



# Clinical Outcomes of Stereotactic Body Radiation Therapy Alone versus Stereotactic Body Radiation Therapy after Incomplete Transarterial Chemoembolization for a Single Small ( $\leq 5$ cm) Hepatocellular Carcinoma

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# INTRODUCTION

- SBRT demonstrates promising results as an alternative treatment option in patients with small HCC unfeasible to locoregional therapy such as surgical resection, RFA, or TACE. (*Liver Cancer 2017 Nov;6(4):264-274*)
- Also, based on a phase III clinical trial on proton beam radiotherapy, high dose radiotherapy has been proved to be comparable to RFA in small HCC. (*J Hepatol. 2021 Mar;74(3):603-612*)
- Based on these results, the number of patients receiving SBRT without prior TACE continue to rise.
- However, there are only a few number of studies on the efficacy of SBRT alone without prior treatment.
- Therefore, as a means of evaluating the clinical outcomes of SBRT alone, comparison with SBRT after incomplete TACE was made.

# MATERIAL & METHOD

Between 2007 and 2017,  
Patients treated with SBRT for HCC  
without macroscopic vascular invasion or  
extrahepatic metastasis  
 $n = 1014$

## Inclusion Criteria

- Single, small-sized ( $\leq 5$  cm)
- Child-Pugh class A or B7
- ECOG performance status 0-2
- No other primary tumors
- No history of previous radiation therapy

Excluded,  $n = 517$

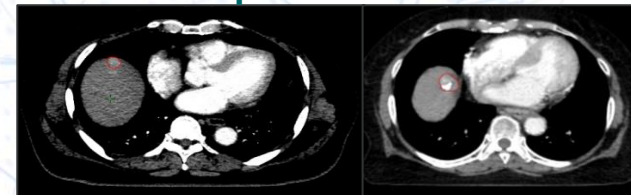
- Double primary cancer,  $n = 55$
- Previous history of radiation therapy,  $n = 204$
- Child-Pugh class C,  $n = 3$
- Combined treatment with TACE,  $n = 47$
- Treatment-naïve,  $n = 15$
- Recurrent after RFA or PEIT,  $n = 65$
- Multiple HCC,  $n = 122$
- Tumor size  $> 5$  cm,  $n = 6$

Total recruited  
 $n = 497$

Lost to follow-up,  $n = 20$

Data available for analysis  
 $n = 477$

## Patient Group



- SBRT Alone group : no prior treatment ( $n = 54$ )
- TACE + SBRT group : incomplete TACE before SBRT ( $n = 423$ )

# MATERIAL & METHOD

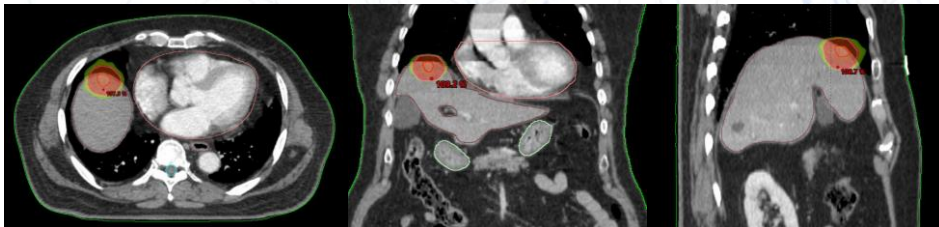
## • SBRT Planning and Treatment

### ▪ RT technique

- Static IMRT (March 2007 – April 2012)
- Volumetric-modulated arc therapy (May 2012 – September 2017)

▪ Median total dose : 45 Gy (30 – 60 Gy)

▪ Median fraction size : 15 Gy (10 – 20 Gy)



### ▪ Dose prescription

- $rV_{15Gy} \geq 700$  ml
- Mean liver dose  $\leq 13$  Gy

### ▪ Dose constraint

	Volume	Dose
Esophagus	2cc	< 21 Gy
Large bowel	2cc	< 21 Gy
Stomach	2cc	< 18 Gy
Duodenum	2cc	< 18 Gy
Spinal cord	2cc	18 Gy

