

SBRT for lung cancer: Boing beyond small inoperable NSCLC

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Early stage lung cancer:

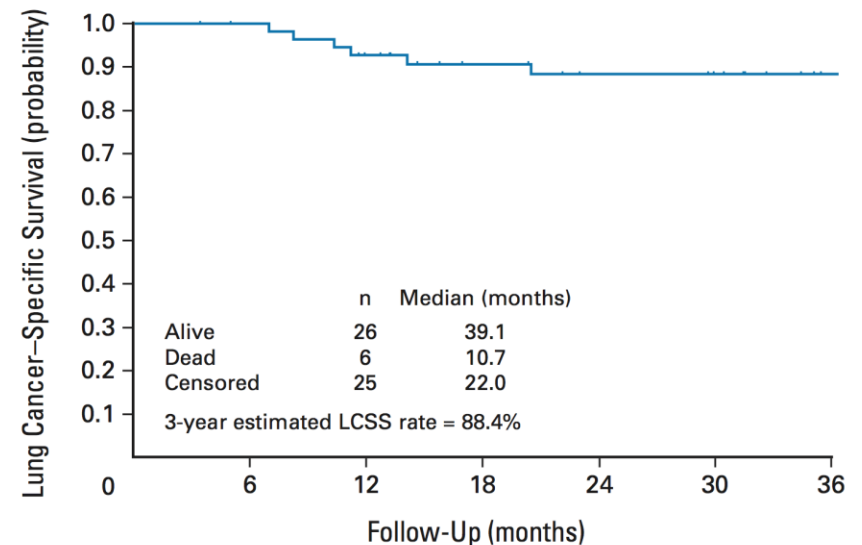
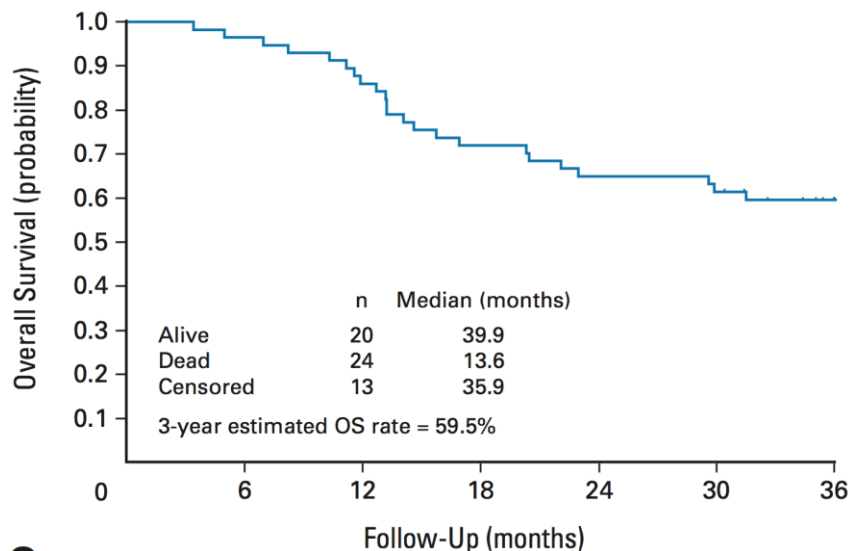
- Surgical resection – standard of care for patients who are candidates for lobectomy.
- >20% of patients cannot tolerate surgery because of comorbidities.
- >30% of patients do not have surgery in US community practice.
- Some patients with high surgical risk are not candidates for lobectomy but could tolerate more limited resection.

3 main populations of early lung cancer pts :

- Standard risk surgical candidates
- High risk surgical candidates
- Medically inoperable

Inoperable patients - prospective studies

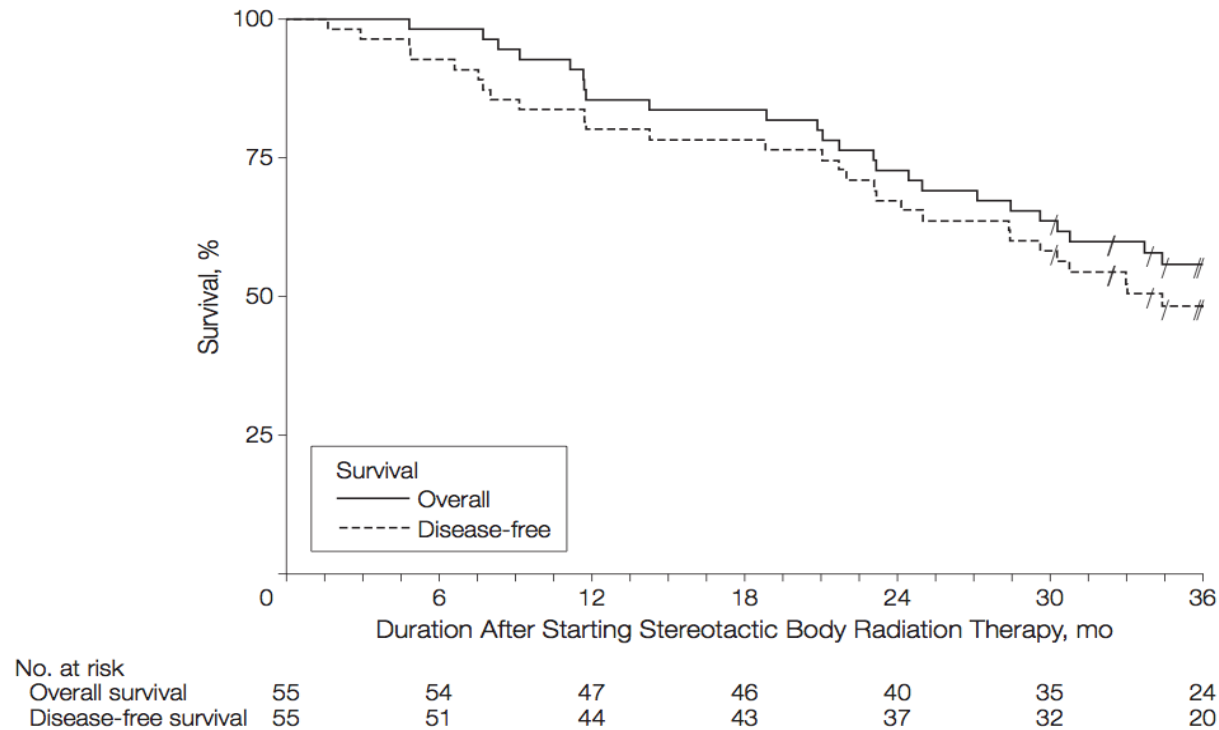
Nordic Study Group – phase II, 57 patients



Baumann et al. JCO 2009

Inoperable patients - prospective studies

RTOG 0236 – phase II, 55 patients

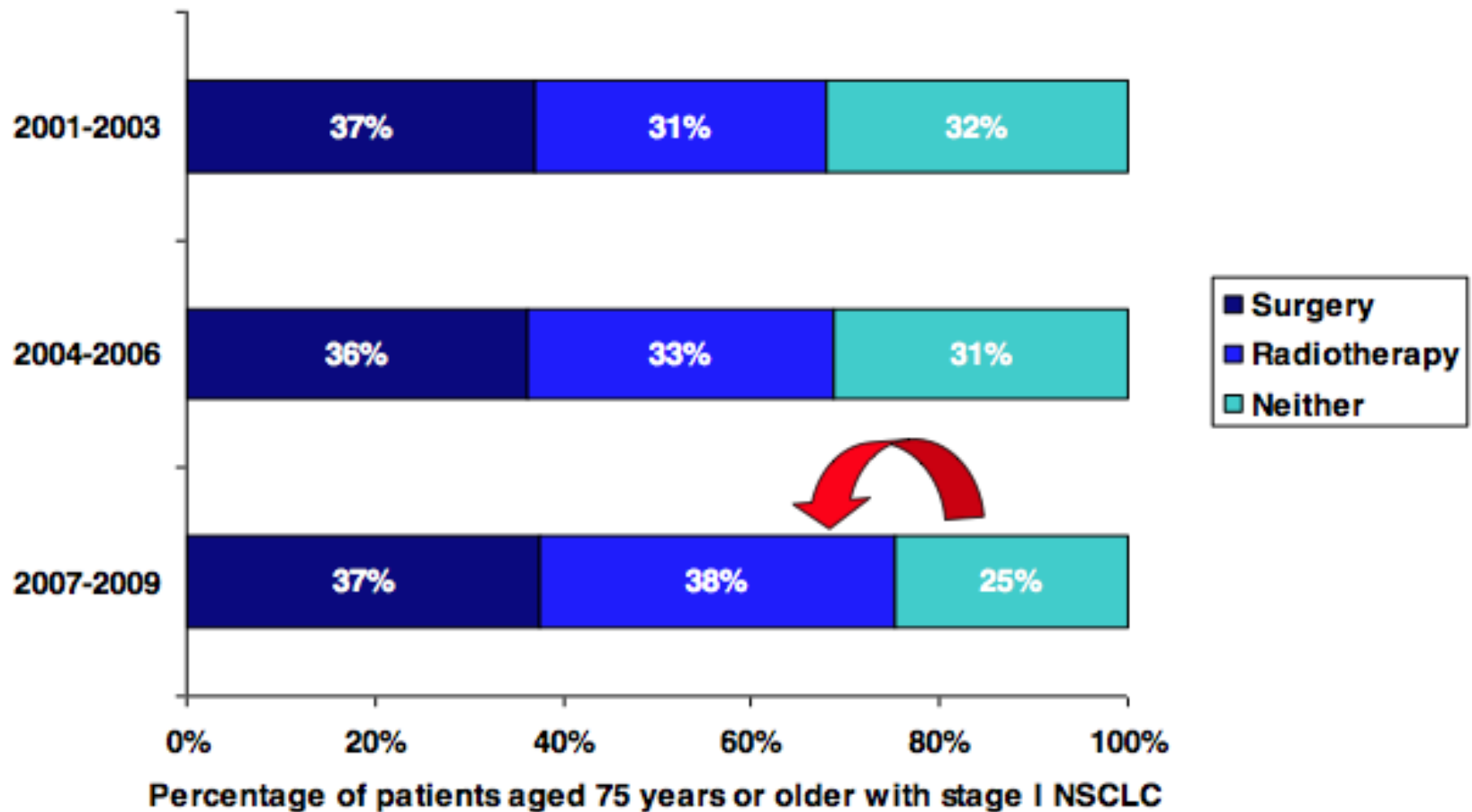


Inoperable patients - prospective studies

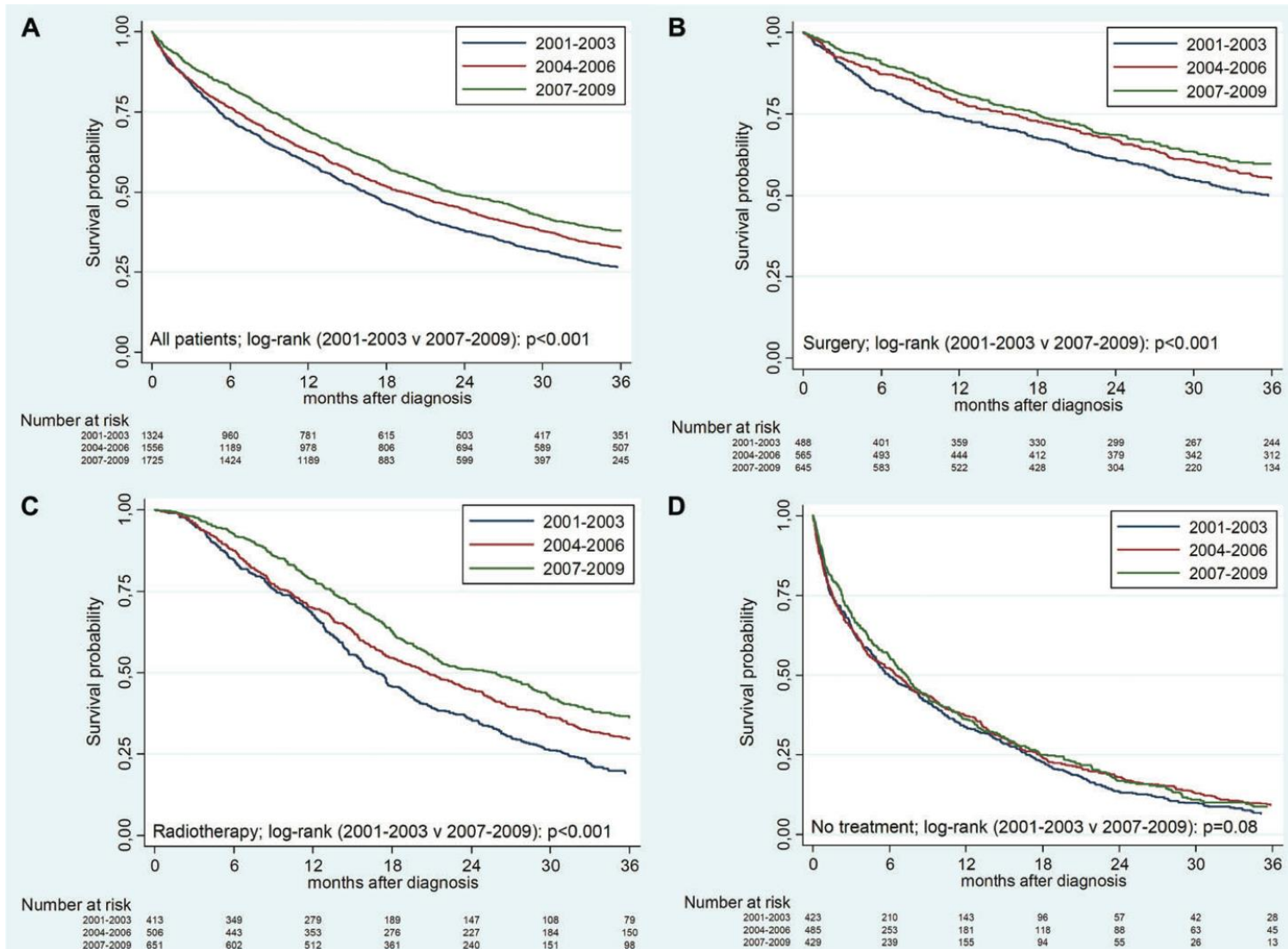
JCOG 0403 (medicaly inoperable arm)

- Phase II stratified: 100 pts eligible
- Stge IA; 48Gy in 4 fractions
- OS 59,9%@3y (90% CI: 51,4%-67,5%)
- Local Control rate 88%@3y

