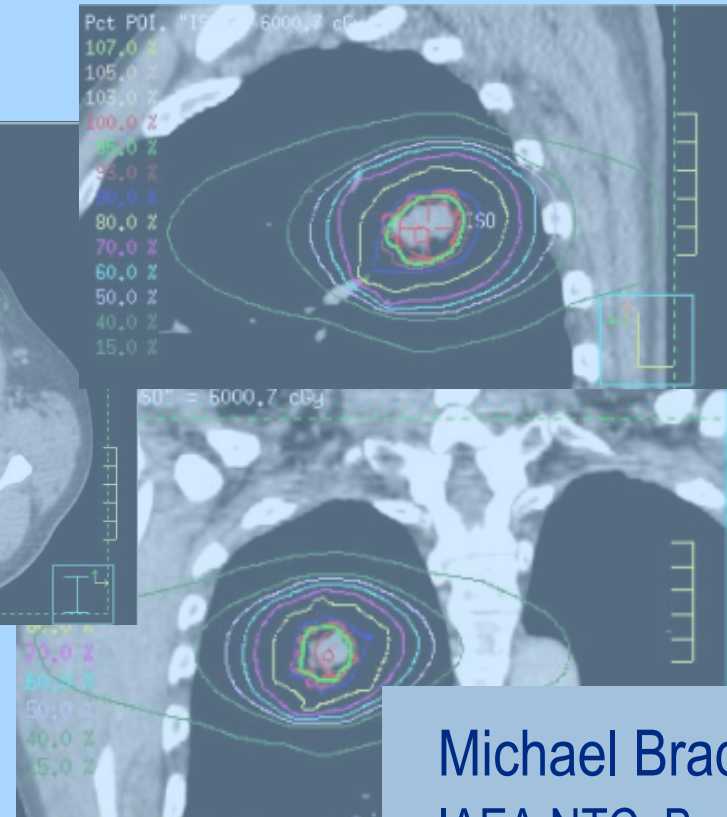


Evaluation of outcome of lung SABR



Michael Brada
IAEA NTC Bratislava
19 March 2018

pollev.com/michaelbrada606

SABR in localised NSCLC



assessing efficacy



prognostic factors



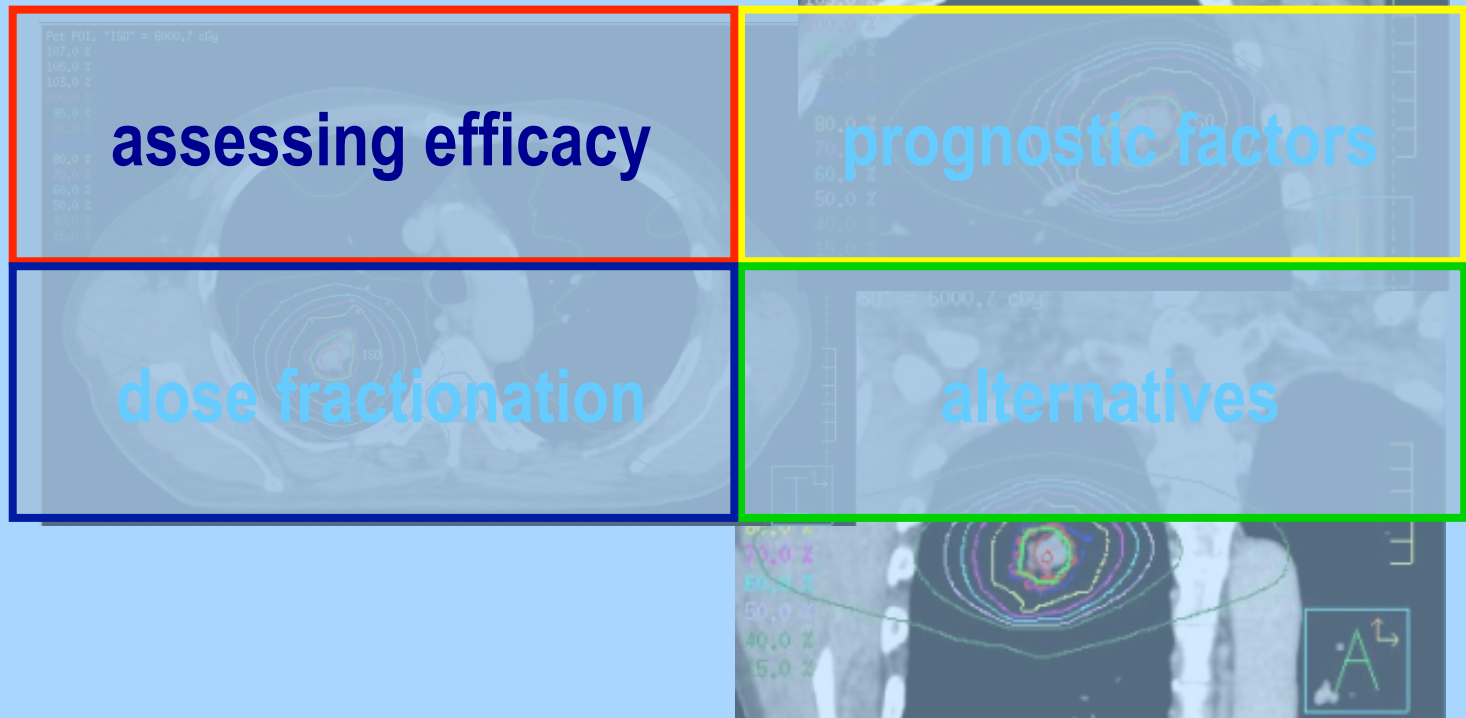
dose fractionation



alternatives

Evaluation of outcome of local treatment in localised NSCLC

SABR in localised NSCLC



Evaluation of outcome of local treatment in localised NSCLC

What are the endpoints for SABR in stage I NSCLC of relevance to the patient

tumour control

toxicity

survival

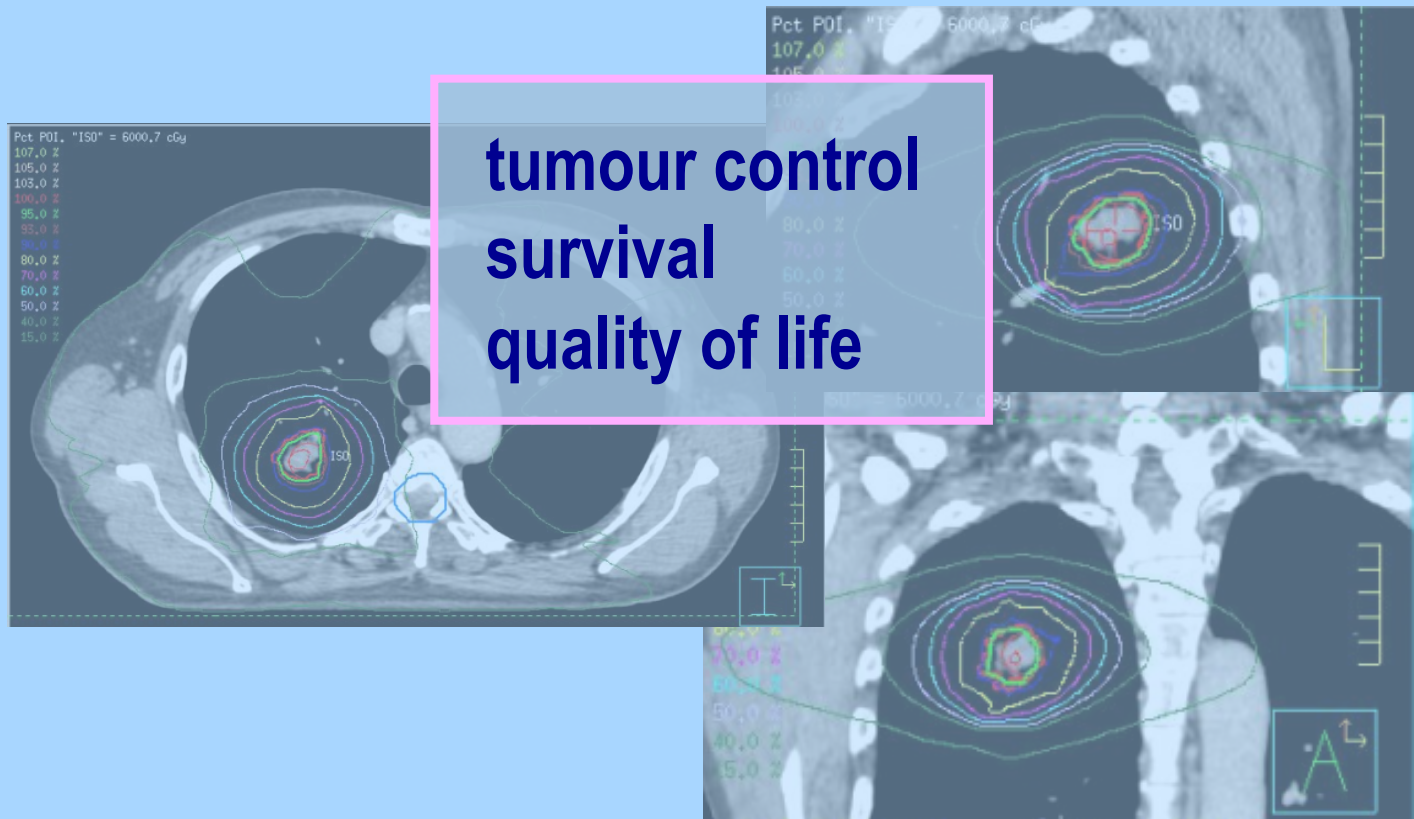
quality of life

