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Prostate Cancer

# Control of Prostate Cancer by Transrectal HIFU in 227 Patients

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**Abstract**

***Purpose:*** To evaluate the results of high-intensity focused ultrasound (HIFU) treatment of localized prostate cancer with reference to disease-related prognostic factors.

***Materials and methods:*** Patients with T1–2 localized prostate cancers, prostate specific antigen (PSA) $\leq$15 ng/ml, Gleason score $\leq$7, prostate volume $\leq$40 cc and no previous radical treatment for prostate cancer were treated with the Ablatherm HIFU device. Follow-up included PSA measurements, and prostate biopsies 3 months after HIFU and in cases of rising PSA. Failure was defined as any positive biopsy or a PSA >1 ng/ml with three consecutive rises.

***Results:*** The study included 227 patients. Mean follow-up was 27 $\pm$ 20 months (12–121 months). Eighty-six percent had negative control biopsies. Median nadir PSA was 0.10 ng/ml. The actuarial 5-year disease-free survival rate (DFSR), combining pathologic and biochemical outcomes, was 66%. DFSR showed a significant decrease when stratified according to initial PSA level: 90% with PSA $\leq$4 ng/ml versus 57% and 61% with PSA between 4.1 and 10, and between 10.1 and 15 ng/ml, respectively. Incontinence and bladder neck stricture decreased with the treatment procedure standardization from 28% and 31% to 9% and 6%, respectively.

***Conclusions:*** HIFU for localized prostate cancer offered high control of local disease with low morbidity. The ability to repeat the HIFU treatment is of major interest.



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## 1. Introduction

Since 1989, in our department transrectal high-intensity focused ultrasound (HIFU) has been studied as a minimally invasive treatment for localized prostate cancer. The first pilot study demonstrated the feasibility of the treatment, and this result has been confirmed by additional short-term evaluations [1,2]. We now present comprehensive data from 227 consecutive patients who underwent this procedure between April 1994 and July 2003.

## 2. Materials and methods

### 2.1. *The HIFU principle*

HIFU produces ultrasound waves that are generated by a spherical transducer. The ultrasound energy is focused on a fixed point. The aim is to treat the entire gland by juxtaposition of elementary lesions. The device has a fixed focal ultrasound transducer and a motorized system for successive movements of the focal point. Contiguous shots (5 s on, 5 s off) are delivered repeatedly to obtain a complete treatment of the whole gland, while preserving the rectal wall and the surrounding tissues. The HIFU-induced necrosis phenomenon has been modeled by the National Institutes of Health and Medical Research (INSERM Unit 556, Lyon, France) [3].

### 2.2. *Equipment*

All patients were treated with the Ablatherm HIFU device (EDAP SA, Lyon, France). From 1993 to 1999, the patients were treated with prototype devices. In 1999, the device was granted the CE label and, after 2000, patients were treated with the commercially available device. The differences between the prototypes and the commercially available devices are described in Table 1.

### 2.3. *Procedure*

In parallel with technical progress, clinical procedures have evolved gradually to attain an efficient level of treatment. The HIFU treatment initially involved just one session for each prostate lobe (1993–1996), followed later by a single session to treat the whole gland. A safety margin of 6 mm was defined for treatment of the apex, taking into consideration heat accumulation and diffusion, to protect the external sphincter—and thus to control the risk of treatment-related incontinence—while nevertheless treating the apical tissue. Similar logic is applied currently to obtain nerve-sparing procedures. The last issue was the risk of prolonged retention after treatment, caused by the sloughing of necrotic tissue, and possible secondary obstruction. This issue was solved by performing a transurethral resection of the prostate (TURP) immediately before the HIFU session and while the patient was under the same anesthesia. The catheter was removed on day 3 post-HIFU. This combined procedure dramatically simplified post-HIFU patient management and comfort. Since 2000, the patients were treated according to the standardized HIFU treatment procedure: hospitalization the day before treatment for rectal preparation, a single session treatment combining TURP and HIFU with a safety margin for treatment of the prostate apex and discharge from hospital at day 4 with no urinary catheter.

### 2.4. *Patient selection and follow-up*

For this study, patient selection was based on the following criteria: localized prostate cancer, clinical stage T1–T2, baseline prostate specific antigen (PSA) $\leq$15 ng/ml, prostate volume $\leq$40 cc, no previous radical treatment for prostate cancer and at least 1 year of follow-up.

All patients were assessed regularly on the following criteria: baseline PSA, post-HIFU PSA measurement at 1, 3, 6 and 12 months then every 6 months, and prostate sextant biopsies performed before inclusion and 3 months after HIFU treatment. Additional control biopsies were performed during follow-up in cases of rising PSA. All the patients satisfying these criteria were included. Assessment criteria included the nadir PSA, the posttreatment negative biopsy rate and the disease-free survival rate (DFSR). Failure was defined as any positive biopsy or a PSA $>$1 ng/ml with three consecutive rises. Kaplan-Meier product-limit methods and log-rank tests were used to evaluate the data. In case of positive prostate biopsy during follow-up without evidence of metastasis, HIFU retreatment was performed. For those retreated, the only considerations were the follow-up time and assessment after the last session.

The need for an adjuvant treatment after single or repeated HIFU was defined by general rules (i.e., a rising PSA level, with or without residual local cancer evidenced by biopsy). External radiation therapy, hormonal deprivation or a combination of both was administered in the light of the patient's general status and life expectancy. Patient status and treatment-related complications were followed up by periodic patient visits and by self-administered questionnaires. Stress incontinence was graduated into three grades. Grade one was

**Table 1 – Development of the device**

| Dates | Device | Transducer frequency (MHz) | Shot duration (s) | Safety features | HIFU sessions | TURP |
|---|---|---|---|---|---|---|
| 1993–1995 | Prototype no. 1 | 2.5 | 4 | No | 1 per lobe | No |
| 1996–1998 | Prototype no. 2 | 3 | 4.5 | Control of the distance rectal wall transducer | 1 per lobe | No |
| 1998–1999 | Prototype no. 3 | 3 | 5 | Rectal cooling | 1 per prostate | No |
| 2000–2003 | Final device | 3 | 5 | Safety features | 1 per prostate | Yes |