

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

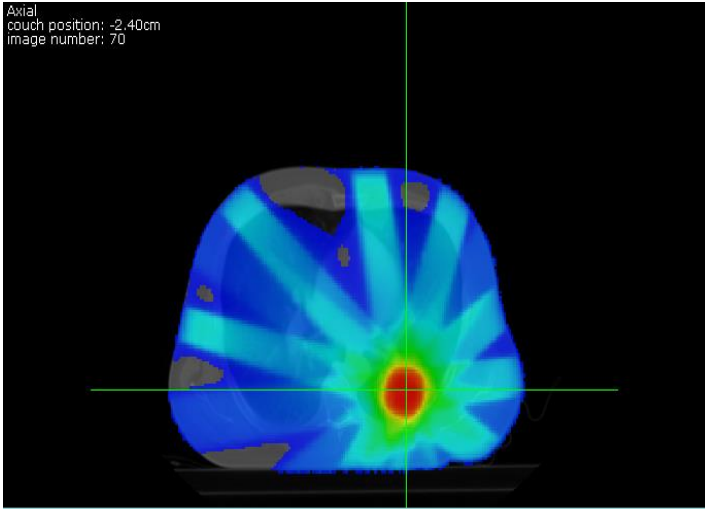


## SABR: The concept

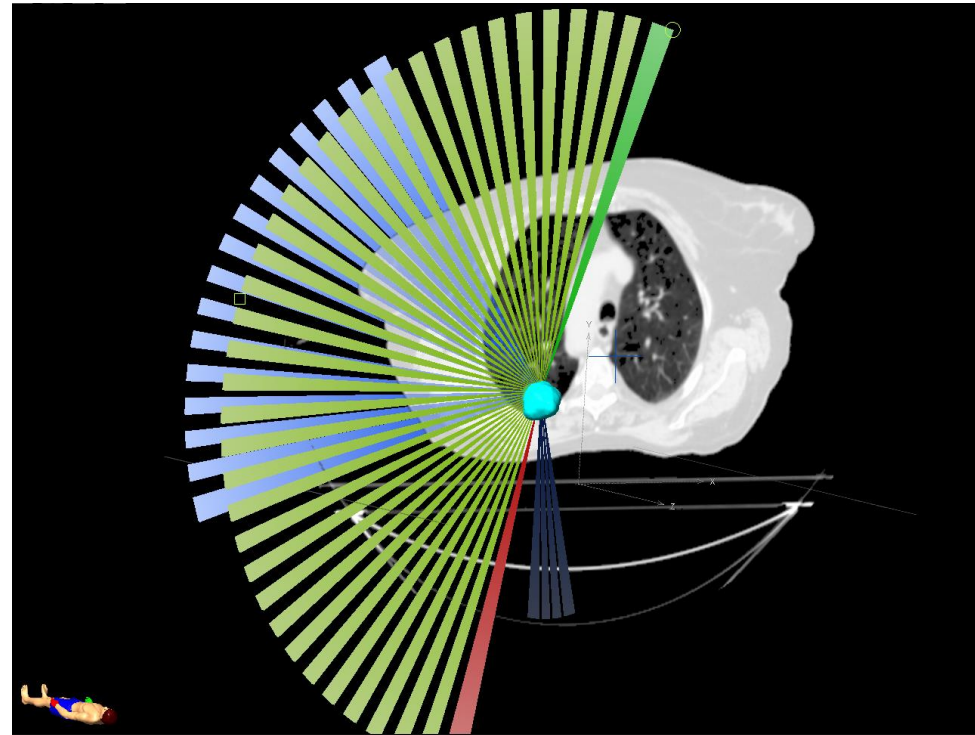
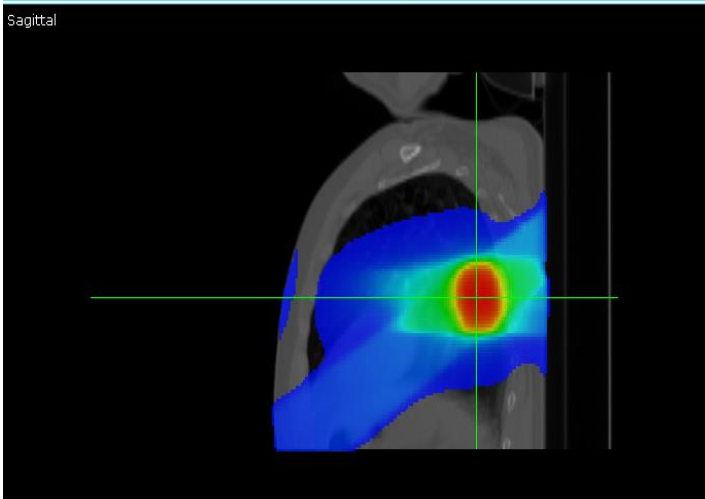
- Very high doses
- 1– 5 (or more) fractions
- Multiple non-opposing beams or arcs
- Steep dose gradients
- Revolutionary