tumour control and toxicity

tumour control and survival

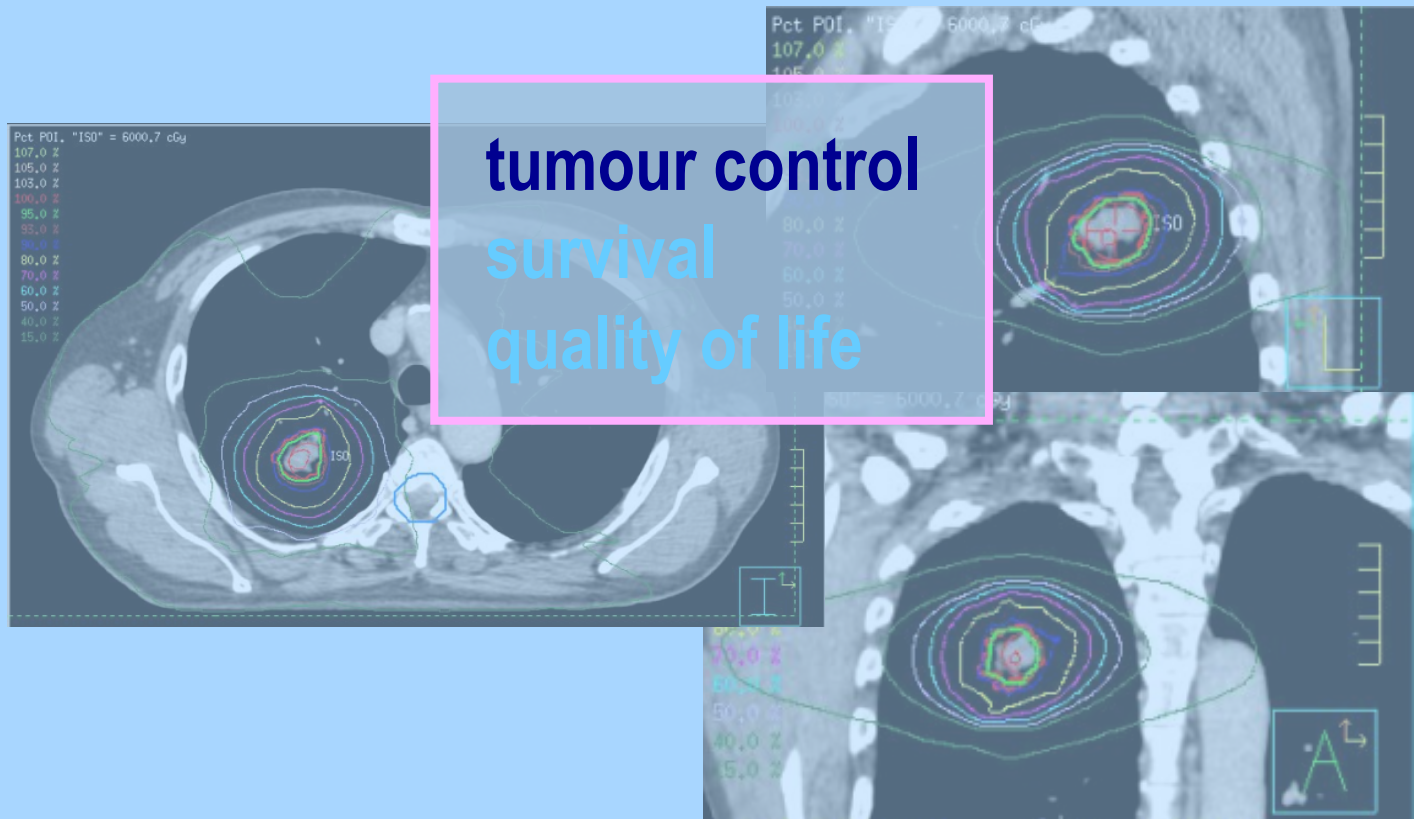
survival and quality of life

Endpoints in patients with early stage NSCLC



Evaluation of outcome of local treatment in localised NSCLC

Endpoints in patients with early stage NSCLC

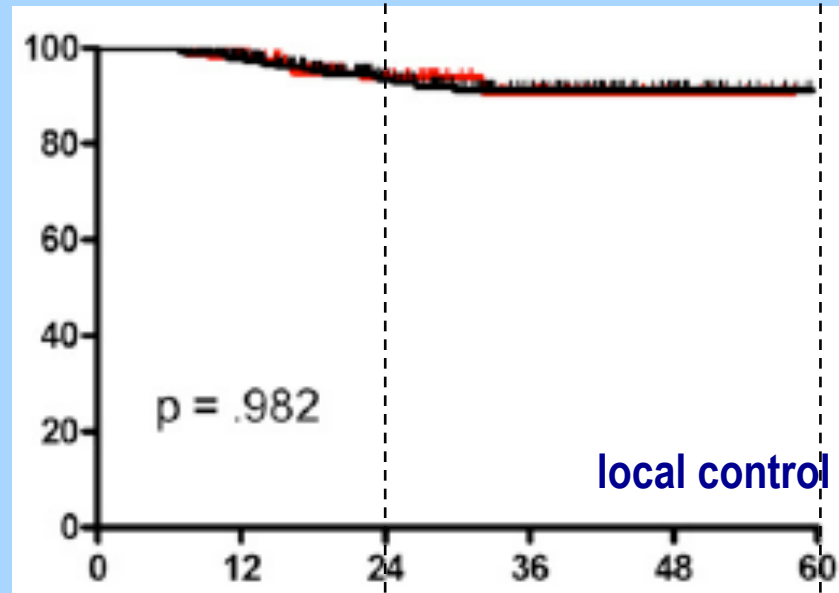


Evaluation of outcome of local treatment in localised NSCLC

SABR for stage I NSCLC

Tumour control

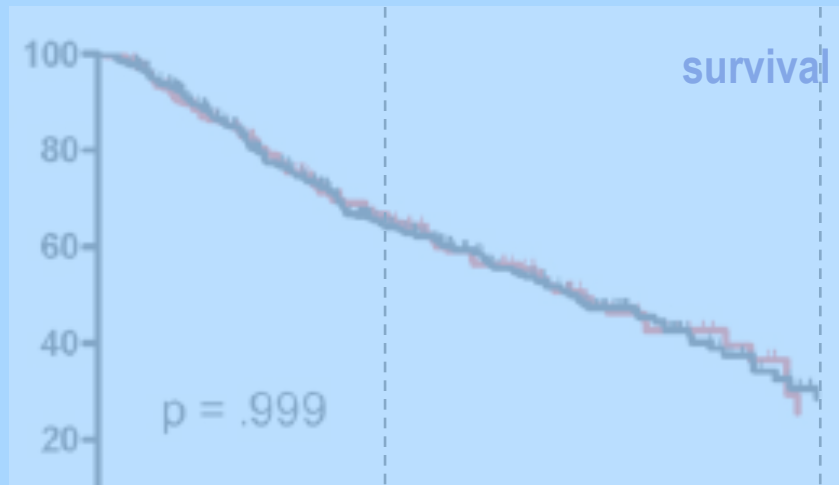
Local progression free survival (%)



VU Amsterdam
591 patients

→ histol. verified
→ histol. unverified

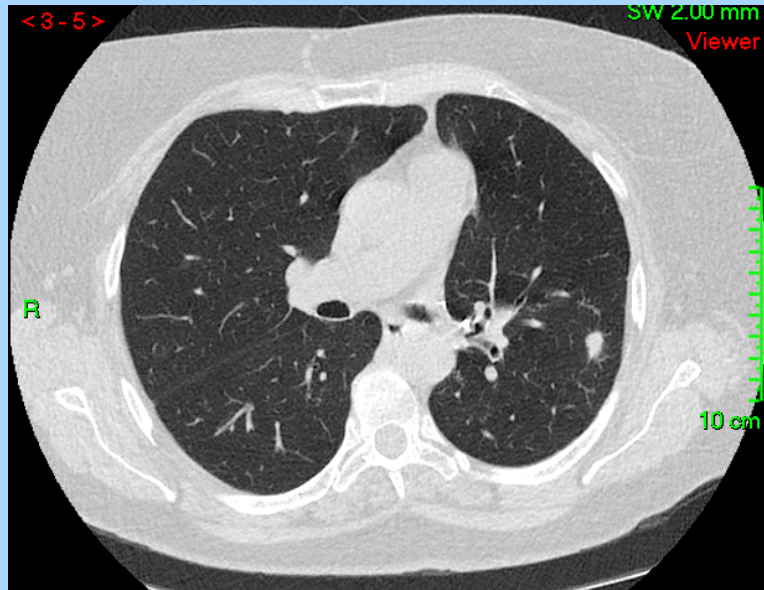
Survival (%)