Netherlands Cancer Registry 2003 - 2009



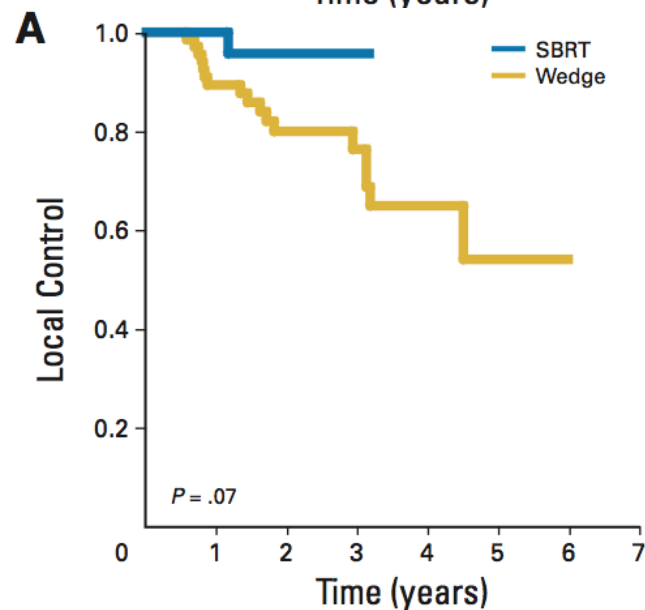
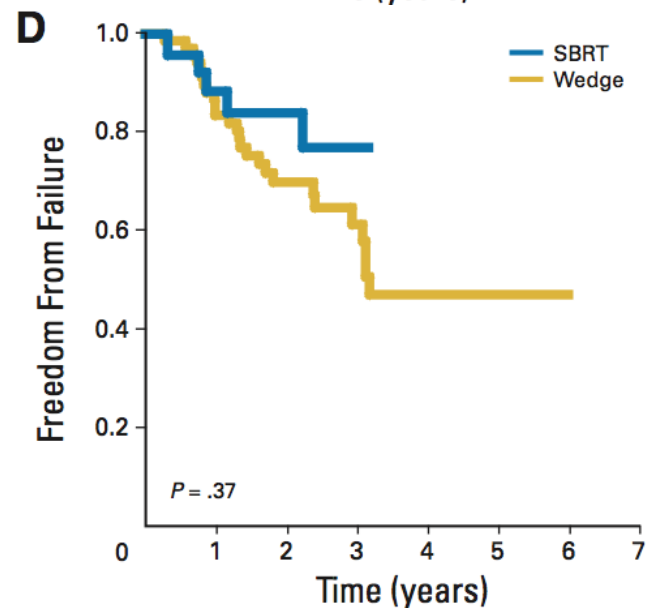
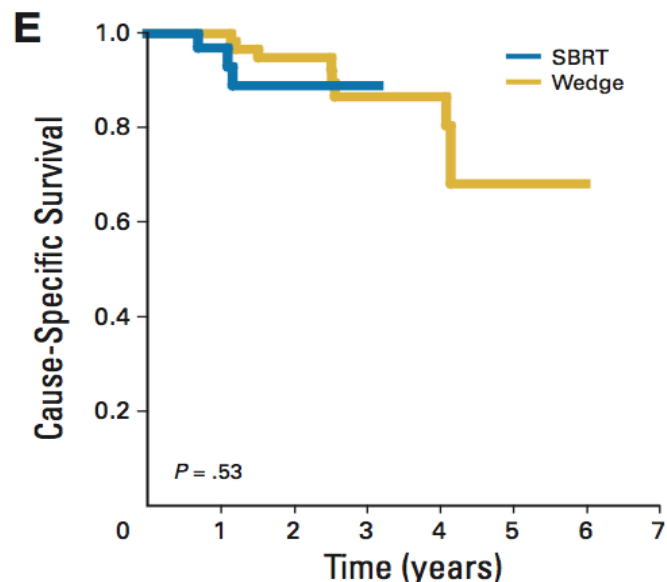
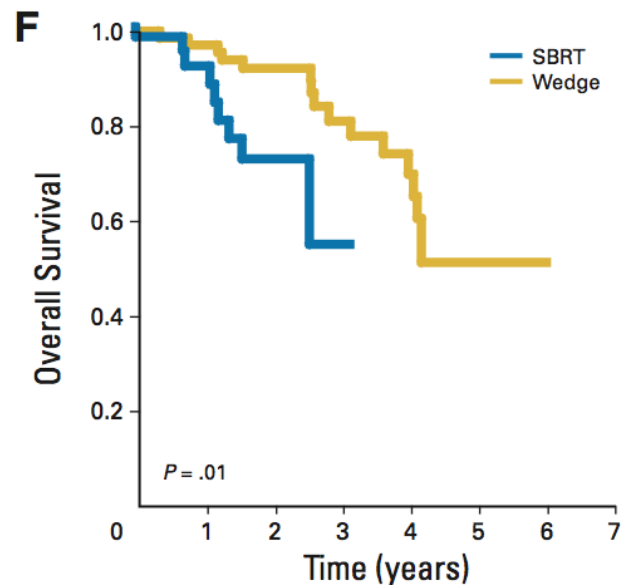
Netherlands Cancer Registry 2003 - 2009



SBRT is standard of care
for medically inoperable
early stage NSCLC

What about high risk/operable
early stage NSCLC?

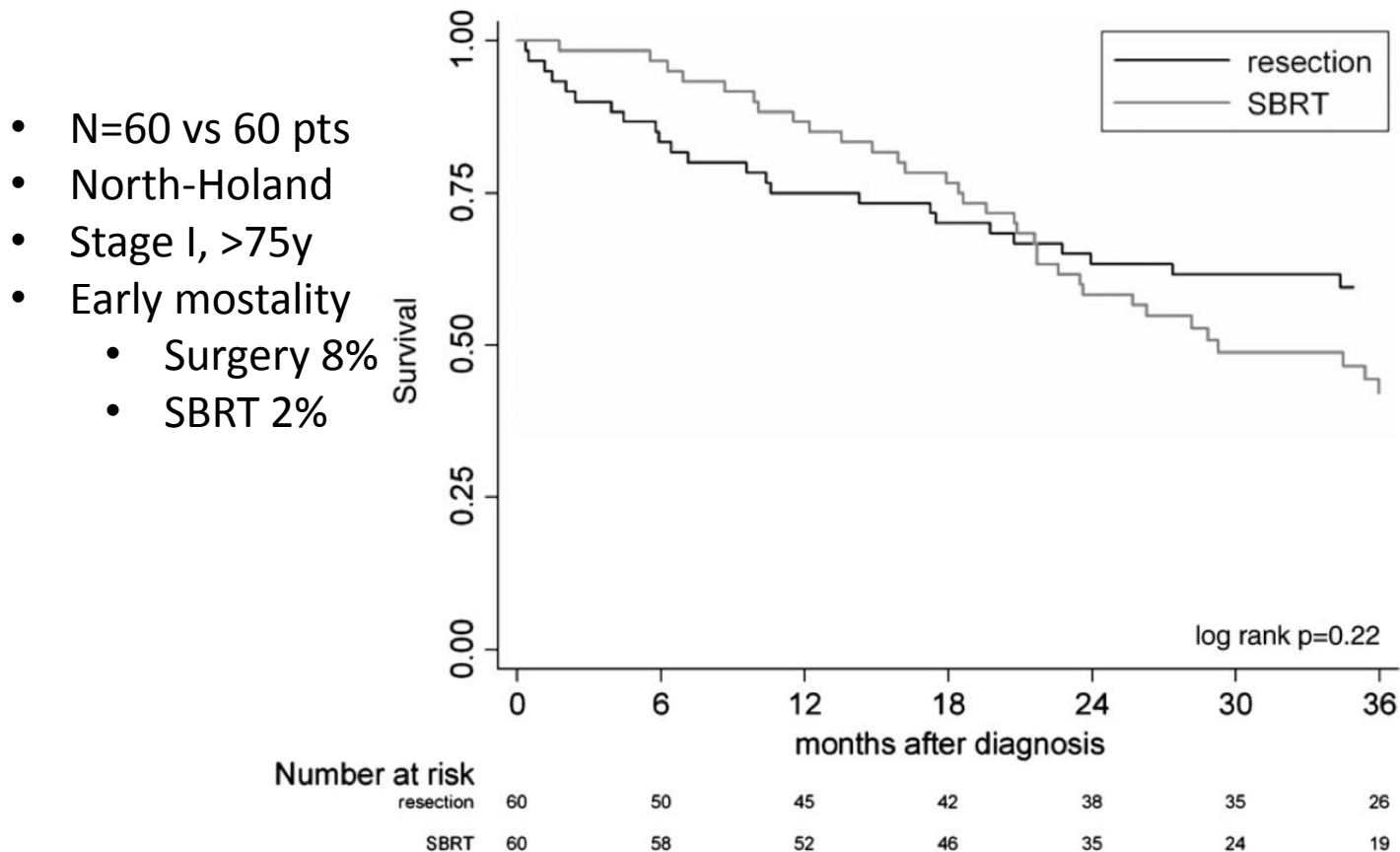
SBRT vs wedge resection – retrospective series



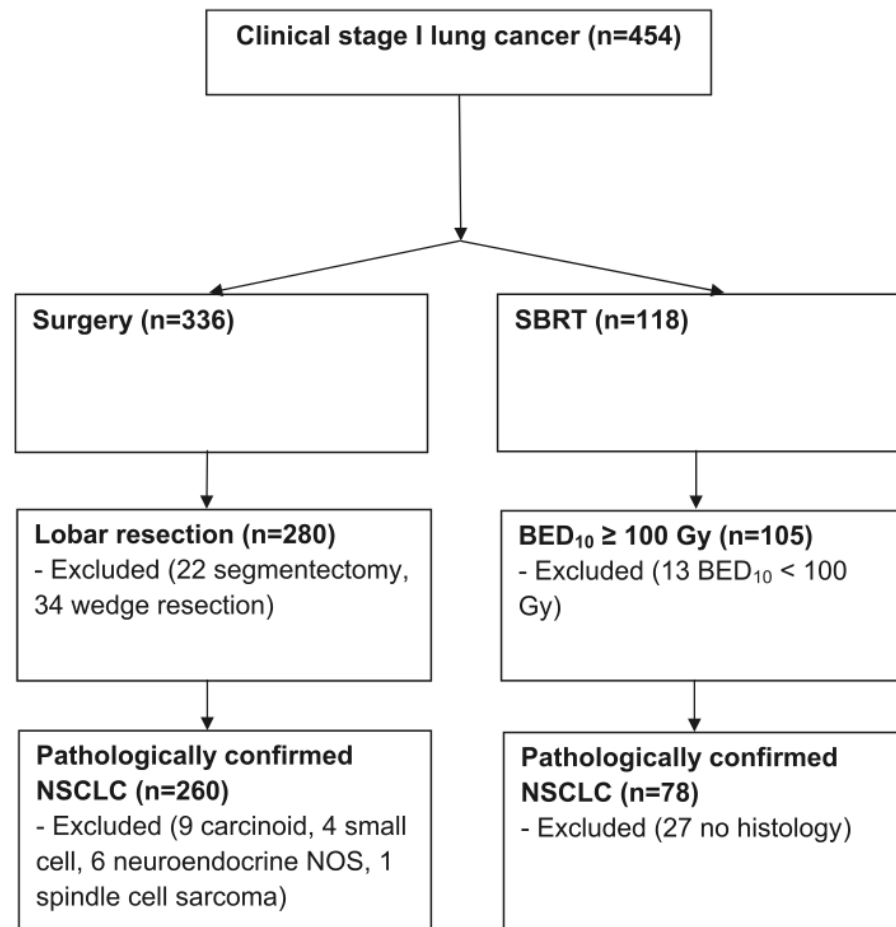
- n=58 vs 69
- Higher age and comorbidity score in SBRT

SBRT vs surgery – population-based matched-pair comparison

Stereotactic radiotherapy versus surgery in stage I NSCLC

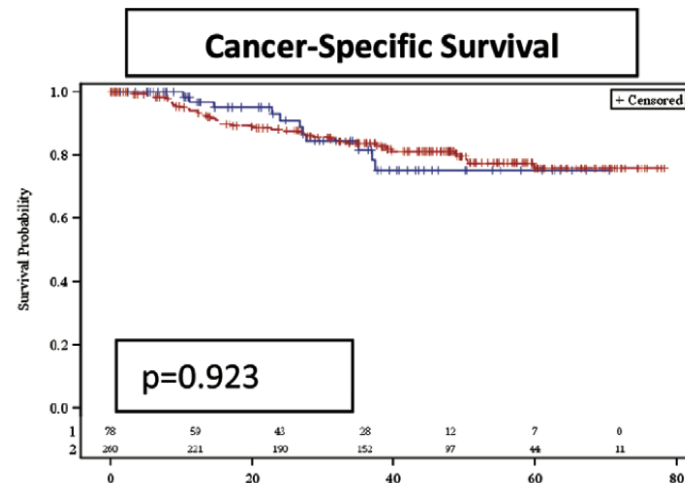
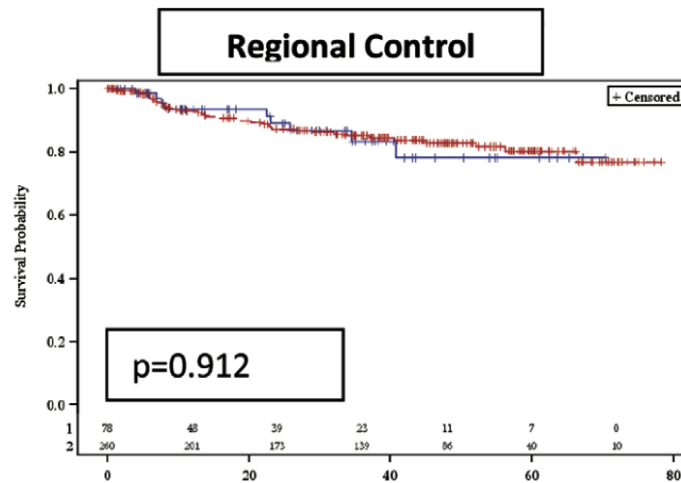
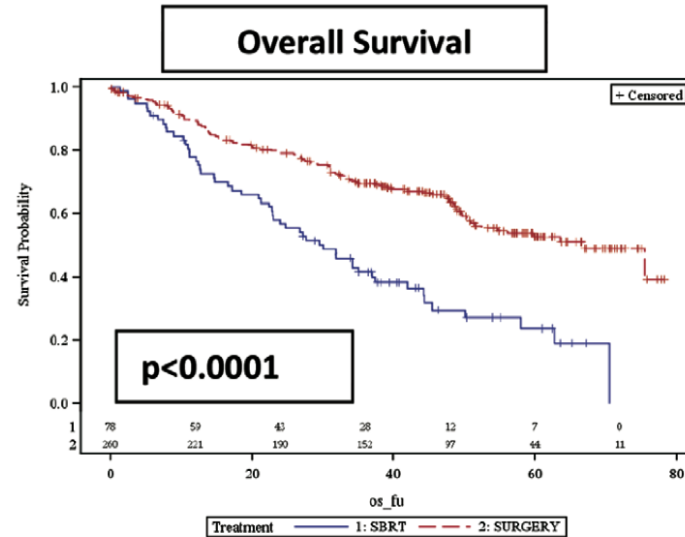
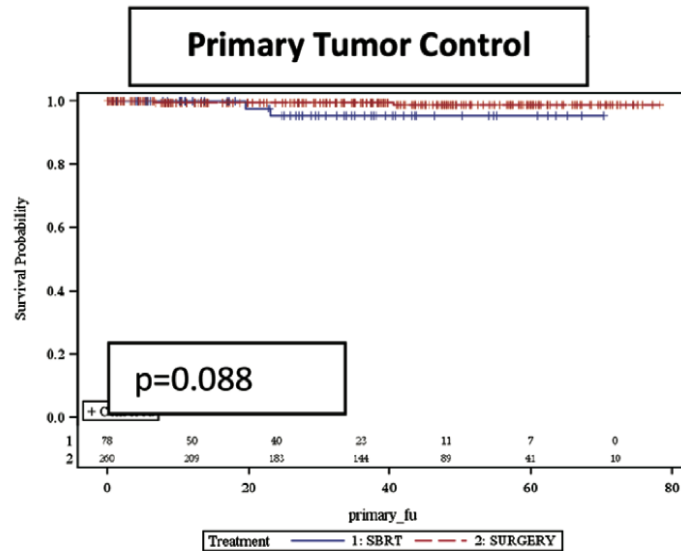