# Multiple intersecting beams or arcs

Axial  
couch position: -2.40cm  
image number: 70



Sagittal

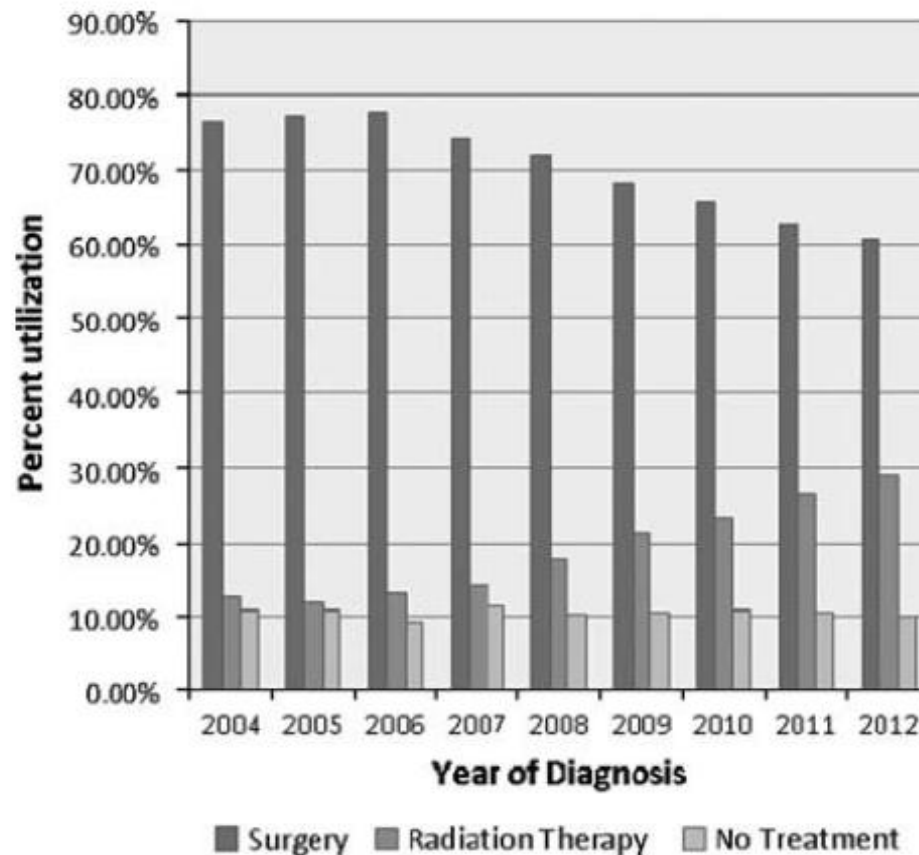


## Biologically Effective Dose

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



# 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.

## The rise of SABR

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

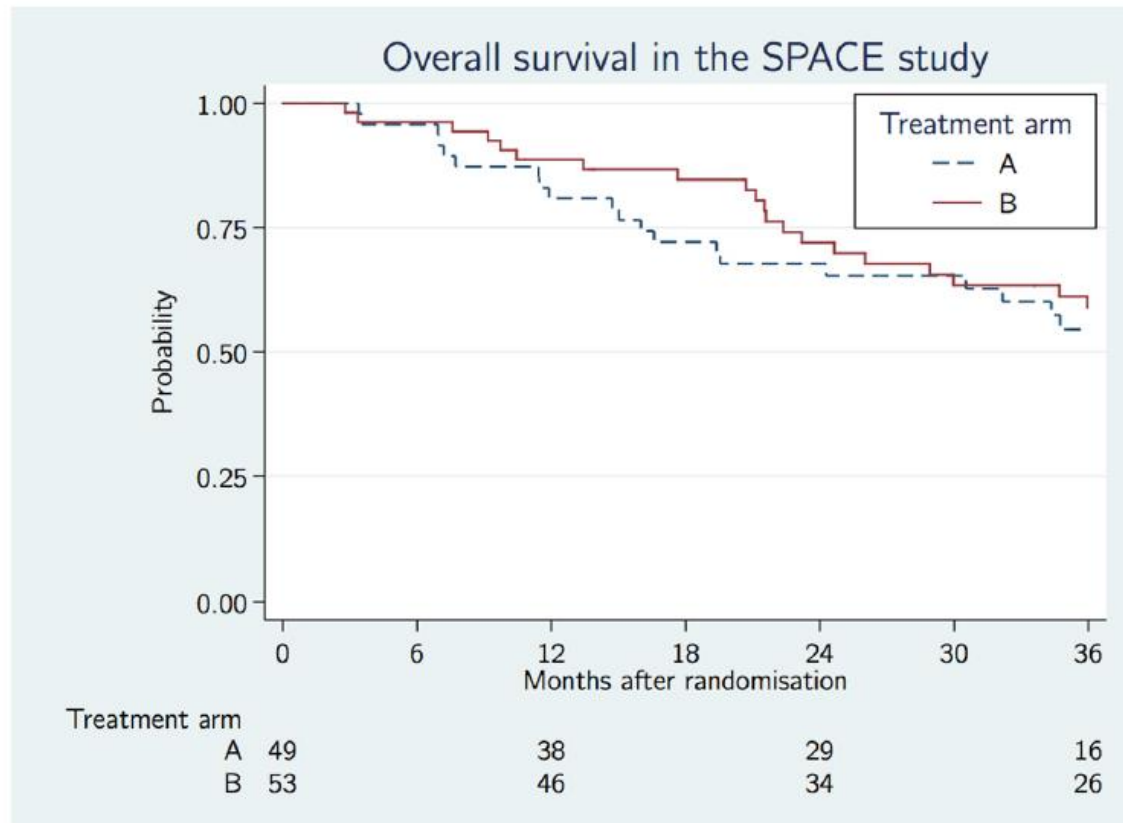


Fig. 2. Overall survival by treatment arm (A = SBRT, B = 3DCRT), ITT analysis. HR = 0.75, 95% CI: 0.43–1.30.