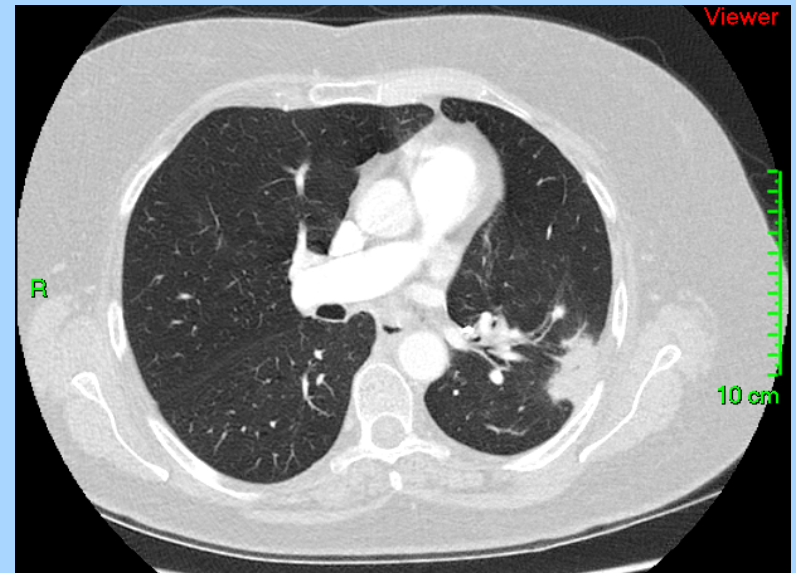
Endpoints of efficacy of SABR in stage I NSCLC

SABR for stage I NSCLC

Tumour control



6.9.13



22.1.15

Endpoints of efficacy of SABR in stage I NSCLC

Endpoints in patients with early stage NSCLC

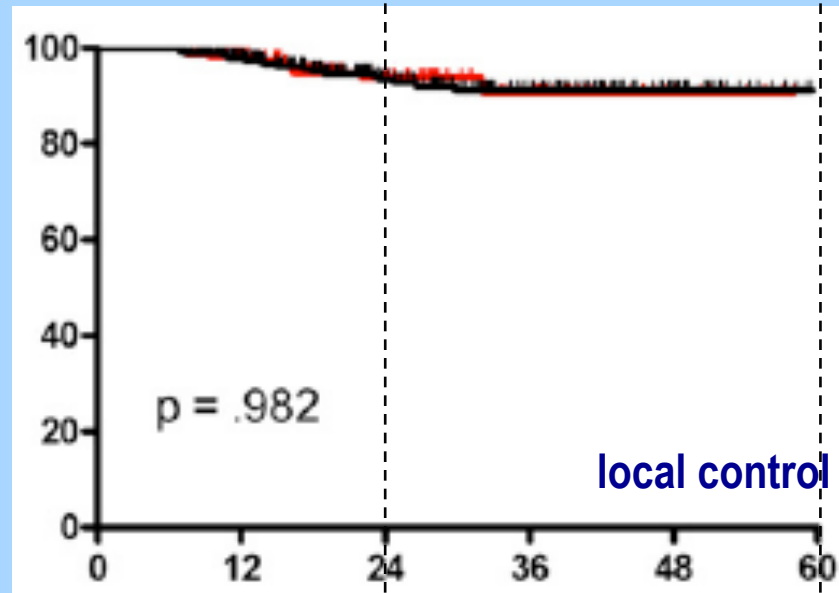


Evaluation of outcome of local treatment in localised NSCLC

SABR for stage I NSCLC

Tumour control

Local progression free survival (%)

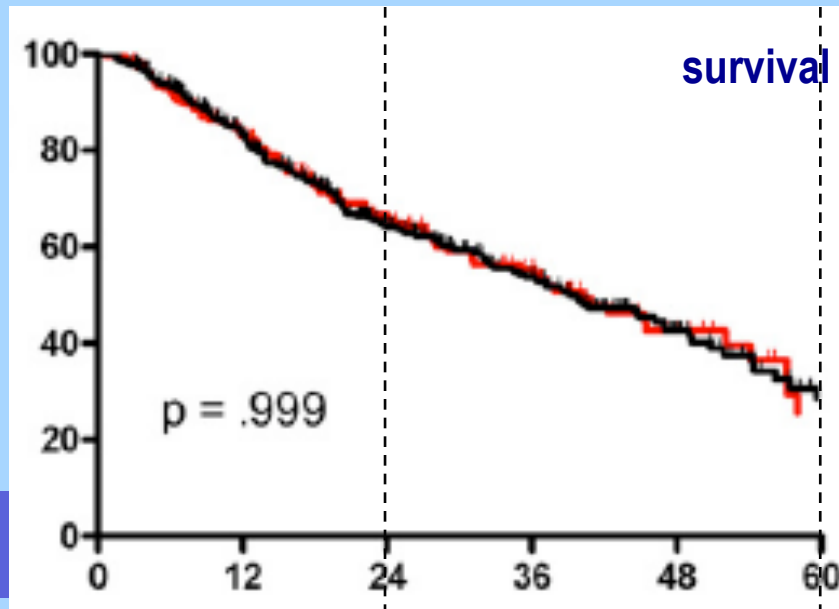


VU Amsterdam
591 patients

→ histol. verified
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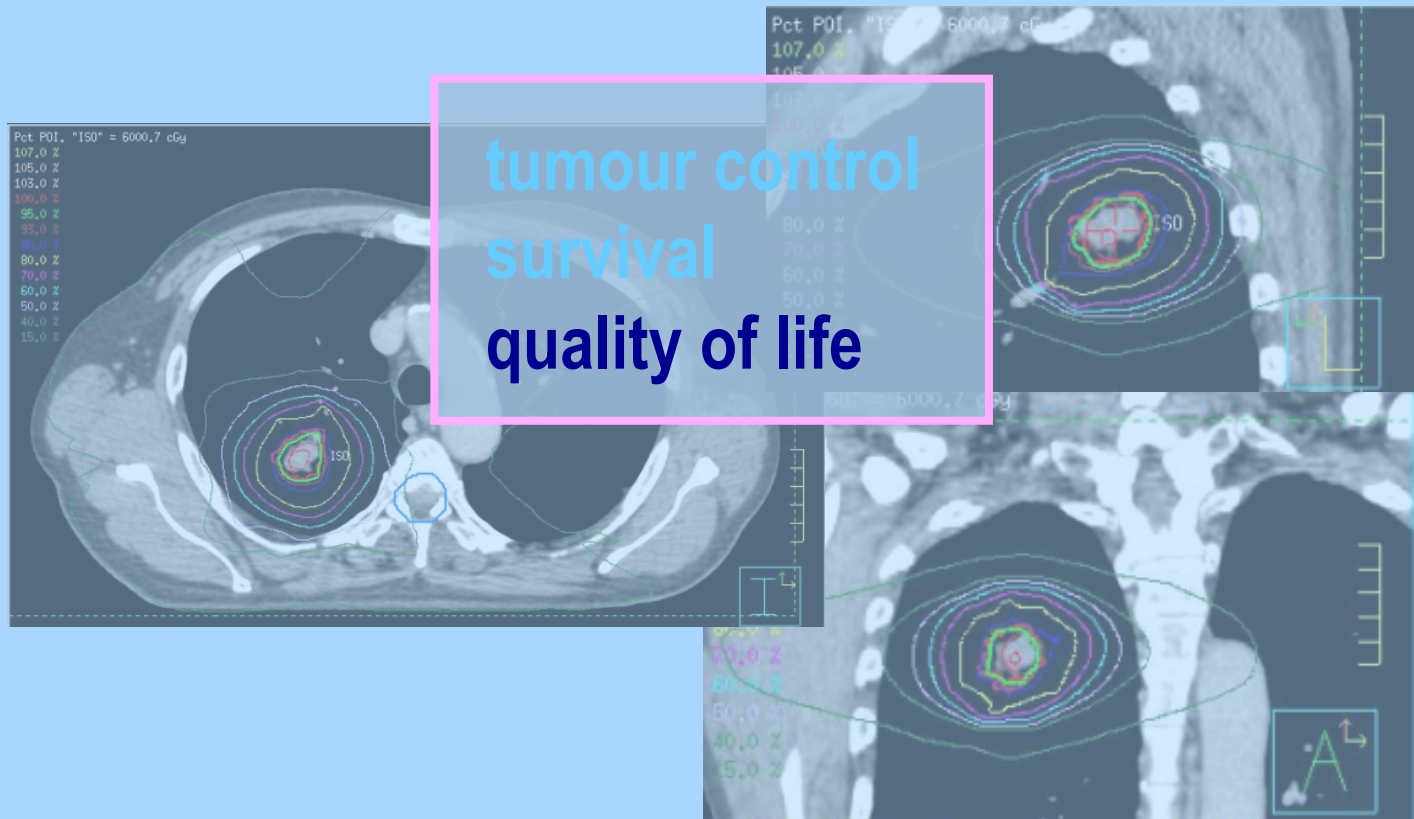
Survival