# RESULT

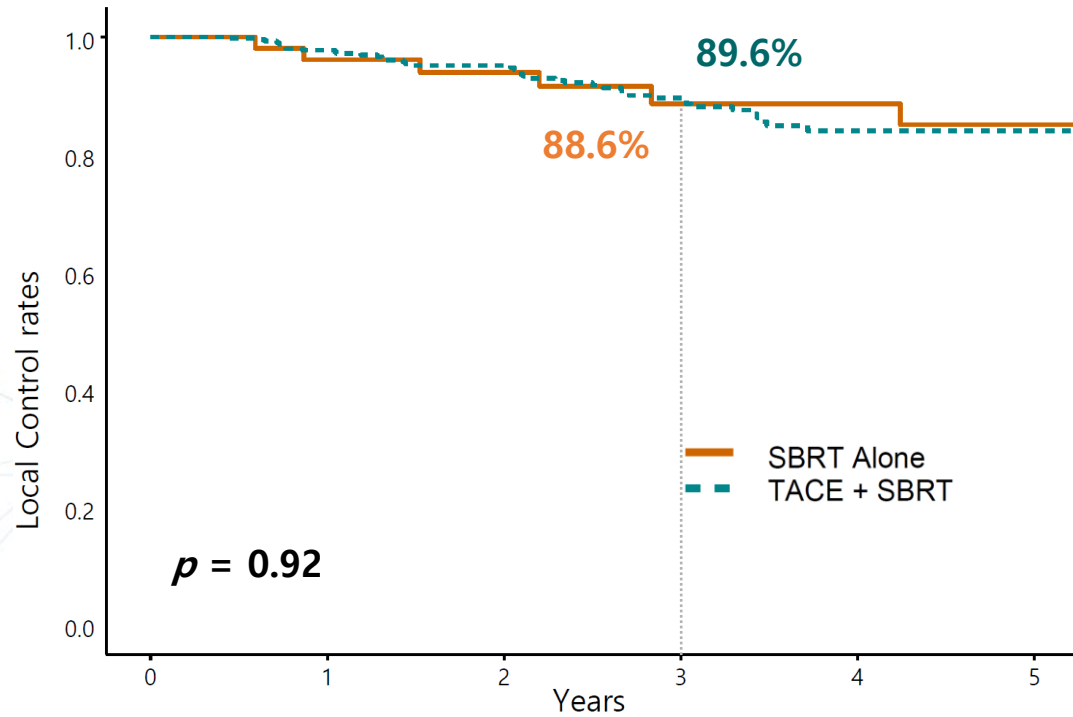
## • Patient Characteristics

Characteristics		SBRT Alone <i>n</i> = 54 (%)	TACE + SBRT <i>n</i> = 423 (%)	<i>p</i> -value
<b>Age</b>	≤ 65 years	39 (72.2)	260 (61.5)	0.165
	> 65 years	15 (27.8)	163 (38.5)	
<b>Sex</b>	Male	42 (77.8)	323 (76.4)	0.951
	Female	12 (22.2)	100 (23.6)	
<b>ECOG PS</b>	0	50 (92.6)	362 (85.6)	0.229
	1-2	4 (7.4)	61 (14.4)	
<b>Child-Pugh class</b>	A	49 (90.7)	379 (89.6)	0.982
	B	5 (9.3)	44 (10.4)	
<b>Etiology</b>	Hepatitis B	39 (72.2)	318 (75.2)	0.761
	Non-Hepatitis B	15 (27.8)	105 (24.8)	
<b>Tumor size (cm), median (IQR)</b>		1.4 (1.2 – 1.7)	1.9 (1.5 – 2.5)	<b>&lt; 0.001</b>
<b>AFP</b>	≤ 20 ng/mL	43 (79.6)	271 (64.1)	<b>0.034</b>
	> 20ng/mL	11 (20.4)	152 (35.9)	
<b>Number of prior treatment sessions, median (IQR)</b>		2 (1 – 3)	3 (2 – 5)	<b>&lt; 0.001</b>
<b>BED</b>	< 112.5 Gy	5 (9.3)	37 (8.7)	1.000
	≥ 112.5 Gy	49 (90.7)	386 (91.3)	

Abbreviations : ECOG PS, Eastern Cooperative Oncology Group performance status; IQR, interquartile range; AFP, alpha-fetoprotein; BED, biologically effective dose