- 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)

## TROG 09.02 CHISEL: Patient eligibility

- 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

## TRGOG 09.02 CHISEL Study design

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

```
graph TD; A["Stratify:  
T1 vs T2a  
Medically inoperable vs medically operable  
Randomize 2:1"] --> B["54 Gy 3 fx in 2 weeks  
or  
48 Gy 4 fx in 2 weeks"]; A --> C["66 Gy 33 fx in 6.5 weeks  
or  
50 Gy 20 fx in 4 weeks"];
```

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

66 Gy 33 fx in 6.5 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

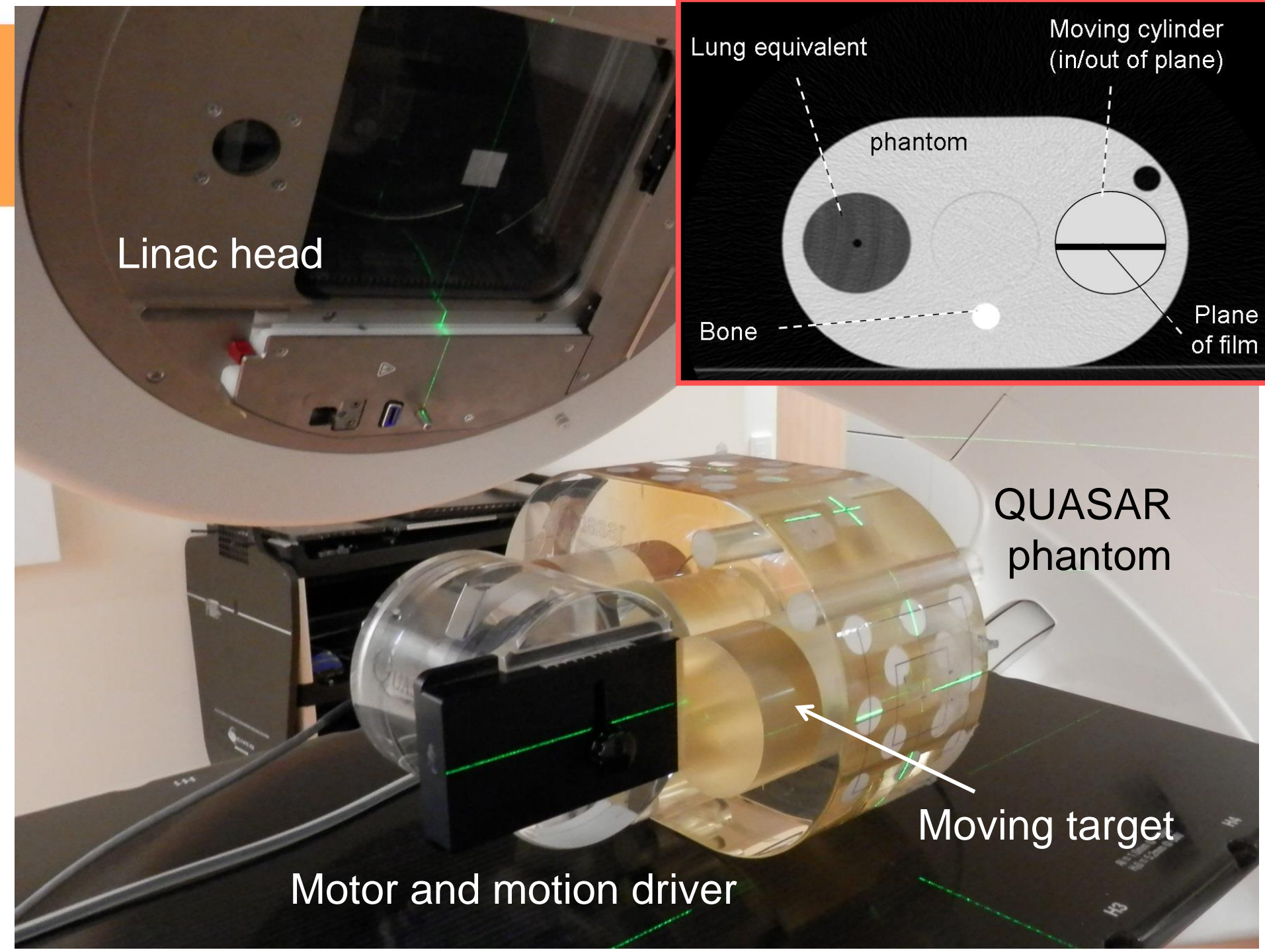
Bone

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

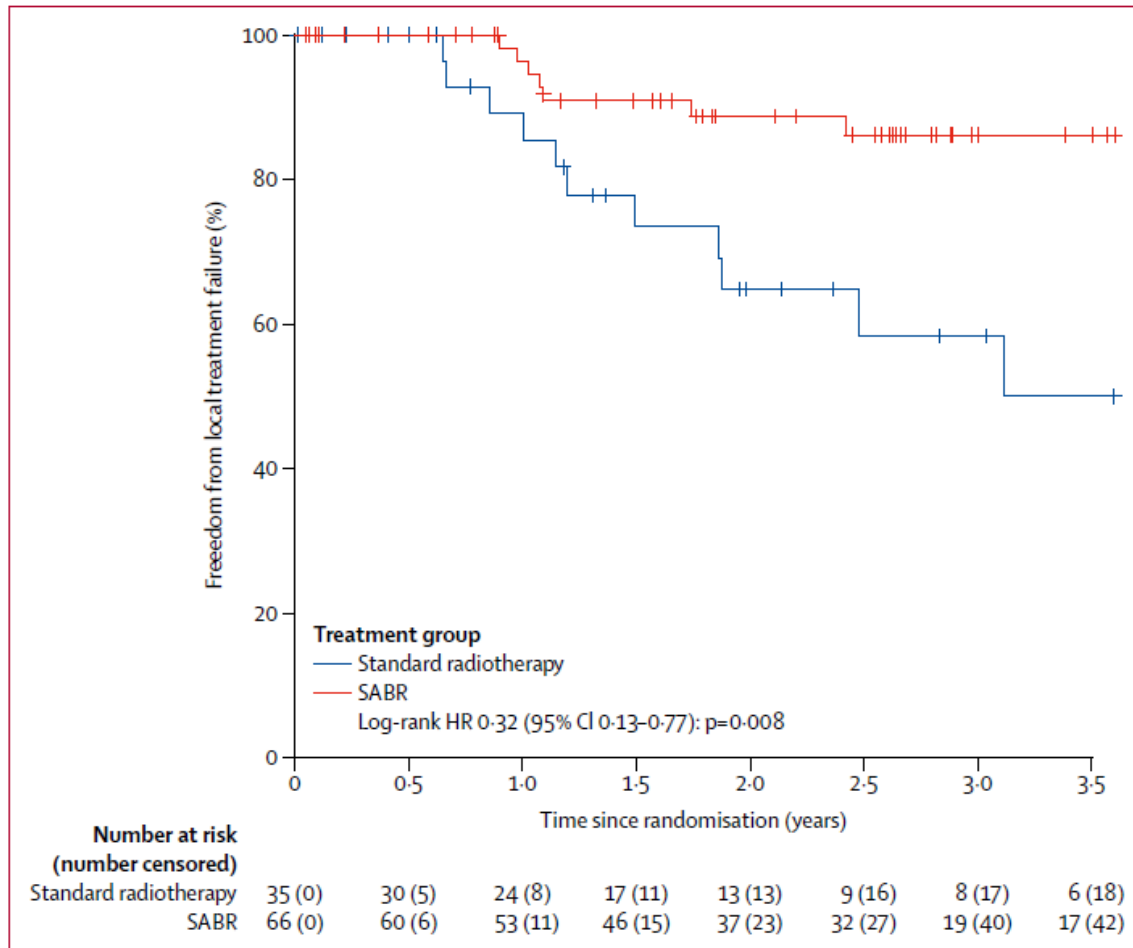
## Summary

**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.

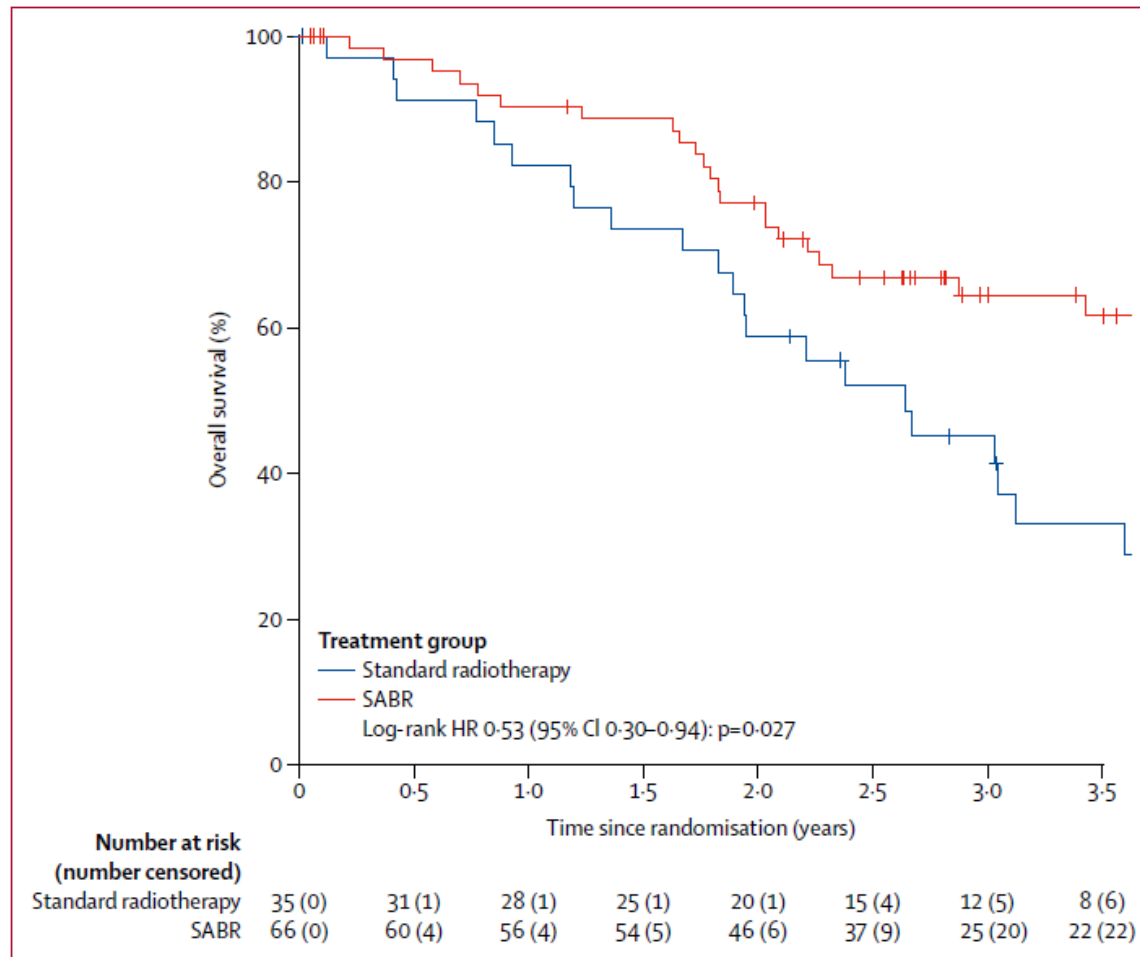
*Lancet Oncol* 2019

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[http://dx.doi.org/10.1016/S1470-2045\(18\)30896-9](http://dx.doi.org/10.1016/S1470-2045(18)30896-9)

