Supplementary

Supplementary file (Part 4 paper)

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Table S4-1 Short-term mortality

Ordered by use of adjustment, extent of resection, time period

1st author year (reference)	Source	Years	n	Age [a]	CCS ≥2 [a]	Resection extent	Adjusted/ Confid	% 90-day mortality			Comments
								SBRT	Surg	P	
Stokes 2018 (1)	NCDB	04-13	27,200	-	17/15 [b]	Surg [c]	H	2.8	4.2	<.001	
Razi 2021 (2)	NCDB	04-15	2,073	≥80 [d]	CC =0 [e]	Lobe	H	0.7	3.6	.03	VATS
Razi 2021 (2)	NCDB	04-15	2,665	≥80 [d]	CC =0 [e]	Lobe	H	0.7	6.7	.01	Open
Chang 2021 (3)	US ×1	15-17	160	69	0	Lobe	M	0	0	-	VATS
Dong 2020 (4)	China ×1	12-16	104	67/68	19/23 [f]	Lobe	M	[0] [g]	[2] [g]	-	VATS
Yu 2015 (5)	SEER	07-09	1,078	≥67 [d]	40/42 [f]	Lobe + SL	L	2.2	6.1	.005	
Verstegen 2013 (6)	Dutch ×6	-	128	68/71	45/45	Lobe	L	0	1.6	-	VATS
Mayne 2020 (7)	NCDB	04-15	558	73/73	24/24	W	H	2.9	2.9	NS	≥90-day delayed W
Bryant 2018 (8)	VA	06-15	3.435	66/71	39/39	Lobe	-	1.4	3.6	-	
Kasteljin 2015 (9)	Dutch ×1	08-11	228	67/72	-	Lobe [h]	-	0	4	-	
Stokes 2018 (1)	NCDB	04-13	67,684	-	17/15 [b]	Lobe	-	2.9	3.5	-	
Boyer 2017 (10)	VA	01-10	8,671	67/73 [b]	27/38 [b]	Lobe	-	0.4	2.7	-	Open
Boyer 2017 (10)	VA	01-10	3,673	67/73 [b]	27/38 [b]	Lobe	-	0.4	1.5	-	VATS
Hamaji 2015 (11)	Japan ×1	03-09	517	74/73	-	Lobe	-	[0] [g]	[0] [g]	-	VATS
Shirvani 2014 (12)	SEER	03-09	7,604	≥65 [d]	16/27	Lobe	-	1.3	4	.008	
Shirvani 2012 (13)	SEER	01-07	6,655	≥65 [d]	23/44	Lobe	-	0.8	4.1	-	
Crabtree 2014 (14)	US ×1	04-10	609	66/74	36/67	Lobe+SL	-	[0.7] [g]	[1.1] [g]	NS	
Bryant 2018 (8)	VA	06-15	1,083	69/71	46/39	SL	-	1.4	2.5	-	
Stokes 2018 (1)	NCDB	04-13	23,742	-	17/15 [b]	SL	-	2.9	3.3	-	
Crabtree 2013 (15)	Ph II [i]	04-10	266	70/73	20/22	SL	-	0	2.4	NS	
Boyer 2017 (10)	VA	01-10	3,506	67/73 [b]	27/38 [b]	SL	-	0.4	1.8	-	VATS
Boyer 2017 (10)	VA	01-10	4,239	67/73 [b]	27/38 [b]	SL	-	0.4	2.5	-	Open
Shirvani 2014 (12)	SEER	03-09	1,885	≥65 [d]	22/27	SL	-	1.3	3.7	.008	
Shirvani 2012 (13)	SEER	01-07	1,401	≥65 [d]	36/44	SL	-	0.8	4.1	-	
Average [j]								1.1	3.2		

Inclusion criteria: studies comparing 90-day mortality of SBRT vs. surgery, 2000-21, with >50 pts per arm. Light green shading highlights statistically significant differences (lighter shade = univariable; darker = multivariable); Red font highlights potential weakness (disparity between arms of ≥5 years average age or ≥10% proportion of CCS≥2).

[a], for surgery/SBRT cohort; [b], for entire study cohort, not specifically this subset; [c], any surgical resection, including pneumonectomy (2%); [d], minimum age for inclusion; [e], Charlson comorbidity score of 0 and recommended to have surgery but refused; [f], ≥3; [g], 30-day mortality (in brackets because not directly comparable to 90-day mortality); [h], 10% pneumonectomy and 5% sublobar; [i], comparison of 2 phase II trials (RTOG0236 2004-06 and ACOSOG Z4032 2006-10); j, Excluding 30-day results.

CCS, Charlson comorbidity score; Confid, confidence in attribution of outcome to the intervention; H, high confidence that outcome can be attributed to the intervention; L, low confidence that outcome can be attributed to the intervention; NCDB, national cancer database (US); NS, not statistically significant; Ph, phase; SBRT, Stereotactic Body Radiotherapy; SEER, Surveillance, Epidemiology, and End Results database; SL, sublobar; Surg, surgery; VA, Veterans Health Administration Database (US); VATS, video-assisted thoracic surgery; W, wedge.

