

CHISEL: A randomized phase III trial of stereotactic ablative body radiotherapy (SABR) vs conventional radiotherapy for inoperable stage I non-small cell lung cancer

TROG 09.02, ALTG 09.05
Trial Registration NCT01014130

Trial Chair: David Ball

The Tasman Sea

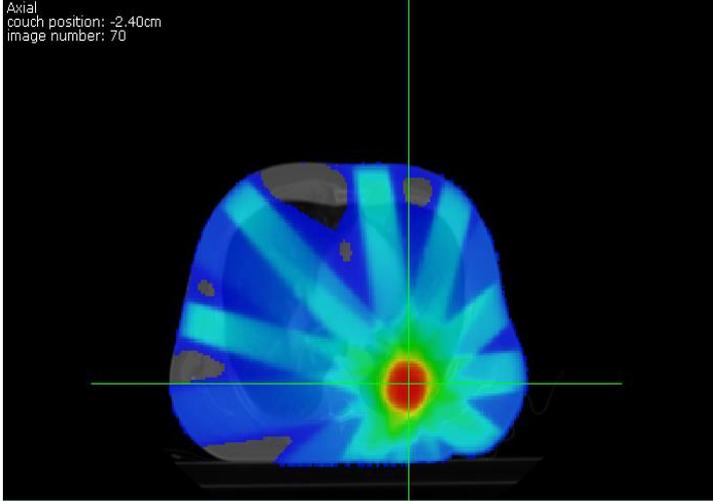


SABR: The concept

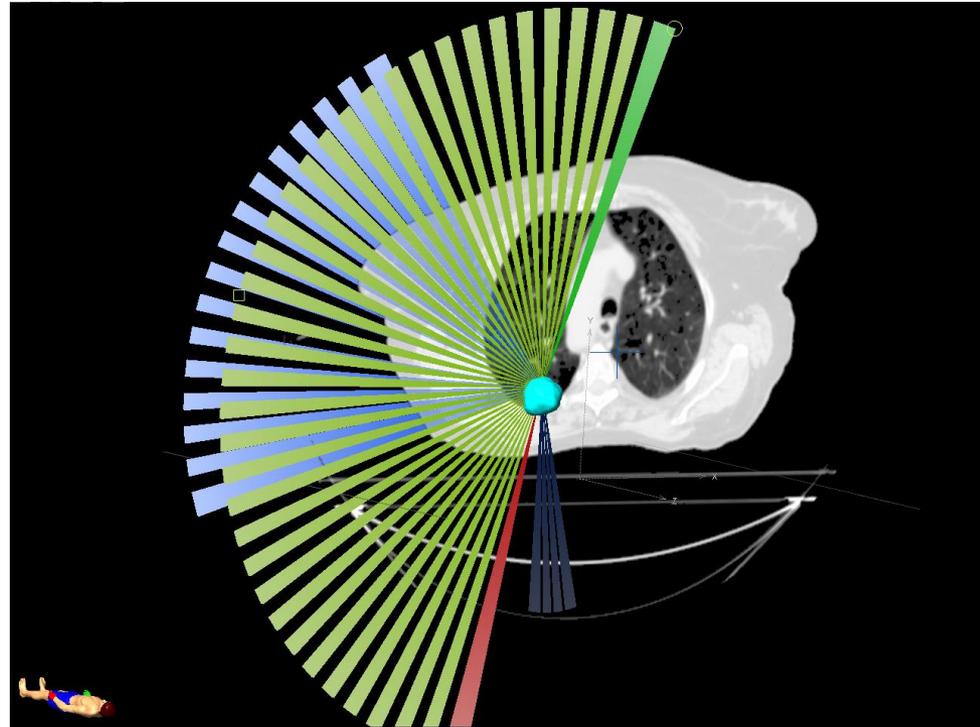
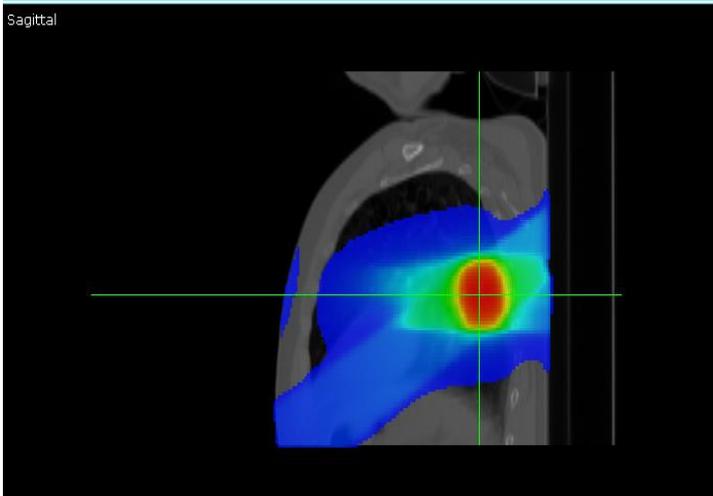
- Very high doses
- 1– 5 (or more) fractions
- Multiple non-opposing beams or arcs
- Steep dose gradients
- Revolutionary

Multiple intersecting beams or arcs

Axial
couch position: -2,40cm
image number: 70



Sagittal



Biologically Effective Dose

	<u>Early</u> $\alpha/\beta=10\text{Gy}$	<u>Late</u> $\alpha/\beta=3\text{Gy}$
4F x 12 Gy	105 Gy ₁₀	240 Gy ₃
3F x 18 Gy	151 Gy ₁₀	378 Gy ₃

