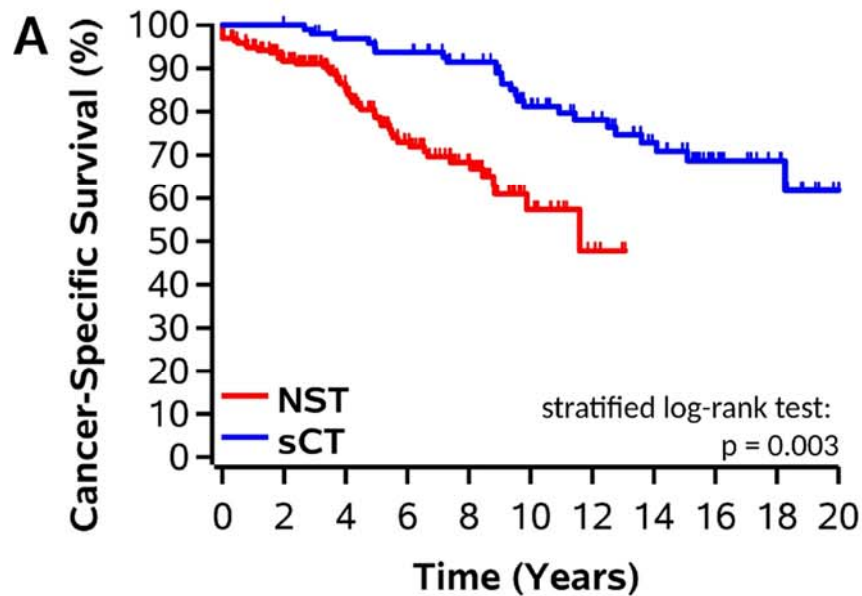


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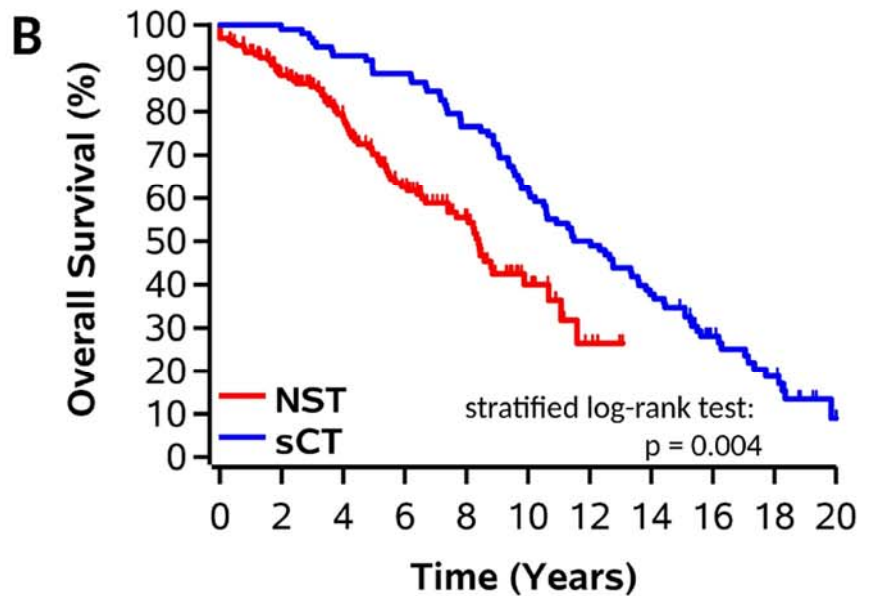
APPENDIX

Supplementary Fig. 1. Kaplan-Meier plot for survival outcomes for matched patients (NST and sCT) from date of biochemical failure. NST: no salvage treatment; sCT: salvage transperineal cryotherapy.



