

Single application of high-intensity focused ultrasound (HIFU) in clinically localized prostate cancer– Late oncological results and comparative cancer control efficacy with different HIFU device generations

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Abstract

Purpose: To report late oncological outcomes in men with localized T1-T3 prostate cancer following single-session HIFU performed under the conception of whole-gland therapy.

Material and methods: This retrospective single-center study enrolled patients, who were uniformly treated by whole-gland ablation between December 2002 and September 2012. Treatment involved two generations of Ablatherm devices, the Maxis[®] (A1) and the Integrated Imaging[®] (A2). Outcome measures were overall survival, cancer-specific, metastasis-free, biochemical-free, and disease-free survival. Biochemical failure was assessed using PSA nadir+2 and nadir+1.2 failure definitions. Disease failure was defined as positive control biopsy and/or PSA failure (nadir+2 ng/ml). Kaplan–Meier analyses were performed for survival estimates. Multivariate analysis was performed using Cox models.

Results: Of 357 study patients, 146 (40.9%), 124 (34.7%) and 87 (24.4%) exhibited low-, intermediate- and high-risk disease (D'Amico), respectively. Median patient age was 70 yrs. Median follow-up was 6.5 yrs. (interquartile range, 4.3-8.9). The 10-year overall, cancer-specific and metastasis-free survival rates were 68%, 95% and 91%, respectively. The 8-year biochemical-free survival rates according to risk grouping were 93%, 76% and 48%, or 81%, 62% and 45% for nadir+2 and nadir+1.2 failure definitions. The 8-year disease-free survival (DFS) rates were 76%, 49% and 42%, respectively. 8-year estimates of DFS differed between the HIFU-devices A1 and A2 (54% vs. 74%, $p < .001$). The device generation predicted disease failure (hazard ratio .51, $p = .001$) independent from risk group, pre-treatment PSA level and Gleason sum.

Conclusions: Success with single-session HIFU does not depend solely on tumor determinants. Ablation is more efficacious with the technically advanced A2 HIFU device.

Abbreviations: ADT: Androgen deprivation therapy; AS: Active surveillance; ASA: American society of anaesthesiologists; BFS: Biochemical failure-free survival; DFS: Disease-free survival; HIFU: High-intensity focused ultrasound; HR: Hazard risk; IMRT: Intensity-modulated radiation therapy; IQR: Interquartile range; MFS: Metastasis-free survival; PCa: Prostate cancer; PCSS: Prostate cancer specific survival; RT: Radiotherapy.

Introduction

High-intensity focused ultrasound (HIFU) ablates the prostate *in situ*. The curative potential for the treatment of localized prostate cancer (PCa) was already recognized in the 1990s [1,2] subsequently, the use of HIFU therapy expanded to include the treatment of localized PCa with high risk of tumor progression [3,4]. In Europe, extensive experience has been gained using Ablatherm HIFU devices (EDAP-TMS, Vaulx-en-Velin, France). Recent reports on late outcomes show that cancer control rates following HIFU are associated with the risk groups of tumor recurrence (D'Amico [5]), suggesting a strong impact of tumor determinants on oncological results [6-8]. However, these reports included repeat HIFU treatment, with a mean of 1.2 to 1.4 HIFU treatments per patient, which confounds the interpretation of HIFU

efficacy and raises the question whether the initial tumor ablation was performed adequately on all patients.

Under-treatment of PCa due to an inadequate HIFU approach was addressed by Blana *et al.* who marked the significance of complete prostate ablation as a prerequisite of tumor eradication; whole-gland therapy requires that all parts of the gland are exposed to the traversing ultrasound and ablation should avoid leaving gaps of untreated tissue [9]. The ability to treat the entire gland may also be influenced by the technical standard of the apparatus. Recent studies involved different commercially available HIFU device generations and even prototypes. The most important factor was the lack of visual real-time control of the on-going procedure until 2005 [10,11], leaving a risk of under-treatment due to discrepancies between plan and performance.