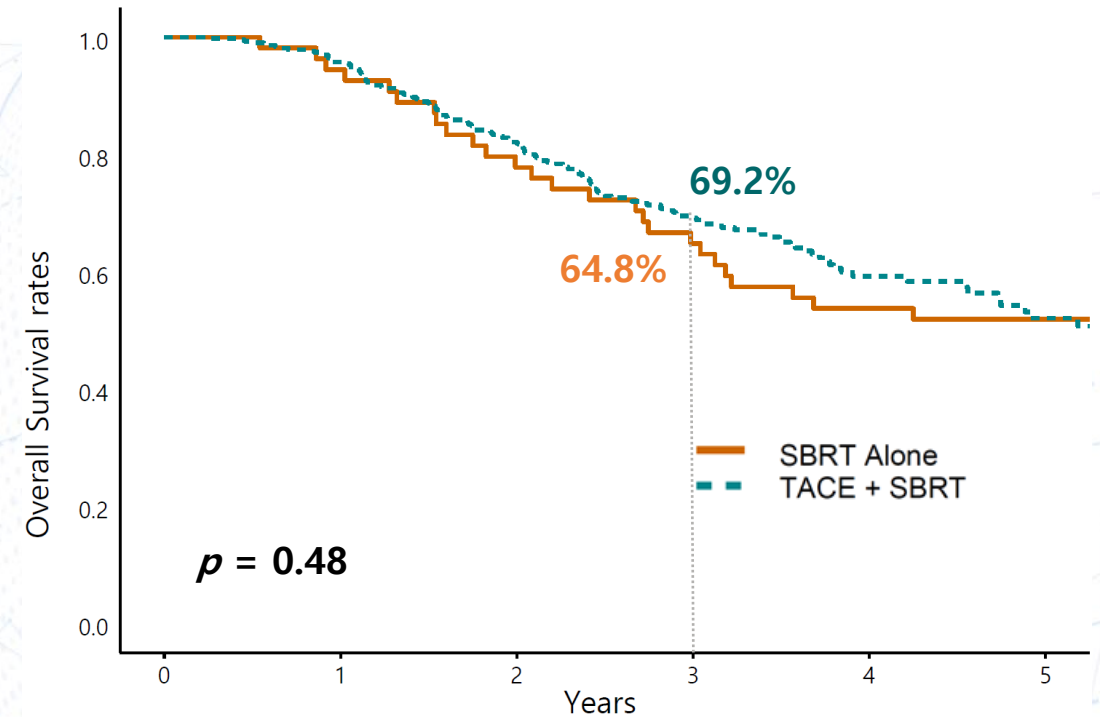
# RESULT

- Local Control by treatment



Number at risk		0	1	2	3	4	5
New	54	48	40	29	26	21	
Treated	423	364	276	189	70	38	

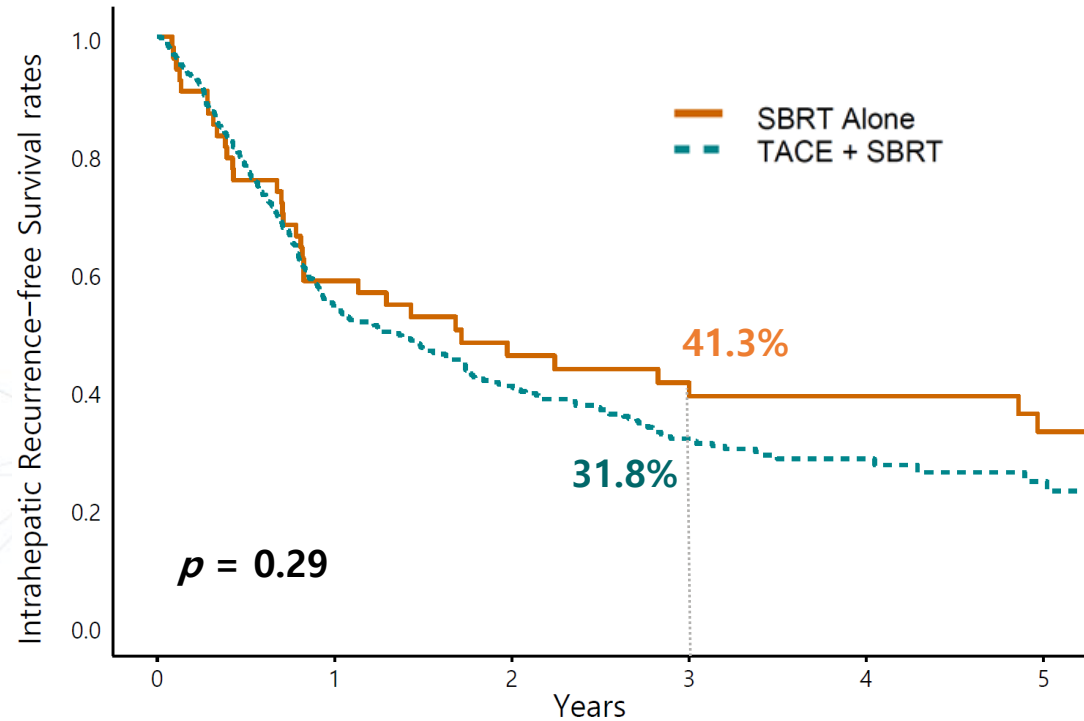
- Overall Survival by treatment