Number at risk

NST	196	145	103	72	47	16	4					
sCT	98	97	91	87	75	61	49	37	21	12	2	

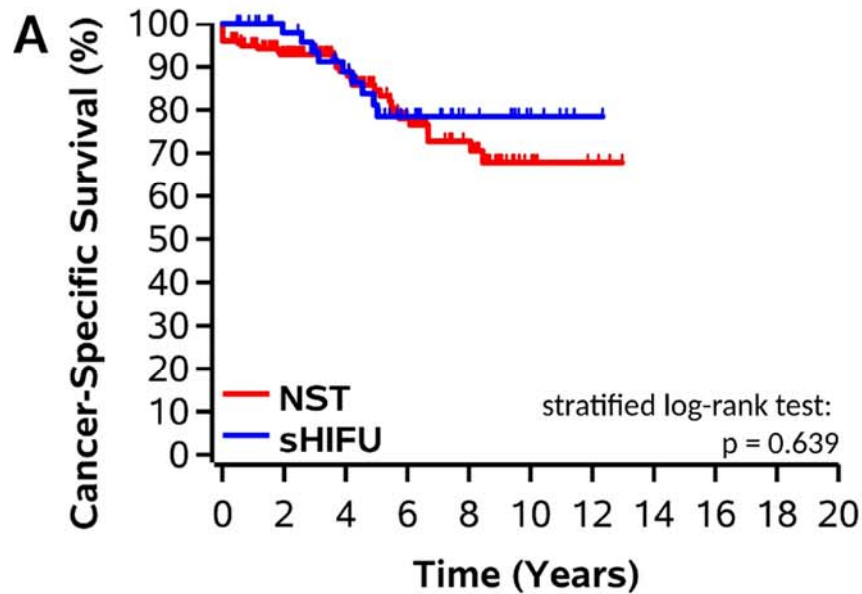


Number at risk

NST	196	145	103	72	47	16	4				
sCT	98	97	91	87	75	61	49	37	21	12	2

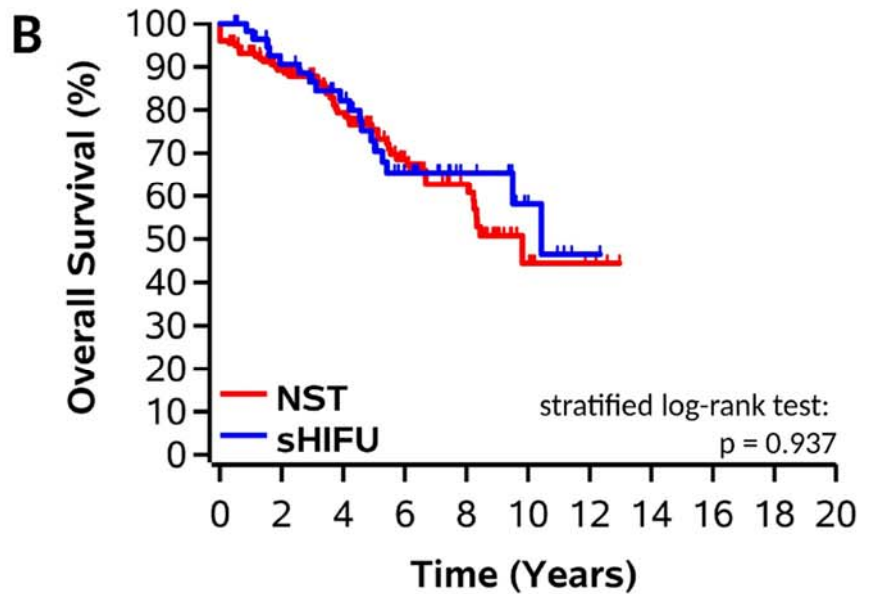
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Supplementary Fig. 2. Kaplan-Meier plot for survival outcomes for matched patients (NST and sHIFU) from date of biochemical failure. NST: no salvage treatment; sHIFU: salvage transrectal high intensity focused ultrasound ablation.