Survival (%)



stage I NSCLC

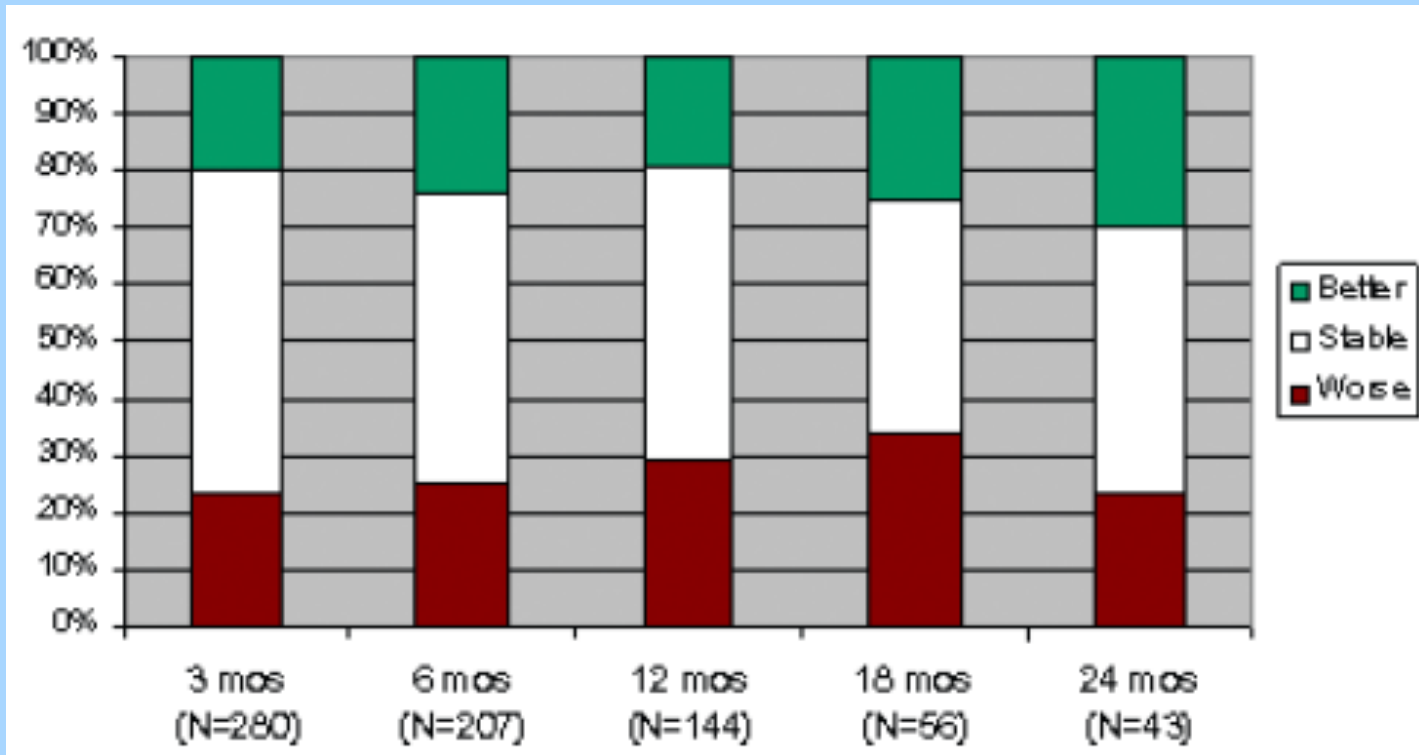
Endpoints in patients with early stage NSCLC



Evaluation of outcome of local treatment in localised NSCLC

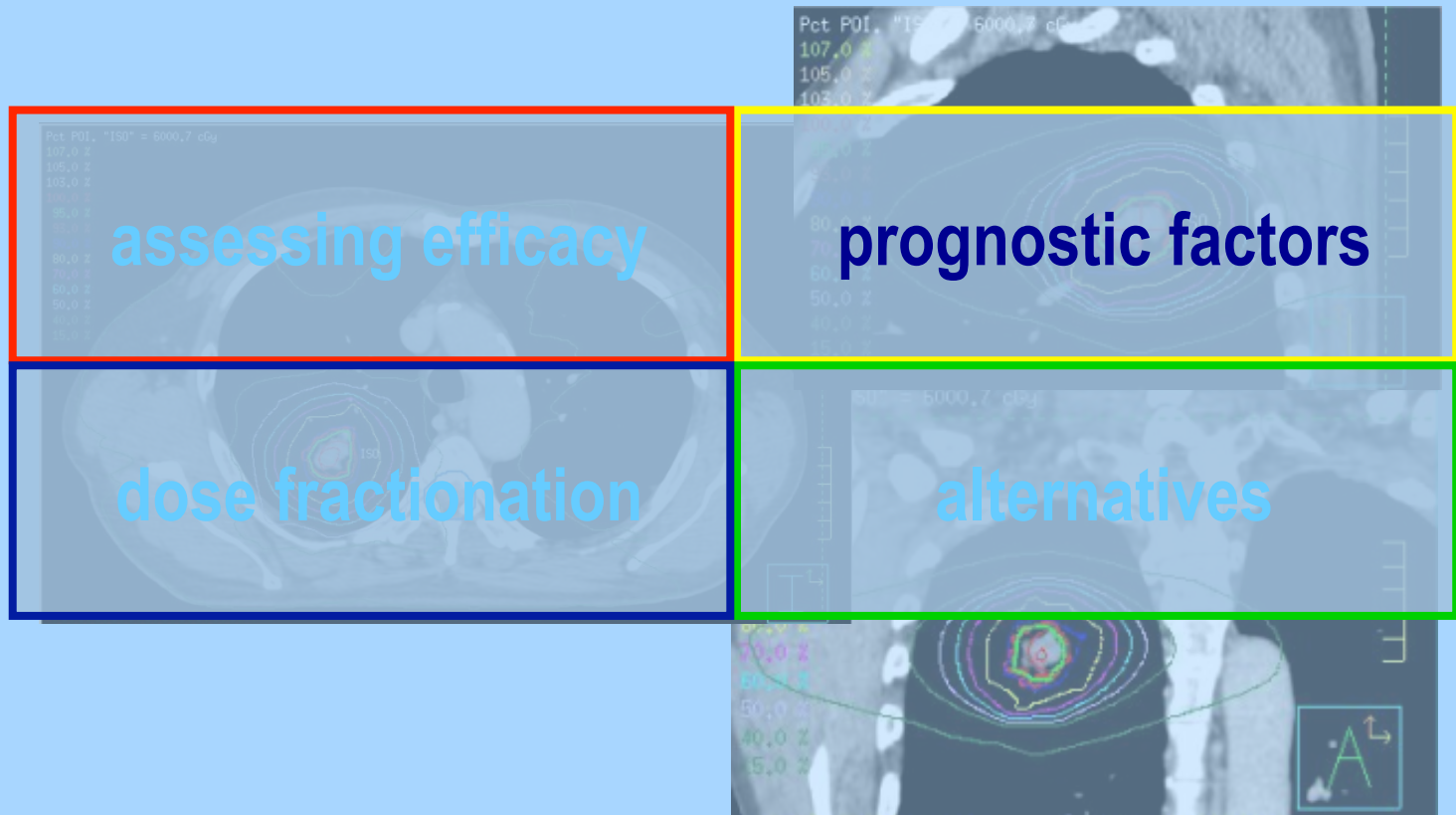
Quality of life after SABR (EORTC QLQ C30)

Change in global QOL score



SABR and quality of life (QOL)

SABR in localised NSCLC



Evaluation of outcome of local treatment in localised NSCLC

Prognostic factors for survival in Stage I NSCLC treated with SABR

age

comorbidity

performance status

tumour size

A, B & C

A, C & D

A, B, C & D

Independent predictors of survival

<i>Variable</i>	<i>p</i> (<i>multivariate</i>)
performance status (ECOG)	0.0000019
operability	0.007
Charlson comorbidity index	0.02

779 patients, 5 centres

Evaluation of outcome of local treatment in localised NSCLC

Independent predictors of survival

<i>Variable</i>	<i>p</i> (multivariate)
tumour size	<0.0001
age	<0.0001
performance status (KPS)	<0.001
Charlson comorbidity index	0.048
gender	0.0165