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Table S4-2A Toxicity of SBRT by post-treatment period
Ordered by post-treatment period, central/peripheral

1[st] author year (reference)	Source	yrs	n	% PS ≥2	% Inoperable	f-u period (mo)	% Central	% Gr 2 toxicity	% Gr ≥3 toxicity	% Specific toxicity Gr ≥3									
										Pulmonary [a]	Dyspnea	Cough	Pleural Effus	Fatigue	Chest wall [b]	Esophagitis	Hemoptysis	Dermatitis	Br Plexopathy
Short-term																			
Park 2015 (16)	US ×1	07-13	140	26	-	0-3	0	-	-	10		-	-	1.4	0	0	0.7	0	0
Taremi 2012 (17)	PrCT	04-08	108	-	100	0-3	18	-	4	0	1.8		0	0.9	0.9	0	0	0	-
Mangona 2015 (18)	US ×1	05-11	77	-	-	0-6	0	3	2	2.1	-	-	0	0	0	-	-	0	-
Sun 2017 (19)	PrCT	04-08	65	28	78	0-6	12	-	5	1.5	0	-	-	0	0	-	0	3.1	0
Claude [c] 2020 (20)	PrCT	09-11	106	-	100	acute	0	-	10	0.9	8.5	0	-	-	0.9	0	0	0.9	-
Nestle [d] 2020 (21)	PrCT	11-14	100	24	100	0-7.5	27	-	-	3.6	13	-	-	-	-	2.5	-	0	-
Park 2015 (16)	US ×1	07-13	111	24	-	0-3	100	-	-	2.7		-	-	0.9	0	0.9	0	0	0
Haasbeek [e] 2011 (22)	NL ×1	03-09	63	32	100	0-3	100	10	2	0		0	0	0	1.6	0	0	0	-
Mangona 2015 (18)	US ×1	05-11	79	-	-	0-6	100	10	2	1.4	-	-	0	0	0	-	-	0	-
Bezjak 2019 (23)	PrCT	09-13	120	16	100	0-12	100	-	5	2.2	-	-	3.4	-	-	-	-	-	-
Intermediate-term																			
Park 2015 (16)	US ×1	07-13	140	26	-	>3	0	-	-	7.9		-	-	0	1.4	0	0	0	0
Taremi 2012 (17)	PrCT	04-08	108	-	100	>3	18	-	6	0.9	1.8		0	0	2.8	0	0	0	-
Mangona 2015 (18)	US ×1	05-11	58	-	-	6-24	0	23	5	1.7	-	-	1.7	0	3.4	-	-	1.7	-
Nestle [d] 2020 (21)	PrCT	11-14	100	24	100	≥8	27	-	-	1.2	13	-	-	-	-	2.7	-	0	-
Stephans [f] 2018 (24)	US ×1	03-12	600	-	-	~24	24	-	-	1.2	-	-	-	-	0.6 [g]	-	-	-	-
Park 2015 (16)	US ×1	07-13	111	24	-	>3	100	-	-	6.3		-	-	0	0	0	1.8	0	0
Bezjak 2019 (23)	PrCT	09-13	120	16	100	>12	100	-	22	6.5	4.3	-	1.1	-	-	3.3	3.3	-	-
Mangona 2015 (18)	US ×1	05-11	58	-	-	6-24	100	16	5	0	-	-	0	3.4	0	-	-	1.7	-
Unspecified term																			
Nagata 2015 (25)	PrCT	04-08	169	7	59	-	0	-	10	6.5	8.9	2.4	-	-	1.8	-	-	0	0
Ball 2019 (26)	PrCT	09-15	66	0	88	-	0	-	12	0	4	4	0	2	0	0	0	0	-
Singh 2019 (27)	RCT	08-15	98	-	100	-	0	7	14	7	9	2	-	-	-	-	-	-	-
Cheung 2014 (28)	PrCT	06-08	80	20	100	-	0	-	-	10.1	13.8	7.5	-	6.3	1.3	0	1.3	0	-
Inoue 2018 (29)	PrCT	09-14	62	5	31	-	0	-	14	9.7	9.7	-	-	-	-	-	-	-	-
Baumann 2008 (30)	PrCT	03-05	57	-	95	-	0	35	21	1.8	7	1.8	3.5	1.8	3.5	0	0	0	-
Timmerman 2010 (31)	PrCT	04-06	55	15	100	-	0	31	27	16		-	-	1.8	-	1.8	0	3.6	-
Fakiris 2009 (32)	PrCT	-	70	36	100	-	31	-	17 [h]	5.7		-	2.9	-	-	-	1.4	1.4	-
Onishi 2004 (33)	PrCT	95-03	245	19	65	-	-	-	-	2.4	-	-	1.6	-	0.8	0.8	-	0.8	-
Modh [i] 2014 (34)	US ×1	06-11	125	31	100	-	81	34	8	2.4	3.2	-	-	-	0.8	1.6	-	-	-

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Table S4-2B Overall toxicity of SBRT in operable *vs*. inoperable patients