# CHISEL: Time to local treatment failure



# CHISEL: Overall survival



# Survival at timepoints

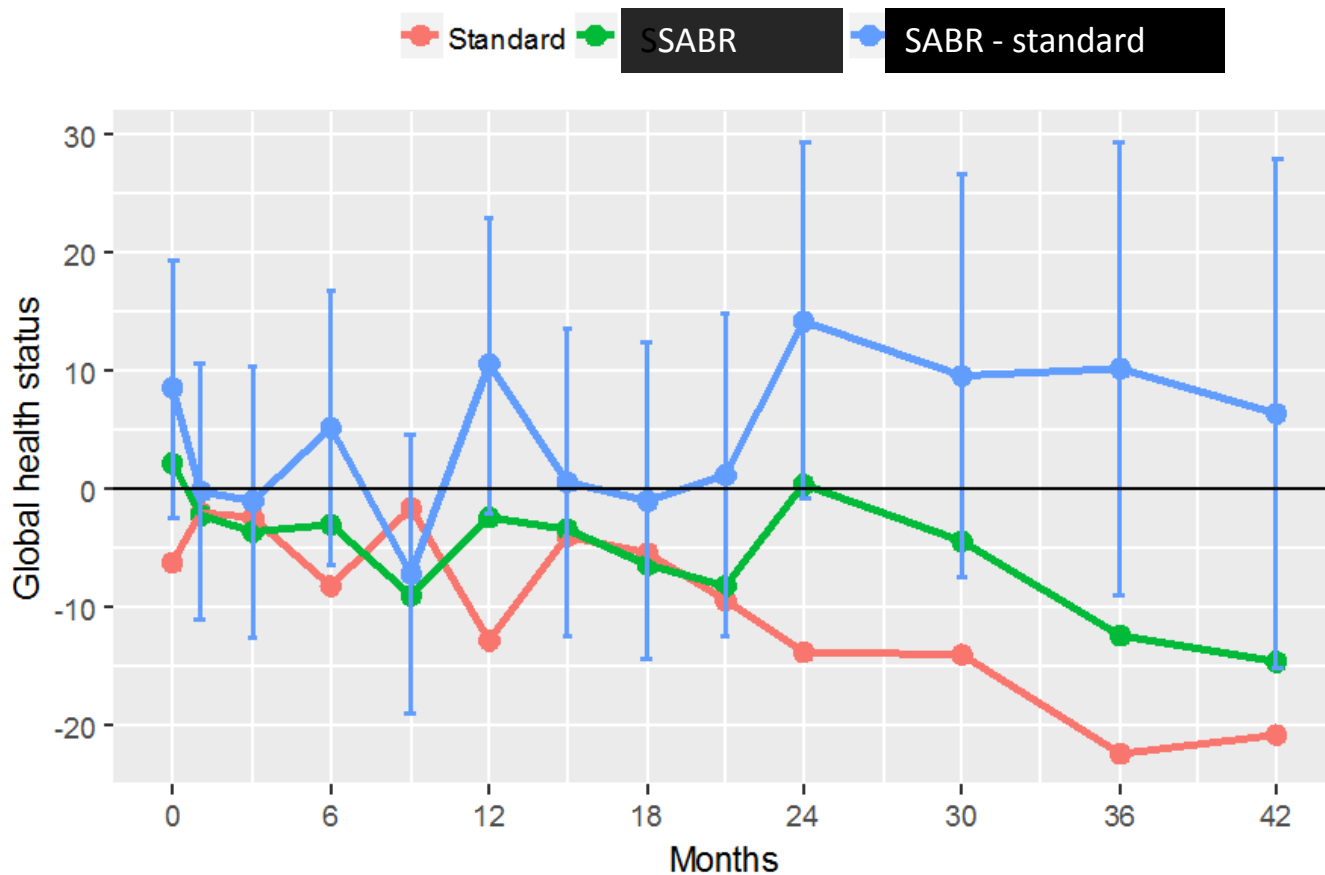
Time (years)	Overall Survival (%) [95% CI]	
	Treatment Arm=Standard radiotherapy	Treatment Arm=SABR
1	82% [70%, 96%]	90% [83%, 98%]
2	59% [44%, 78%]	79% [69%, 90%]
3	45% [31%, 66%]	66% [55%, 79%]