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Received: January 15, 2021; **Accepted:** January 25, 2021; **Published:** February 08, 2021

In the present study, we evaluated the late oncological efficacy with HIFU following single-session whole-gland ablation for localized PCa. Two generations of Ablatherm devices were involved. The study focused on oncological outcomes, whereas treatment-related morbidity had already been reported elsewhere [12].

Patients and methods

This retrospective single-center study enrolled patients with clinically localized PCa who underwent a single session of whole-gland HIFU treatment as a first-line therapy with curative intent at the Asklepios Clinic Hamburg-Barmbek between December 2002 and September 2012. All men were unsuitable candidates for radical prostatectomy due to age or comorbidity and were unwilling to undergo radiotherapy (RT).

Patients were stratified into risk categories of tumor recurrence according to D'Amico [5]. Criteria for the high-risk category were modified to include patients with tumor stage cT3 (TNM 2002). Extracapsular tumor extension and lymph node status was assessed with CT or MRI. Staging included bone scans in men with PSA ≥ 10 ng/ml. Patients with apical prostate tumor or metastases were not considered for local HIFU treatment.

Excluded from the study were men who received organ-preserving HIFU ablation (treating only parts of the gland [13]). Patients on androgen deprivation therapy (ADT) were not excluded. ADT was discontinued at the time of HIFU therapy.

One operator (D.P.) conducted 94% of all HIFU procedures. Treatment involved the use of two commercially available Ablatherm devices, the Maxis' device and (after February 2006) the Integrated Imaging' device, hereafter addressed respectively as devices A1 and A2. The A2-device allowed for the more precise targeting of the prostate and TRUS-based visual real-time control of the ongoing procedure [10,11].

The intention of whole-gland treatment is the destruction of the prostate with a safety margin of 6 mm from the apex to preserve the urethral sphincter. Our ablation technique included an overlap of treatment zones to avoid leaving gaps of untreated tissue [9]. With enlarged glands, anterior margins were ablated with a second pass. Glands with an excess in height (>2.6 cm [TRUS]) required prostate resection prior to HIFU to adjust the gland size to the limited penetration depth of the ultrasound beam (approximately 30 mm).

Postoperative follow-up included serial PSA measurements. Control biopsies were recommended after 6 months and in cases of rising PSA. The metastatic status was assessed in case of a PSA doubling time ≤ 6 months. Follow-up data were obtained by periodical patient contacts or medical records. Cause of death was identified from physician correspondence. The data were collected in an Access database (prospectively established in 2002). The use of prospectively collected data for outcome evaluations was approved by the local ethics committee.

Outcome measures were overall survival (OS), prostate cancer-specific survival (PCSS), biochemical failure-free survival (BFS), disease-free survival (DFS) and metastasis-free survival (MFS). Biochemical failure was defined according to the ASTRO Phoenix definition (PSA nadir +2 ng/ml [14]) and the Stuttgart definition (PSA nadir +1.2 ng/ml [15]). Disease failure was expressed as positive biopsy and/or biochemical relapse (nadir+2 definition), whichever occurred first. The type and sequence of salvage treatment was also recorded.

Statistical analysis was performed using StataSE v.13 (StataCorp LP, College Station, USA). Categorical variables were compared using Fisher's exact test. Quantitative variables were compared with the Mann-Whitney-U-test. The Kaplan-Meier method was used to construct survival curves, which were compared using the log-rank test. The Cox regression model was used to estimate the prognostic relevance of different variables on disease failure. The follow-up period was defined as the interval between HIFU treatment and the last available monitoring data or the date of death. Median (IQR) follow-up time was established with the inverse Kaplan-Meier method. A p-value <0.05 was considered statistically different.