Ordered by Operable/Inoperable category, central/peripheral

1st author year (reference)	source	yrs	n	% PS ≥2	% Inoperable	f-u period (mo)	% Central	% Gr 2 toxicity	% Gr ≥3 toxicity	% Specific toxicity Gr ≥3: Pulmonary [a]	Dyspnea	Cough	Pleural Effus	Fatigue	Chest wall [b]	Esophagitis	Hemoptysis	Dermatitis	Br Plexopathy
Operable patients																			
Nagata 2015 (25)	PrCT	04-08	65	3	0	-	0	-	6	4.6	4.6	0	-	-	1.5	-	-	0	0
Lagerwaard 2012 (35)	NL ×1	03-10	177	-	0	late	19	-	-	2.3	0	0	-	0	2.8	-	-	-	-
Inoperable patients																			
Nagata 2015 (25)	PrCT	04-08	104	9	100	-	0	-	13	8.7	11.5	1	-	-	1.9	-	-	0	0
Ball 2019 (26)	PrCT	09-15	66	0	88	-	0	-	12	0	4	4	0	2	0	0	0	0	-
Singh 2019 (27)	RCT	08-15	98	-	100	-	0	7	14	7	9	2	-	-	-	-	-	-	-
Baumann 2008 (30)	PrCT	03-05	57	-	95	-	0	35	21	1.8	7	1.8	3.5	1.8	3.5	0	0	0	-
Timmerman 2010 (31)	PrCT	04-06	55	15	100	-	0	31	27	16		-	-	1.8	-	1.8	0	3.6	-
Taremi 2012 (17)	PrCT	04-08	108	-	100	>3	18	-	6	0.9	1.8		0	0	2.8	0	0	0	-
Nestle [d] 2020 (21)	PrCT	11-14	100	24	100	≥8	27	-	-	1.2	13	-	-	-	-	2.7	-	0	-
Fakiris 2009 (32)	PrCT	-	70	36	100	-	31	-	17 [h]	5.7		-	2.9	-	-	-	1.4	1.4	-
Haasbeek [e] 2011 (22)	NL ×1	03-09	63	32	100	>3	100	14	6	3.2		0	0	0	3.2	0	0	0	-
Modh [i] 2014 (34)	US ×1	06-11	125	31	100	-	81	34	8	2.4	3.2	-	-	-	0.8	1.6	-	-	-
Bezjak 2019 (23)	PrCT	09-13	120	16	100	>12	100	-	22	6.5	4.3	-	1.1	-	-	3.3	3.3	-	-

Inclusion criteria (Table S4-2A,S4-2B): Prospective data of SBRT toxicity by grade, 2000-2021, ≥50 patients (i.e. prospective trial or a prospectively collected institutional database). Light yellow shading highlights major focus of table; red font highlights potential weakness (accrual before 2000).

[a], pneumonitis, hypoxia, pneumonia; [b], pain, rib fracture; [c], excluding symptom present pre-treatment; [d], 44% of lung tumors were metastases from extrathoracic cancer; [e], central tumors treated with 8 fractions of 7.5 Gray; [f], various regimens: 60 Gy/3 fx (21%), 50 Gy/5 fx (60%), 30 Gy/1 fx (14%), 60 Gy/8 fx (5%); [g], rate only among peripheral tumors; [h], 10% for peripheral *vs.* 27% for central tumors; i many with BED10 <100.

Br, brachial; Effus, effusion; f-u, follow-up; Gr, grade; NL, Netherlands; PrCT, prospective controlled trial; PS, performance status (ECOG): RCT, randomized controlled trial; yrs, years.

Table S4-3 Percent change from preoperative values in lung function following SBRT

Ordered by general *vs.* compromised patients and study size

1st author year (reference)	Study type	Years	N	PFT Base-line	Interval to PFT (mo)	Absolute Δ [a]	% with relative decrease of		% with relative increase of		Comments
							≥25% [b]	≥10% [b]	≥10% [b]	≥25% [b]	
FEV1 %											
Takeda 2013 (36)	Retro	05-10	141	-	12-75 [c]	- 2	16 [d]	42	-	-	Mostly normal patients
Stone 2015 (37)	PrCT	05-12	127	67%	12	- 2	8	34	-	-	
Regnery 2020 (38)	Retro	12-19	107	70%	12	- 8 [e]	-	-	-	-	Central, ultra-central
Guckensberger 2013 (39)	Retro	98-10	93	63% [f]	12	- 8	22	47	13	3	
Mangona 2015 (18)	P-DB	05-11	69	-	6-24	-	12	-	-	-	
Stephans 2009 (40)	Retro	04-07	68	50%	≥6	- 2	7 [d]	14	13	3 [d]	
Baumann 2008 (30)	PrCT	03-05	48	64%	14	- 3	-	-	-	-	
Mathieu 2015 (41)	PrCT	10-13	45	68%	12	0	-	-	-	-	
Bral 2011 (42)	PrCT	07-09	40	-	12 [g]	- 3	15 [h]	33 [h]	-	-	
Navarro 2016 (43)	PrCT	08-12	35	62%	12	- 4	-	-	-	-	
Ferrero 2015 (44)	PrCT	12-13	30	75%	10	- 11 [e]	37 [h]	53 [h]	-	-	
Videtik 2013 (45)	PrCT	08-09	21	62%	12	- 6 [e]	-	-	-	-	
Stanic 2014 (46)	PrCT	04-06	20	61%	24	- 6	10	49	-	-	
Bauman 2008 (30)	PrCT	03-05	34	44%	16	0	-	-	-	-	COPD
Takeda 2013 (36)	Retro	05-10	27	-	12-75 [c]	0	22 [d]	39	-	-	GOLD III, IV
Average				64% [i]		- 4	17	39	13	3	
DLCO %											
Stone 2015 (37)	PrCT	05-12	127	51%	12	- 5	12	37	-	-	
Mangona 2015 (18)	P-DB	05-11	69	-	6-24	-	25	-	-	-	
Mathieu 2015 (41)	PrCT	10-13	45	63%	12	- 6	-	-	-	-	
Guckensberger 2013 (39)	Retro	98-10	42	52% [f]	12	- 12	26	62	10	5	
Stephans 2009 (40)	Retro	04-07	41	57%	≥6	- 3	7 [d]	34	12	5 [d]	
Bral 2011 (42)	PrCT	07-09	40	-	12 [g]	- 3	20 [h]	33 [h]	-	-	
Navarro 2016 (43)	PrCT	08-12	35	54%	12	- 1	-	-	-	-	
Ferrero 2015 (44)	PrCT	12-13	30	67%	10	- 15 [e]	37 [h]	53 [h]	-	-	
Videtik 2013 (45)	PrCT	08-09	21	62%	12	- 17 [e]	-	-	-	-	
Stanic 2014 (46)	PrCT	04-06	13	61%	24	- 6	40	67	-	-	
Average				58%		- 8	24	48	11	5	