Growth of SABR in USA

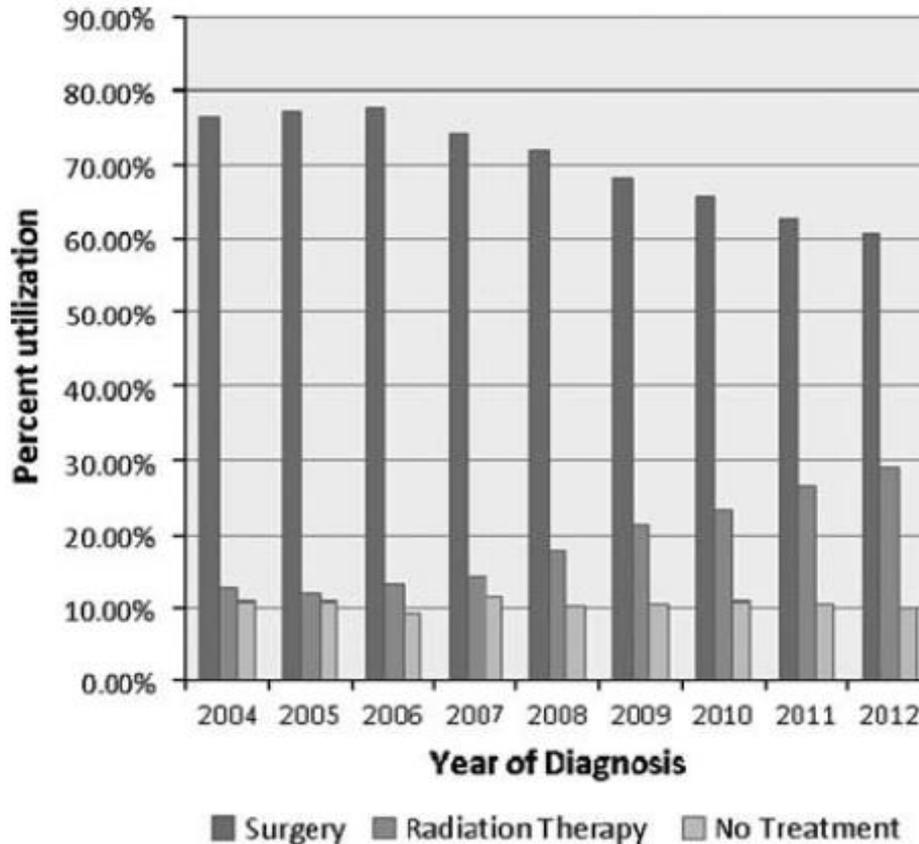


FIGURE 1. Utilization of surgery, radiation therapy, or observation for patients with stage IA non-small cell lung cancer treated in the United States.

SABR is one of the great success stories of modern thoracic radiotherapy

- for peripheral stage I lung cancers
- based on non-randomised evidence
- excellent local control but ?survival

The SPACE trial

- The SPACE trial compared SABR with conventionally fractionated radiotherapy
 - no differences in overall or progression free survival
 - PET/CT staging: 65%
 - ECOG 2: 24%
 - 4D CT planning not mandatory

The SPACE trial

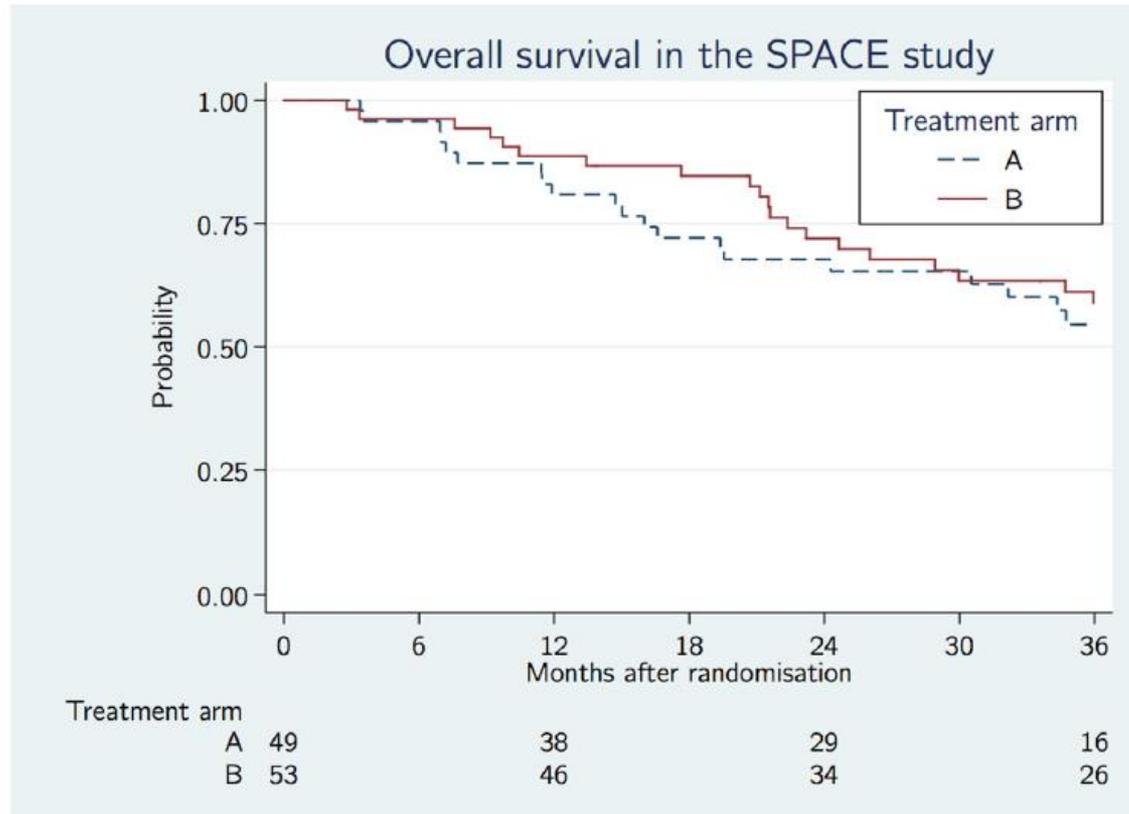


Fig. 2. Overall survival by treatment arm (A = SBRT, B = 3DCRT), ITT analysis. HR = 0.75, 95% CI: 0.43–1.30.