Results

A total of 357 patients aged 55 to 82 years were enrolled in the study. According to the ASA risk classification, 129 (36.1%) men exhibited an elevated perioperative risk (ASA III-IV). HIFU was delivered with the A1-device in 139 patients, and the A2-device in 218 patients. Baseline characteristics are summarized in Table 1. Most patients underwent prostate surgery prior to HIFU, either for BPH (resulting in incidental carcinoma) or synchronously with HIFU Procedures were TURP (n=281), adenomectomy (n=7), or laser enucleation (n=5). Prior to HIFU, 112 (31.6%) men received ADT for median (IQR) 10 (6-24) weeks. Treatment characteristics are summarized in Table 2. The prostate size (pre-plan) allowed for complete HIFU ablation in all but 5 (1.4%) glands which exhibited an excess in height, thereby limiting the ablation of anterior margins. With both devices, the ablation technique was similarly extensive; the treatment volume exceeded the measured prostate volume (pre-plan) by factor 2.1 (mean 2.2).

Survival

Median (interquartile range [IQR]) follow-up was 6.5 (4.3-8.9) years (95th percentile:10.5). The vital status was evaluable for 356 (99.7%) men. The 10-year OS-rate was 68% (95%-CI, 58-76%) (Figure 1). Patients aged >75 years were more likely to die than those aged 55 to 65 years (hazard ratio [HR], 2.32 [95%-CI, 1.33-4.10], $p=0.003$). Amongst the oldest men, the risk of death was associated with an elevated perioperative risk (ASA III-IV) at the time of HIFU (HR, 2.72 [95%-CI, 1.34-5.47], $p=0.005$).

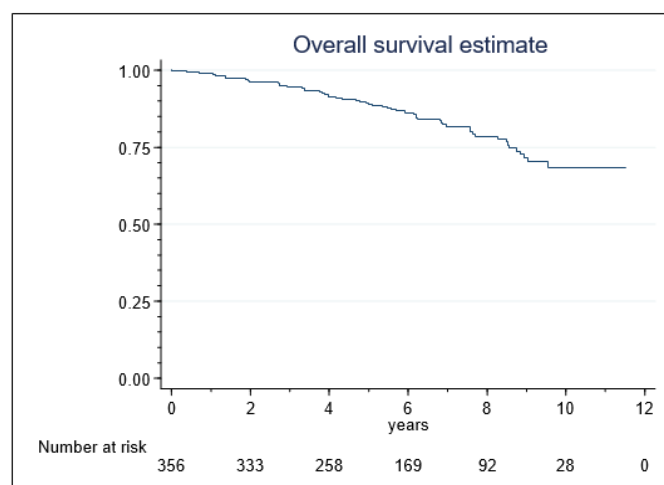


Figure 1. Overall survival in 356 patients following single-session HIFU treatment of localized prostate cancer

Table 1. Baseline characteristics in 357 patients and in subgroups by Ablatherm HIFU devices

	Total	Ablatherm HIFU devices		p value
		Device A1*	Device A2*	
Patients N (100%)	357	139	218	
Age (yrs.)	70 (66-74)	71 (66.5-75)	70 (66-74)	.20
PSA at diagnosis (ng/mL)	7.2 (5.0-10.9)	7.2 (4.8-13.2)	7.2 (5.1-10.4)	.53
Gleason sum				.107
≤ 6	221 (61.9)	90 (64.7)	131 (60.1)	
7	97 (27.2)	30 (21.6)	67 (30.7)	
8 - 10	39 (10.9)	19 (13.7)	20 (9.2)	
Clinical tumor stages**				<.001
T1A/B	46 (12.9)	29 (20.9)	17 (7.8)	
T1C	160 (44.8)	48 (34.5)	112 (51.4)	
T2A	69 (19.3)	22 (15.8)	47 (21.6)	
T2B	38 (10.6)	18 (12.9)	20 (9.2)	
T2C	22 (6.2)	14 (10.1)	8 (3.7)	
T3A/B	22 (6.2)	8 (5.8)	14 (6.4)	
Risk groups (D'Amico)				.071
Low	146 (40.9)	51 (36.7)	95 (43.6)	
Intermediate	124 (34.7)	45 (32.4)	79 (36.2)	
High	87 (24.4)	43 (30.9)	44 (20.2)	
Prostate surgery				<.001
Not performed	64 (17.9)	38 (27.3)	26 (11.9)	
previous for BPH	46 (12.9)	29 (20.9)	17 (7.8)	
synchronous with HIFU	247 (69.2)	72 (51.8)	175 (80.3)	
ADT***				<.001
no	244 (68.4)	72 (51.8)	172 (78.9)	
yes	113 (31.6)	67 (48.2)	46 (21.1)	