Number at risk

NST	177	131	87	54	33	7	3
sHIFU	59	46	37	23	13	6	1



Number at risk

NST	177	131	87	54	33	7	3
sHIFU	59	46	37	23	13	6	1

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Supplementary Table 1. Summary of propensity score matching scenarios							
#	Matching variable	Caliper	Ratio	Cryo/HIFU N	NST n	Total n	Final match
Match #1: NST = vs. Cryotherapy							
1	Logit(PS)	0.2*SD*Logit(PS)	1:1	133	133	266	
2	Logit(PS)	0.2*SD*Logit(PS)	1:2	98	196	294	***
3	Logit(PS)	0.2*SD*Logit(PS)	1:3	71	213	284	
4	Logit(PS)	0.2*SD*Logit(PS)	1:4	61	244	305	
5	PS	0.10*(PS)	1:1	132	132	264	
6	PS	0.10*(PS)	1:2	98	196	294	
7	PS	0.10*(PS)	1:3	73	219	292	
8	PS	0.10*(PS)	1:4	63	252	315	
9	PS	0.15*(PS)	1:1	134	134	268	
10	PS	0.15*(PS)	1:2	99	198	297	
11	PS	0.15*(PS)	1:3	82	246	328	
12	PS	0.15*(PS)	1:4	70	280	350	
Match #2: NST vs. HIFU							
1	Logit(PS)	0.2*SD*Logit(PS)	1:1	92	92	184	
2	Logit(PS)	0.2*SD*Logit(PS)	1:2	67	134	201	
3	Logit(PS)	0.2*SD*Logit(PS)	1:3	55	165	220	
4	Logit(PS)	0.2*SD*Logit(PS)	1:4	46	184	230	

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5	PS	0.10*(PS)	1:1	90	90	180	
6	PS	0.10*(PS)	1:2	66	132	198	
7	PS	0.10*(PS)	1:3	55	165	220	
8	PS	0.10*(PS)	1:4	48	192	240	
9	PS	0.15*(PS)	1:1	92	92	184	
10	PS	0.15*(PS)	1:2	67	134	201	
11	PS	0.15*(PS)	1:3	59	177	236	***
12	PS	0.15*(PS)	1:4	49	196	245	

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Supplement Table 2. Summary of propensity score matching scenarios

Characteristic	All patients	Caliper: 0.2*SD*Logit(PS)				Caliper: 0.10				Caliper: 0.15			
		Ratio: 1:1	Ratio: 1:2	Ratio: 1:3	Ratio: 1:4	Ratio: 1:1	Ratio: 1:2	Ratio: 1:3	Ratio: 1:4	Ratio: 1:1	Ratio: 1:2	Ratio: 1:3	Ratio: 1:4
Match #1: NST vs. cryotherapy													
Cryotherapy, n	186	133	98	71	61	132	98	73	63	134	99	82	70
EBRT, n	982	133	196	213	244	132	196	219	252	134	198	246	280
Age, SD	0.892	0.068	0.027	0.042	0.134	0.074	0.032	0.067	0.080	0.060	0.037	0.060	0.087
Baseline PSA, SD	0.150	0.033	0.108	0.182	0.174	0.038	0.126	0.169	0.145	0.038	0.113	0.122	0.185
T stage, SD													
T1	0.065	0.019	0.039	0.023	0.020	0.039	0.065	0.011	0.039	0.038	0.025	0.010	0.017
T2	0.365	0.048	0.042	0.038	0.049	0.032	0.064	0.000	0.016	0.032	0.021	0.042	0.000
T3	0.433	0.084	0.014	0.023	0.078	0.085	0.014	0.011	0.057	0.084	0.000	0.042	0.018
T4	0.245	—	—	—	—	—	—	—	—	—	—	—	—
Gleason score, SD													
2–5	0.615	0.000	0.039	0.098	0.138	0.000	0.039	0.097	0.136	0.000	0.038	0.091	0.129
6	0.827	0.031	0.020	0.010	0.052	0.031	0.020	0.037	0.008	0.031	0.030	0.065	0.088
7	0.202	0.133	0.043	0.038	0.016	0.134	0.043	0.009	0.072	0.133	0.032	0.083	0.115
8–10	0.317	0.152	0.110	0.000	0.034	0.153	0.110	0.000	0.033	0.152	0.109	0.012	0.010
ADT pre-radiation, SD	0.516	0.140	0.165	0.175	0.186	0.157	0.176	0.151	0.147	0.156	0.164	0.119	0.096
Final match			***										
Match #2: NST vs. HIFU													
HIFU, n	113	92	67	55	46	90	66	55	48	92	67	59	49
EBRT, n	982	92	134	165	184	90	132	165	192	92	134	177	196
Age, SD	1.100	0.086	0.083	0.162	0.225	0.059	0.059	0.157	0.239	0.086	0.083	0.076	0.226
Baseline PSA, SD	0.270	0.046	0.208	0.143	0.079	0.046	0.216	0.140	0.108	0.046	0.208	0.167	0.126
T stage, SD													
T1	0.495	0.155	0.048	0.000	0.025	0.158	0.016	0.040	0.012	0.155	0.048	0.088	0.012
T2	0.061	0.109	0.122	0.050	0.123	0.111	0.077	0.125	0.075	0.109	0.122	0.116	0.063