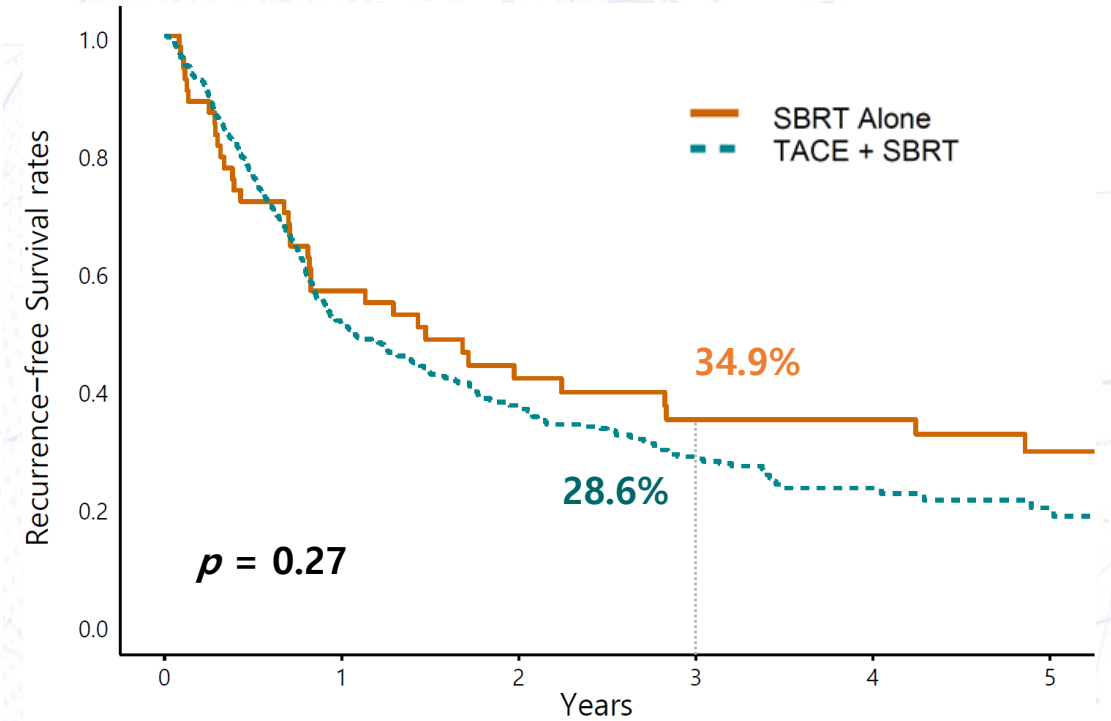
Number at risk		0	1	2	3	4	5
New	54	51	42	35	29	26	
Treated	423	400	317	214	78	48	

# RESULT

- Intrahepatic Recurrence-free Survival by treatment
- Recurrence-free Survival by treatment