Values are median (interquartile range) or N (%)
 *Device A1, Ablatherm Maxis®; Device A2, Ablatherm Integrated Imaging®
 **TNM-classification 2002
 ***ADT, androgen deprivation therapy (preoperative)

Table 2. Treatment characteristics in 357 patients and in subgroups by Ablatherm HIFU devices

	Total	Ablatherm HIFU devices		p value
		Device A1*	Device A2*	
Patients N (100%)	357	139	218	
Prostate volume on TRUS (mL)				
at first visit	28.6 (20.6-38.0)	23.0 (17.0-31.0)	32.0 (24.1-41.0)	<.001
before HIFU [pre-plan]	18 (13-22)	19 (13-24)	17 (13-21)	.011
HIFU treatment data				
Lesions per treatment (No.)	586 (501-668)	629 (505-759)	566 (501-645)	.001
Treatment volume (mL)**	37 (31-43)	40 (32-50)	36 (30-40)	<.001
Treatment duration (min)	145 (125-170)	165 (135-200)	135 (120-155)	<.001
Treatment ratio***	2.1 (1.7-2.5)	2.1 (1.6-2.8)	2.1 (1.8-2.4)	.447

Values are median (interquartile range)
 *Device A1, Ablatherm Maxis®; Device A2, Ablatherm Integrated Imaging®
 **Treatment volume, computed sum of single lesion volumes
 ***Treatment ratio, treatment volume/TRUS-measured prostate volume [pre-plan]

The 10-year PCSS-rate was 95.0%(95-CI,90-98%) (Figure 2). Nine (2.5%) men died of PCa, including 3 (2.4%) and 6 (7.0%) patients in intermediate- and high-risk groups.

Cancer control

The median (IQR) nadir PSA was 0.04 (0.02-0.16) ng/mL, which occurred at 28.3 (14.5-56) weeks. The nadir values in patients with previous ADT (0.04 [0.02-0.17] ng/ml) and men without (0.045 [0.02-0.16] ng/ml) were similarly low (p=.61).

Control prostate biopsies were available for 215 (60.7%) patients and were taken at a median (IQR) of 29.3 (23.7-62.5) weeks after HIFU,

i.e near the time of PSA nadir. Biopsies were positive in 63 (29.3%) men. Men with positive biopsies exhibited higher nadir PSA values (median [IQR], 0.3 [0.05-1.01]) than those with negative biopsies (0.03 [0.01-0.11]) (p<.001). 139 (39.3%) men with very low nadir PSA values (0.03 [0.02-0.09] ng/ml) omitted scheduled biopsy.

Biochemical relapse was recorded in 75 (21.2%) and 100 (28.2%) patients for nadir+2 or nadir+1.2 failure definitions. Table 3 shows the BDF-rates at 5 and 8 years. Depending on the failure definition, BFS-calculation censored 30 (48%) or 18 (29%) of 62 men with local failure as non-failing, as they were transmitted to salvage therapy before PSA relapse occurred.

In total, 104 (29.4%) men exhibited disease failure. First failure event was a positive biopsy in 62 (59.6%) men and PSA progression to nadir+2 in another 42 (40.4%). The overall 8-year DFS-rate was 65% (95%-CI,58-71%). The 8-year DFS-rates in low-, intermediate-, and high-risk patients were 84% (75-91), 61% (51-70) and 42% (30-55), respectively (p<0.001) (Figure 3). In the low- to intermediate-risk disease, treatment with the A2 device was more efficacious than with the older device (Table 4). Preoperative tumor determinants (PSA, Gleason sum, D’Amico risk category) and the HIFU device generation were univariate and multivariate risk factors of DFS, whereas clinical tumor stages and preoperative ADT were not (Table 5).