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T3	0.576	0.082	0.134	0.076	0.147	0.083	0.106	0.138	0.126	0.082	0.134	0.054	0.108
T4	0.245	–	–	–	–	–	–	–	–	–	–	–	–
Gleason score, SD													
2–5	0.629	0.148	0.071	0.111	0.141	0.150	0.072	0.111	0.138	0.148	0.071	0.107	0.137
6	0.455	0.088	0.122	0.164	0.057	0.090	0.141	0.189	0.022	0.088	0.122	0.046	0.043
7	0.197	0.154	0.060	0.086	0.022	0.157	0.077	0.110	0.064	0.154	0.060	0.011	0.010
8–10	0.414	0.149	0.125	0.120	0.096	0.151	0.125	0.120	0.120	0.149	0.125	0.084	0.044
ADT pre-radiation, SD	0.447	0.133	0.069	0.040	0.000	0.135	0.088	0.054	0.034	0.133	0.069	0.089	0.022
Final match:												***	

ADT: androgen deprivation therapy; HIFU: high intensity focused ultrasound; PS: propensity score; PSA: prostate-specific antigen;
SD: standard deviation.

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Supplement Table 3. Univariable and multivariable Cox proportional hazards regression models for NST vs. sCT								
Dependent variable	Cancer-specific survival (date of radiotherapy)		Overall survival (date of radiotherapy)		Cancer-specific survival (date of BF/sCT)		Overall survival (date of BF/sCT)	
Variable	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p
Univariable								
NST vs. sCT	4.05 (2.60, 6.31)	<0.001	3.83 (2.88, 5.11)	<0.001	3.16 (2.17, 4.62)	<0.001	2.87 (2.25, 3.67)	<0.001
Age (pre-radiation, per 5 years)	0.97 (0.89, 1.05)	0.441	1.23 (1.16, 1.32)	<0.001	0.97 (0.89, 1.06)	0.475	1.21 (1.13, 1.29)	<0.001
Baseline PSA (pre-radiation, per 5 ng/mL)	1.05 (1.03, 1.07)	<0.001	1.03 (1.02, 1.05)	<0.001	1.04 (1.02, 1.06)	<0.001	1.02 (1.00, 1.03)	0.127
T stage (pre-radiation)								
T2 vs. T1	1.46 (0.94, 2.27)	<0.001		<0.001		<0.001		<0.001
T3 vs. T1	4.15 (2.68, 6.43)	0.095	1.35 (1.04, 1.76)	0.025	1.37 (0.88, 2.13)	0.168	1.26 (0.97, 1.64)	<0.001
T4 vs. T1	10.80 (5.83, 20.01)	<0.001	2.44 (1.85, 3.21)	<0.001	3.45 (2.23, 5.34)	<0.001	2.00 (1.53, 2.63)	<0.001
		<0.001	6.19 (3.87, 9.89)	<0.001	7.94 (4.21, 14.99)	<0.001	4.35 (2.69, 7.04)	<0.001
Gleason score (pre-radiation)								
7 vs. ≤6	1.96 (1.41, 2.71)	<0.001	1.50 (1.22, 1.85)	<0.001	1.92 (1.38, 2.66)	<0.001	1.38 (1.12, 1.70)	0.002
8–10 vs. ≤6	5.30 (3.76, 7.46)	<0.001	3.12 (2.45, 3.97)	<0.001	4.75 (3.36, 6.71)	<0.001	2.61 (2.06, 3.33)	<0.001
ADT pre-radiation, n (%)	2.46 (1.95, 3.10)	<0.001	1.74 (1.48, 2.06)	<0.001	2.36 (1.87, 2.98)	<0.001	1.60 (1.36, 1.89)	<0.001
Multivariable								
NST vs. sCT	2.64 (1.61, 4.34)	<0.001	2.41 (1.73, 3.36)	<0.001	2.23 (1.42, 3.51)	<0.001	1.87 (1.40, 2.51)	<0.001
Age (pre-radiation, per 5 years)	0.93 (0.84, 1.02)	0.109	1.15 (1.07, 1.24)	<0.001	0.93 (0.84, 1.02)	0.120	1.14 (1.06, 1.23)	<0.001
Baseline PSA (pre-radiation, per 5 ng/mL)	1.01 (0.98, 1.03)	0.621	1.01 (0.99, 1.03)	0.587	0.98 (0.95, 1.01)	0.279	0.98 (0.95, 1.00)	0.075
T stage (pre-radiation)								
T2 vs. T1	1.45 (0.90, 2.32)	0.126	1.25 (0.94, 1.64)	0.121	1.36 (0.85, 2.19)	0.204	1.23 (0.93, 1.62)	0.144