Surgery vs SBRT patterns of failure—retrospective analysis

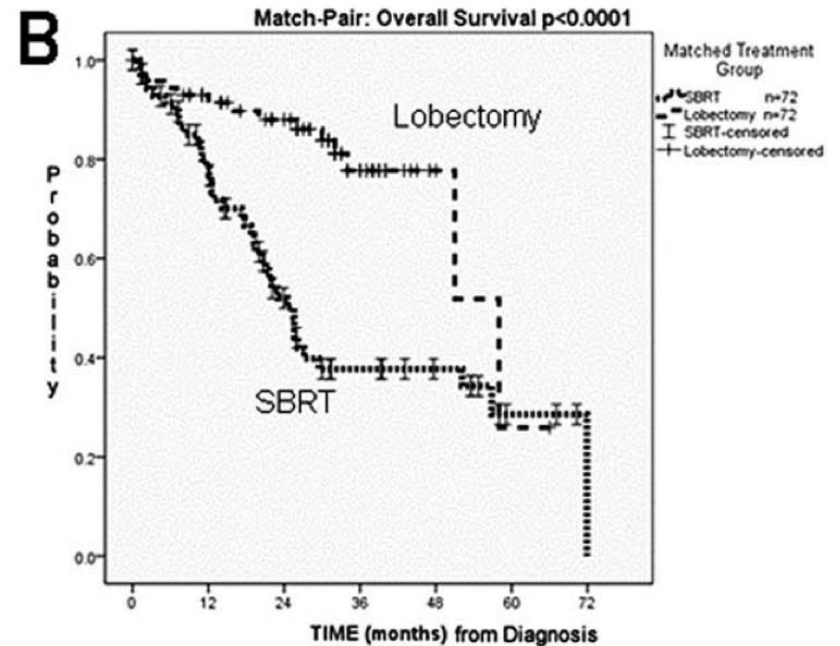
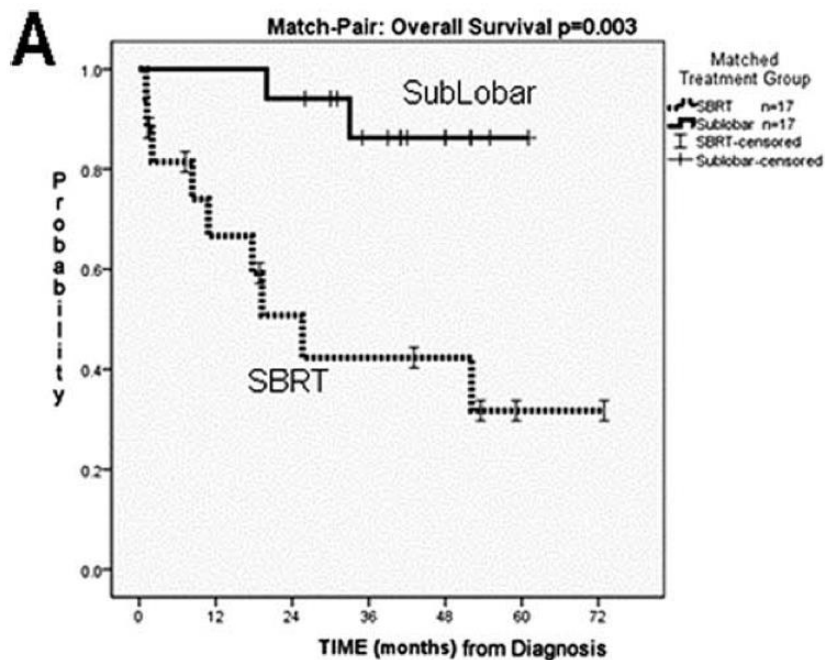


Surgery vs SBRT patterns of failure

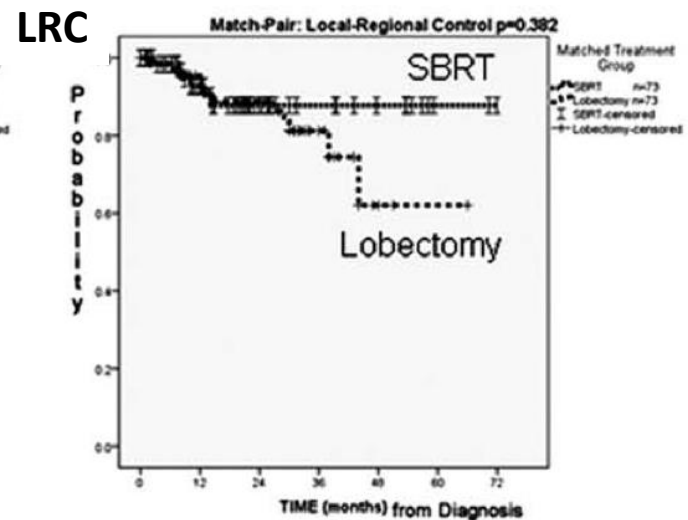
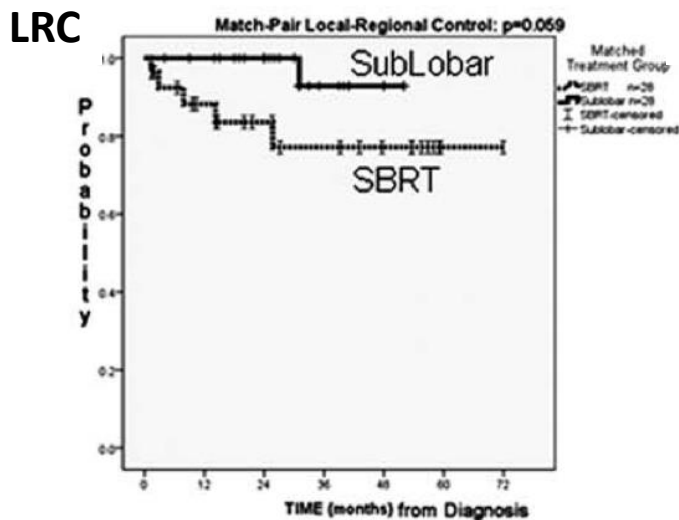
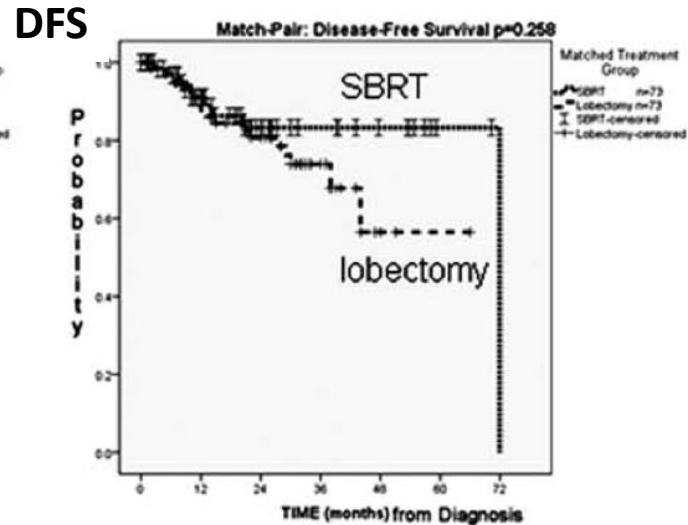
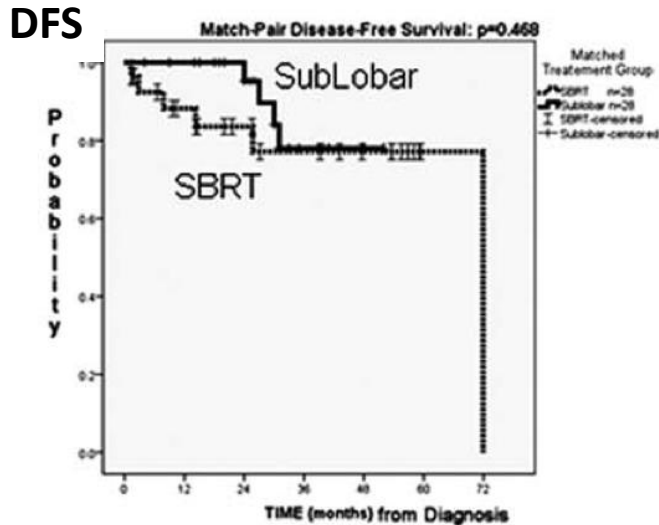
– retrospective analysis



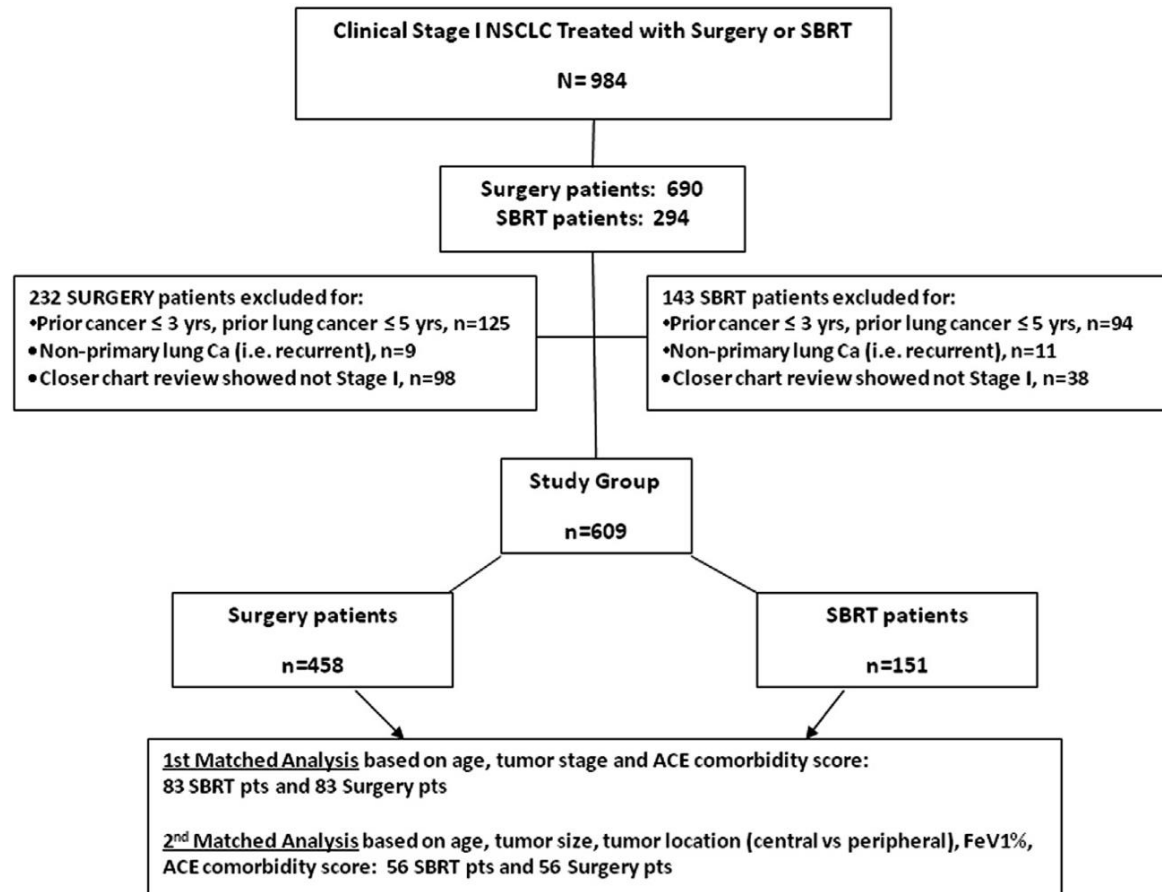
SBRT vs surgery – matched-pair and propensity score comparison