- SABR with a dose of 54 Gy in 3 fractions or 48 Gy in 4 fractions results in superior local control of peripherally located inoperable T1–T2a N0 non-small cell lung cancer compared with conventional radiotherapy (66 Gy in 33 fractions or 50 Gy in 20 fractions)
- Endpoints:
 - Time to local failure (primary)
 - Overall and lung cancer specific survival
 - Toxicities (CTCAE v 4.0)
 - Quality of life (QLQ C30 and LC 13, State-Trait Anxiety Inventory)

- Histologic/cytologic confirmation
- T1-T2a N0 (PET staged)
- ECOG performance status 0-1
- Inoperable or refuse surgery
- Peripheral lesion (>2cm from bifurcation of lobar bronchi)
- Ethics committee approval
- Written informed consent

Stratify:
T1 vs T2a
Medically inoperable vs medically operable
Randomize 2:1

54 Gy 3 fx in 2 weeks
or
48 Gy 4 fx in 2 weeks

66 Gy 33 fx in 6.5 weeks
or
50 Gy 20 fx in 4 weeks

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FULL PAPER

Credentiailling of radiotherapy centres in Australasia for TROG 09.02 (Chisel), a Phase III clinical trial on stereotactic ablative body radiotherapy of early stage lung cancer

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Linac head

Lung equivalent

Moving cylinder
(in/out of plane)

phantom

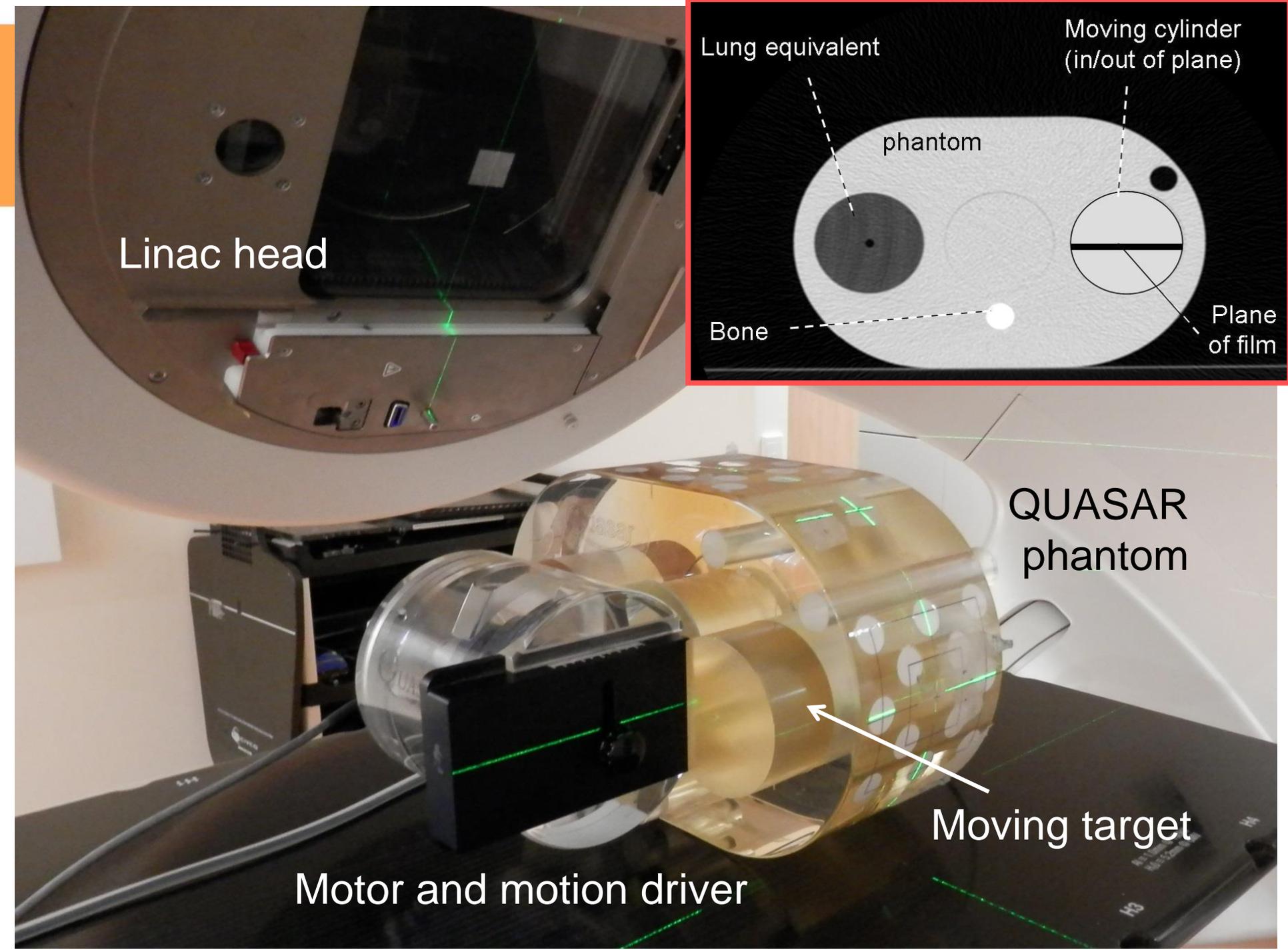
Bone

Plane of film

QUASAR
phantom

Moving target

Motor and motion driver



- Time to failure and survival analyses based on intention to treat
- Assume local failure at 2 years in SABR arm = 10%
in conventional arm = 30%
- 100 patients will have an 80% power to detect a difference with an alpha of 0.05
- Local failure: biopsy, PET or independent blinded expert review
- Recruitment 2009 – 2015, close-out date July 31 2017

Patient characteristics (n =101)

Characteristic	SABR (n=66)	CRT (n= 35)
Male sex	55%	57%
Median age (years)	73	77
Performance status ECOG 1	72%	71%
Ever smoker	97%	100%
T1 stage	71%	69%
Comorbidity (median, range)	9 (6-19)	9 (0-17)
Maximum diameter (mm) (median, IQR)	22.5 19-31	27 20.5-32
Prior cancer	43%	31%
Adenocarcinoma histology	48%	46%

Stereotactic ablative radiotherapy versus standard radiotherapy in stage 1 non-small-cell lung cancer (TROG 09.02 CHISEL): a phase 3, open-label, randomised controlled trial



