52 minutes. A mean of 612 HIFU shots were delivered and the requested HIFU lesion length was 20 mm. In 4 cases (13%) histological examination of TURP chips revealed cancer. Mean hospital stay was 3 days.

**Oncological results.** Posttreatment efficacy results were considered in all patients at a median followup of 20 months (range 3 to 38). A total of 22 patients (73.3%) had negative followup biopsies at 1 year and a mean PSA of 0.9 ng/ml (range 0.0 to 2.6) after this single HIFU session. None of these patients needed any adjuvant treatment (table 1).

Five patients (16.7%) had positive followup biopsies at 1 year and were re-treated with HIFU only without combined resection or incision. Four of these patients had negative followup biopsies 6 months after HIFU re-treatment and had a mean PSA of 0.4 ng/ml (range 0.1 to 0.9). The remaining patient had a positive followup biopsy after HIFU re-treatment and then received intermittent hormone therapy. In 3 patients (10.0%) posttreatment PSA was high (greater than 4 ng/ml), ie, a mean of 6.3 ng/ml (range 4.2 to 8.0). They underwent external beam radiation therapy (2) or intermittent hormone treatment (a 79-year-old man) without any attempt at a second HIFU treatment. In total the treatment delivered by 1 or 2 HIFU sessions resulted in negative biopsy and PSA control in 86.6% of the patients.

**Functional results.** Questionnaires were administered a mean of 10 months after treatment to evaluate continence status, urinary symptoms, health related quality of life and sexual function.

**Continence Status:** All patients were continent before treatment. After treatment only 1 patient presented with stress incontinence, and urine leakage and pad use were still persistent at 1 year of followup.

**Urinary Symptoms:** Mean baseline I-PSS was 7.5 (range 1 to 20, median 6), including 6 patients with a score of greater than 12. After treatment mean I-PSS was 6.7 (range 1 to 20, median 5) with a mean paired difference of -0.9. Two patients had a score of greater than 12.

**Quality of Life:** Health related quality of life was assessed using the I-PSS-quality of life item with a range of 0—delighted to 6—terrible. Before treatment the mean score was 2.4 (range 0 to 6, median 2). The mean posttreatment score was 1.6 (range 0 to 5, median 1) and the mean paired difference was -0.7. After treatment 12% of the patients were unsatisfied with quality of life (score 4 or greater) vs 37% before treatment.

**Sexual Function:** Before treatment 14 patients had a sexual life with normal erections, 11 reported partial loss of potency and 5 patients were impotent. Of the 14 patients who had previously been potent with normal erections 11 (78.6%) reported no changes in potency status after treatment, while 3 (21.4%) reported the partial or total loss of potency. Of the 11 patients who previously reported decreased potency erection capacity almost disappeared in 5 (45.5%), while it was unchanged in the other 6 (54.5%). In total a decrease in sexual function was observed in 32% of the patients.

TABLE 1. Pathological results of HIFU combined with TURP or BNI

HIFU	No. Neg Biopsies/ Total No. (%)	No. Pos Biopsies/ Total No. (%)
1	22/30 (73.3)	8/30 (26.7)
2	4/5 (80.0)	1/5 (20.0)
Total	26/30 (86.7)	4/30 (13.3)

After first HIFU 8 patients with positive biopsies were treated with hormone therapy or radiotherapy (3), or repeat HIFU without combined TURP (5).

TABLE 2. Complications after HIFU combined with TURP or BNI

	No. Pts (%)
Acute urinary retention	2 (6)
Urinary infection	3 (10)
Hematuria	22 (66)
Prostatorectal fistula	0
Anal pain	0
Fecal incontinence	0
Urinary incontinence	1 (3)
Total No.	28

**Treatment related morbidity.** Reported side effects were observed at immediate followup (table 2). Of the patients 75% reported mild hematuria for 2 to 3 weeks after treatment. This hematuria did not require any intervention and it resolved spontaneously. Mild urgency was reported by 50% of the patients, which resolved within 3 weeks. An asymptomatic urinary tract infection diagnosed in 3 patients was managed by appropriate medications. Two patients experienced an acute urinary retention at the removal of the transurethral catheter at day 2 after treatment; another tube was placed for 3 additional days, and then removed without further complications. No anal pain, incontinence, prostatorectal fistula or delayed morbidity was reported.

#### DISCUSSION

The transrectal HIFU application for localized prostate cancer was used 10 years ago by Gelet et al.<sup>6</sup> The first patients in the European Multicentric Study<sup>12</sup> now have more than 7 years of followup.

Due to HIFU related edema a urinary catheter was placed for 2 to 3 weeks at the end of the procedure. To avoid this risk of prolonged urinary retention, we performed TURP or bladder neck incision. It may be performed before or immediately after the HIFU procedure with different advantages for the 2 options. When performed after HIFU delivery, the advantage is to avoid any clotting since the gland was already coagulated by HIFU prior to resection. When performed before HIFU delivery, HIFU completes the hemostasis and global management using the same anesthesia is easier.

At immediate followup patients are somewhat amazed by the absence of postoperative pain and the improvement in urinary status due to resection or incision. This functional improvement, and the sharp and rapid decrease in PSA are important components in their improved quality of life perception. The HIFU related stress incontinence case, which still persisted after 1 year, was likely due to over treatment of the apex. The patient presented with positive apical biopsies on each side. Today fewer shots are delivered for apex treatment and control of heat diffusion can be considered additional security. Posttreatment impotence is sometimes observed only 1 to 2 months after treatment. It may be due to progressive fibrosis of the neurovascular bundles when too many shots are delivered laterally.

#### CONCLUSIONS

The combination of endoscopic resection or incision of the prostate with HIFU treatment decreases urinary catheterization time and improves posttreatment urinary status without additional morbidity. We are still collecting data on more patients for confirmation with longer term evaluation.

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