	0	1	2	3	4	5
New	54	30	21	18	16	11
Treated	423	203	131	80	28	15



	0	1	2	3	4	5
New	54	29	19	15	15	10
Treated	423	193	121	74	26	14

# RESULT

- **Toxicity**

- Acute toxicity

CTCAE Grade	SBRT Alone <i>n</i> = 54 (%)					TACE + SBRT <i>n</i> = 423 (%)				
	1	2	3	4	5	1	2	3	4	5
Nausea	5 (9.3)	0	0	0	0	21 (5.0)	5 (1.2)	0	0	0
Abdominal pain	2 (3.7)	0	0	0	0	8 (1.9)	1 (0.2)	0	0	0
Anorexia	0	0	0	0	0	7 (1.7)	8 (1.9)	0	0	0
AST/ALT elevation	16 (29.6)	0	0	0	0	105 (24.8)	1 (0.2)	0	0	0
Bilirubin elevation	8 (14.8)	0	0	0	0	110 (26.0)	3 (0.7)	0	0	0

- Non-classic radiation induced liver disease

	SBRT Alone <i>n</i> = 54 (%)	TACE + SBRT <i>n</i> = 423 (%)
CTCAE grade ≥2	2 (3.7)	22 (5.2)
Child-Pugh score ≥ 2 elevation	0	10 (2.4)



# RESULT

## • Univariate and Multivariate Analysis of Prognostic Factor

### Local Control

### Overall Survival

Variables	Univariate		Multivariate		Univariate		Multivariate	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
<b>RT aim</b> SBRT alone (vs. TACE + SBRT)	0.96 (0.43 – 2.15)	0.918	-	-	1.16 (0.77 – 1.77)	0.479	-	-
<b>Age</b> > 65 years (vs. ≤ 65 years)	1.89 (1.07 – 3.33)	<b>0.029</b>	1.84 (1.04 – 3.26)	<b>0.036</b>	1.48 (1.10 – 1.98)	<b>0.009</b>	1.53 (1.13 – 2.06)	<b>0.006</b>
<b>Sex</b> Female (vs. Male)	1.69 (0.92 – 3.12)	0.091	-	-	1.02 (0.72 – 1.44)	0.915	-	-
<b>ECOG PS</b> 1-2 (vs. 0)	1.08 (0.48 – 2.41)	0.850	-	-	1.82 (1.29 – 2.57)	<b>0.001</b>	1.36 (0.95 – 1.95)	0.092
<b>Child-Pugh class</b> B (vs. A)	1.22 (0.44 – 3.41)	0.703	-	-	3.35 (2.33 – 4.81)	<b>&lt; 0.001</b>	3.03 (2.05 – 4.46)	<b>&lt; 0.001</b>
<b>Etiology</b> Non-HBV (vs. HBV)	1.01 (0.53 – 1.94)	0.976	-	-	1.38 (1.01 – 1.88)	<b>0.045</b>	-	-
<b>Tumor size</b>	1.40 (1.02 – 1.93)	<b>0.039</b>	1.36 (1.00 – 1.89)	<b>0.049</b>	1.24 (1.05 – 1.46)	<b>0.011</b>	1.13 (0.96 – 1.34)	0.145
<b>AFP</b> > 20ng/mL (vs. ≤ 20 ng/mL)	0.78 (0.41 – 1.47)	0.444	-	-	1.54 (1.15 – 2.06)	<b>0.004</b>	1.32 (0.98 – 1.77)	0.072
<b>Number of prior treatment sessions</b>	1.01 (0.93 – 1.11)	0.774	-	-	1.06 (1.02 – 1.10)	<b>0.005</b>	1.05 (1.01 – 1.09)	<b>0.028</b>
<b>BED</b> ≥ 112.5 Gy (vs. < 112.5 Gy)	0.99 (0.97 – 1.00)	0.186	-	-	0.50 (0.98 – 1.00)	<b>0.017</b>	0.65 (0.42 – 1.00)	<b>0.050</b>

Abbreviations : HR, hazard ratio; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; AFP, alpha-fetoprotein; BED, biologically effective dose