Metastases developed in 17 (4.8%) patients and occurred in 14 men within 5 years after HIFU. The 10-year MFS-rate was 91% (95%-CI 83-95%) (Figure 4). High risk patients were exposed to an elevated risk of developing metastases (HR, 17.8 [95%-CI, 2.29-138.6], p= 0.006). Lymph node involvement was present in six men and distant metastases were recorded in the remainder.

Salvage treatment was introduced to 85 (24.0%) patients. 36 (10.2%) men with persistent local tumor received therapy with curative intent, either repeat HIFU (n=24), radiotherapy (n=7), or prostatectomy (n=5). 49 (13.8%) comorbid men received only palliative ADT. Chemotherapy was initiated in 6 (1.7%) men with metastases.

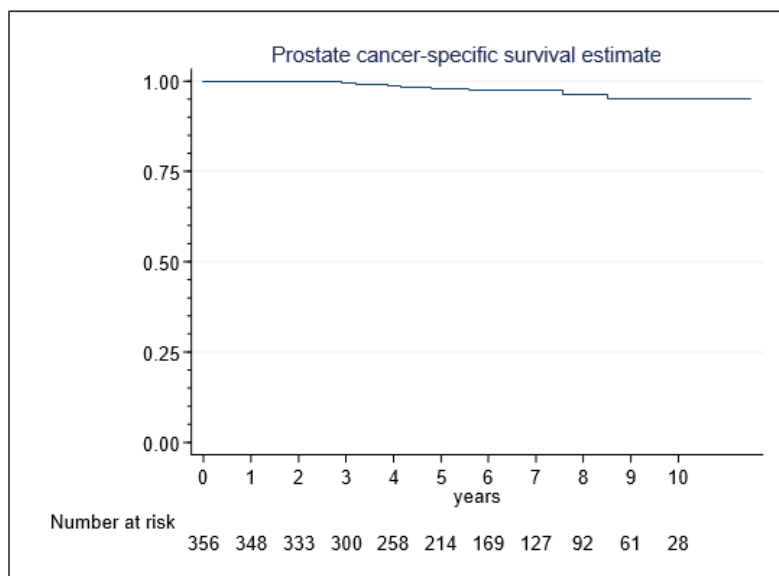


Figure 2. Prostate cancer-specific survival in 356 patients following single-session HIFU treatment of localized prostate cancer

Table 3. Biochemical failure-free survival probabilities in 354 patients according to Nadir+2 and Nadir+1.2 failure definitions, stratified by D’Amico risk groups

Variables	Biochemical failure definition									
	Nadir+2 definition					Nadir+1.2 definition				
	5 years		8 years		p value	5 years		8 years		p value
	No. at risk	Ŝ(t) [95%-CI]	No. at risk	Ŝ(t) [95%-CI]		No. at risk	Ŝ(t) [95%-CI]	No. at risk	Ŝ(t) [95%-CI]	
All cohort	178	82% [77-86]	67	74% [68-80]		159	73% [68-78]	56	65% [58-71]	
Risk groups (D’Amico)										
Low	84	98% [93-99]	35	93% [83-97]	Ref.	76	89% [82-94]	29	81% [70-89]	Ref.
Intermediate	54	78% [68-84]	19	76% [66-83]	.009	49	69% [59-77]	16	62% [51-71]	.008
High	40	62% [51-72]	13	48% [35-60]	.001	34	54% [42-64]	11	45% [33-57]	.002

Ŝ(t) [95%-CI]= Estimated survival function in percentage with 95% confidence interval

Table 4. Disease failure-free survival probabilities according to the HIFU device generation, stratified by D’Amico risk groups