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T3 vs. T1	2.66 (1.64, 4.30)	<0.001	1.76 (1.31, 2.37)	<0.001	2.29 (1.41, 3.72)	<0.001	1.61 (1.19, 2.18)	0.002
T4 vs. T1	4.15 (2.09, 8.24)	<0.001	3.11 (1.86, 5.20)	<0.001	3.78 (1.86, 7.71)	<0.001	3.06 (1.79, 5.23)	<0.001
Gleason score (pre-radiation)		<0.001		<0.001		<0.001		
7 vs. ≤6	1.53 (1.08, 2.16)	0.017	1.19 (0.95, 1.49)	0.124	1.47 (1.03, 2.09)	0.034	1.09 (0.87, 1.36)	<0.001
8–10 vs. ≤6	2.95 (2.01, 4.32)	<0.001	1.95 (1.49, 2.54)	<0.001	2.75 (1.87, 4.06)	<0.001	1.75 (1.34, 2.30)	0.479
ADT pre-radiation, n (%)	1.41 (1.08, 1.85)	0.011	1.33 (1.10, 1.60)	0.003	1.51 (1.15, 1.98)	0.003	1.39 (1.15, 1.68)	<0.001

p<0.05 shown in bold. ADT: androgen deprivation therapy; BF: biochemical failure; CI: confidence interval; NST: no salvage treatment; PSA: prostate-specific antigen; sCT: salvage cryotherapy.

Supplement Table 4. Univariable and multivariable Cox proportional hazards regression models for NST vs. sHIFU								
Dependent variable	Cancer-specific survival (date of radiotherapy)		Overall survival (date of radiotherapy)		Cancer-specific survival (Date of BF/sHIFU)		Overall survival (Date of BF/sHIFU)	
Variable	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p
Univariable								
NST vs. sHIFU	4.27 (2.31, 7.88)	<0.001	4.84 (3.14, 7.45)	<0.001	2.86 (1.60, 5.10)	<0.001	2.38 (1.63, 3.46)	<0.001
Age (pre-radiation, per 5 years)	0.95 (0.87, 1.04)	0.278	1.19 (1.11, 1.28)	<0.001	0.93 (0.85, 1.02)	0.118	1.13 (1.05, 1.21)	<0.001
Baseline PSA (pre-radiation, per 5 ng/mL)	1.04 (1.03, 1.06)	<0.001	1.03 (1.01, 1.04)	<0.001	1.04 (1.02, 1.06)	<0.001	1.02 (1.00, 1.04)	0.116
T stage (pre-radiation)		<0.001		<0.001		<0.001		<0.001
T2 vs. T1	1.50 (0.94, 2.41)	0.089	1.74 (1.28, 2.36)	<0.001	1.42 (0.89, 2.27)	0.147	1.60 (1.18, 2.17)	0.003
T3 vs. T1	4.14 (2.63, 6.52)	<0.001	2.80 (2.05, 3.81)	<0.001	3.38 (2.15, 5.33)	<0.001	2.18 (1.60, 2.98)	<0.001
T4 vs. T1	10.26 (5.49, 19.17)	<0.001	6.89 (4.23, 11.22)	<0.001	7.25 (3.80, 13.80)	<0.001	4.50 (2.73, 7.42)	<0.001

