Twelve Years' Experience with High-Intensity Focused Ultrasound (HIFU) Using Sonablate™ Devices for the Treatment of Localized Prostate Cancer

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Abstract. To report on the long-term results of high-intensity focused ultrasound (HIFU) in the treatment of localized prostate cancer. Patients with clinical Stage T1c-T3N0M0, biopsy proven, localized prostate cancer, with a serum prostate specific antigen (PSA) level of <30 ng/ml, any Gleason score were included. All patients underwent HIFU using the Sonablate™ (S) device and were required to have a minimal follow-up of 2 years after the last HIFU session to be included in this analysis. Four different generation HIFU devices, S200, S500, S500 version 4 and S500 TCM, have been used for this study. Biochemical failure was defined according to the Phoenix definition (PSA nadir+2ng/ml). Seven hundred and fifty-three men with prostate cancer were included. The patients were divided into two groups: in the Former group, 421 patients were treated with S200 and 500 from 1990 to 2005; in the Latter group, 332 patients were treated with S500 ver. 4 and TCM from 2005 to 2009. The mean age, PSA, Gleason score, operation time, and follow-up period in the Former and Latter groups were 68 and 67 years, 11.3 and 9.7 ng/ml, 6.2 and 6.6, 167 and 101 min, and 49 and 38 months, respectively. The biochemical disease-free rate (BDFR) in the groups at 5 years was, respectively, 67% and 53%, and was 50% at 10 years in the Former group ($p<0.0001$). The BDFR in patients in the low-, intermediate-, and high-risk groups in the Former group at 5 and 10 years were 68% and 65%, 52% and 48%, and 43% and 40%, respectively ($p<0.0001$). The BDFR in patients in the low-, intermediate-, and high-risk groups in the Latter group at 5 years were 83%, 76%, and 42% ($p<0.0001$). The negative prostate biopsy rate in the Former and Latter groups was 81% and 93%, respectively. Postoperative erectile dysfunction was noted in 45%, 38%, and 24% of patients at 6 months, 12 months, and 2 years after HIFU. The results after long-term follow-up have indicated that HIFU is an efficient and safe treatment for patients with localized prostate cancer, especially low- and intermediate-risk patients.

Keywords: benign prostatic hyperplasia, prostate cancer, high-intensity focused ultrasound

INTRODUCTION

Prostate cancer is the leading malignancy in men and the second leading cause of death due to cancer in the United States. Recently, a number of alternative minimally invasive treatments have been developed localized prostate cancer. High-intensity focused ultrasound (HIFU) is one of the newer of ablation therapy for available for

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men with prostate cancer [1-5]. This report describes the 12-years experience with 753 consecutive patients treated with HIFU for clinical stage T1c-3N0M0 localized prostate cancer.

MATERIAL AND METHODS

Patients with clinical Stage T1c-T3N0M0, biopsy proven, localized prostate cancer, with a serum prostate specific antigen (PSA) level of <30 ng/ml, any Gleason score were included. All patients underwent HIFU using the Sonablate™ device and were required to have a minimal follow-up of 2 years after the last HIFU session to be included in this analysis. Four different generation HIFU devices, Sonablate (S)-200, S500, S500 version 4 (V4) and TCM (Focus Surgery Inc., Indianapolis, IN USA), have been used for this study. Biochemical failure was defined according to the Phoenix definition (PSA nadir + 2 ng/ml). Treatment module includes the ultrasound power generator, multiple transrectal probes of different focal, the probe positioning system, and a cooling system. The transrectal HIFU probes use proprietary transducer technology with low-energy ultrasound (4 MHz) for imaging of the prostate and for the delivery of high-energy ablative pulses (site intensity, 1300 - 1680 W/cm^2). Details of the HIFU techniques have been previously published [1-3]. Many improvements and newly developed functions have been added to each device to shorten the time of operation and to improve the clinical outcome (Table 1). Cycle was shortened from 16 to 6 s/focus lesion. Angle widened from 70 to 90°. Each volume was enlarged from 2x2x10 mm^3 to 3x3x12 mm^3. Doppler system was added to detect the neurovascular bundle. STACK and TCM systems were added in V4 and TCM devices. STACK system can refine the treatment plan at any time before or during the procedure. TCM system can monitor temperature of each lesion color change. For example, green means temperature of the focus lesion 48℃, yellow 65℃ and orange 95℃.