SBRT vs surgery – matched-pair comparison and propensity score comparison

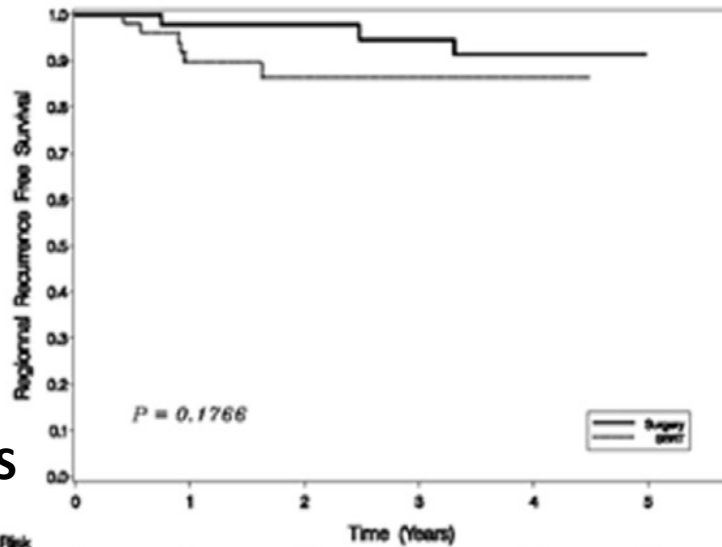


SBRT vs surgery – retrospective propensity-score matched comparison

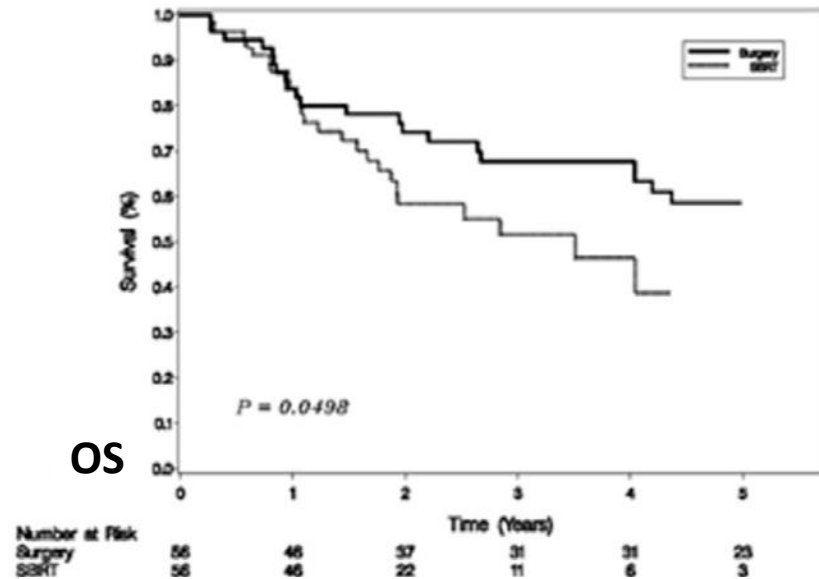


SBRT vs surgery – retrospective analysis

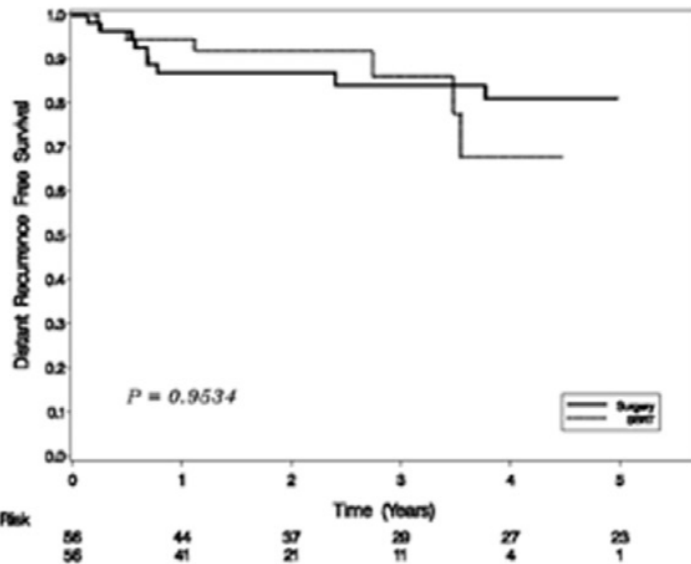
RPFS



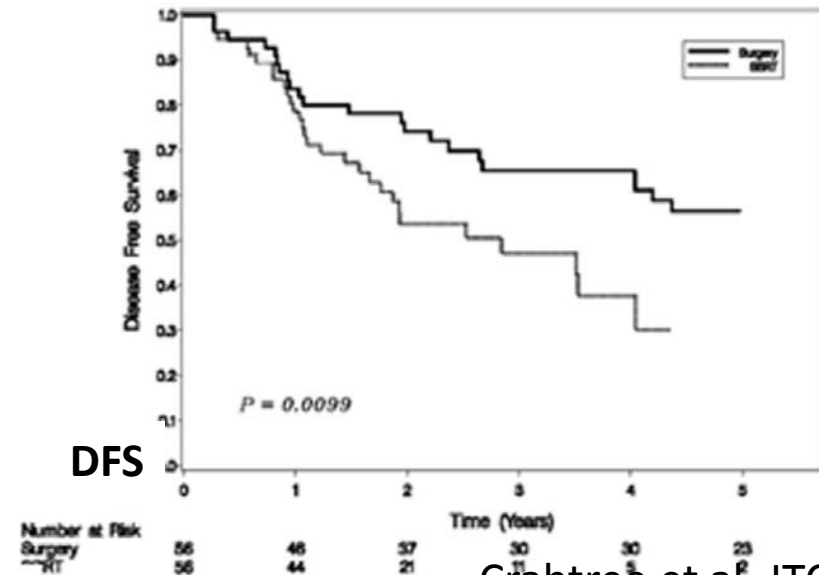
OS



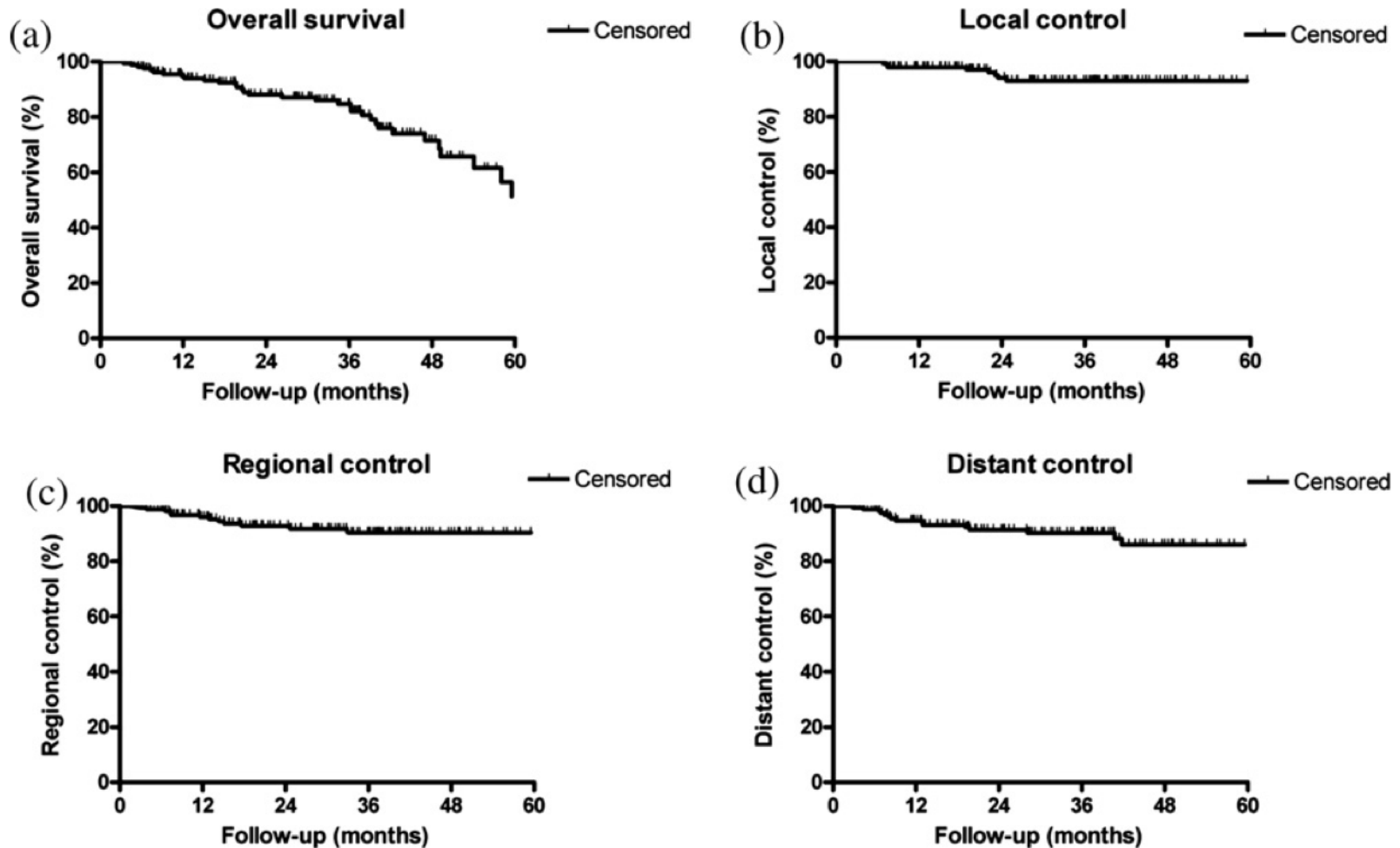
DPFS



DFS

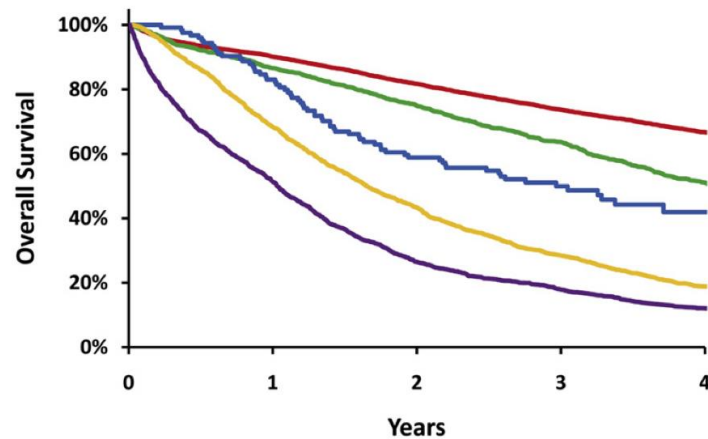


SBRT for potentially operable patients – retrospective analysis



SEER-Medicare retrospective analysis

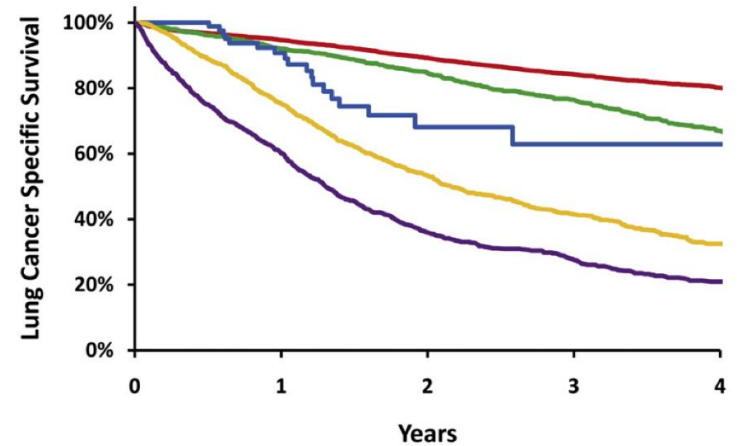
A



Number at Risk

Lobectomy	6531	5338
Sublobar Resection	1278	958
SBRT	124	73
Conventional Rad.	1614	702
No Treatment	1378	366

B



Number at Risk

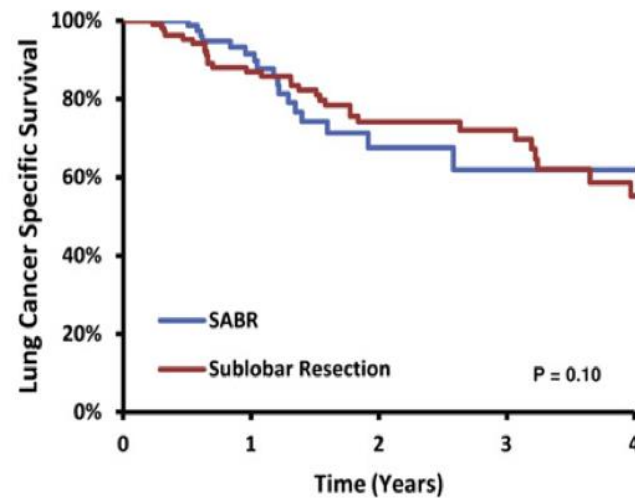
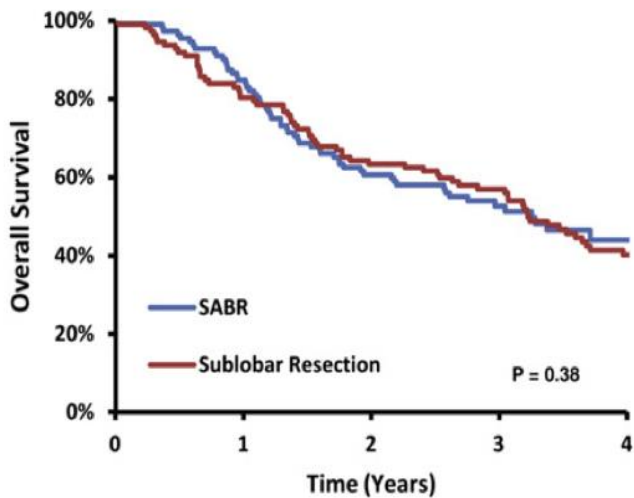
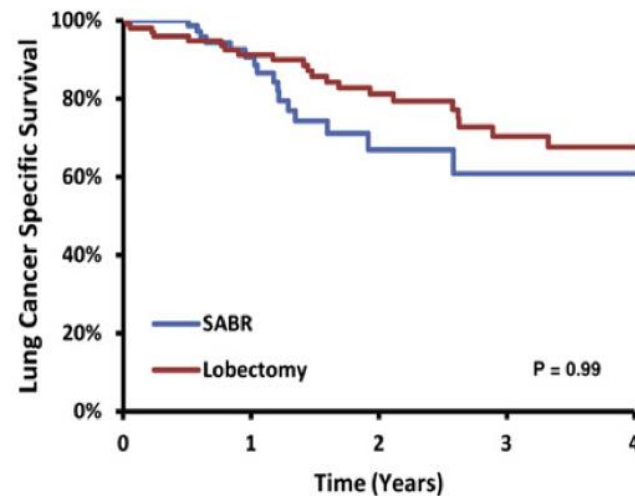
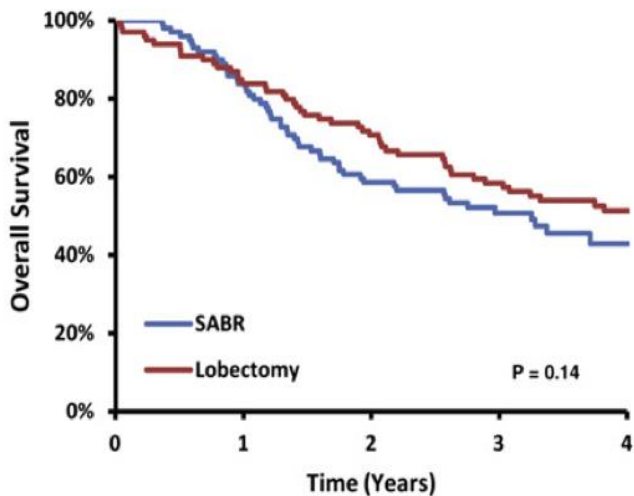
Lobectomy	6531	3783	1824
Sublobar Resection	1278	647	262
SBRT	124	17	<11
Conventional Rad.	1614	492	118
No Treatment	1378	251	64