600 patients, Cleveland Centre

Evaluation of outcome of local treatment in localised NSCLC

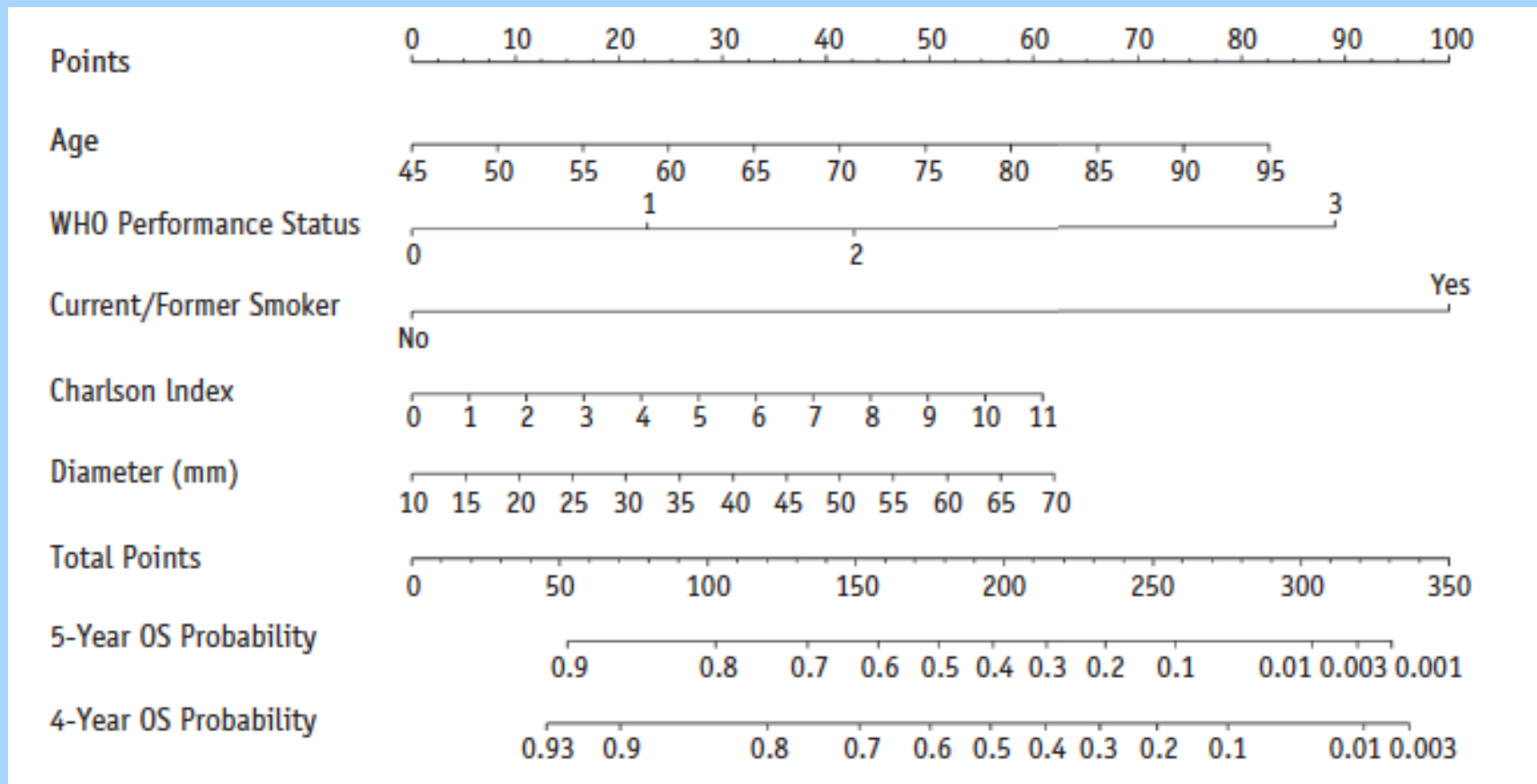
Independent predictors of survival

<i>prognostic factors</i>	<i>adverse</i>
tumour size (diameter)	$\geq 2\text{cm}$
WHO performance status	≥ 2
Charlson comorbidity index	≥ 3
age	≥ 75

703 patients, VUMC Amsterdam

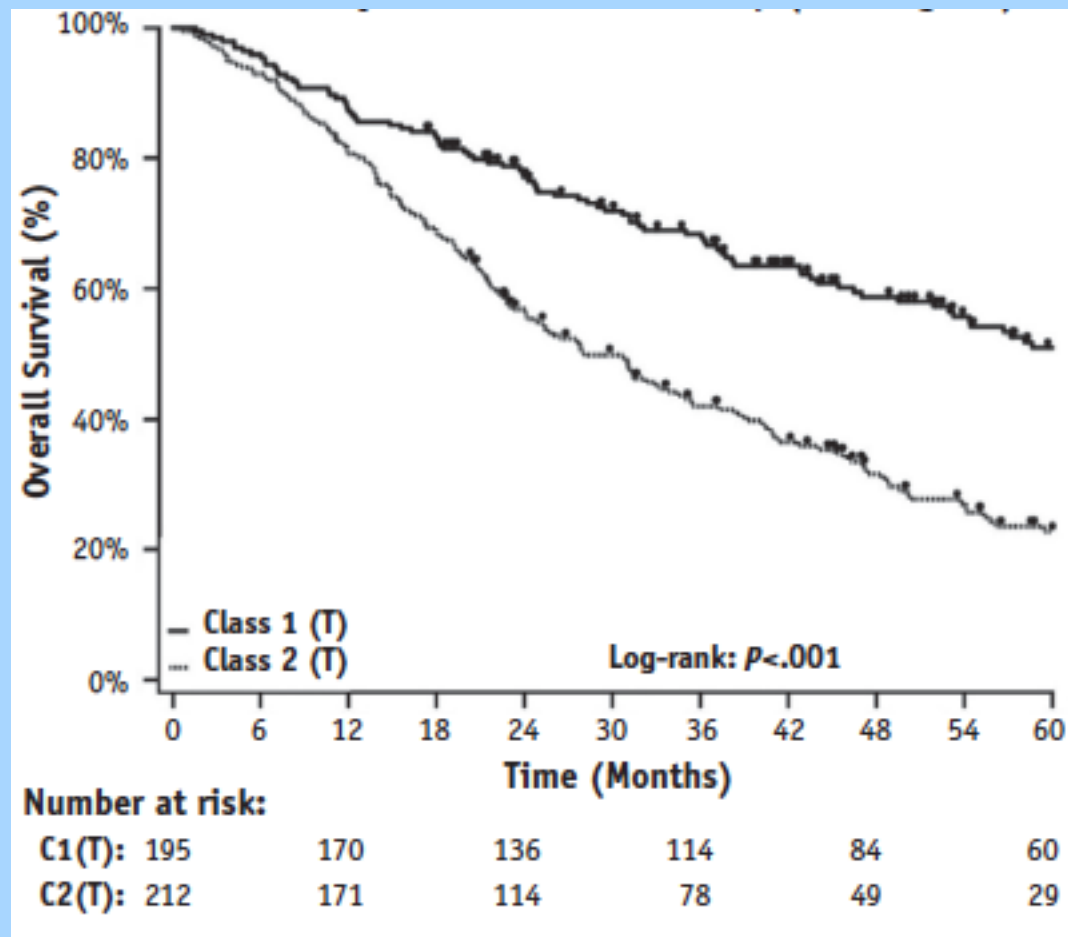
Independent prognostic factors for survival