TABLE 1. Improved and new developed functions in each device

Type (Period)	SB200 (93'-01')	SB500 (01'-05')	SB500 ver.4 (05'-08')	Tissue Change Monitor (07'-)
Cycle (sec)	15	9	6	6
Sector Angle	70	90	90	90
Focus volume (c.c.)	2x2x2mm (0.04cc)	3x3x12mm (0.108cc)	3x3x12mm (0.108cc)	3x3x12mm (0.108cc)
Doppler system	No	Yes	Yes	Yes
Conti-Cooling	No	Yes	Yes	Yes
Three Dimension	No	Yes	Yes	Yes
STACK system	No	No	Yes	Yes
TCM system	No	No	No	Yes

None of the patients received androgen deprivation or other anticancer therapy before documentation of a biochemical failure. All patients were fully informed of the details of this treatment and provided written consent preoperatively.

RESULTS

The mean age, PSA, Gleason score, operation time, and follow-up period in the Former and Latter groups were 68 and 67 years, 11.3 and 9.7 ng/ml, 6.2 and 6.6, 167 and 101 min, and 49 and 38 months, respectively (Table 2).

TABLE 2. Characteristics each generation HIFU device

	SB200/500 (99'-05')	SB500 ver.4/TCM (05'-09')	Total
No. of Pts	421	332	753
Age	68±7	67±7	67±7
PSA (ng/ml)	11.3±6.1	9.7±4.9	10.6±5.7
Gleason score	6.2±1.3	6.6±1.1	6.4±1.2
Prostate vol.(c.c.)	23.6±9.5	23.6±7.8	23.5±9.1
Ope time(min)	167±53	101±26	131±55
Follow-up (month)	49±33	38±16	44±27
Neg. Prostate Bx (%)	81%	93%	86%

The biochemical disease-free survival rate (GCFR) in S200, S500, V4 and TCM groups were 55%, 50%, 66% and 78%, respectively (p=0.0004, FIGURE 1). The BDFR in the Former and Latter groups at 5 years was, respectively, 67% and 53%, and was 50% at 10 years in the Former group (p<0.0001, FIGIRE 2). The BDFR in patients in the low-, intermediate-, and high-risk groups in the Former group at 5 and 10 years were 68% and 65%, 52% and 48%, and 43% and 40%, respectively (p<0.0001, FIGURE 3). The BDFR in patients in the low-, intermediate-, and high-risk groups in the Latter group at 5 years were 83%, 76%, and 42% (p<0.0001, FIGURE 4). The negative prostate biopsy rate in the Former and Latter groups was 81% and 93%, respectively (TABLE 2). Multivariate analyses revealed that pretreatment PSA levels (hazard ratio 1.052; p<0.0001; 95% CI 1.032–1.072), neoadjuvant hormonal therapy (hazard ratio 1.769; p<0.0001; 95% CI 1.389–2.257), and stage (p<0.0001) were statistically significant variables. Postoperative erectile dysfunction was noted in 45%, 38%, and 24% of patients at 6 months, 12 months, and 2 years after HIFU.