n=10923

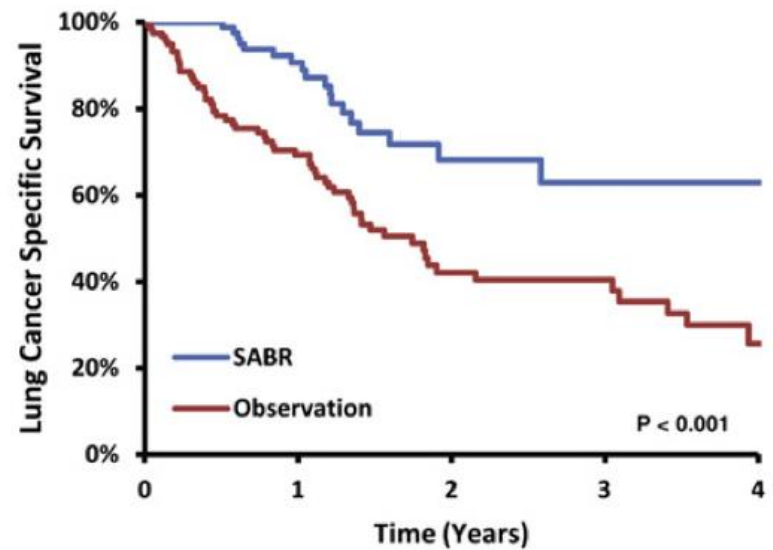
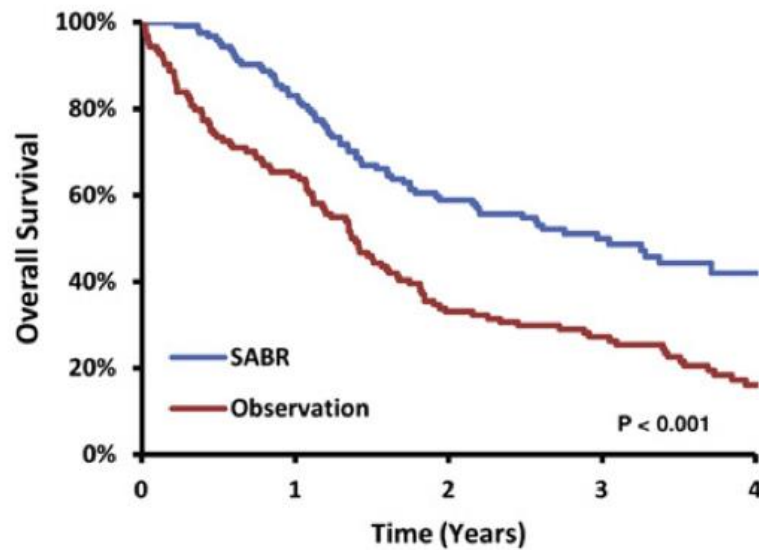
Age $\geq 66y$

Stage 1

SEER-Medicare retrospective analysis



SEER-Medicare retrospective analysis



SBRT vs surgery for operable pts – prospective trials

STARS phase III (MDACC/international)

- Standard risk operable, <4cm size
- CyberKnife SBRT vs lobectomy

ROSEL phase III (Netherlands)

- Operable, peripheral location, <3cm size
- SBRT vs lobectomy

ACOSOG Z 4099/RTOG 1021 phase III (USA)

- High risk operable, peripheral location, <3cm
- SBRT vs sublobar resection

SBRT efficacy summary:

- Consistent outcomes across series, including prospective cooperative trials:
 - Tumor control >85-90%@3y
 - OS – 50-60%@3y for medically inoperable pts
 - OS – 76%@3y for operable patients (JCOG0403)
- SBRT is comparable to surgery in non randomized comparisons – good options for high-risk/elderly patients

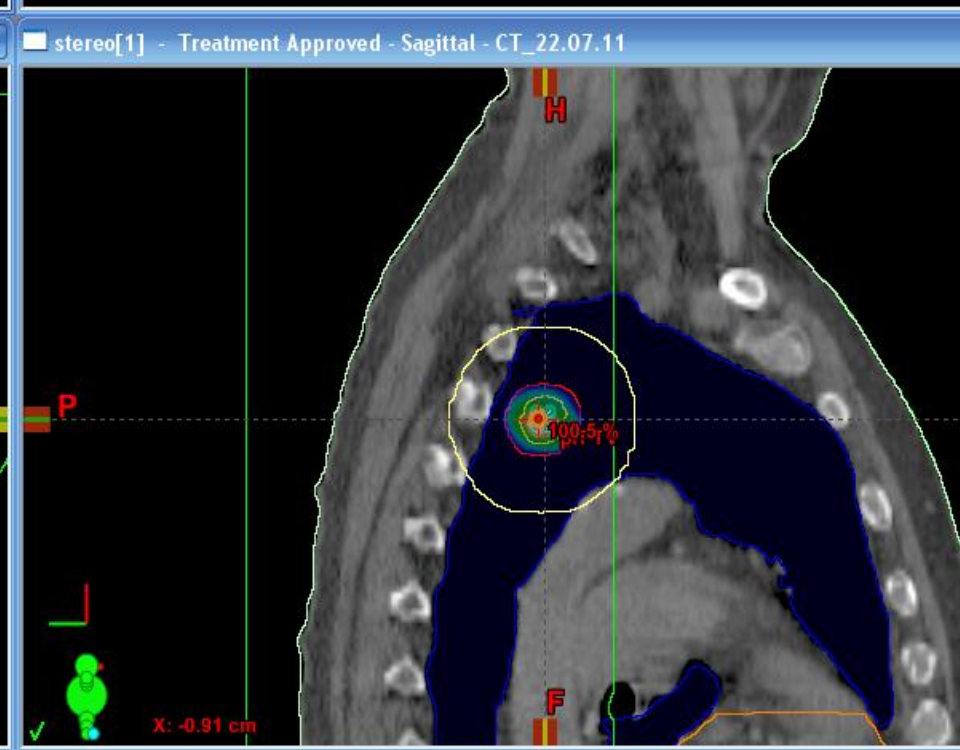
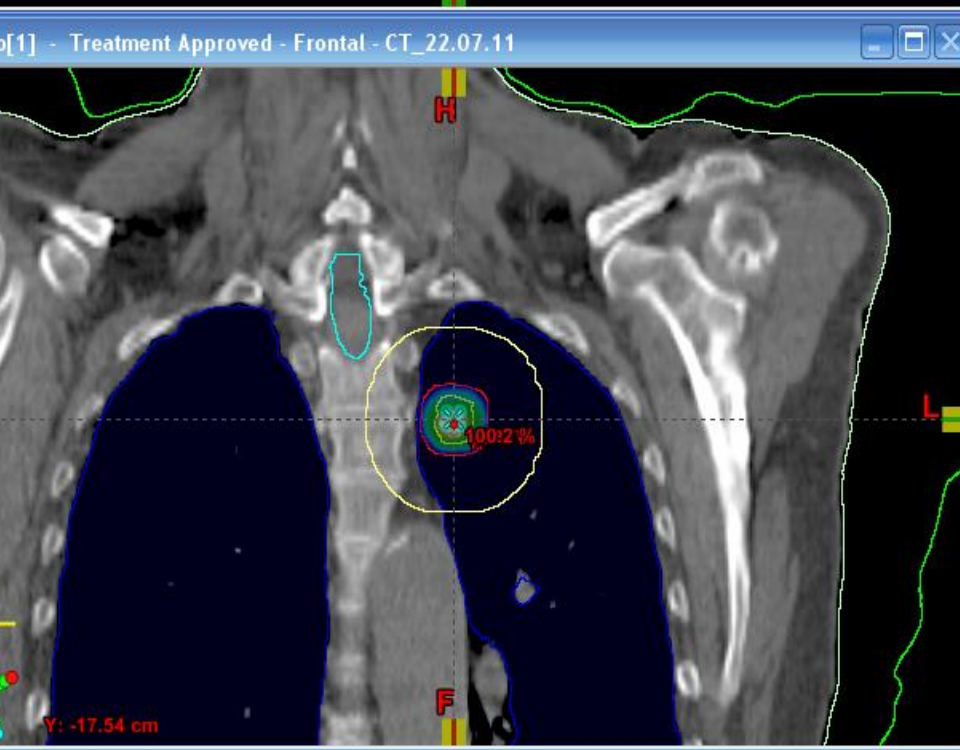
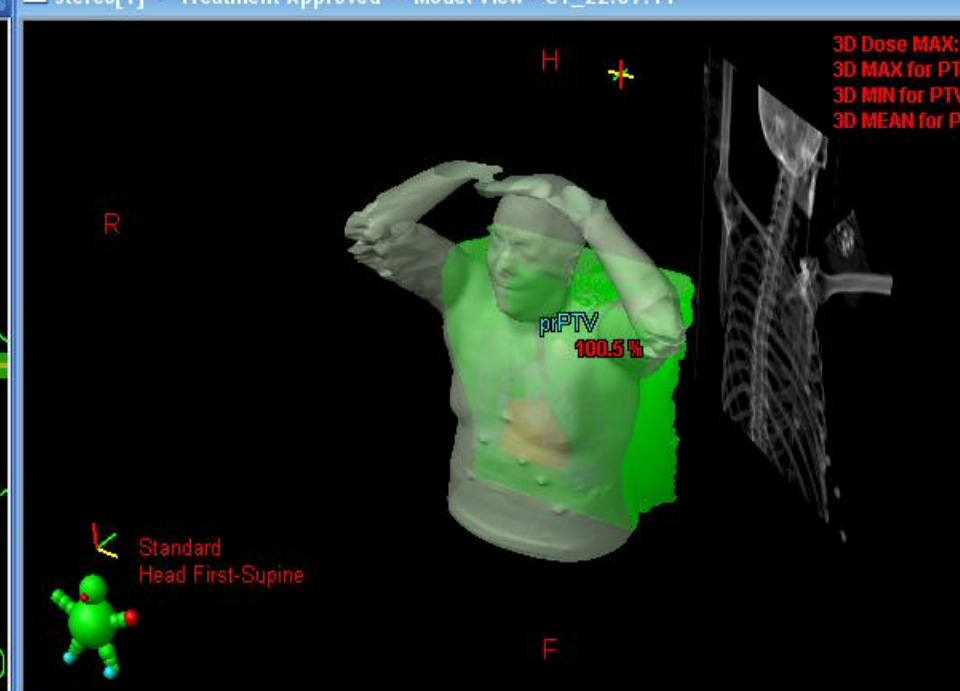
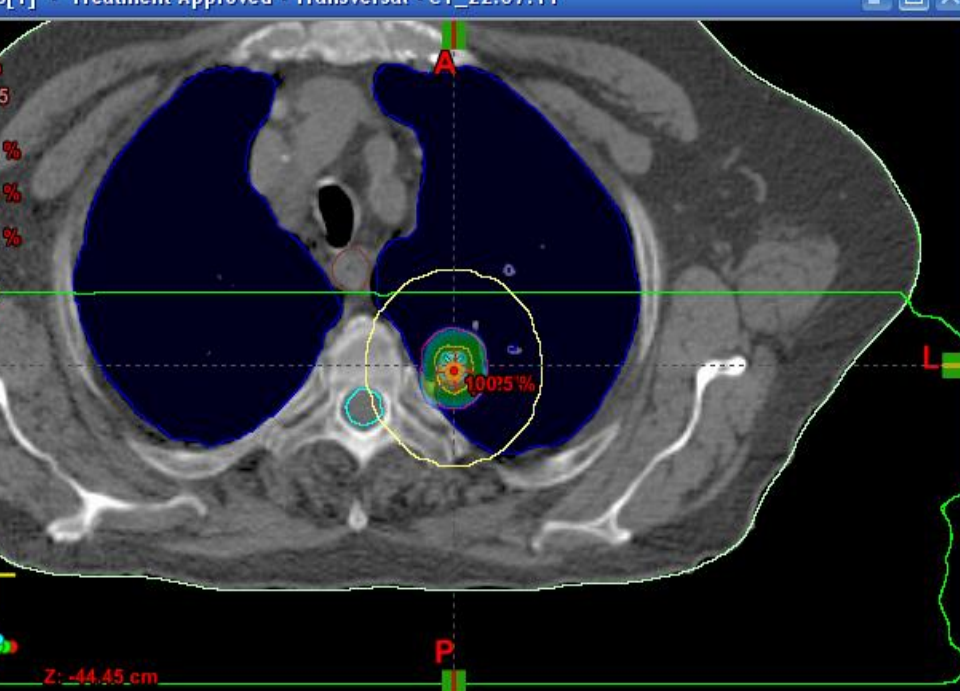
What about incomplete/clinical staging
without surgery?