# RESULT

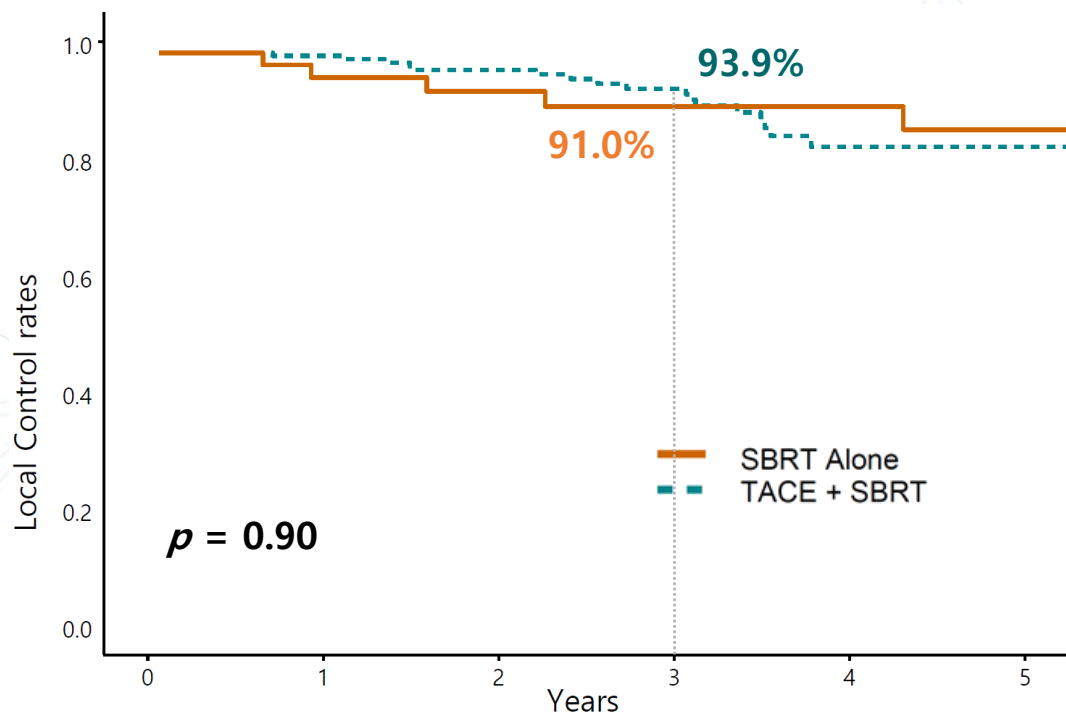
## • Patient Characteristics – After Propensity Score Matching

Characteristics		SBRT Alone <i>n</i> = 54 (%)	TACE + SBRT <i>n</i> = 423 (%)	<i>p</i> -value
<b>Age</b>	≤ 65 years	35 (70.0)	135 (66.2)	<b>0.728</b>
	> 65 years	15 (30.0)	69 (33.8)	
<b>Sex</b>	Male	38 (76.0)	152 (74.5)	<b>0.971</b>
	Female	12 (24.0)	52 (25.5)	
<b>ECOG PS</b>	0	46 (92.0)	186 (91.2)	<b>1.000</b>
	1-2	4 (8.0)	18 (8.8)	
<b>Child-Pugh class</b>	A	45 (90.0)	181 (88.7)	<b>0.995</b>
	B	5 (10.0)	23 (11.3)	
<b>Etiology</b>	Hepatitis B	36 (72.0)	148 (72.5)	<b>1.000</b>
	Non-Hepatitis B	14 (28.0)	56 (27.5)	
<b>Tumor size (cm), median (IQR)</b>		1.4 (1.3 – 1.7)	1.6 (1.2 – 2.0)	<b>0.185</b>
<b>AFP</b>	≤ 20 ng/mL	40 (80.0)	140 (68.8)	<b>0.158</b>
	> 20ng/mL	10 (20.0)	64 (31.4)	
<b>Number of prior treatment sessions, median (IQR)</b>		2 (1 – 3)	2 (1 – 4)	<b>0.102</b>
<b>BED</b>	< 112.5 Gy	4 (8.0)	17 (8.3)	<b>1.000</b>
	≥ 112.5 Gy	46 (92.0)	187 (91.7)	

Abbreviations : ECOG PS, Eastern Cooperative Oncology Group performance status; IQR, interquartile range; AFP, alpha-fetoprotein; BED, biologically effective dose