Nomogram



Independent prognostic factors for survival

Training set - two prognostic groups



Independent prognostic factors for survival

Independent predictors of survival

summary

performance status

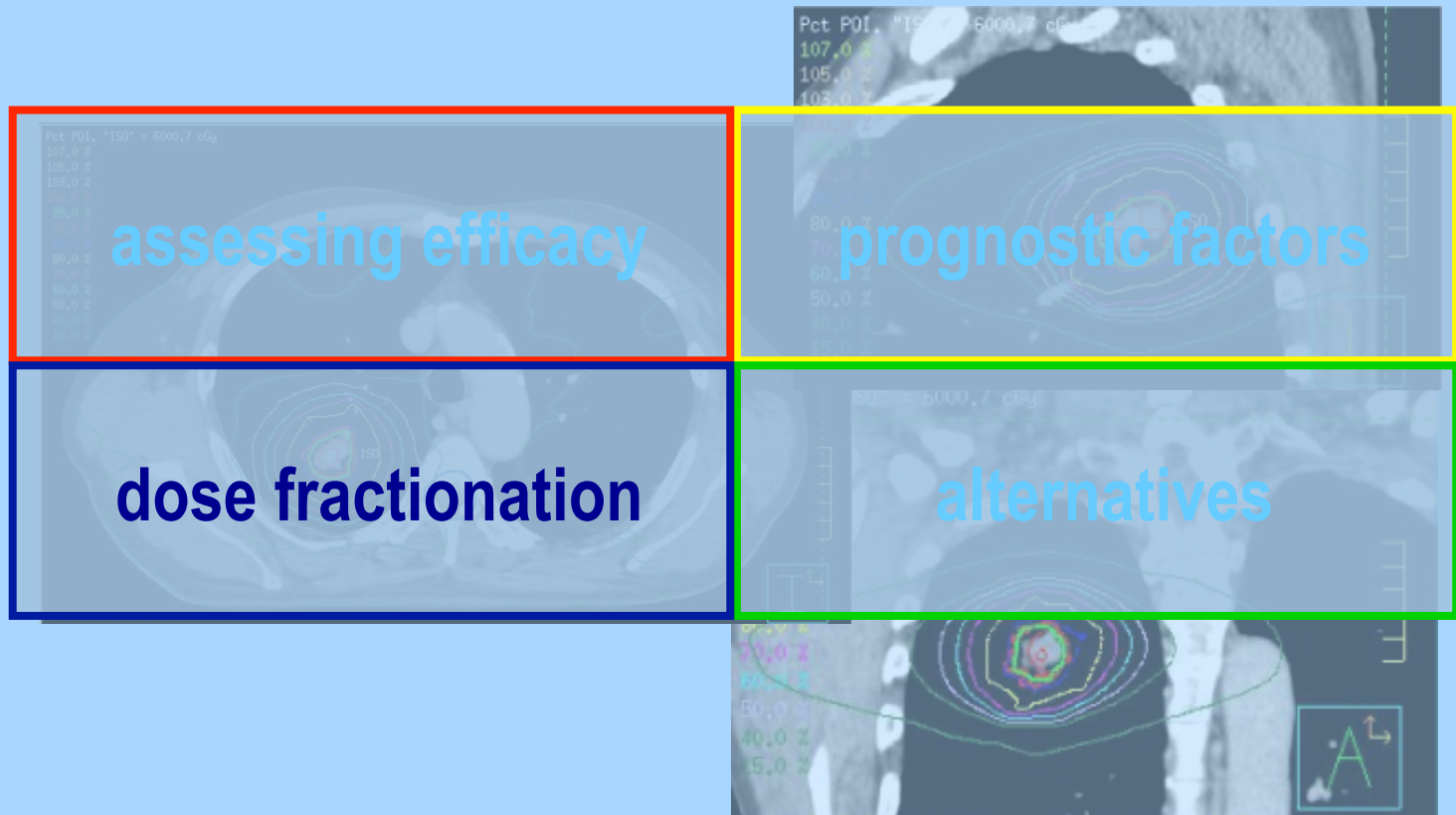
comorbidity

age

tumour size

Independent prognostic factors for survival

SABR in localised NSCLC



Evaluation of outcome of local treatment in localised NSCLC

SABR dose and outcome

Higher dose is associated with
longer survival

Different dose fractionation
regimens have similar survival
outcomes

Higher dose is associated with
improved tumour control

Minimum dose should be
100Gy BED

Radical radiotherapy – dose escalation

Locally advanced
NSCLC



Phase I/II

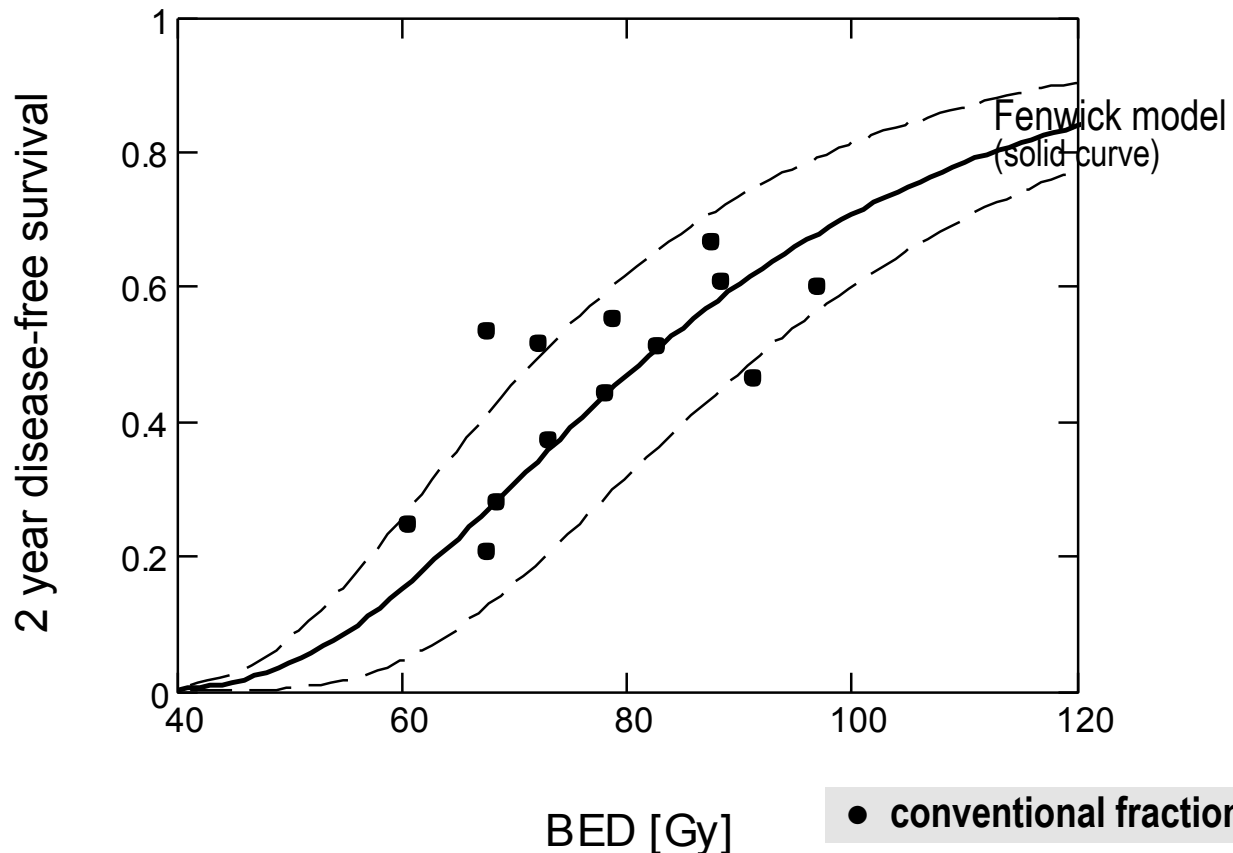


increasing RT dose
(related to normal lung DVH)

Improving lung cancer radiotherapy

Summary of published phase I/II studies (1201 patients, 8 publications)

2 year local progression free survival (corrected for stage distribution)

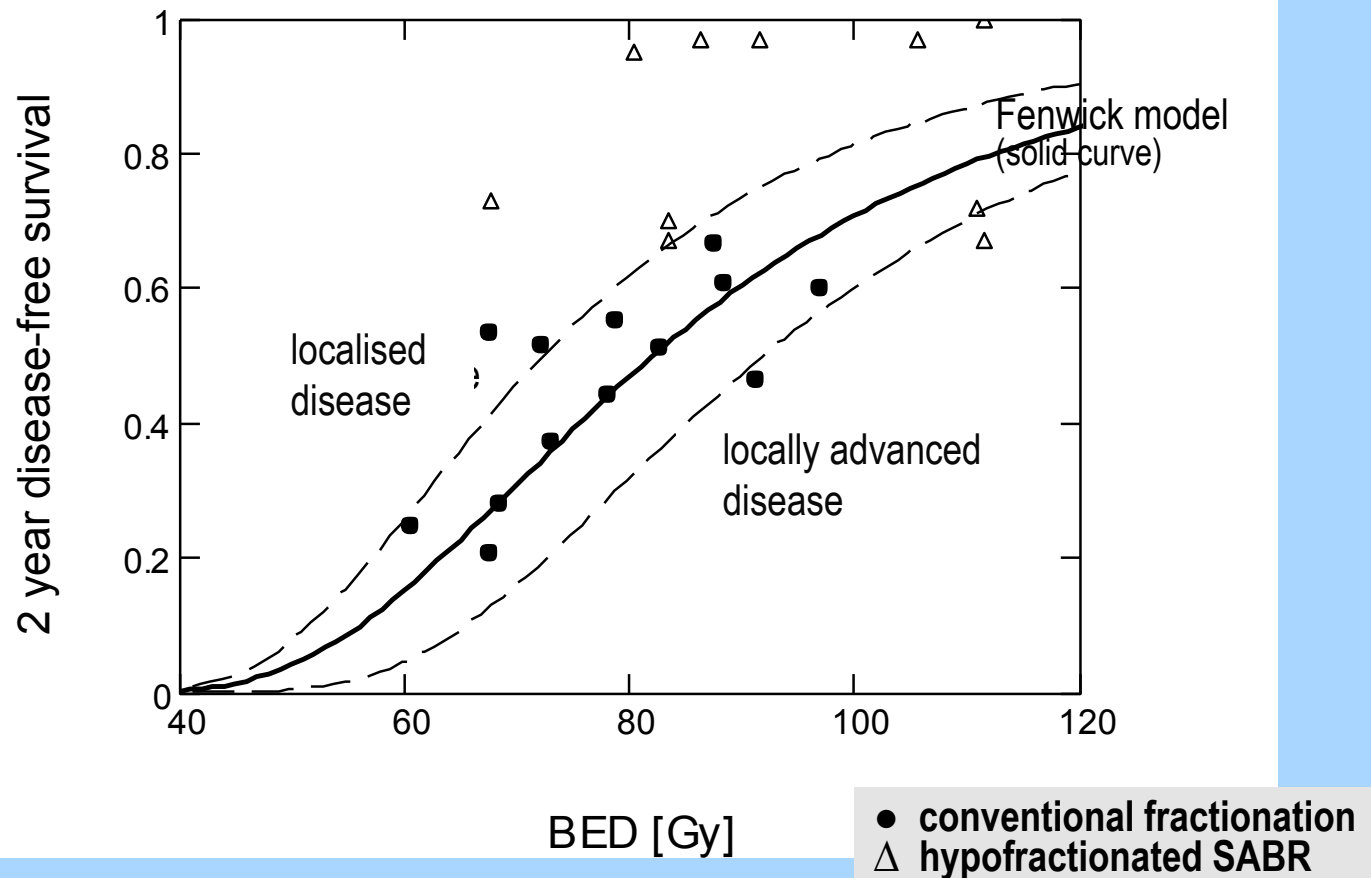


corrected for dose fractionation/time and stage distribution

Dose response in non-small cell lung cancer (NSCLC)