David Ball, G Tao Mai, Shalini Vinod, Scott Babington, Jeremy Ruben, Tomas Kron, Brent Chesson, Alan Herschtal, Marijana Vanevski, Angela Rezo, Christine Elder, Marketa Skala, Andrew Wirth, Greg Wheeler, Adeline Lim, Mark Shaw, Penelope Schofield, Louis Irving, Benjamin Solomon, on behalf of the TROG 09.02 CHISEL investigators

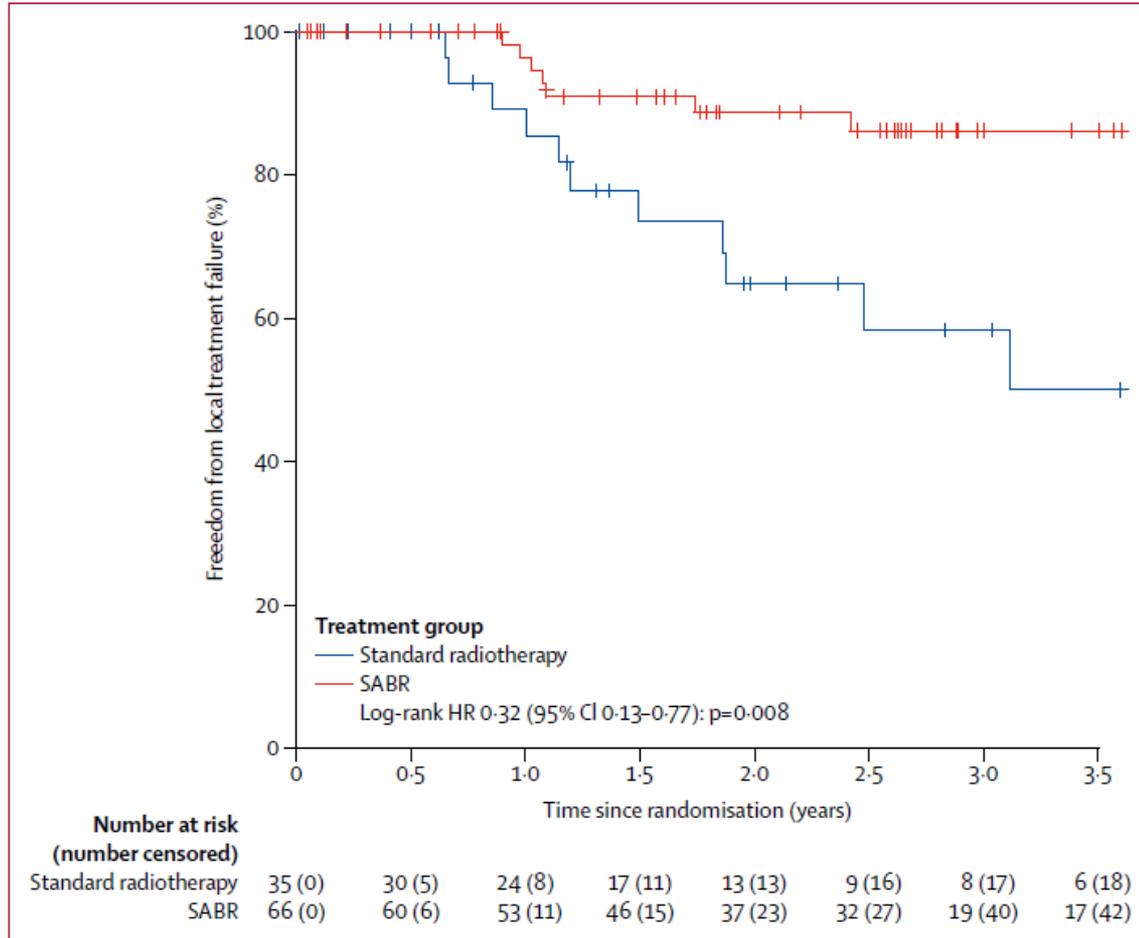
Summary

Background Stereotactic ablative body radiotherapy (SABR) is widely used to treat inoperable stage 1 non-small-cell lung cancer (NSCLC), despite the absence of prospective evidence that this type of treatment improves local control or prolongs overall survival compared with standard radiotherapy. We aimed to compare the two treatment techniques.

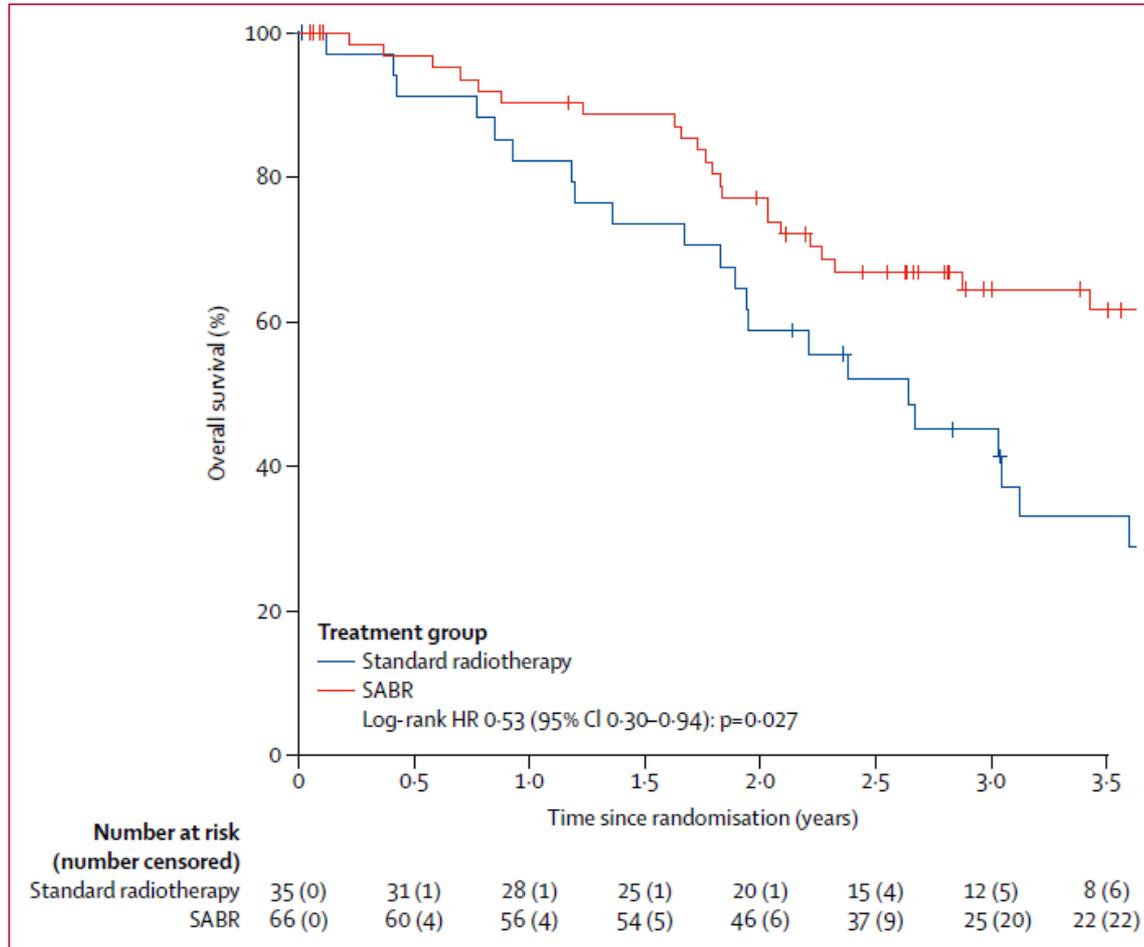
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CHISEL: Time to local treatment failure