# RESULT

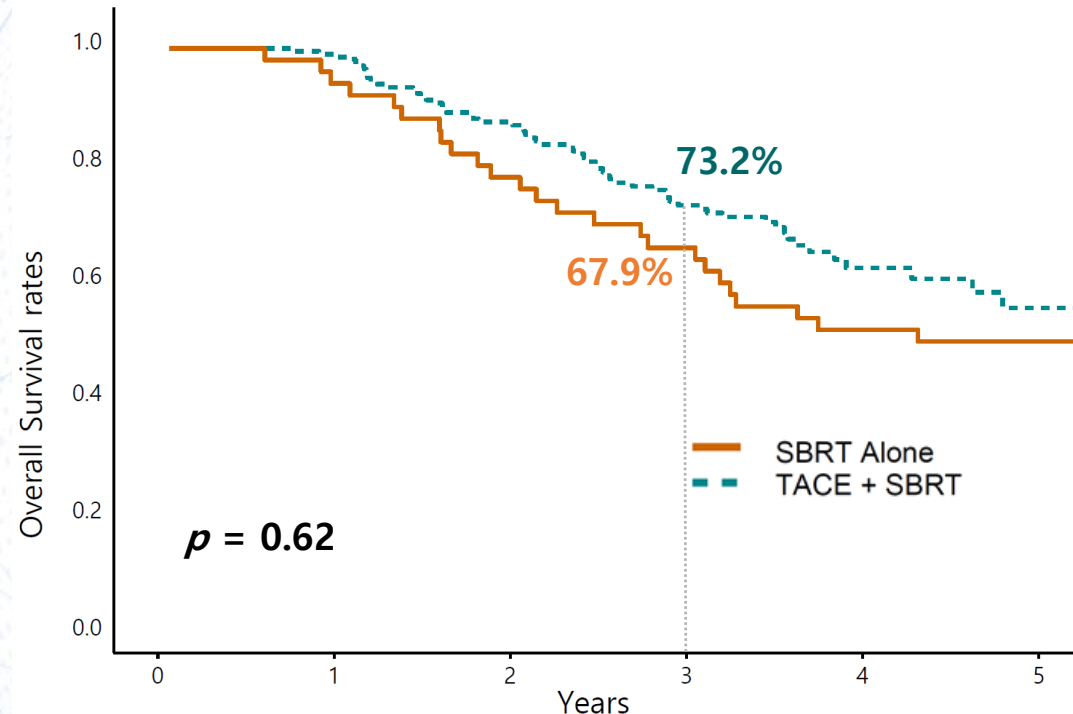
- Local Control by treatment  
– propensity score matching