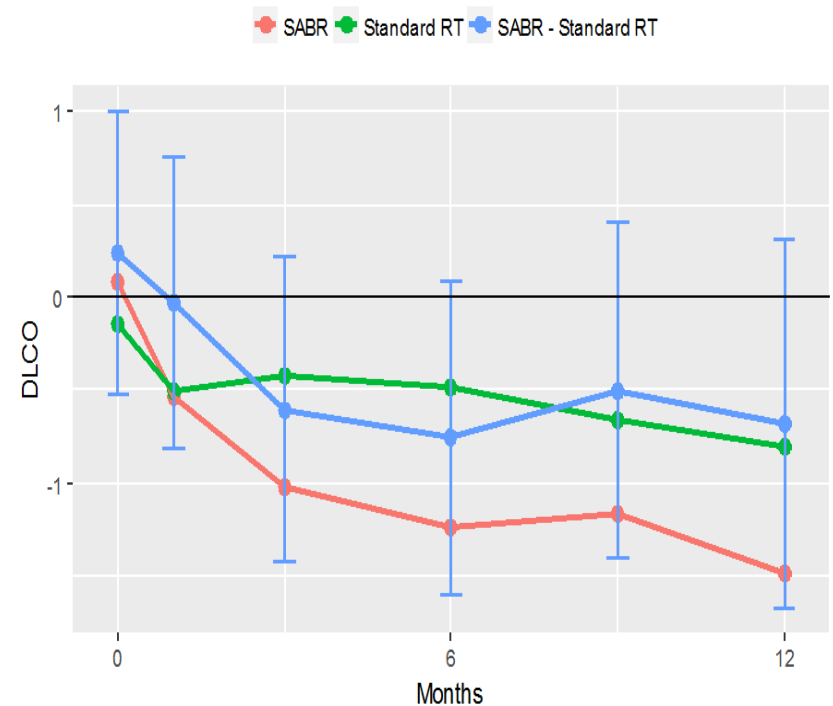
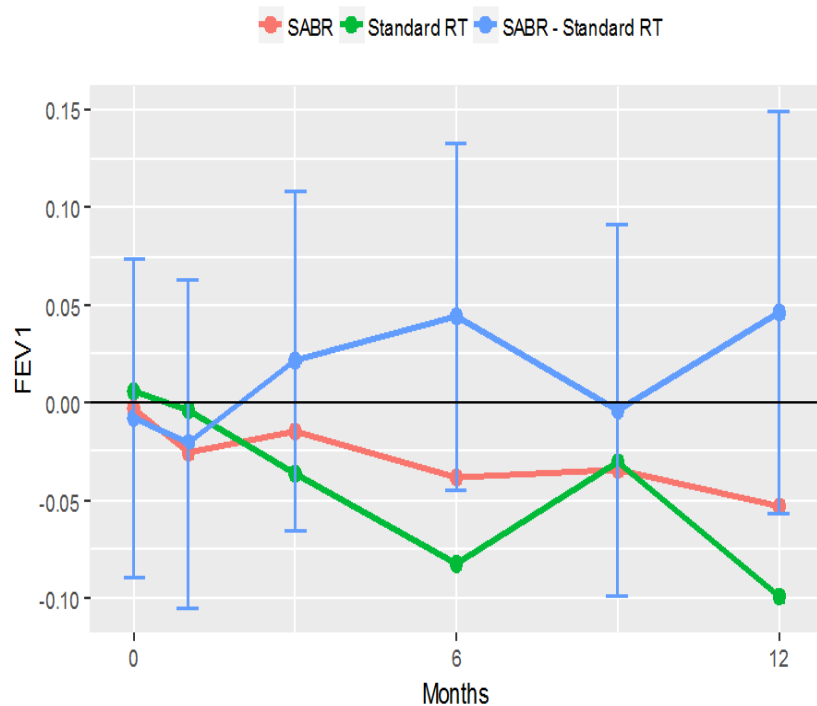
## Grade 3+ toxicities by arm

	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

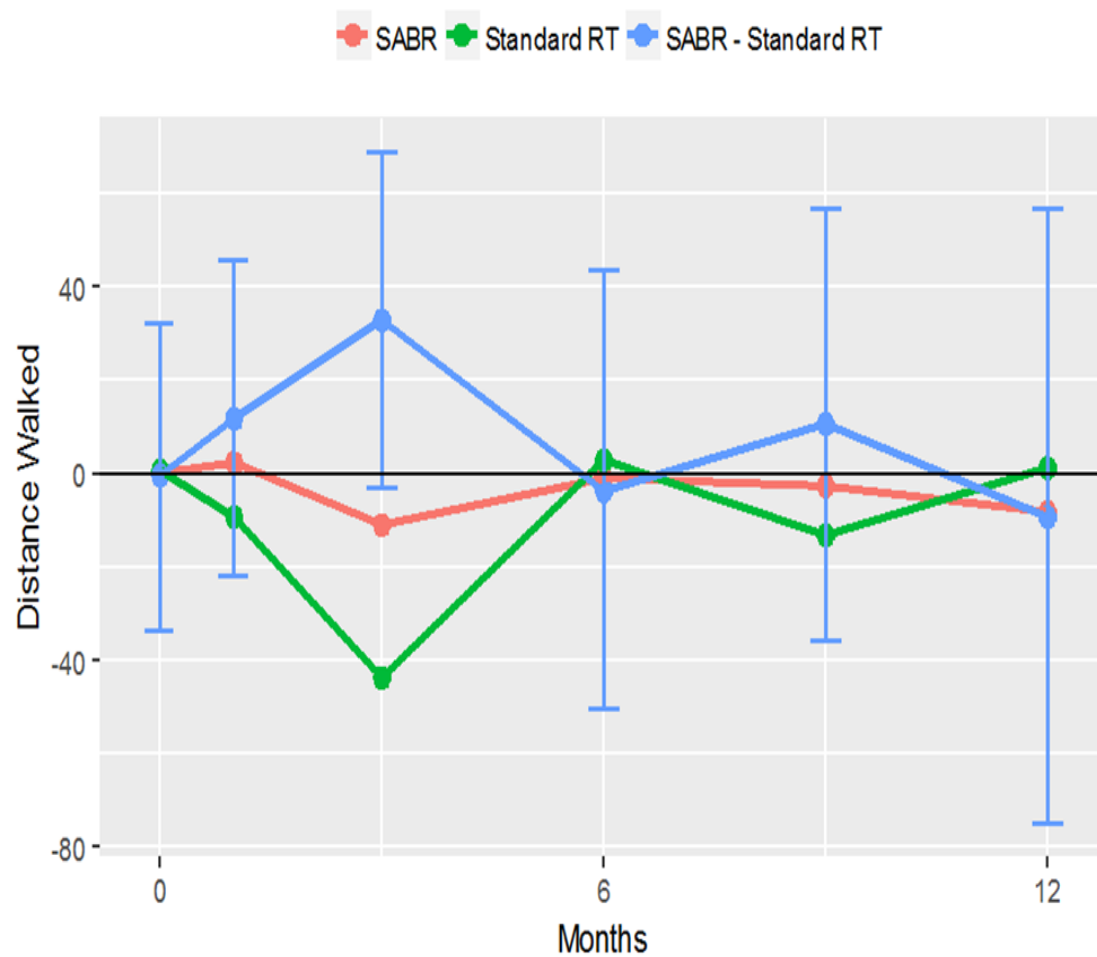
# TROG 09.02 CHISEL: QOL



# 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

David Ball, Tao Mai, Shalini Vinod, Scott Babington, Jeremy Ruben, Angela Rezo, Christine Elder, Marketa Skala, Andrew Wirth, Greg Wheeler, Adeline Lim, Mark Shaw, Hien Le, Nick Nedev