CHISEL: Overall survival

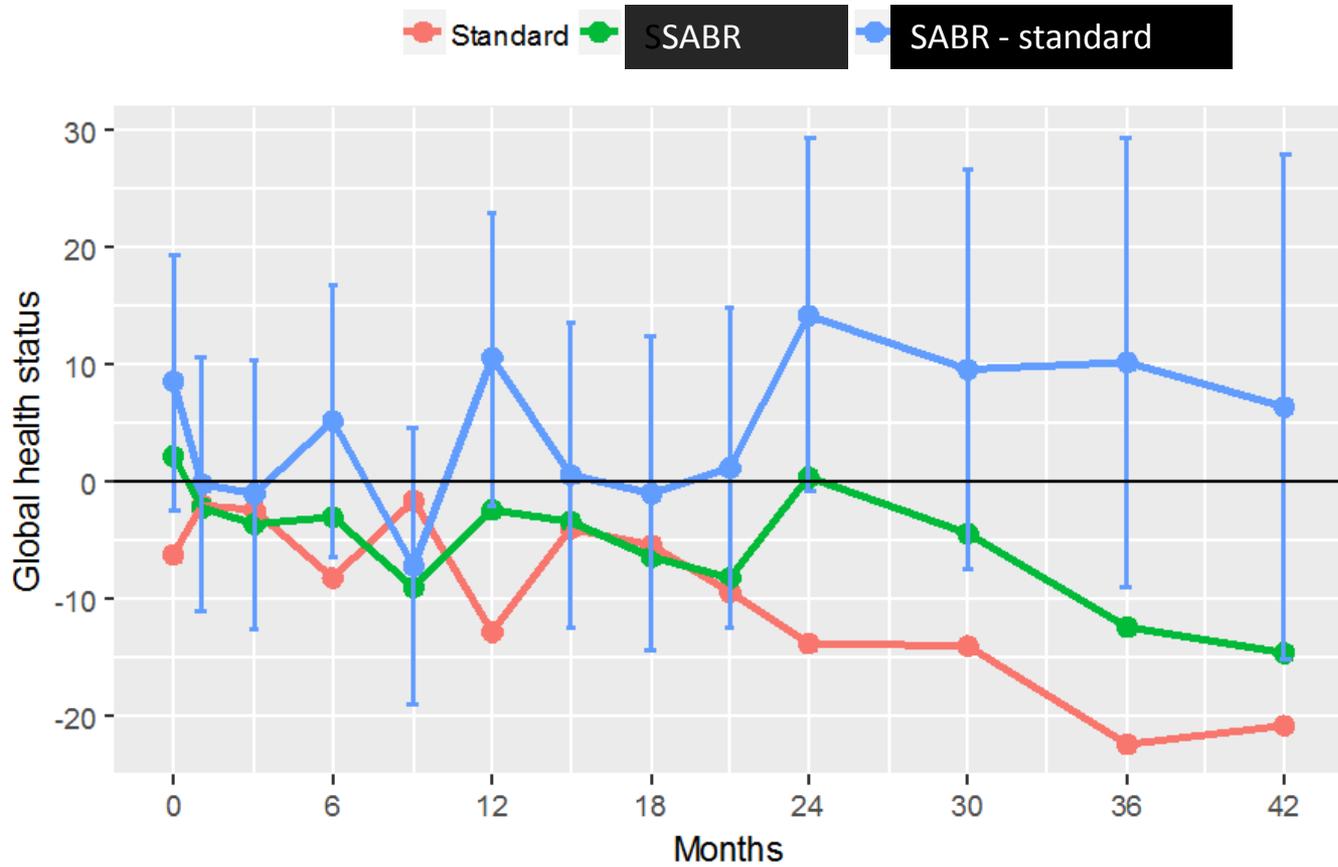


Survival at timepoints

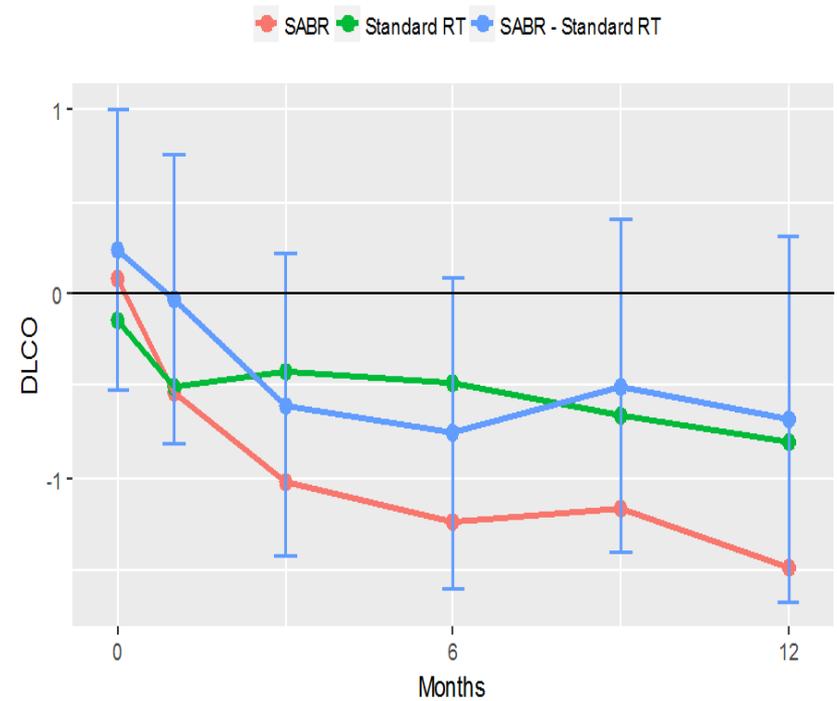
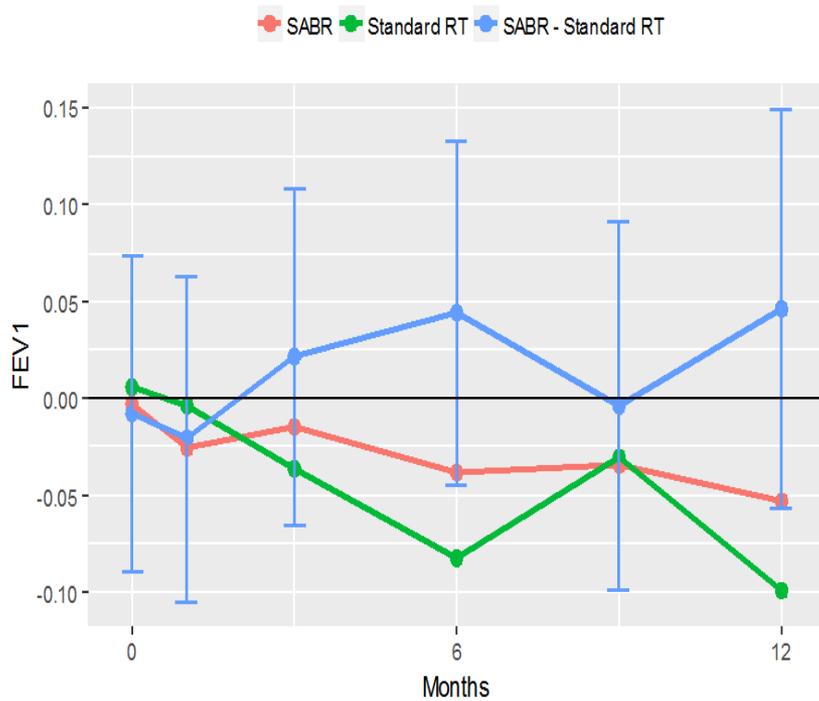
Time (years)	Overall Survival (%) [95% CI]	
	Treatment Arm=Standard radiotherapy	Treatment Arm=SABR