Number at risk

New	50	44	36	27	24	19
Treated	204	180	139	100	34	17

- Overall Survival by treatment  
– propensity score matching

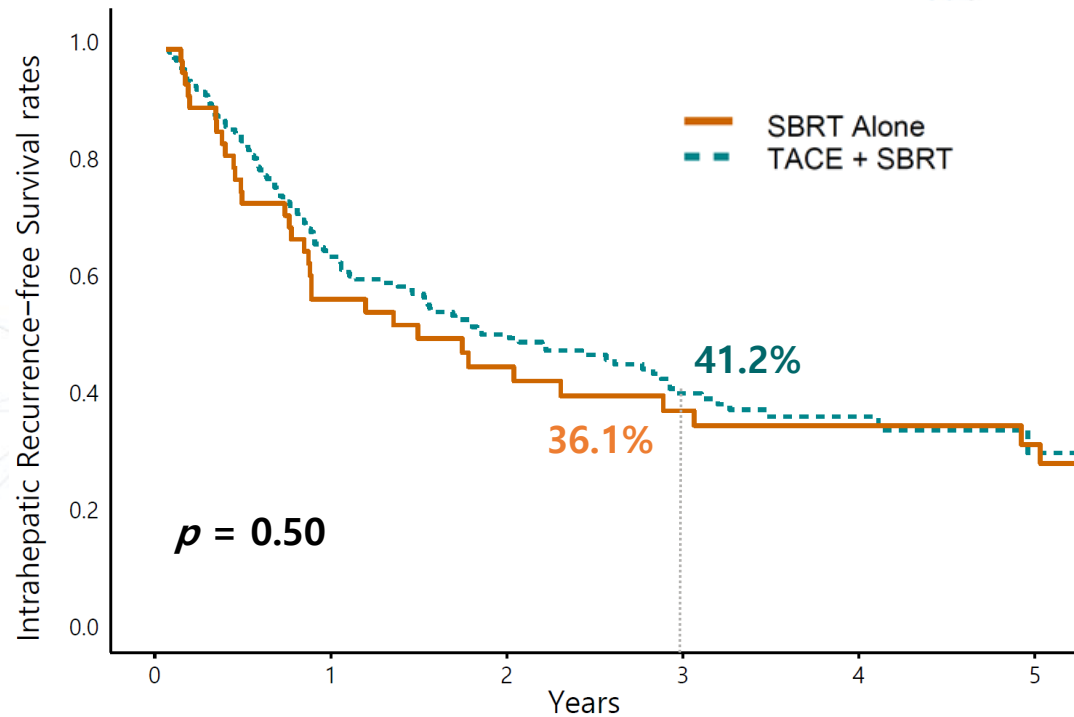


Number at risk

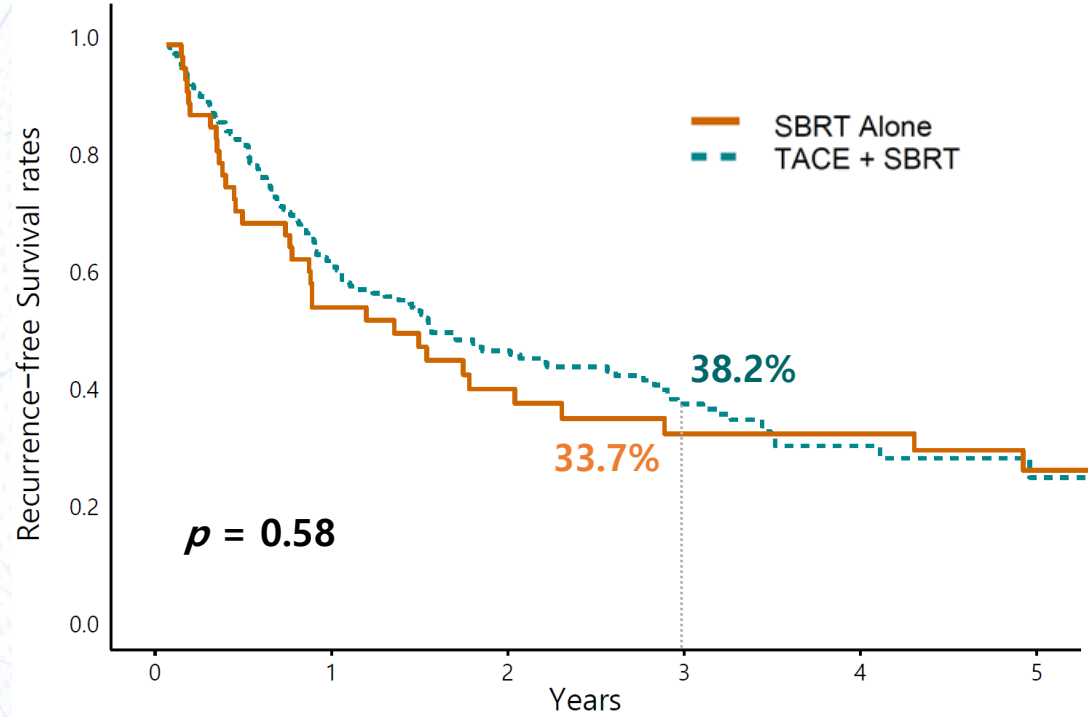
New	50	47	38	32	26	24
Treated	204	198	160	111	38	21

# RESULT

- Intrahepatic Recurrence-free Survival by treatment – propensity score matching
- Recurrence-free Survival by treatment – propensity score matching



Number at risk		0	1	2	3	4	5
New	50	27	18	15	14	9	
Treated	204	114	76	48	17	7	



Number at risk		0	1	2	3	4	5
New	50	26	16	13	13	8	
Treated	204	110	72	47	16	7	

# CONCLUSION

- There were no differences between SBRT Alone group and TACE + SBRT group in terms of local control and survival.
- Prospective studies on comparison between SBRT alone and RFA are needed, for SBRT to establish itself as a curative treatment option in small HCC.