Inclusion criteria: studies involving SBRT reporting a change in pulmonary function tests, published 2000-2021, ≥20 patients total; Red font indicates study weakness (variable and long intervals).

[a], average of absolute differences per patient from baseline to follow-up % value; [b], relative difference from baseline; [c], variable time period; [d], ≥20% decrease or increase; [e], unmatched (difference of the averages of cohorts with baseline and with follow-up results); [f] taken from another publication of the patients involved (47); [g], 3 months data if 12 months data missing; [h], unclear when (toxicity at any time); [i], without double counting the poor PFT subsets.

Δ, change (from baseline); COPD, chronic obstructive pulmonary disease; DLCO, diffusing capacity of the lung for carbon monoxide; FEV1, forced expiratory volume in 1 second; GOLD III, IV, global initiative for chronic obstructive lung disease class III and IV; mo, months; NS, not statistically significant; P-DB, analysis of prospectively collected database; PFT, pulmonary function test; PrCT, prospective controlled trial; retro, retrospective study.

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Table S4-4 Toxicity in patients with ILD

	SBRT	Particle therapy	Ablation	Surgery
N studies	13	4	3	30
N patients	122	23	46	1709
% operable	29%	25%	0	100%
% non-IPF ILD	69%	50%	67%	60%
Treatment-related ILD toxicity [a]	25%	18%	25%	12%
Treatment-related mortality [a]	16%	4%	9%	2%

Data taken from a systematic review by Chen *et al.* (48). [a], average of studies weighted by study size. ILD, interstitial lung disease; IPF idiopathic pulmonary fibrosis; SBRT, stereotactic body radiotherapy.

Table S4-5A Summary of general evidence

	SBRT (v Open L)		SBRT (v Open SL)		SBRT (v VATS L)		SBRT (v VATS SL)		Abl (v SL)		Abl (v SBRT)	
	Effect	Conf	Effect	Conf	Effect	Conf	Effect	Conf	Effect	Conf	Effect	Conf
Short-term (90-day) outcomes												
Mortality	↑↑ [a]	+++	↑↑ [a]	+++	↑ [a]	+++	↑ [a]	+++	=/↑	0	↓	
Morbidity	↑ [a]	+	↑ [a]	+	↑ [a]	+	↑ [a]	+	=/↑	0	↓	
QOL	↑↑ [a]	+	↑↑ [a]	+	↑↑ [a]	+	↑↑ [a]	+	-	-	-	-
Pain	↑↑ [a]	+	↑↑ [a]	+	↑↑ [a]	+	↑↑ [a]	+	↑↑	Extpol	-	-
Intermediate (1-2 year) outcomes												
Δ FEV1	↑	+	=	0	↑	+	=	0	=	0	-	-
Dyspnea	↑	+	=	0	↑	+	=	0	-	-	-	-
QOL	↑↑	+	↑↑	0	=	0	=	0	= /↑↑ [b]	0	=	0
Pain	↑↑	+	↑↑	0	=	0	=	0	= /↑↑ [b]	0	-	-
Toxicity	= [a]	0	= [a]	0	= [a]	0	= [a]	0	-	-	-	-
Long-term (5-year) outcomes												
OS	↓↓↓	+++	↓↓	+++	↓↓↓	+++	↓↓	+++	↓↓↓	+	↓	+
LCSS	↓↓↓	+	↓↓	+	↓↓↓	+	↓↓	+	↓↓↓	+	-	-
FFR	↓↓	+	-	-	↓↓	+	-	-	-	-	-	-
LR- FFR	↓	+	-	-	↓	+	-	-	-	-	-	-

Legend (Table S4-5A-S4-5C): Qualitative assessment of the impact of treatment approaches on various key outcome measures and the confidence in the evidence. Differences are categorized by degree of clinically meaningful differences (defined in insert). The reference (for improvement or worsening) is the treatment in parentheses.

Effect	
↑↑↑	2x meaningful improvement
↑↑	Meaningful improvement
↑	Somewhat better
=	Similar
↓	Somewhat worse
↓↓	Meaningful worsening
↓↓↓	2x meaningful worsening

Confidence in/consistency of evidence	
++++	Very high
+++	High
++	Moderate
+	Low
0	Very low
Extpol	Extrapolation

A clinically "meaningful" difference is defined as ≥10-unit difference, with "somewhat" being half of the meaningful difference. The units of measure (for categories in parentheses) are: normalized scale points (QOL); 5-year actuarial rate (OS, LCSS); actuarial rate or simple incidence (recurrence, FFR); incidence of Gr ≥3 treatment related complications (morbidity); absolute change in % FEV1 (PFTs in compromised patients). Different thresholds of "meaningful" are: 90-day mortality (2% difference); PFTs in healthy patients (20% difference in FEV1%).