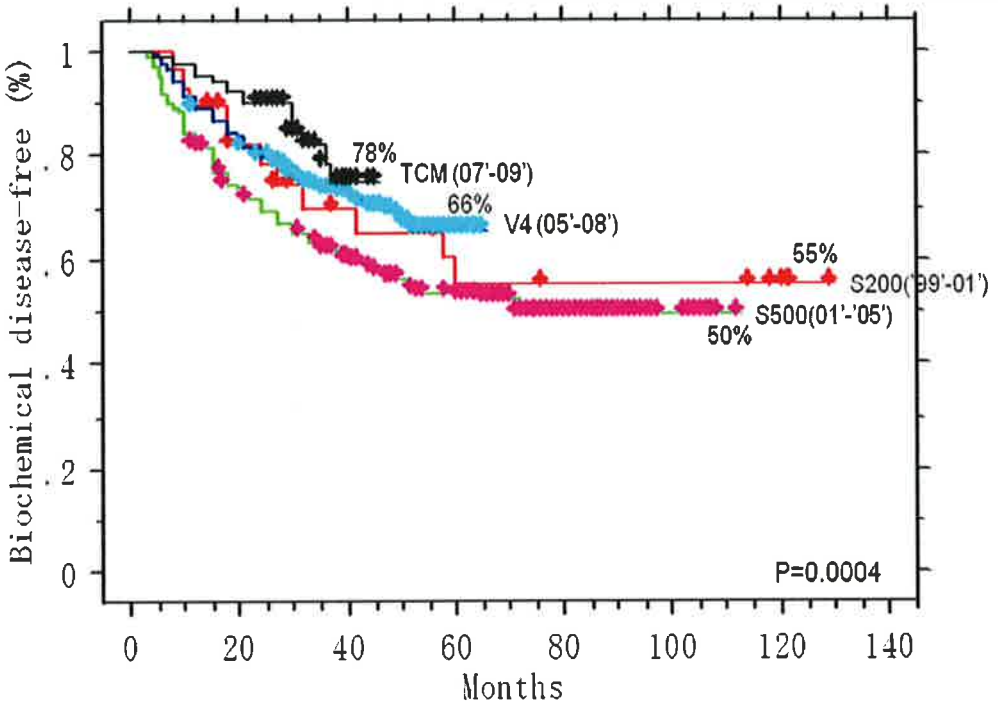

FIGURE 1. Biochemical disease-free survival rates in each group.

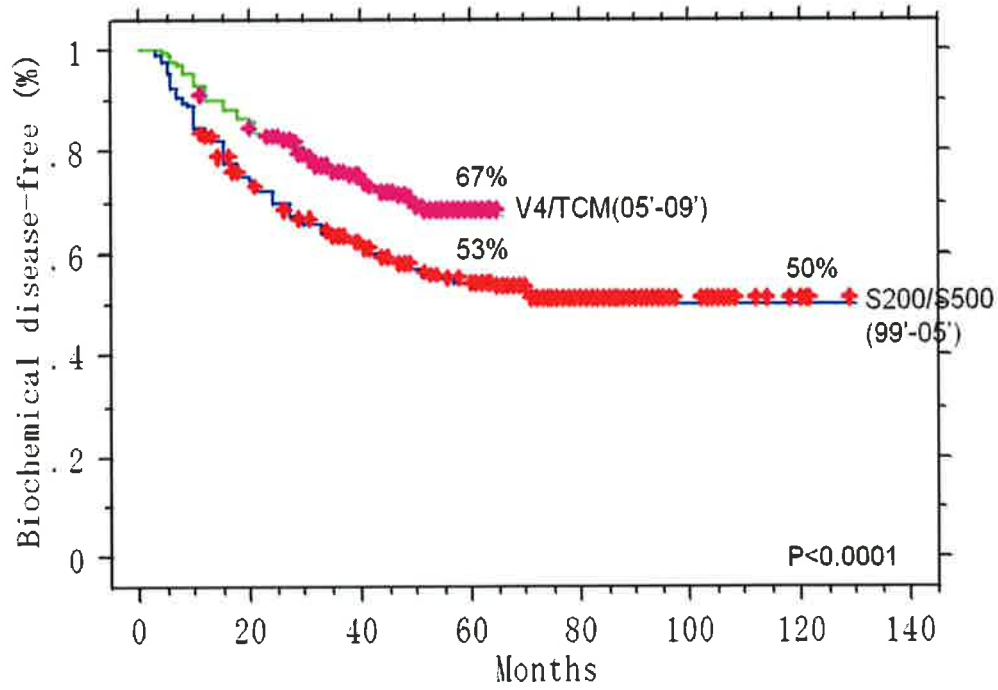

FIGURE 2. Biochemical disease-free survival rate in the Former and Latter groups.