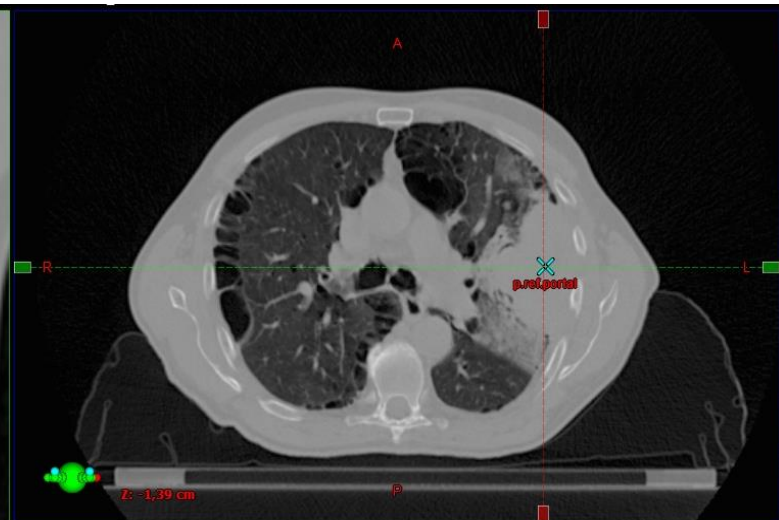
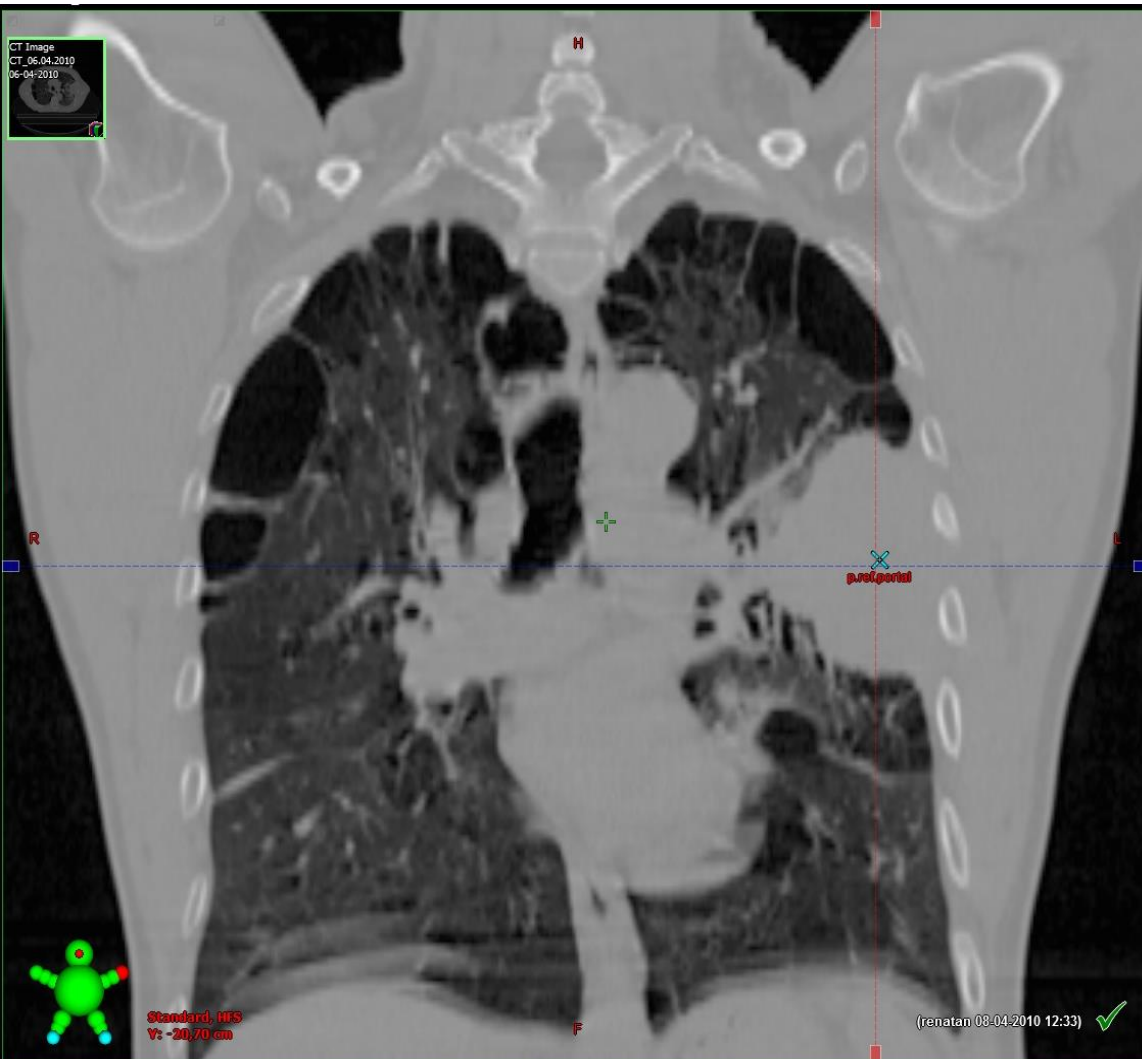
Pattern of relapse after SBRT:

Patterns of failure according to tumor size in selected studies.

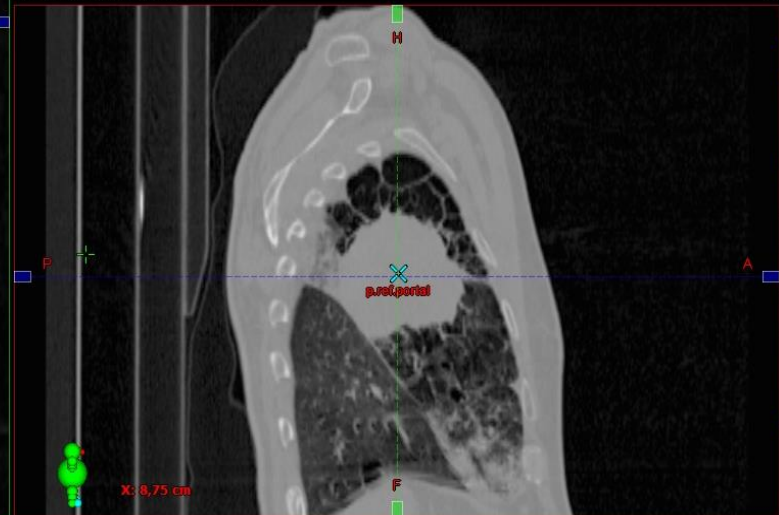
	Tumor size (cm)	% >T1	Total dose/# fractions	BED _{iso} (Gy ₁₀)	BED _{periphery} (Gy ₁₀)	% Local failure	% Regional failure	% Distant failure
Baumann et al. [29]	≤9 Median 3.7	60	30–45 Gy/3–4	112.5–219.4	60–112.5	T1: 3 T2: 13, $p < 0.05$ Increased local, regional, and distant recurrence in T2 tumors noted	<5	25
Baumann et al. [30]	≤5 Median 2.5	30	45 Gy/3	219.4	112.5	4 Local failures, all T2; 3 yr estimated failures (local, regional, and distant mets), $p = 0.02$: T1: 18 T2: 41	5	16; 24 at 3 yrs
Koto et al. [33]	≤5	38.7	45–60 Gy/3–8	105–112.5	90.5–95.2	T1: 22.1 T2: 60	6.5	19.4
Nagata et al. [34]	≤4	28.9	48 Gy/4	105.6	n/a	T1: 3 T2: 0	T1: 9.4 T2: 0	T1: 15.6 T2: 30.8
Onishi et al. [36]	≤5.8 Median 2.8	36.2	30–84 Gy/1–14	57.6–180	n/a	T2 > T1, $p < 0.05$	11.3	19.8
Takeda et al. [38]	n/a	39.7	50 Gy/5	140.6	100	T1: 7 T2: 4, $p = ns$	T1 vs. T2, $p = ns$	T1 vs. T2, $p = ns$
Chang et al. [41]	<4	n/a	40 Gy/4	105.6	80	T2: 2/3 failures in 7 patients who received 40 Gy/4	7.7	15.4
Hata et al. [45]	≤4.2 Median 2.5	47.6	50–60 Gy/10	86.3–111	75–96	T1: 0 T2: 10	0	19
Hof et al. [46]	≤5	59.5	19–30 Gy/1	55.1–120	38.3–81.6	<12 cm ³ : 0 ≥12 cm ³ : 20 $p = 0.078$	9.5	31
Lagerwaard et al. [48]	≤6	41	60 Gy/8	145.3	105	T1: 1.6 T2: 5.5, $p = ns$	T1 < T2, $p = 0.04$	T1 < T2, $p = 0.04$
Le et al. [49]	≤6.2 Median 3.9	70	15–30 Gy/1	64.3–215.6	37.5–120	T1: 0% T2: >20 Gy: 17% <20 Gy: 49%	Regional + DM: 40	
Onishi et al. [53]	≤6	57.1	60 Gy/10	125.3	96	6 overall (2 pts); all T2	4/5 Regional + distant mets (14%): T2	
Van der Voort van Zyp et al. [60]	≤10 Median 2.7	44.3	60 Gy/3	277.1	180	T1: 0 T2: 11, $p = 0.085$	11	17
Inoue et al. [61]	≤4.5	19.1	30–70 Gy/2–10	75–119	n/a	≤2 cm: 3.4 >2 cm: 5.3	≤2 cm: 5.2 >2 cm: 10.5	≤2 cm: 10.3 >2 cm: 17.5
Guckenberger et al. [62]	<5	68.3	26–48 Gy/1–8	138.1–168.9	76.8–93.6	All failures from primary NSCLC are ≥T2	All T2	T1: 16.7 T2: 42.1 T3: 88.9
Onimaru et al. [63]	≤7 Median 2.7	39.0	40–48 Gy/4	80–105.6	57.6–75.3	T2 > T1, $p = 0.0373$ T2: 40 Gy > 48 Gy, $p = 0.0015$	n/a	n/a

SBRT for large tumors

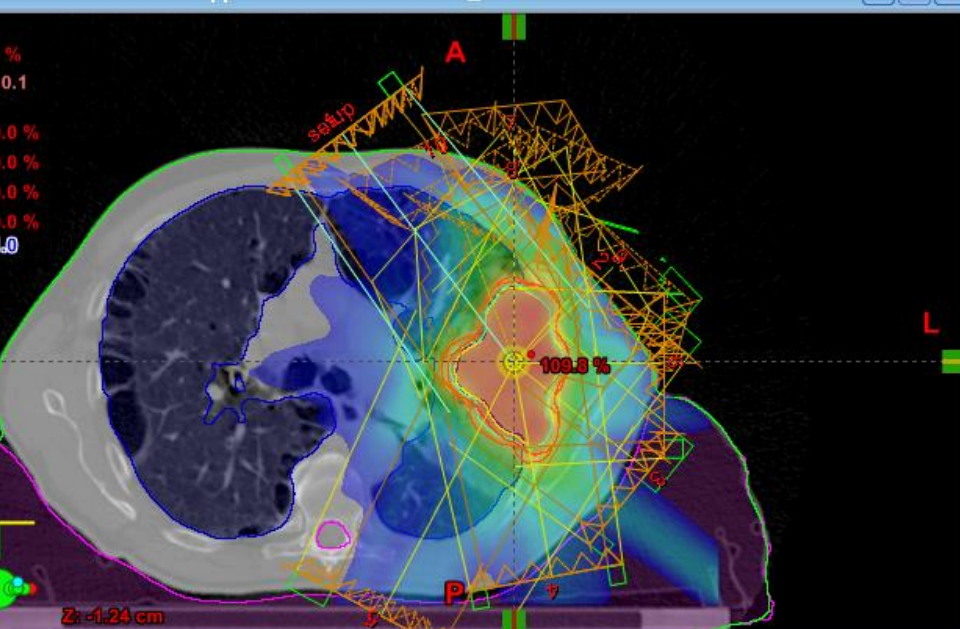




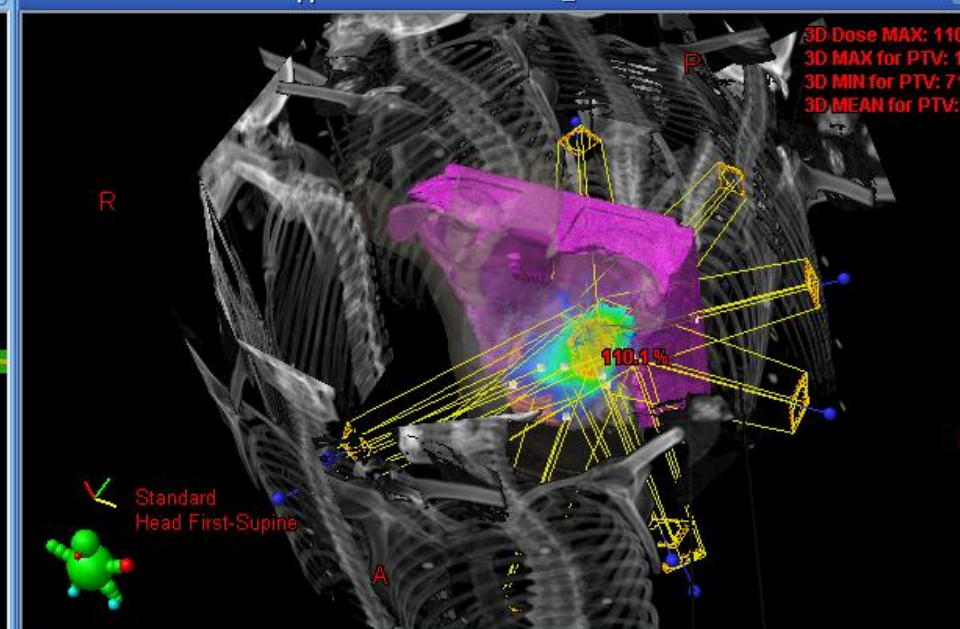
Sagittal - CT_06.04.2010 - 06-04-2010 11:38