[a], data not parsed by resection extent; [b], equal for VATS, better for Ablation *vs.* Open surgery.

Δ FEV1, change in FEV1 ≥6 months; Abl, ablation; Conf, confidence in the evidence; Extpol, extrapolation (indirect evidence); FFR, freedom from recurrence (only recurrence counts as an event); Gr, grade; HR, hazard ratio; LCSS, lung cancer specific survival (only death due to lung cancer counts as an event); Lobe, lobectomy; LR-FFR, locoregional freedom from recurrence; OS, overall survival; PFT, pulmonary function tests; QOL, quality-of-life; VATS, video-assisted thoracic surgery.

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Table S4-5B Summary of evidence in older patients

	SBRT (v Open L/SL)		SBRT (v VATS L/SL)		Abl (v SL)		Abl (v SBRT)	
	Effect	Conf	Effect	Conf	Effect	Conf	Effect	Conf
Short-term (90-day) outcomes								
Mortality	↑↑	++	↑↑	++	=/↑	0	↓	0
Morbidity	↑	+	↑	+	=/↑	0	↓	0
QOL	↑↑	Extpol	↑↑	Extpol	-	-	-	-
Pain	↑↑	Extpol	↑↑	Extpol	↑↑	Extpol	-	-
Intermediate (1-2 year) outcomes								
Δ FEV1	-	-	-	-	-	-	-	-
Dyspnea	-	-	-	-	-	-	-	-
QOL	↑↑	0	=	Extpol	= /↑↑ [b]	0	=	0
Pain	↑↑	0	=	Extpol	= /↑↑ [b]	0	-	-
Toxicity	=	0	=	0	-	-	-	-
Long-term (5-year) outcomes								
OS	↓↓	+	↓↓	+	↓↓↓	+	↓	+
LCSS	↓↓	+	↓↓	+	↓↓↓	+	-	-
FFR	-	-	-	-	-	-	-	-
LR- FFR	-	-	-	-	-	-	-	-

Table S4-5C Summary of evidence in compromised patients

	SBRT (v Open L/SL)		SBRT (v VATS L/SL)		Abl (v SL)		Abl (v SBRT)	
	Effect	Conf	Effect	Conf	Effect	Conf	Effect	Conf
Short-term (90-day) outcomes								
Mortality	↑↑↑	Extpol	↑↑	Extpol	=/↑	Extpol	↓	Extpol
Morbidity	↑↑ [a]	Extpol	↑ [a]	Extpol	=/↑	Extpol	↓	Extpol
QOL	↑↑ [a]	Extpol	↑↑ [a]	Extpol	-	-	-	-
Pain	↑↑ [a]	Extpol	↑↑ [a]	Extpol	↑↑	Extpol	-	-
Intermediate (1-2 year) outcomes					-			
Δ FEV1	-	-	-	-	-	-	-	-
Dyspnea	-	-	-	-	-	-	-	-
QOL	↑↑	Extpol	=	Extpol	= /↑↑ [b]	Extpol	=	Extpol
Pain	↑↑	Extpol	=	Extpol	= /↑↑ [b]	Extpol	-	-
Long-term (5-year) outcomes								
OS	↓	+	↓	+	↓↓	0	↓	0
LCSS	↓	+	↓	+	↓↓	0	-	-
FFR	-	-	-	-	-	-	-	-
LR- FFR	-	-	-	-	-	-	-	-

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SBRT vs Lobectomy

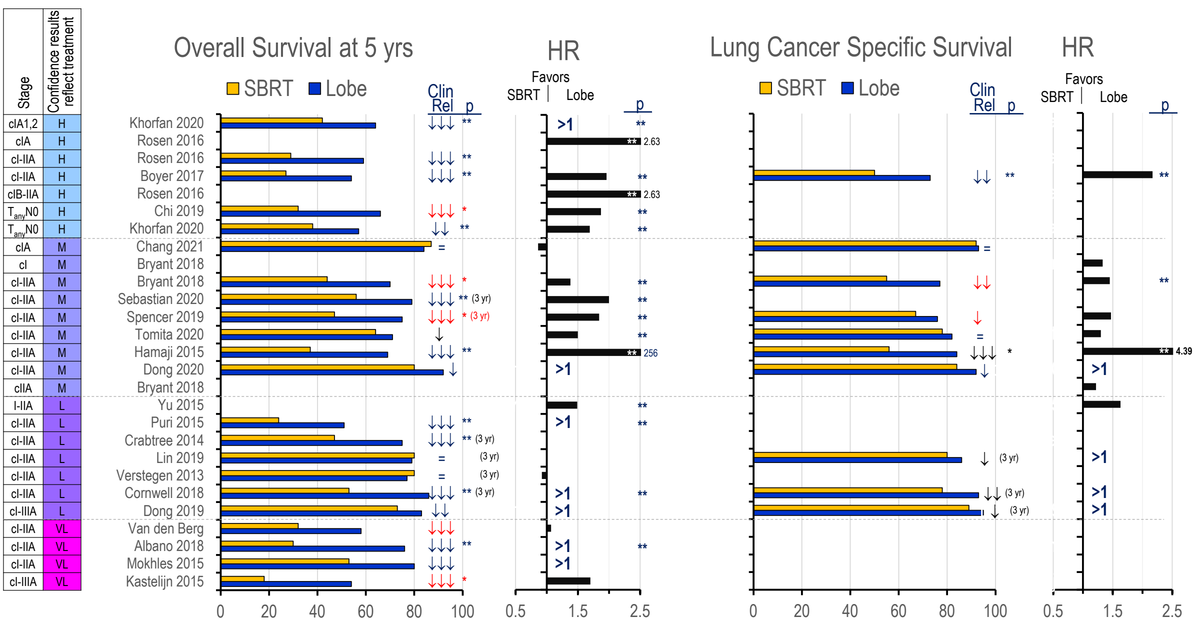

Figure S4-1A Graphic depiction of outcomes in Table 1: SBRT *vs*. lobectomy.