Summary of published phase I/II studies including SABR

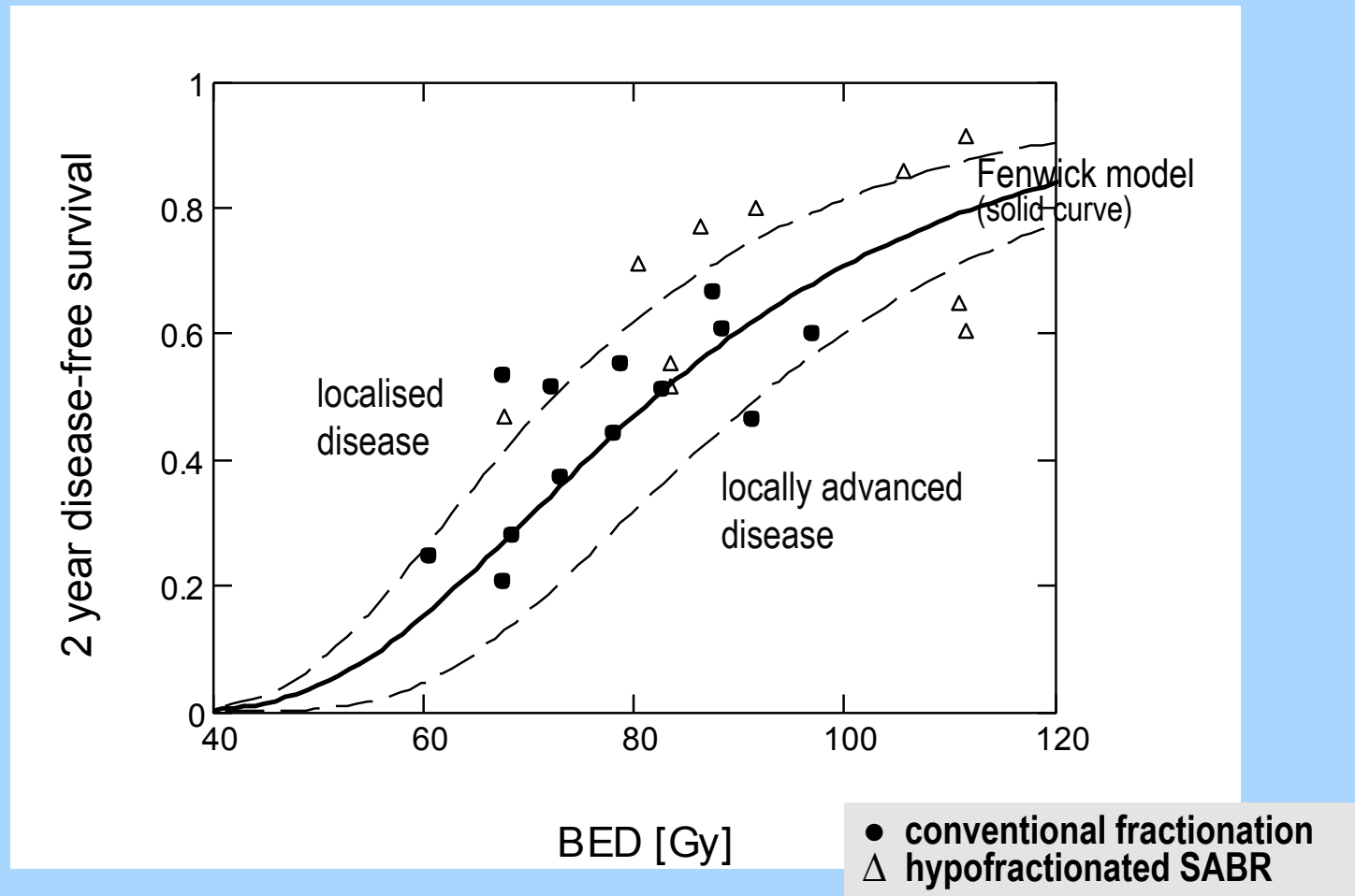
2 year local progression free survival



Dose response in non-small cell lung cancer (NSCLC)

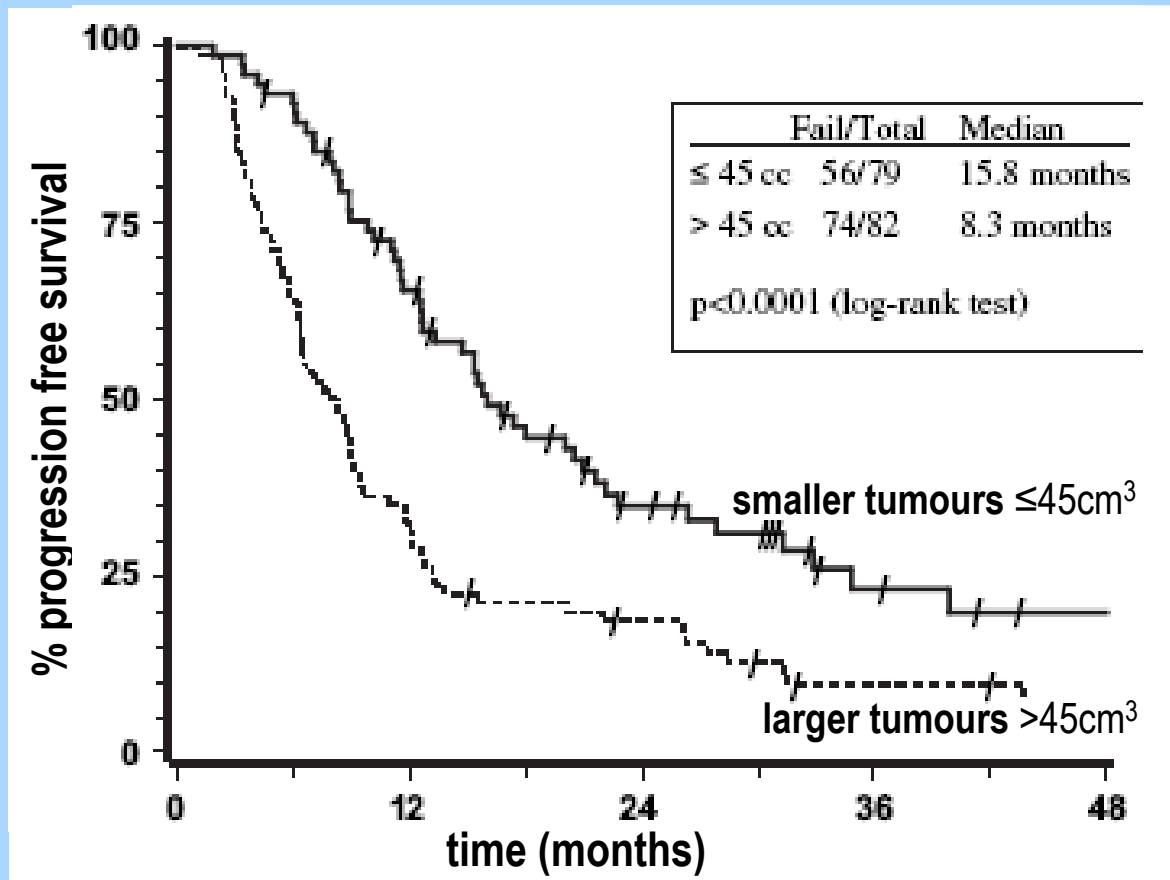
Summary of published phase I/II studies including SABR

2 year local progression free survival (corrected for stage distribution)



Dose response in non-small cell lung cancer (NSCLC)

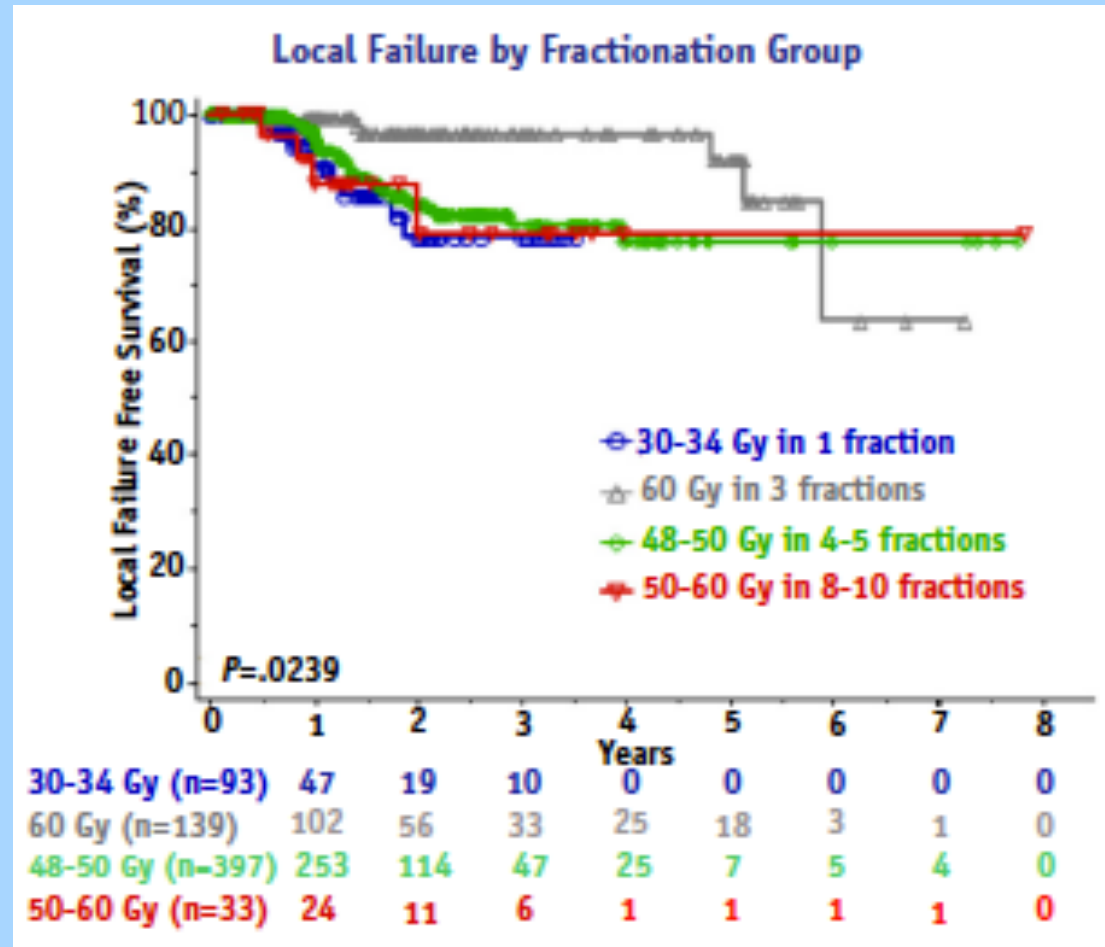
RTOG 93-11 Phase I/II dose escalation study in NSCLC