Tomas Kron, Brent Chesson,  
Alan Herschtal, Marijana Vanevski

Ben Solomon, Lou Irving

Penny Schofield

Consumers: David<sup>+</sup> and Barbara Wenzel



# Acknowledgments

## **Radiation Oncologists Reviewers**

David Ball	Steven David
Andrew Wirth	Shankar Siva
Mark Shaw	Scott Babington
Michael Lim Joon	Tao Mai
Nikki Plumridge	

## **Radiation Therapists/ Physicists Reviewers**

Tomas Kron	Alisha Moore
Brent Chesson	Andy Cousins
Mark Burns	Natalie Clements
Max Enge	Michelle Mauro

## **Radiotherapy Case Reviewers**

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Olivia Cook	Monica Harris	

## **Local failure reviewers**

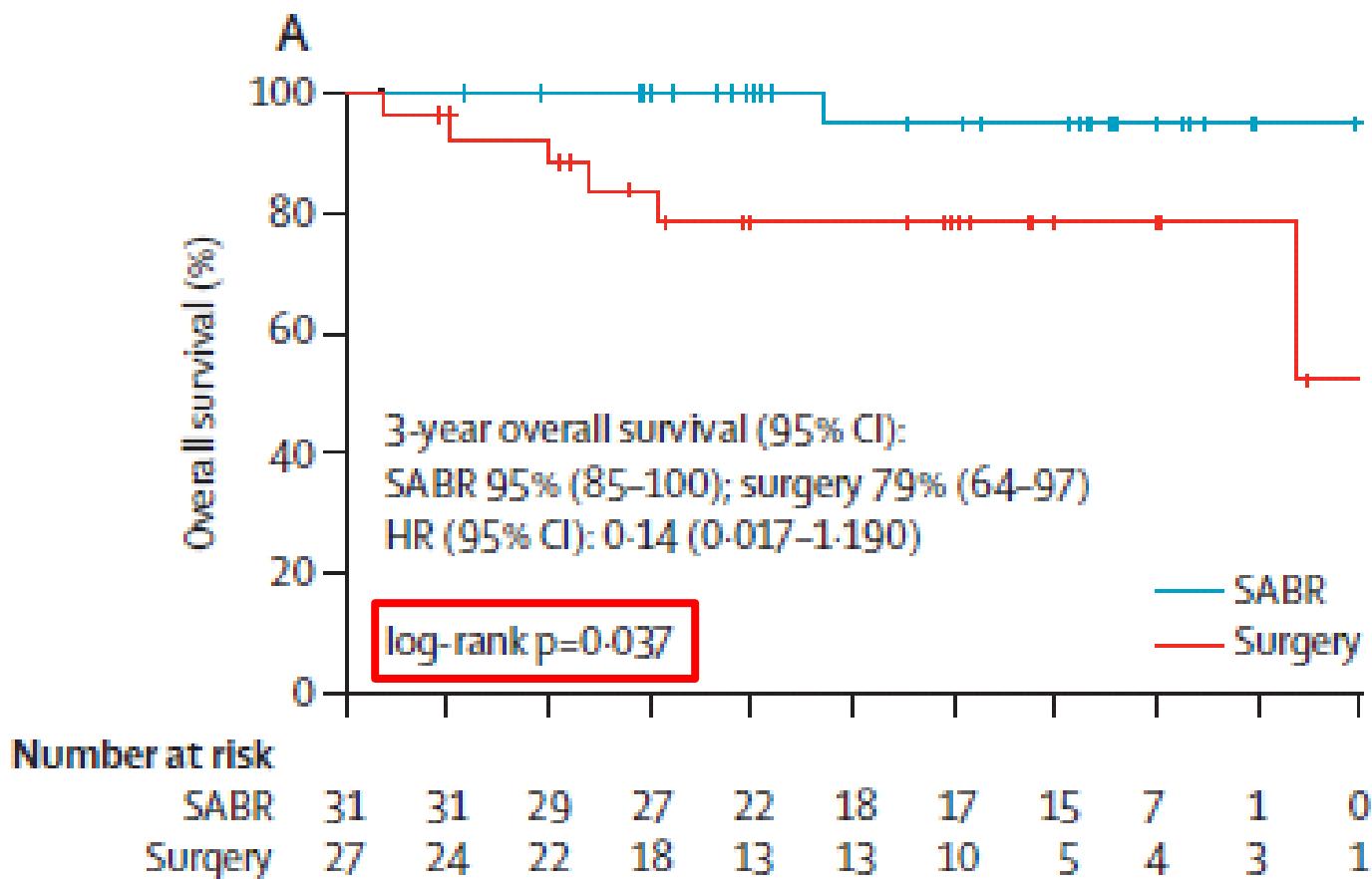
Sam Ellis	Dayanethee Krishna	Kate Moodie
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**Marijana Vanevski and all the clinical trial coordinators**