SBRT vs Sublobar Resection

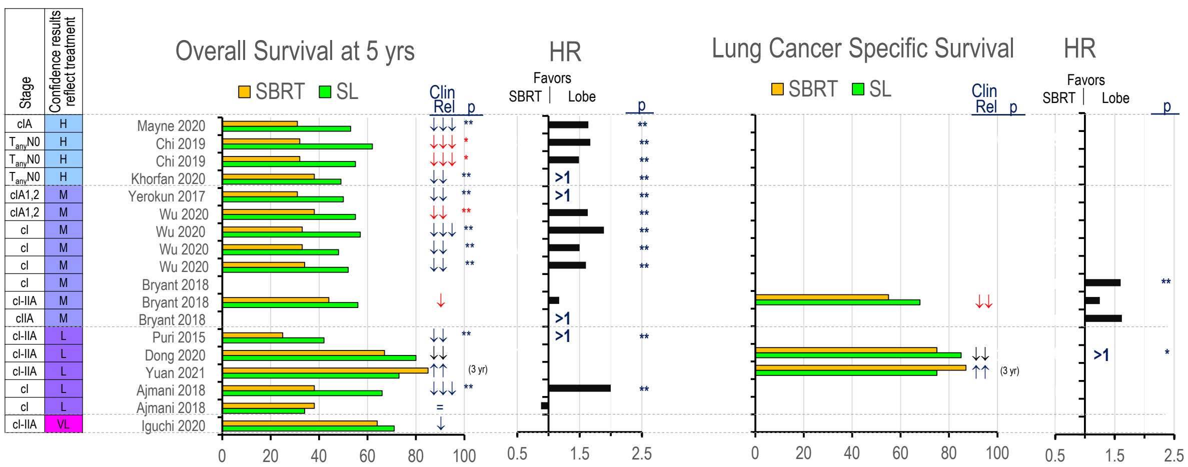

Figure S4-1B Graphic depiction of outcomes in Table 2: SBRT *vs*. sublobar resection.

Legend (Figure S4-1A,S4-1B): Graphic depiction of outcomes in *Table 1* and *Table 2*. Figure rows correspond to the respective table rows. Also depicted is the confidence that the outcomes reflect the treatment (*vs*. confounders), the level of clinical relevance and statistical significance. The HR reference is the surgical resection, i.e. HR >1 reflects worse outcome compared with surgery.

Confidence results reflect the treatment	
VH	Very High
H	High
M	Moderate
L	Low
VL	Very Low
See Table 1 for details	

Relevance of Effect	
↑↑↑	2× meaningfully better
↑↑	Meaningfully better
↑	Somewhat better
=	Similar
↓	Somewhat worse
↓↓	Meaningfully worse
↓↓↓	2× meaningfully worse

The HR reference is the surgical resection, i.e. HR >1 reflects worse outcome compared with surgery.
Red font indicates unadjusted survival rates
* reported as statistically significant by univariable analysis; ** reported as statistically significant by multivariable analysis; Clin Rel, clinical relevance of effect. A clinically relevant difference is defined as ≥5-point difference in the 5-year actuarial rate (overall survival, lung cancer specific survival). Details of this categorization is provided in the part 1 paper (*Tab. S1-1*) (49). HR, hazard ratio; Lobe, lobectomy; SBRT, stereotactic body radiotherapy; Seg, segment; SL, sublobar resection; W, wedge; yrs, years