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Gleason score (pre-radiation)								
7 vs. ≤6	1.62 (1.13, 2.32)	<0.001	1.37 (1.07, 1.75)	<0.001	1.50 (1.04, 2.16)	<0.001	1.23 (0.96, 1.58)	<0.001
8–10 vs. ≤6	4.53 (3.12, 6.57)	0.009	2.94 (2.24, 3.85)	0.013	3.81 (2.61, 5.55)	0.029	2.35 (1.79, 3.08)	0.094
ADT pre-radiation, n (%)	2.30 (1.80, 2.94)	<0.001	1.63 (1.36, 1.94)	<0.001	2.24 (1.75, 2.87)	<0.001	1.51 (1.26, 1.81)	<0.001
Multivariable								
NST vs. sHIFU	2.88 (1.48, 5.62)	0.002	2.76 (1.71, 4.45)	<0.001	1.89 (1.00, 3.61)	0.052	1.46 (0.95, 2.26)	0.088
Age (pre-radiation, per 5 years)	0.92 (0.84, 1.02)	0.109	1.12 (1.04, 1.21)	0.003	0.93 (0.84, 1.02)	0.135	1.12 (1.03, 1.21)	0.006
Baseline PSA (pre-radiation, per 5 ng/mL)	1.00 (0.98, 1.03)	0.743	1.01 (0.98, 1.03)	0.644	0.99 (0.96, 1.02)	0.408	0.98 (0.96, 1.01)	0.166
T stage (pre-radiation)		<0.001		<0.001		<0.001		<0.001
T2 vs. T1	1.35 (0.83, 2.19)	0.229	1.49 (1.09, 2.05)	0.012	1.30 (0.80, 2.11)	0.294	1.46 (1.07, 2.00)	0.018
T3 vs. T1	2.56 (1.57, 4.16)	<0.001	1.99 (1.43, 2.77)	<0.001	2.26 (1.38, 3.70)	0.001	1.84 (1.32, 2.58)	<0.001
T4 vs. T1	4.01 (2.02, 8.00)	<0.001	3.52 (2.07, 6.01)	<0.001	3.59 (1.76, 7.35)	<0.001	3.33 (1.92, 5.79)	<0.001
Gleason score (pre-radiation)		<0.001		<0.001		<0.001		<0.001
7 vs. ≤6	1.40 (0.96, 2.04)	0.078	1.16 (0.90, 1.49)	0.260	1.31 (0.89, 1.91)	0.168	1.04 (0.80, 1.34)	0.789
8–10 vs. ≤6	2.73 (1.82, 4.10)	<0.001	1.94 (1.45, 2.60)	<0.001	2.48 (1.65, 3.73)	<0.001	1.71 (1.28, 2.29)	<0.001
ADT pre-radiation, n (%)	1.37 (1.04, 1.81)	0.025	1.29 (1.06, 1.58)	0.012	1.48 (1.12, 1.96)	0.007	1.37 (1.12, 1.68)	0.003

p<0.05 shown in bold. ADT: androgen deprivation therapy; BF: biochemical failure; CI: confidence interval; NST: no salvage treatment; PSA: prostate-specific antigen; sHIFU: salvage transrectal high intensity focused ultrasound ablation.