**The patients and their families**

**The funders: Cancer Australia, New Zealand Cancer Society, Genesis Oncology Trust**

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

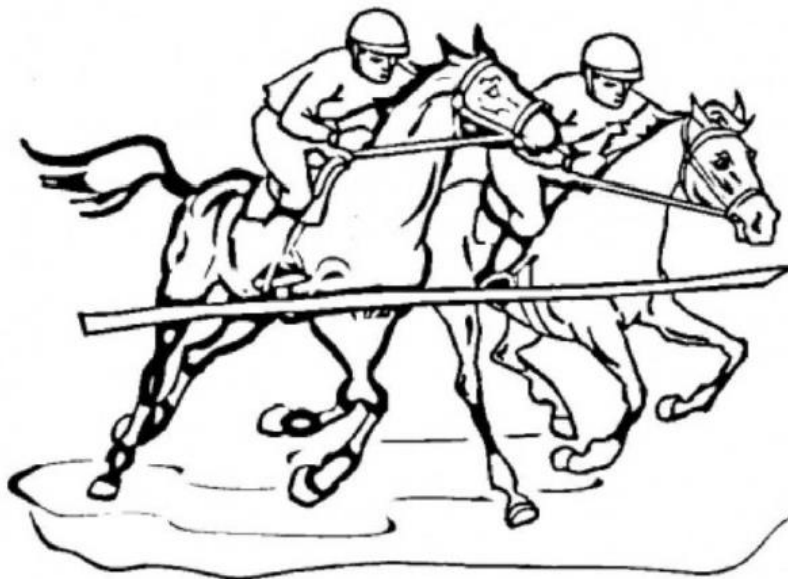


# *Joint Lung Cancer Trialist's Coalition*

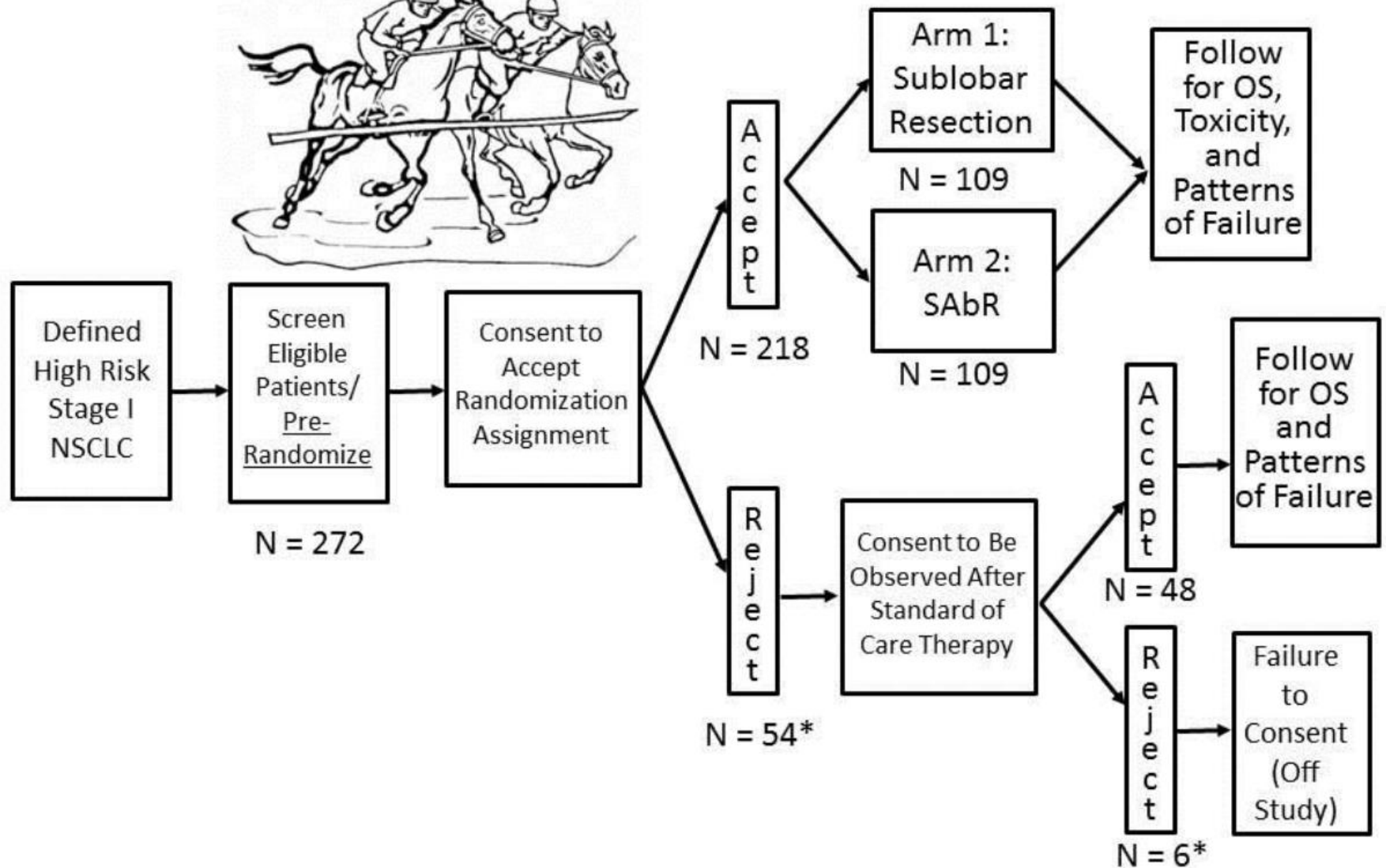
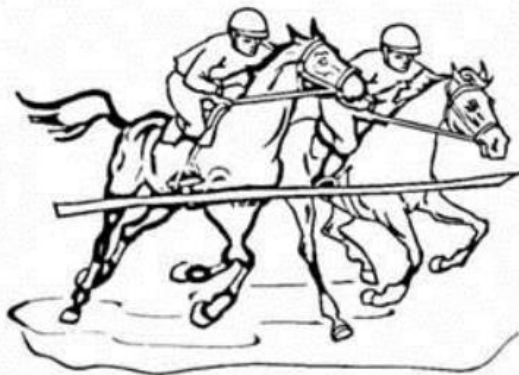
## *JoLT - Ca*

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?