1	82% [70%, 96%]	90% [83%, 98%]
2	59% [44%, 78%]	79% [69%, 90%]
3	45% [31%, 66%]	66% [55%, 79%]

Grade 3+ toxicities by arm

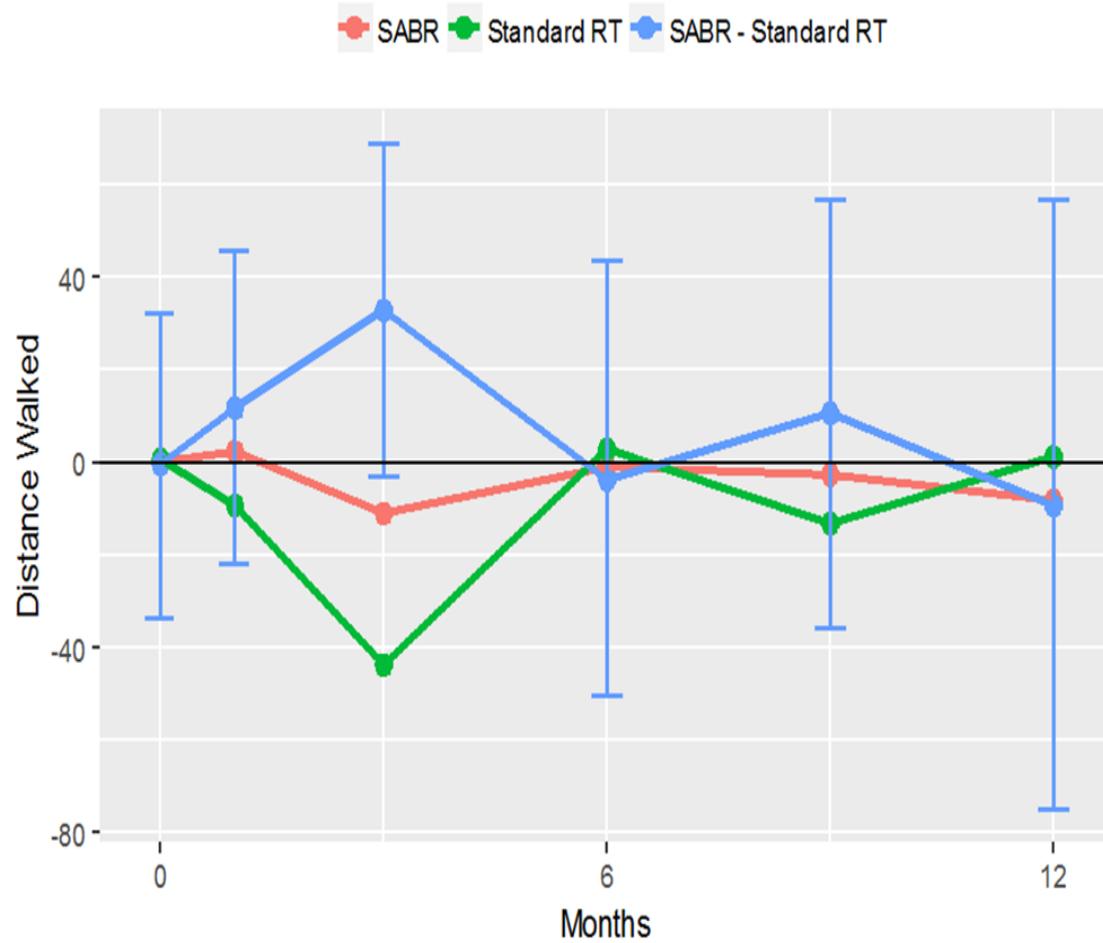
	SABR	Conventional
Dyspnoea	2 (1 grade 4)	0
Cough	2	0
Fatigue	1	0
Chest wall pain/pain	1	2
Lung infection	1	0
Hypoxia	1	0
Weight loss	1	0