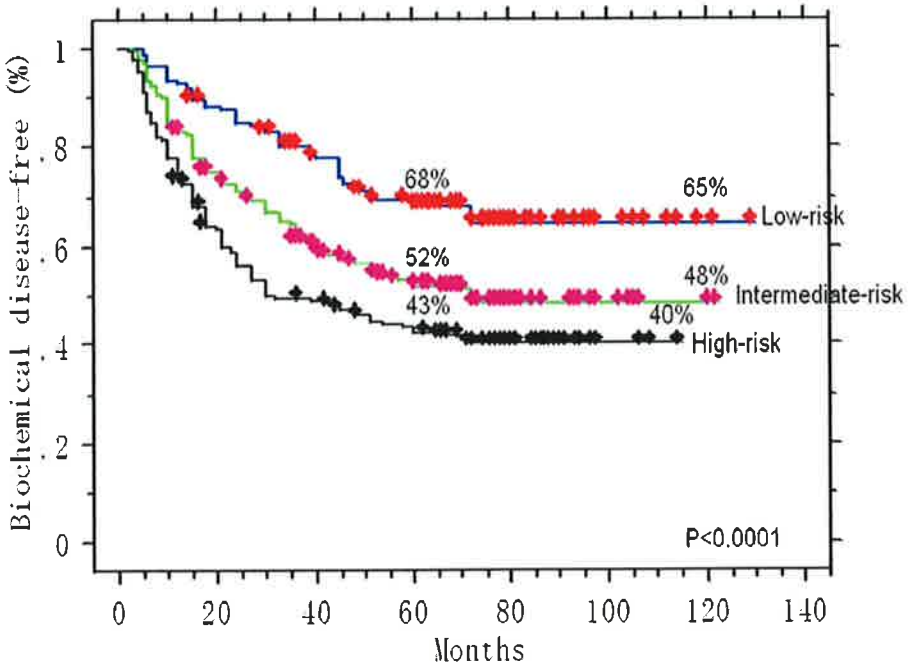

FIGURE 3. Biochemical disease-free survival rate in patients with low-, intermediate- and high-risk groups in the Former group (1999-2005).

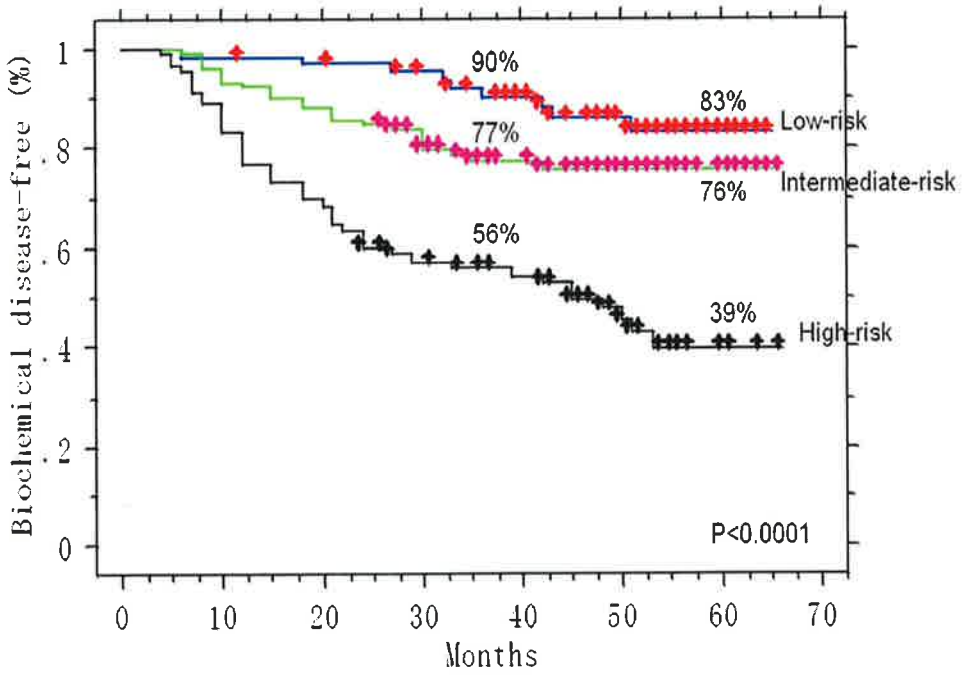

FIGURE 4. Biochemical disease-free survival rate in patients with low-, intermediate- and high-risk groups in the Latter group (2005-2009).

DISCUSSION

Clinical outcome of HIFU for localized prostate cancer was encouraged. Especially, operation time was shortened and % of negative prostate biopsy after HIFU was improved. Biochemical disease-free survival rates were also improved from 50% in Former group (1993-2005) to 67% in the Latter (2005-2009) group. When we compare to other alternative such as surgery and radiation therapy, HIFU showed a similar clinical outcome and lower morbidity. Especially, a rate of incontinence and erectile dysfunction after HIFU were lower than others. However, it needs a further development to achieve more safe and good clinical outcome. In near future, many patients might be home in just 30 min HIFU treatment.

CONCLUSIONS

For many reasons, HIFU appears highly attractive as a minimally invasive treatment for localized prostate cancer. HIFU treatment requires no incision or puncture and it is bloodless, it can be performed on an outpatient basis and repeatable. The rate of clinical outcome has significantly improved over the years due to technical improvements in the device.

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