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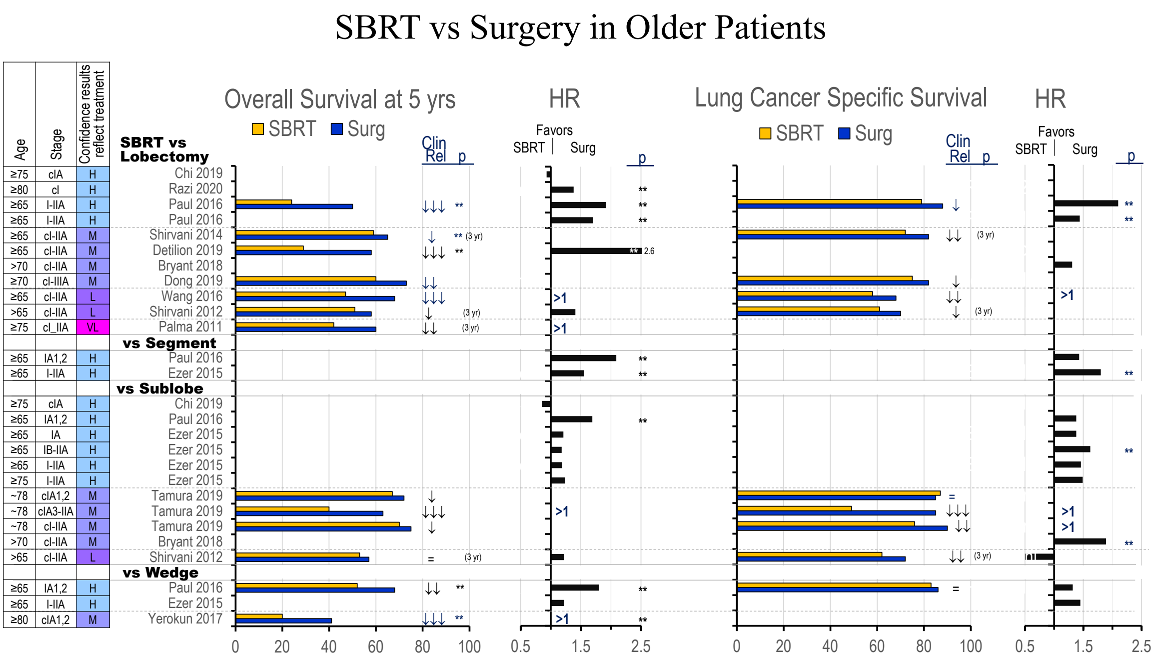

Figure S4-2 Graphic depiction of outcomes in *Table 5*: SBRT *vs.* surgical resection in older patients.

Graphic depiction of outcomes in *Table 5*. Figure rows correspond to the respective table rows. Also depicted is the confidence that the outcomes reflect the treatment (*vs.* confounders), the level of clinical relevance and statistical significance. The HR reference is the surgical resection, i.e. HR >1 reflects worse outcome compared with surgery. Red font indicates unadjusted survival rates. See legend for Figure S4-1A,S4-1B for further explanation.

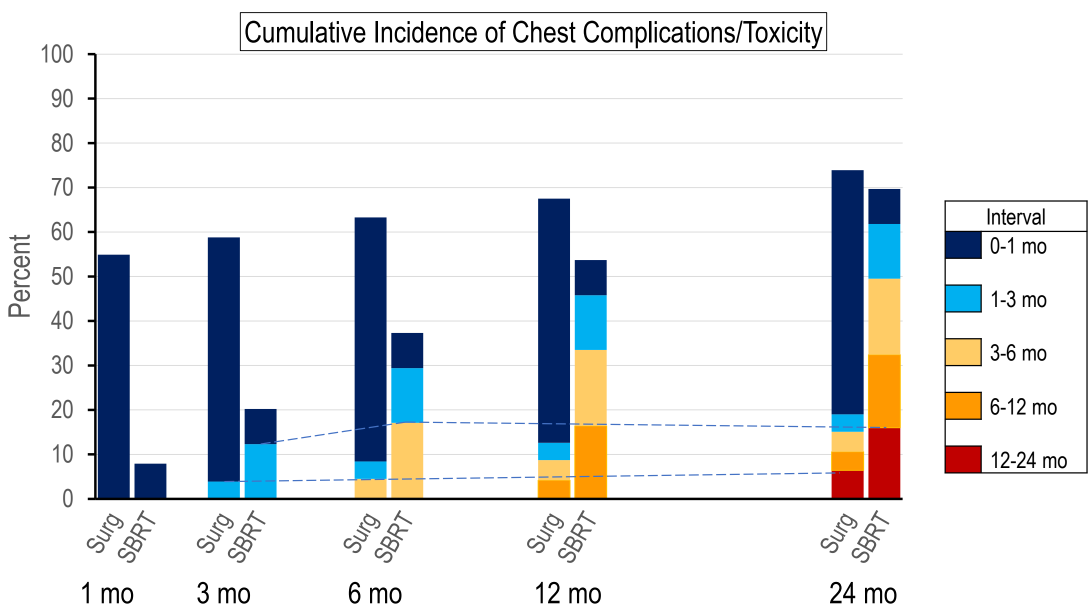

Figure S4-3 Cumulative incidence of morbidity.

Cumulative incidence of complications/toxicity after SBRT *vs.* surgery (data from SEER-Medicare, 2007-09, 1078 propensity-matched patients age ≥67). Depicted is the cumulative occurrence of a new diagnosis of conditions that can be summarized as chest morbidity (cardiac, pulmonary or esophageal conditions). mo, months; SBRT, stereotactic body radiotherapy; Surg, surgery. Data from Yu *et al.*, Cancer 2015 (5).