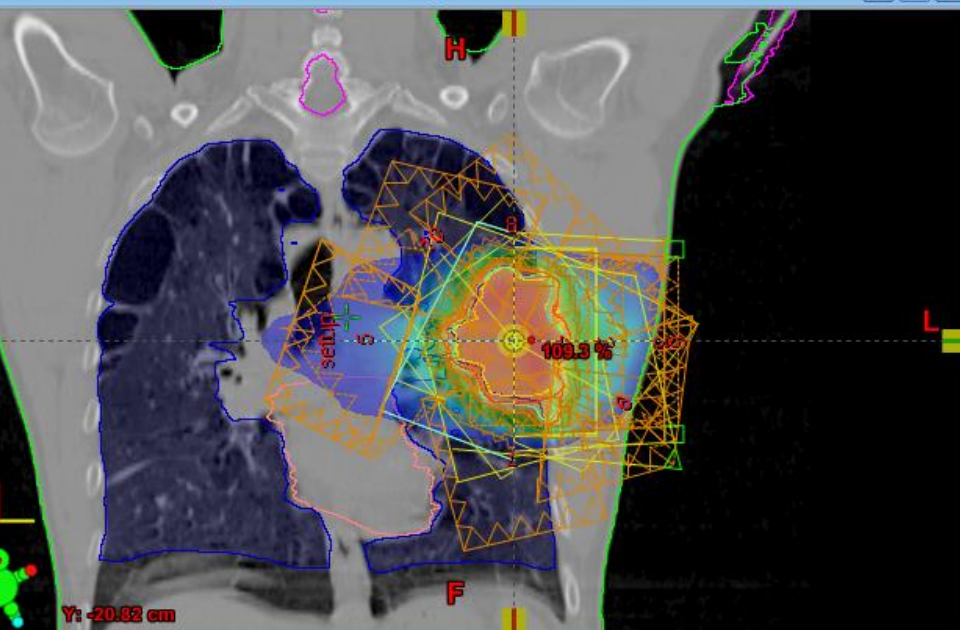
imrt2PTV - Treatment Approved - Transversal - CT_06.04.2010



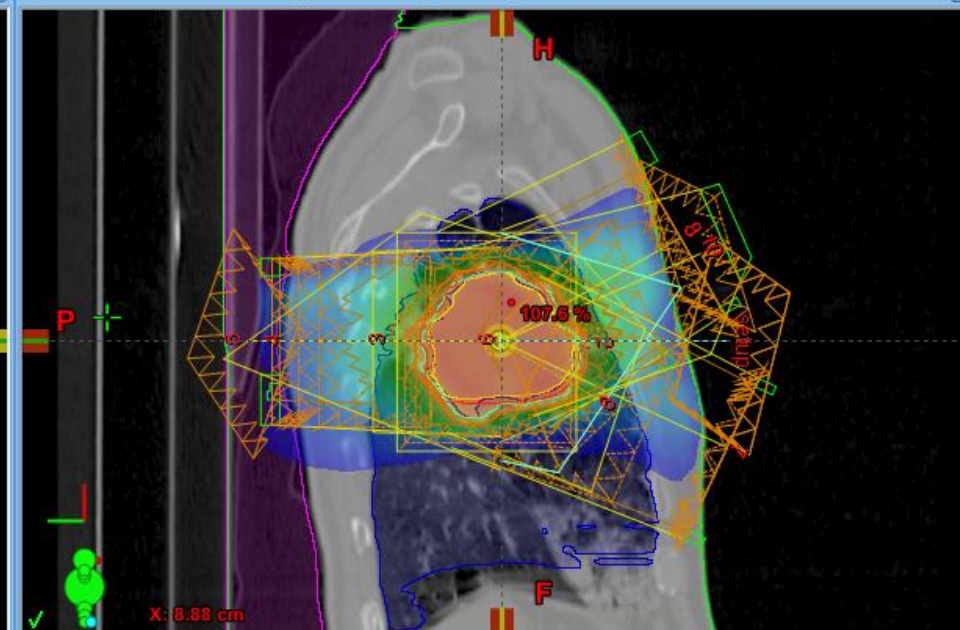
imrt2PTV - Treatment Approved - Model View - CT_06.04.2010



imrt2PTV - Treatment Approved - Frontal - CT_06.04.2010

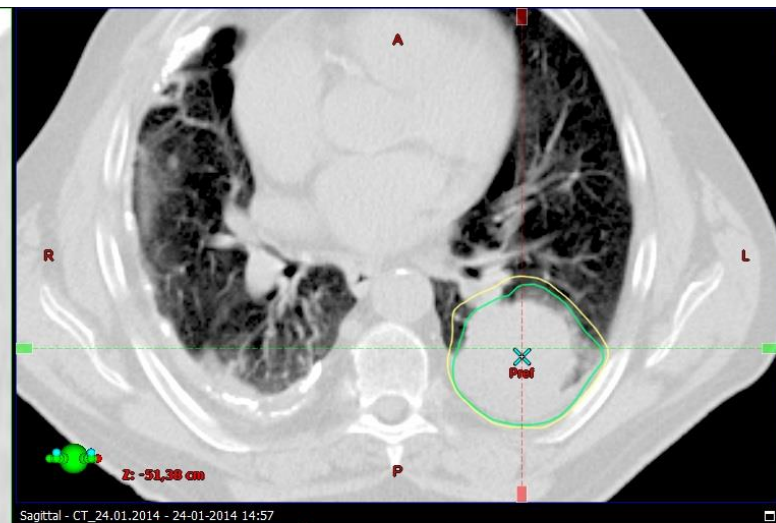
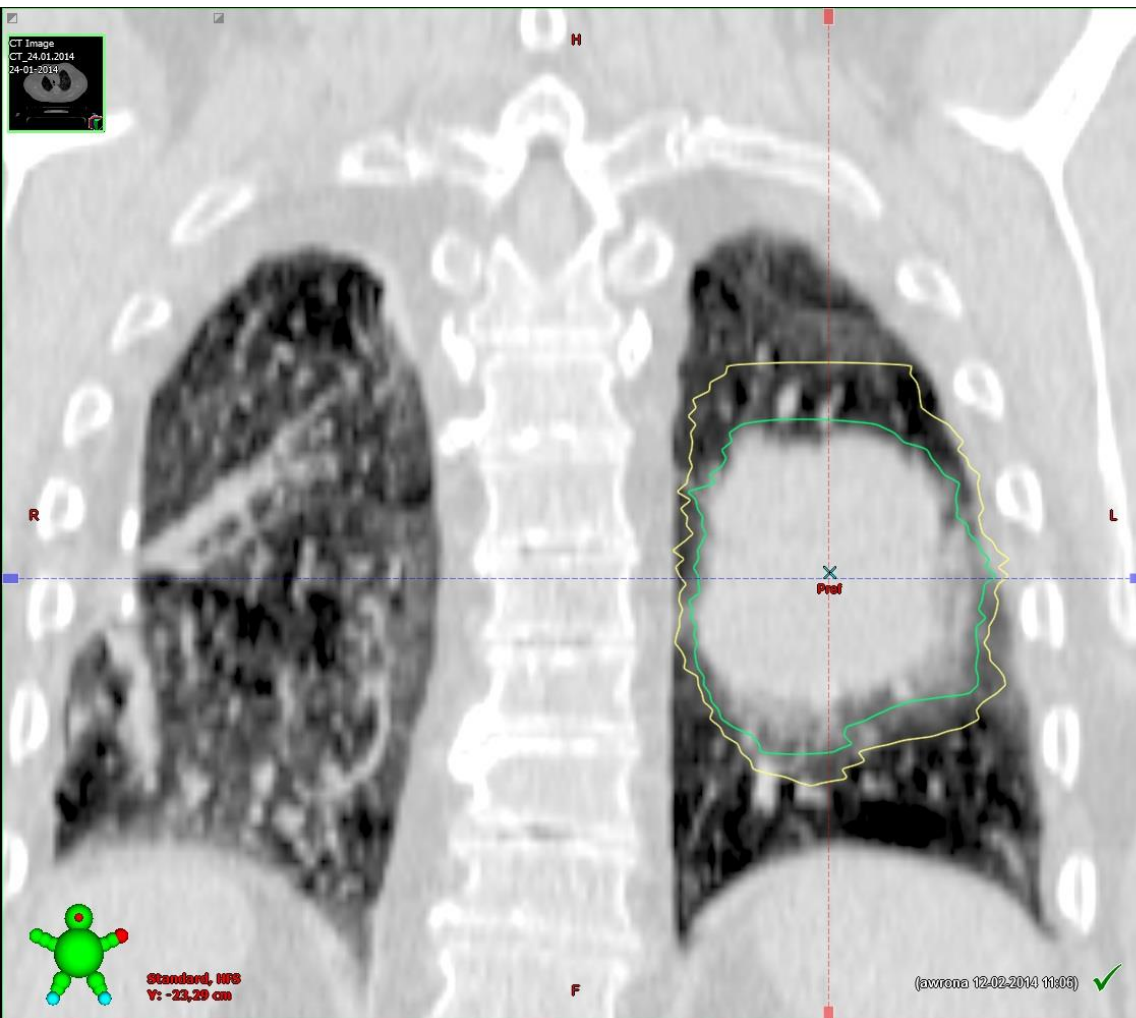


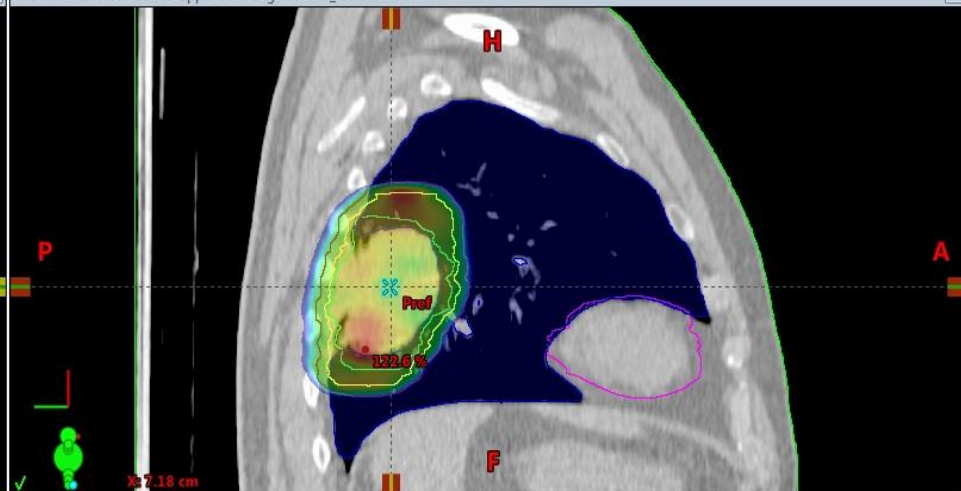
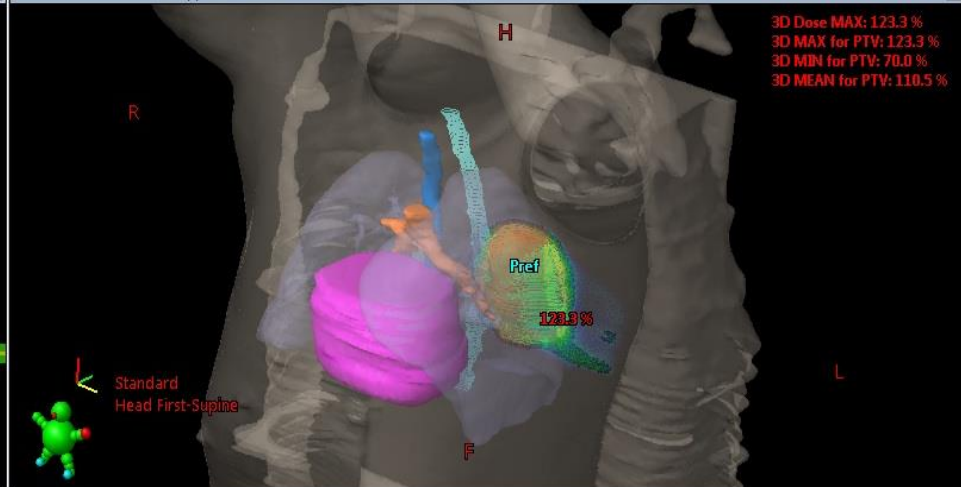
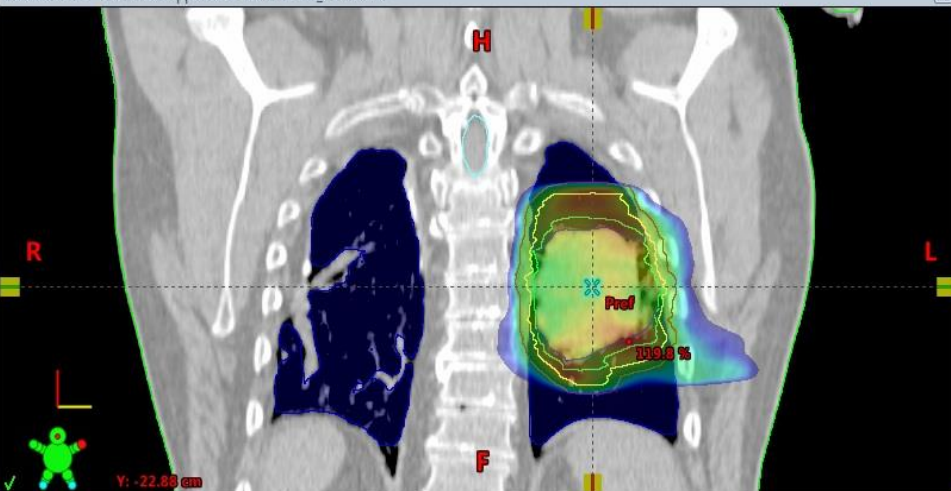
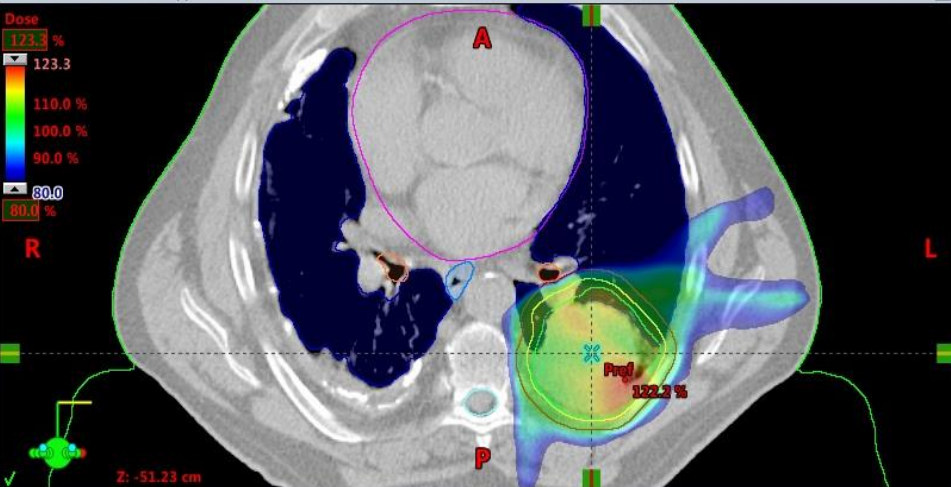
imrt2PTV - Treatment Approved - Sagittal - CT_06.04.2010