Variables	HIFU device generation								p value**
	HIFU device A1* (n= 136)				HIFU device A2* (n= 218)				
	5 years		8 years		5 years		8 years		
	No. at risk	Ŝ(t) [95%-CI]	No. at risk	Ŝ(t) [95%-CI]	No. at risk	Ŝ(t) [95%-CI]	No. at risk	Ŝ(t) [95%-CI]	
All cohort	71	62% [53-70]	51	54% [45-62]	85	81% [75-86]	6	74% [65-81]	<.001
Risk groups (D’Amico)									
Low		84% [70-92]		79% [64-88]		93% [85-97]		89% [75-95]	.092
Intermediate		49% [34-63]		47% [31-61]		76% [64-85]		73% [59-82]	.007
High		51% [35-65]		38% [22-53]		64% [45-77]		50% [31-67]	.360

Ŝ(t) [95%-CI] = Estimated survival function in percentage with 95% confidence interval
 * Device A1, Ablatherm Maxis®; Device A2, Ablatherm Integrated Imaging®
 ** Device A1 vs. A2

Table 5. Univariate and multivariate analysis of disease-free survival

Variables	Univariate analysis			Multivariate analysis		
	HR	95%-CI	p value	HR	95%-CI	p value
PSA at diagnosis	1.02	1.01 - 1.04	.001	1.02	1.01 - 1.03	<.001
Gleason sum	1.25	1.01 - 1.55	.041	1.31	1.06 - 1.62	.013
Clinical tumor stages*						
T1-T2a	1	-		-	-	-
T2b	1.43	.81 - 2.53	.211	-	-	-
T2c-T3b	.69	.36 - 1.31	.254	-	-	-
Risk groups (D'Amico)						
Low	1	-		1	-	
Intermediate	2.16	1.15 - 4.07	.017	2.32	1.27 - 4.25	.006
High	2.48	1.09 - 5.63	.030	2.03	.98 - 4.25	.058
ADT**						
yes	1	-		-	-	
no	.93	.60 - 1.44	.736	-	-	
HIFU device						
A1	1	-		1	-	
A2	.51	.33 - .79	.002	.51	.34 - .78	.001

HR, hazard ratio; 95%-CI, 95% confidence interval
 * TNM 2002
 ** ADT, Androgen deprivation therapy (preoperatively)

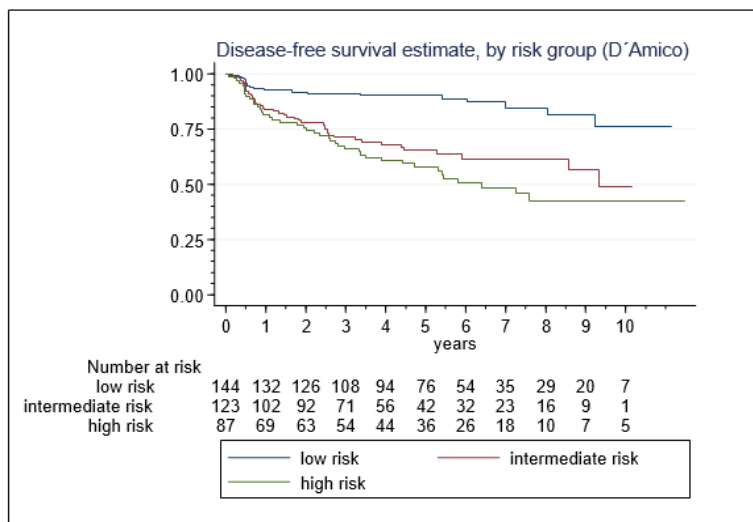


Figure 3. Disease-free survival in 354 patients following single-session HIFU treatment of localized prostate cancer, by D'Amico risk groups