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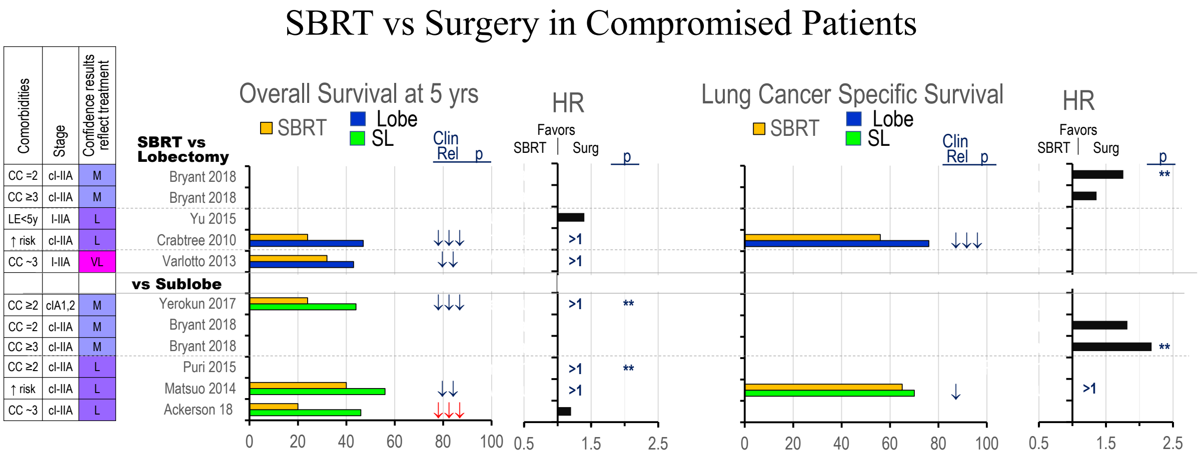

Figure S4-4 Graphic depiction of outcomes in *Table 6*. SBRT *vs.* surgical resection in compromised patients.

Graphic depiction of outcomes in *Table 6*. Figure rows correspond to the respective table rows. Also depicted is the confidence that the outcomes reflect the treatment (*vs.* confounders), the level of clinical relevance and statistical significance. The HR reference is the surgical resection, i.e. HR >1 reflects worse outcome compared with surgery. Red font indicates unadjusted survival rates. See legend for Figure S4-1A,S4-1B for further explanation.

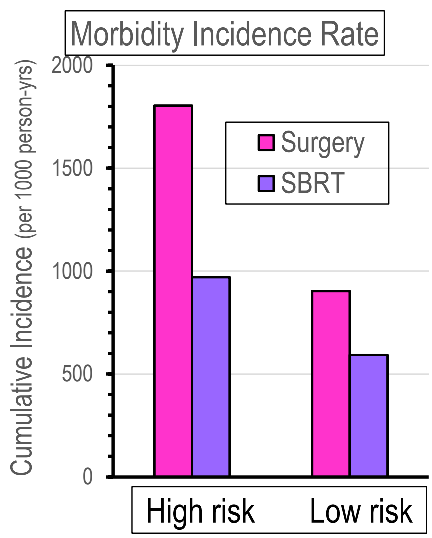

Figure S4-5 Cumulative incidence of morbidity in high- and low-risk cohorts.

Incidence rate (per 1,000 person-years) of morbidity after SBRT *vs.* surgery in propensity-matched cohorts of high- and low-risk patients (defined as < or ≥5-year life expectancy using the SEER-Medicare non-cancer cohort and age, sex and Elixhauser comorbidity). Morbidity involved a new diagnosis of relevant cardiac, pulmonary or esophageal conditions. Data from Yu *et al.*; Cancer 2015 (5).

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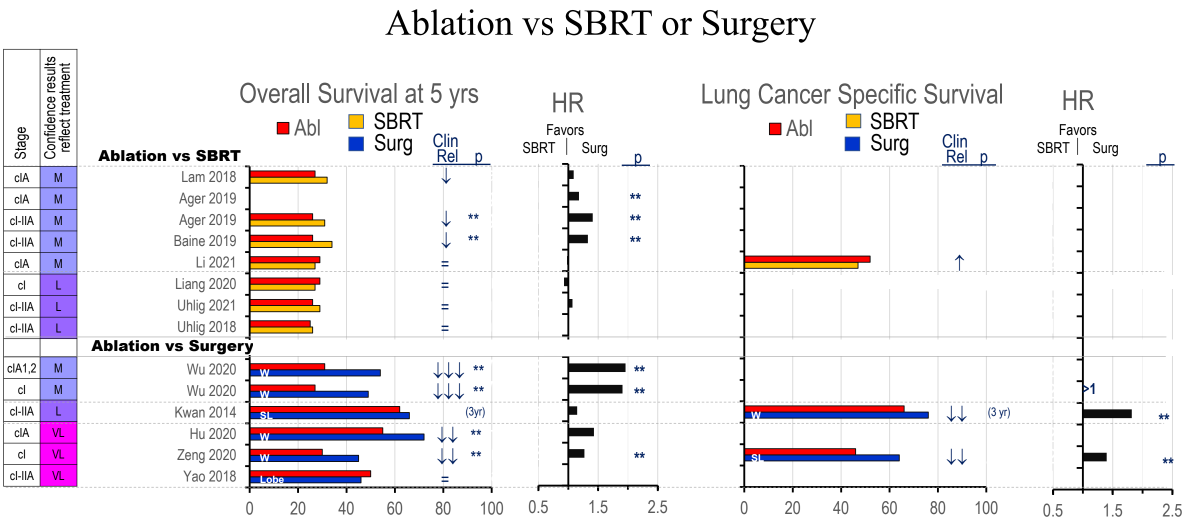

Figure S4-6 Graphic depiction of outcomes in *Table* 7: ablation *vs.* SBRT or surgical resection.

Graphic depiction of outcomes in *Table* 7. Figure rows correspond to the respective table rows. Also depicted is the confidence that the outcomes reflect the treatment (*vs.* confounders), the level of clinical relevance and statistical significance. The HR reference is SBRT or surgical resection, i.e. HR >1 reflects worse outcome compared with SBRT or surgery. Red font indicates unadjusted survival rates. See legend for Figure S4-1A,B for further explanation.

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