Changes in pulmonary function FEV1 and DLCO



6 minute walk test



Conclusions

- In patients with inoperable peripheral stage I NSCLC, SABR resulted in longer time to local failure and improved overall survival compared with conventionally fractionated radiotherapy
- Treatment was well tolerated, with only one grade 4 toxicity (dyspnoea) in one SABR patient
- SABR should be regarded as the standard of care in this patient group



TROG 09.02 CHISEL: **Investigators**

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Tomas Kron, Brent Chesson,

Alan Herschtal, Marijana Vanevski

Ben Solomon, Lou Irving

Penny Schofield

Consumers: David⁺ and Barbara Wenzel

Acknowledgments

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Mark Burns Natalie Clements
Max Enge Michelle Mauro

Radiotherapy Case Reviewers

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Olivia Cook Monica Harris

Local failure reviewers

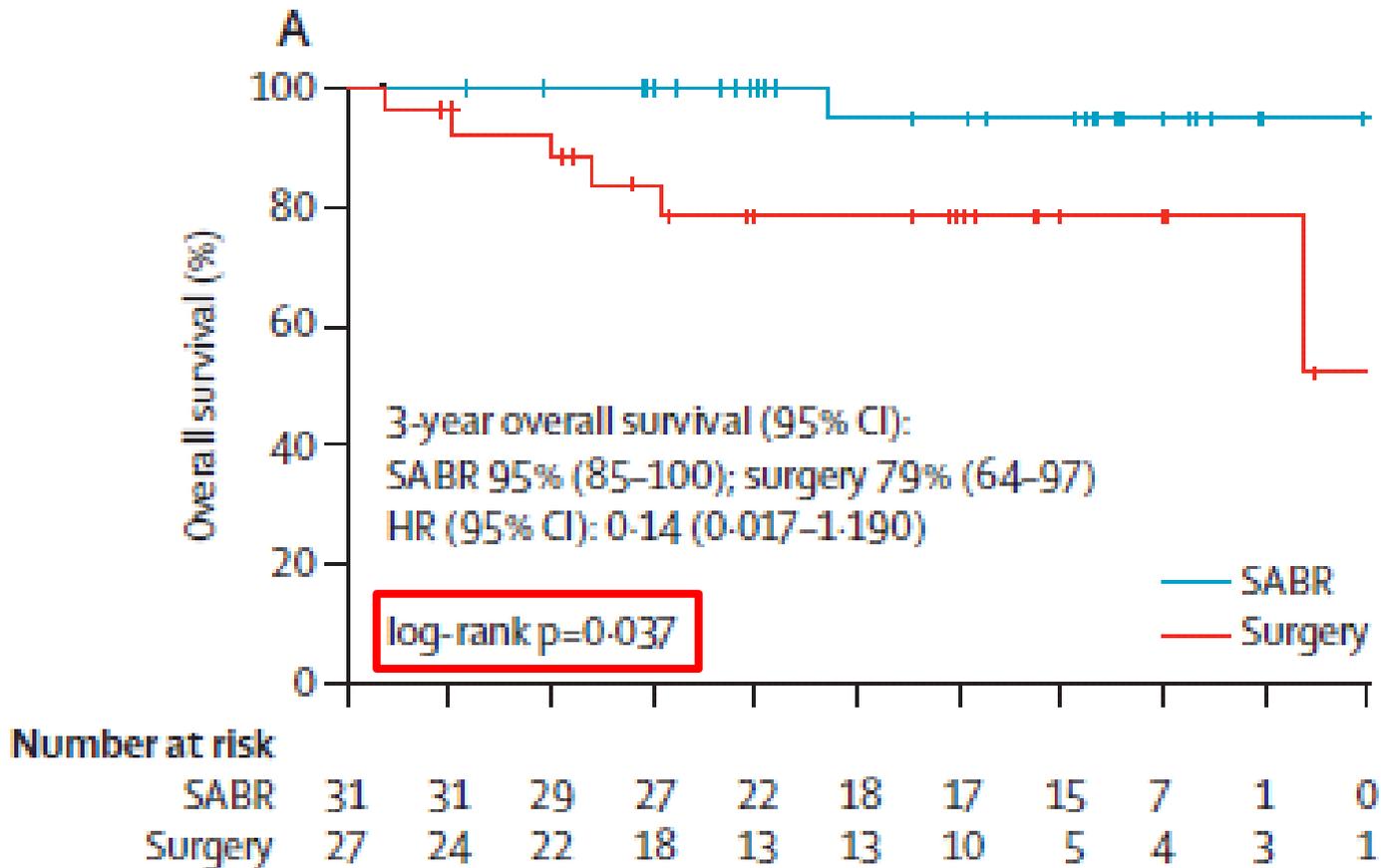
Sam Ellis Dayanethee Krishna Kate Moodie

Marijana Vanevski and all the clinical trial coordinators

The patients and their families

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Pooled results of STARS and ROSEL
SABR vs surgery: overall survival