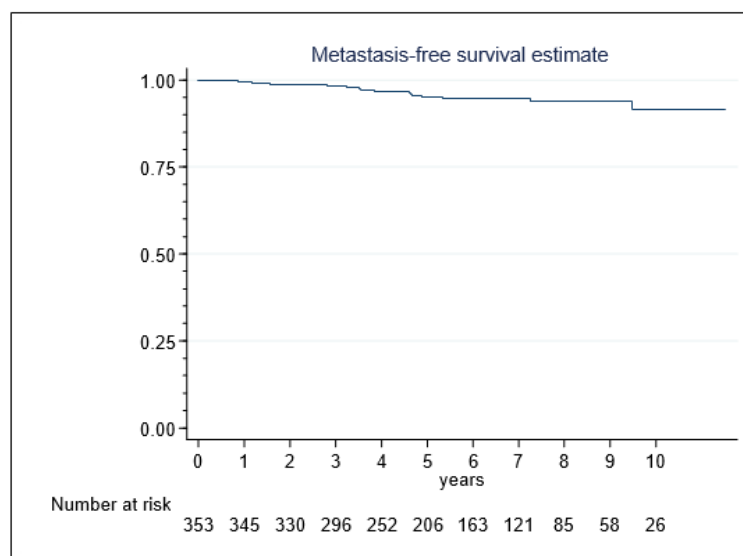


Figure 4. Metastasis-free survival in 353 patients following single-session HIFU treatment of localized prostate cancer

Discussion

The present study assessed late oncological outcomes following single-session HIFU treatment of localized PCa performed under the conception of whole-gland therapy. Differences to all previous reports concern the more extensive ablation technique, resulting in a higher volume ratio (treated/measured prostate volume) in this study (mean 2.2 vs. 1.3-1.9), and the more frequent use of the technically advanced A2 device (application rate 61% vs. 26-29%) [7,8].

In all, 84% of patients with low-risk disease attained a disease-free status at 8 years, with rates of cancer control declining in patients with intermediate- and high-risk disease. In a multivariate analysis, higher pre-treatment PSA values and biopsy Gleason scores were independent predictors of disease failure. In studies of radical prostatectomy, both variables were key factors for the risk of extra-prostatic disease extension [16]. Accordingly, the under-treatment of a considerable proportion of tumors in higher risk groups might reflect understaging prior to therapy.

However, the efficacy of HIFU was not solely dependent on tumor characteristics. Treatment proved to be more efficacious with the A2 HIFU device. The risk of disease failure decreased by approximately 50%. The 8-year DFS-rates tend to be higher in low-risk disease (89% vs. 79%) and increased significantly in intermediate-risk disease (73% vs. 47%), while better outcomes in high-risk tumors (50% vs. 38%) were not statistically significant.

These differences are remarkable, since the ablation technique was similarly extensive with both devices to ensure complete tumor eradication. A principal difference exists between the devices related to control facilities and the precision of the treatment conduct. With the A2 HIFU device a new electronic probe was introduced, which allowed visually directed ablation and a more accurate targeting of the prostate, thereby avoiding gaps between plan and performance and an under-treatment during therapy [10,11]. Our study suggests that these technological advances were associated with a greater efficacy of single-session HIFU.

The composite definition of disease failure used in this study is based on positive biopsy or PSA progression to nadir+2 ng/ml. The biopsy execution rate of 61% compares to rates between 55% and 77% in other recent case-series [7,8]. Locally persistent tumor detected by scheduled biopsy near the time of PSA nadir was the primary event in 59.6% of men who failed, while the remainder eventually experienced PSA relapse without confirmation of local failure. This underlines the value of early post-HIFU biopsy especially if PSA nadir does not reach undetectable levels [17]. Presumably, treatment failure would have ultimately been recognized earlier if biopsies had been taken in all patients with rising PSA values. This is important if secondary curative treatment is intended, which provides more favorable clinical results before the PSA level rises to >0.5 ng/ml; such less pronounced rises in the PSA level imply smaller tumor foci which are difficult to detect by imaging [18].