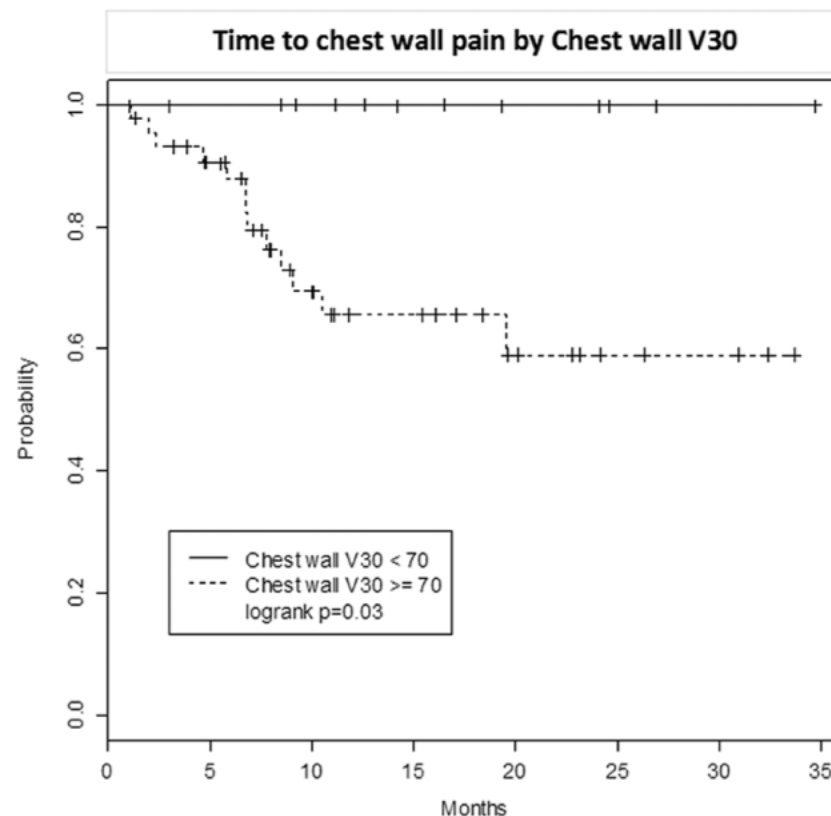
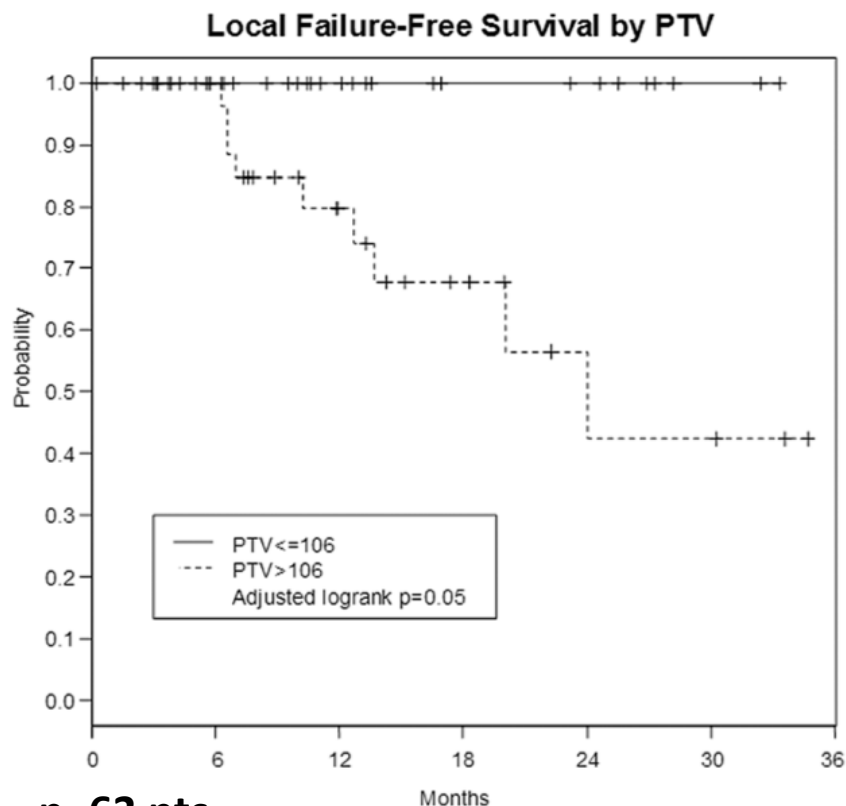
☐ Plan Objectives ☐ Optimization Objectives ☐ Dose Statistics ☐ Calculation Models ☐ Plan Sum

Field X	X1	X2	Field Y	Y1	Y2	X1	X2	Y1	Y2	SSD	MU	Re
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Large tumors – retrospective analysis



n=63 pts

Stage T2-T4

LFFS@2y=75%

OS@2y=57%

Large tumors – retrospective analysis

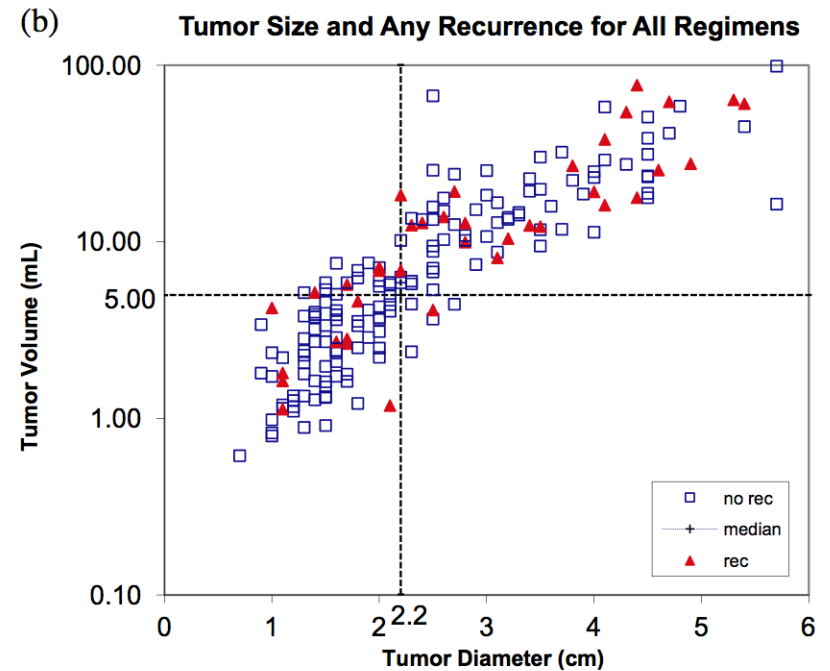
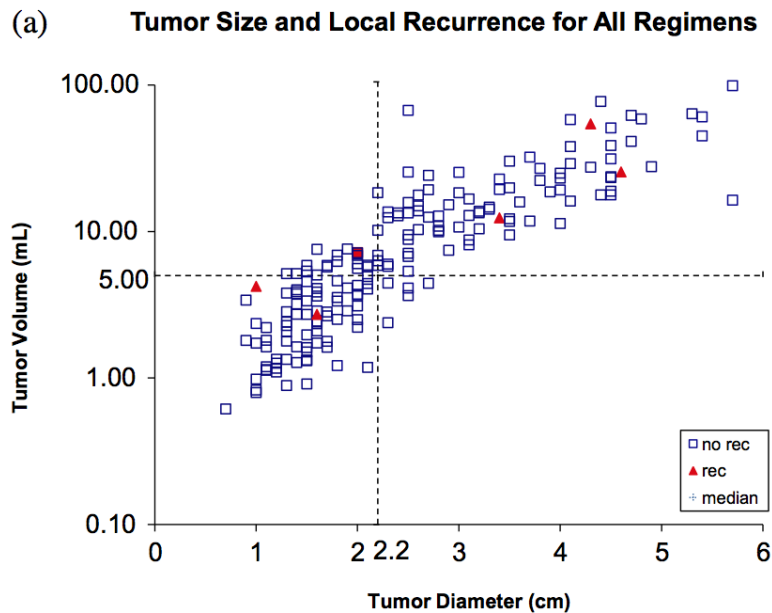


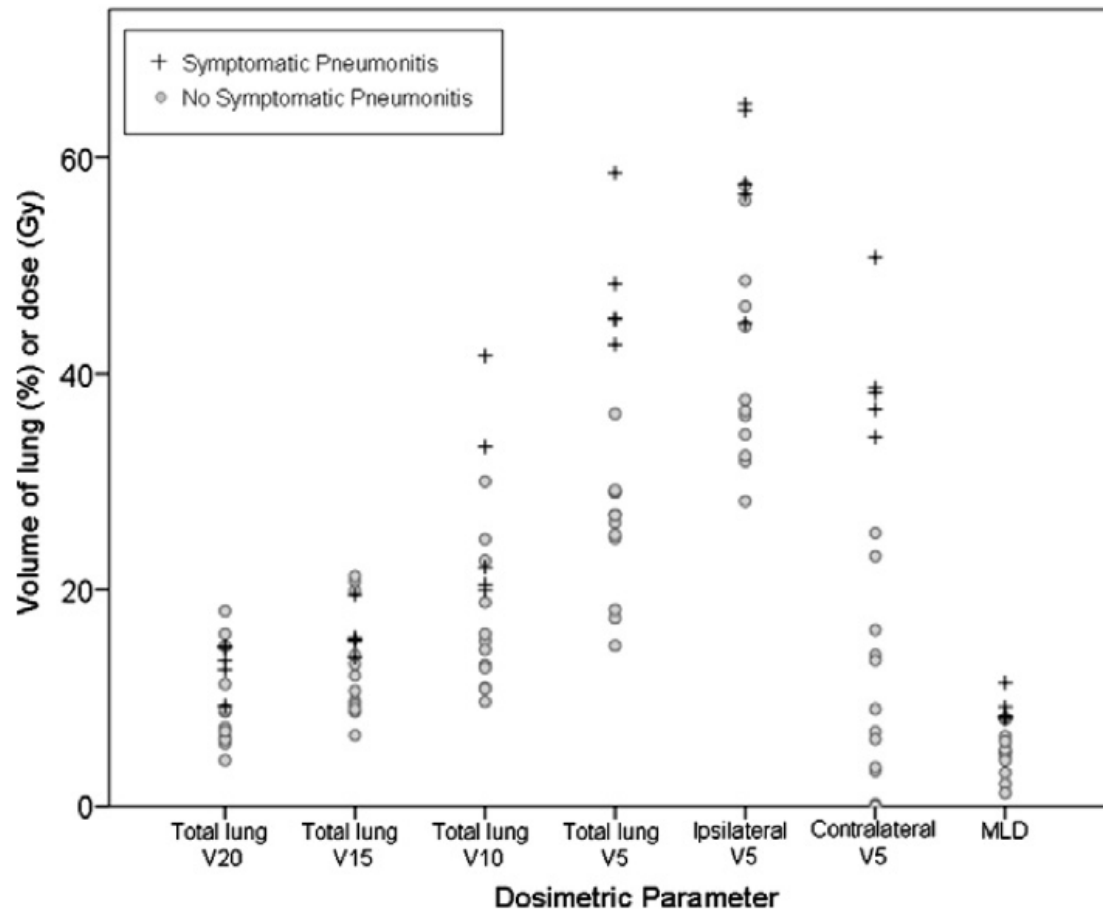
Fig. 3. Scatterplot of tumor size and local (A) and any (B) recurrences for all regimens.

n=185

Stage I, inoperable

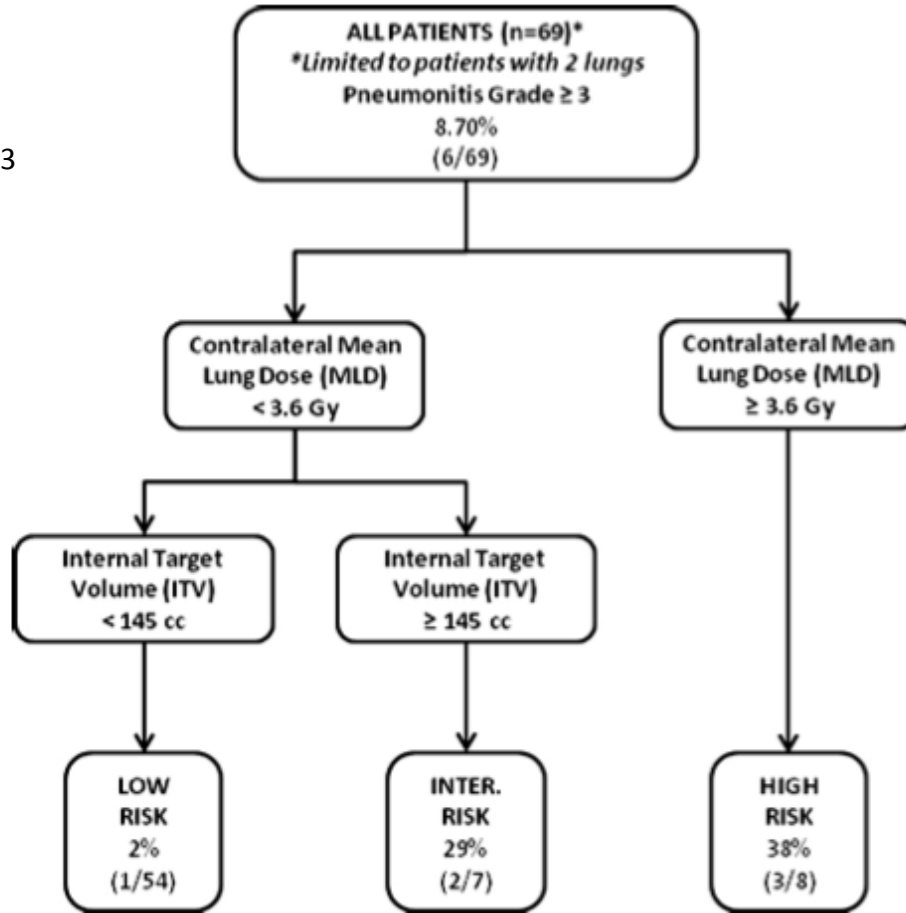
Large tumors – retrospective analysis

- Symptomatic Pneumonitis



Risk of symptomatic pneumonitis after SBRT for large tumors

Median PTV=150cm³
Grade ≥ 3 RP=10%



SBRT for large tumors - summary

- Effective local therapy
- Higher risk of distant failures
- Higher risk of symptomatic pneumonitis
- More data needed!