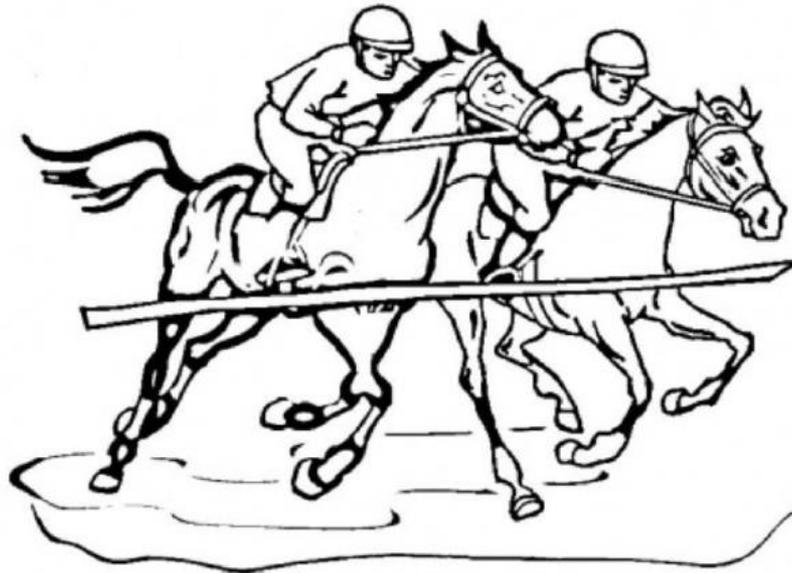


Joint Lung Cancer Trialist's Coalition

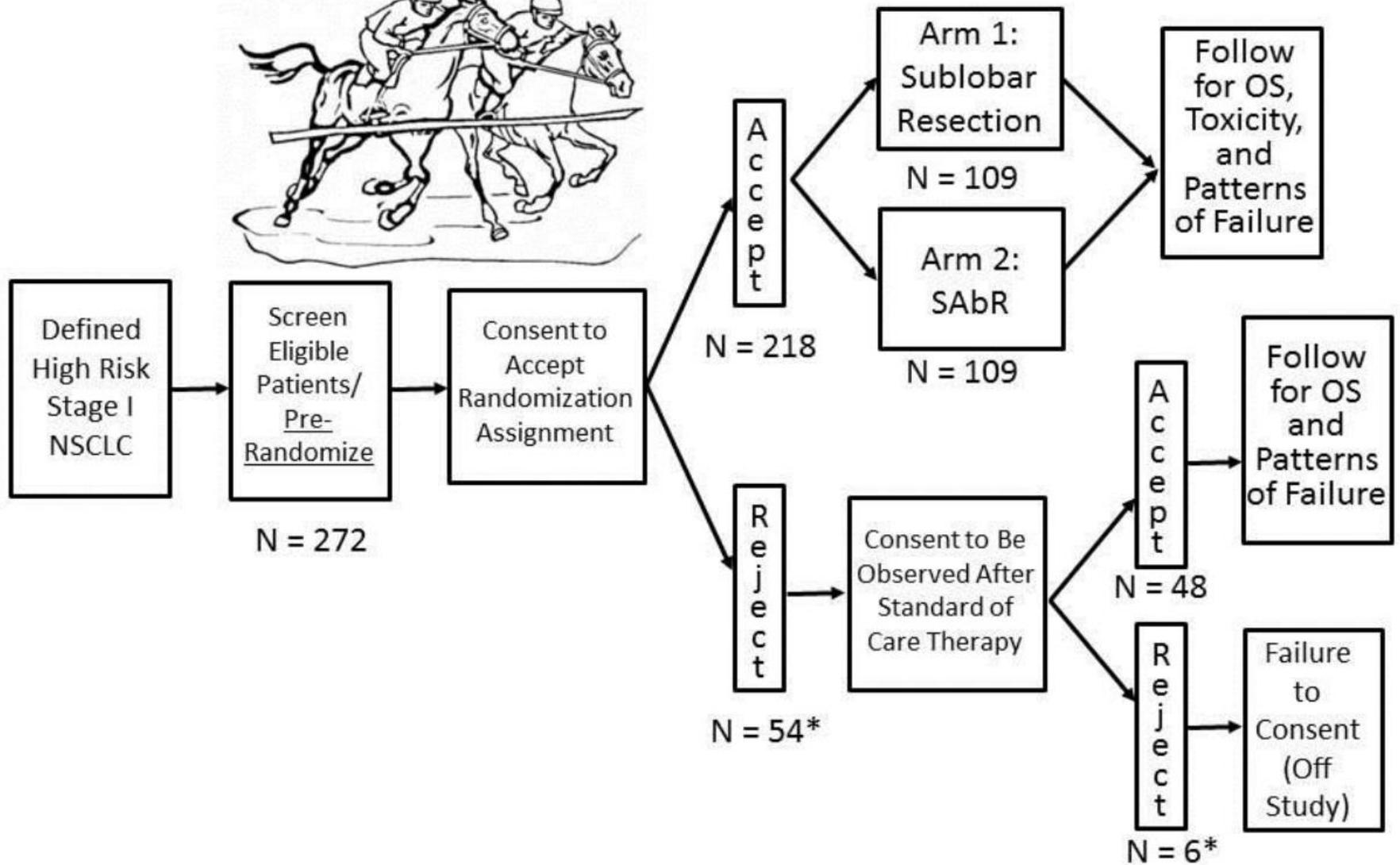
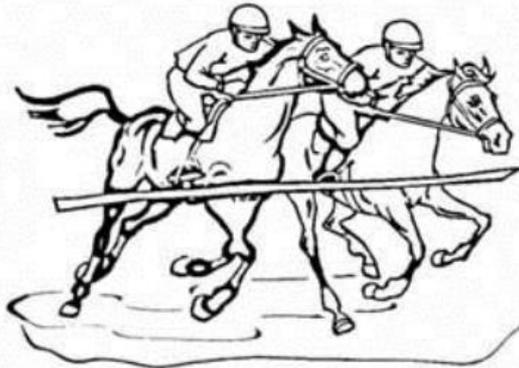
JoLT - Ca

A Randomized Phase III Study of Sublobar Resection (SR) versus Stereotactic Ablative Radiotherapy (SAbR) in High Risk Patients with Stage I Non-Small Cell Lung Cancer (NSCLC)

The STABLE-MATES Trial



STABLEMATES Trial Schema



Questions?