Disease-free survival has also been reported according to strict biochemical failure definitions, either PSA progression to nadir+2 ng/ml, or to nadir+1.2 ng/ml [15]. This study shows that both definitions are not very accurate for the calculation of disease-free rates, since men with early proven local failure, transmitted to salvage therapy before PSA relapse occurred, were misclassified as cured. Therefore, the composite disease failure definition may provide a more consistent picture of the cancer-control efficacy from single-session HIFU.

However, biochemical failure has been widely used as a measure of late oncological outcomes after HIFU treatment and most authors applied the nadir+2 definition originally designed to monitor biochemical response following RT [14].

Recently, Crouzet *et al.* reported 8-year multicenter outcomes in 1002 patients treated with Ablatherm HIFU. The median follow-up length (6.4 yrs.) corresponded to our study (6.5 yrs.). The BFS-rates were 76%, 63%, and 57% in low-, intermediate-, and high-risk disease, respectively. The study included results of repeated HIFU administrations with a mean of 1.4 treatments per patient, suggesting that in many patients a single HIFU ablation was not efficacious and complete tumor destruction required multiple treatments. The corresponding 8-year BFS-rates (nadir+2 definition) obtained in our study were 93%, 76% and 48%, respectively. Accordingly, the biochemical cancer control rates with single-session HIFU were superior in low- and intermediate-risk disease, while patients with high-risk disease might marginally benefit from multiple treatments. Moreover, the MFS-rates (94% vs. 91%) and PCSS-rates (97% vs. 95%) at ten years were similar. In all, our data underline the curative potential of a single HIFU ablation, but also the limited efficacy to eradicate high-risk PCa.

Radiotherapy (RT) is an established primary treatment modality in elderly men [19]. With modern dose-escalated RT, Zumsteg *et al.* attained 8-year BFS-rates (nadir+2 definition) of 90.3%, 77.3% and 57.1% in low-, intermediate-, and high-risk patients (IMRT, radiation dose 81 Gy) [20]. Vora *et al.* reported 9-year BFS-rates of 77.4%, 69.9% and 53.3%, respectively (IMRT, 75.6 Gy) [21]. Compared with single-session HIFU, results from these studies indicate equivalent BFS-rates in low-risk and intermediate-risk disease and an additional benefit from RT in high-risk disease. The 10-year MFS-rates (95%) and PCSS-rates (96.2%) reported by Alicikus *et al.* were similar [22]. However, whether a single application of HIFU represents a curative alternative to modern RT, applied over 4-6 weeks, requires long-term evaluation in prospective randomized trials or matched cohort studies.

We consider patients with low- to intermediate-risk disease as candidates for single-session HIFU treatment, whereas men with high-risk tumors are not treated safely even with whole-gland technique. Prostate size is not a limitation if prostate resection is considered as a part of the treatment protocol. Age >75 yrs. is not a contraindication, but treatment recommendation should be made cautiously in case of men with significant comorbidity.

Active surveillance (AS) is considered to be an alternative to interventional therapy in prostate tumors of low risk, even though these glands may harbor unfavorable pathology [23]. If the selection criteria for AS are limited to low-volume low-risk disease to minimize the risk of disease progression, active therapy remains an indication in patients with a more pronounced tumor burden and especially in those who experience disease progression under AS [19,23]. Whole-gland HIFU therapy is a valuable option for many of these men. Whether focal HIFU is a treatment alternative in low or intermediate risk disease, remains to be determined.

There are inherent limitations in this study, including its retrospective nature and design as a single arm study without control group. The data reflect single-center experience and may not be generally applicable. The median follow-up was only 6.5 years a length of time during which most prostate cancers are unlikely to result in metastatic spread or mortality.

Conclusions

The curative potential of single-session whole-gland therapy with HIFU has improved due to technological advances. Candidates for treatment are patients with organ-confined low- to intermediate-risk PCa.

Conflict of interest

Dietrich Pfeiffer acted as a trainer for EDAP-TMS.

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