$45\text{cm}^3 \approx 4.5 \text{ cm diameter sphere}$

Tumour size and disease control

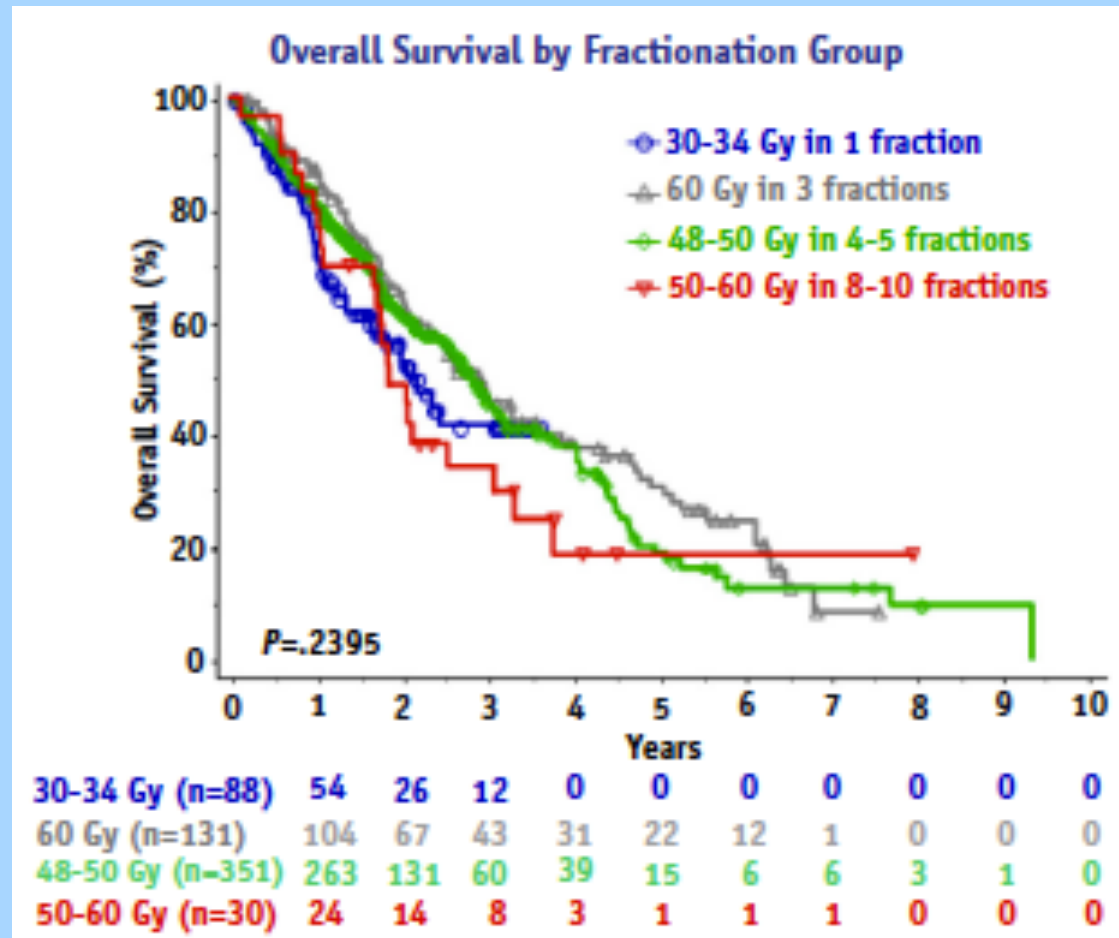
Local control & dose fractionation



600 patients, Cleveland Centre

Evaluation of outcome of local treatment in localised NSCLC

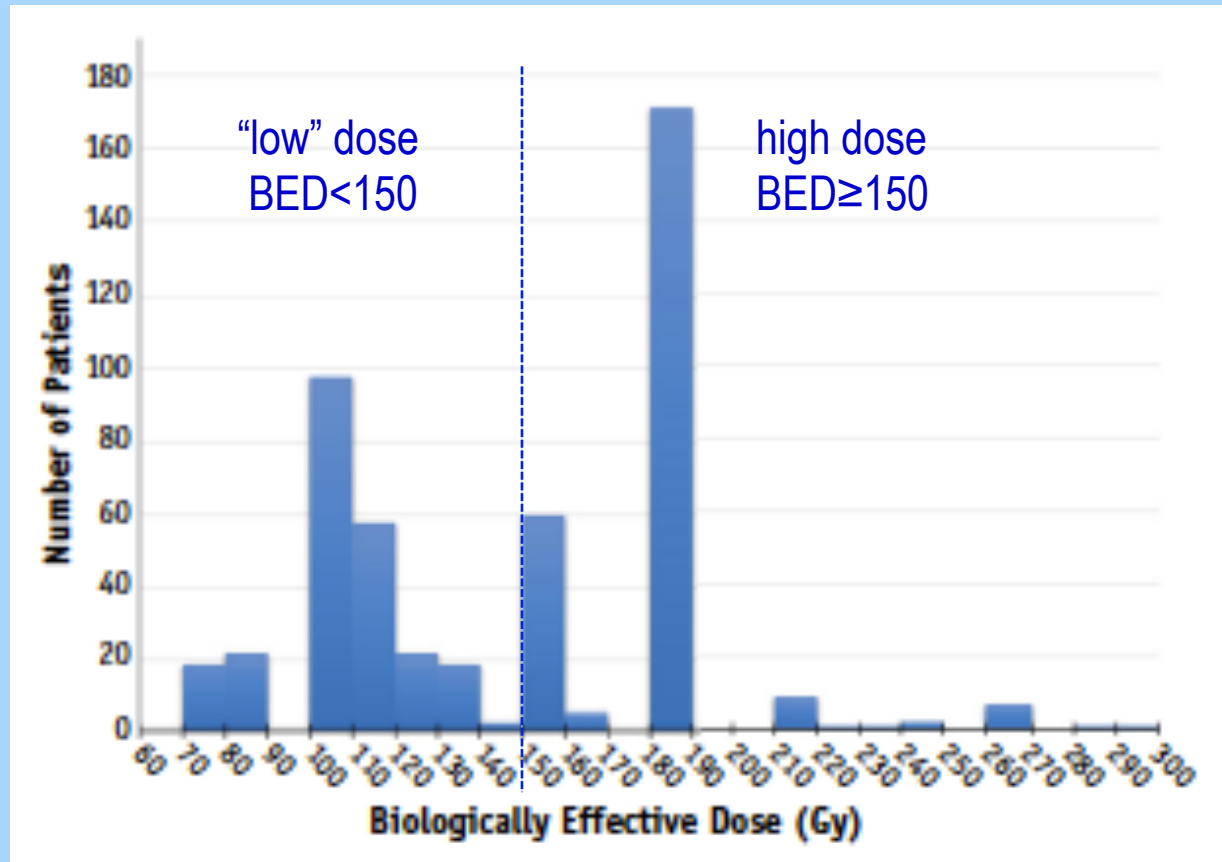
Survival & dose fractionation



600 patients, Cleveland Centre

Evaluation of outcome of local treatment in localised NSCLC

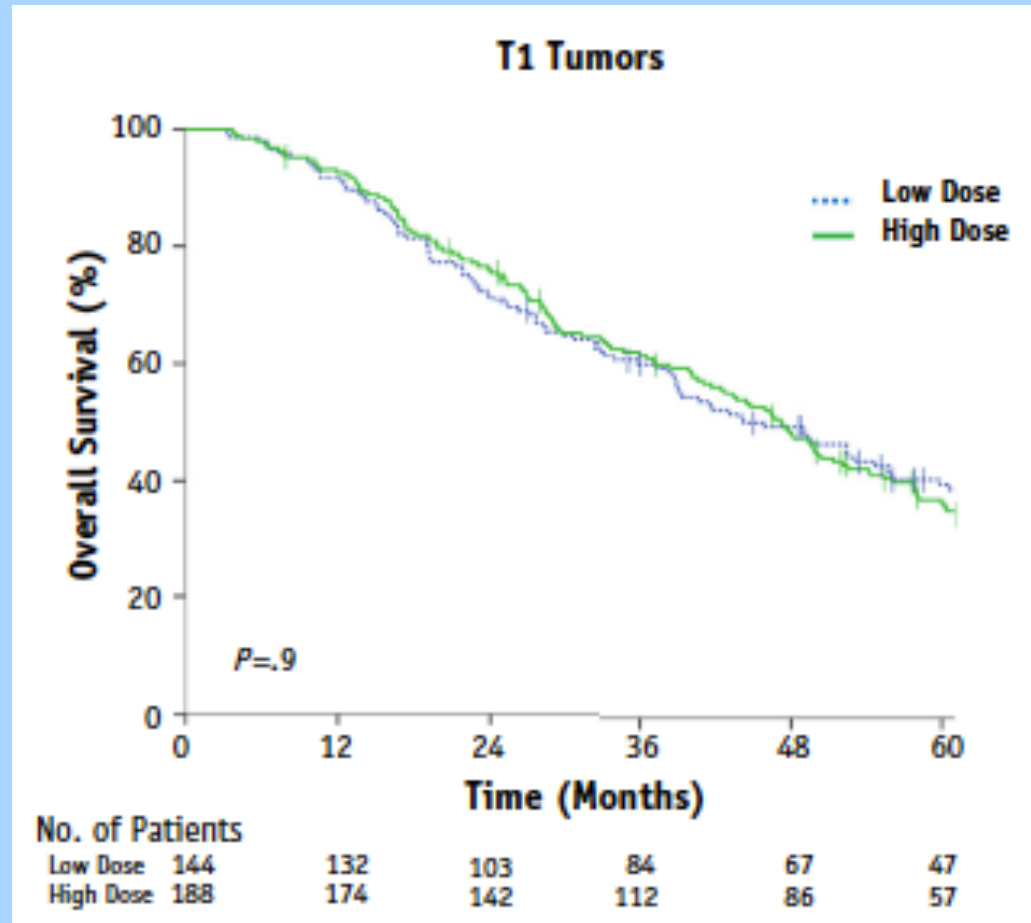
Survival & dose fractionation



495 patients, Stage I NSCLC & SABR, National Cancer Database, us

Evaluation of outcome of local treatment in localised NSCLC

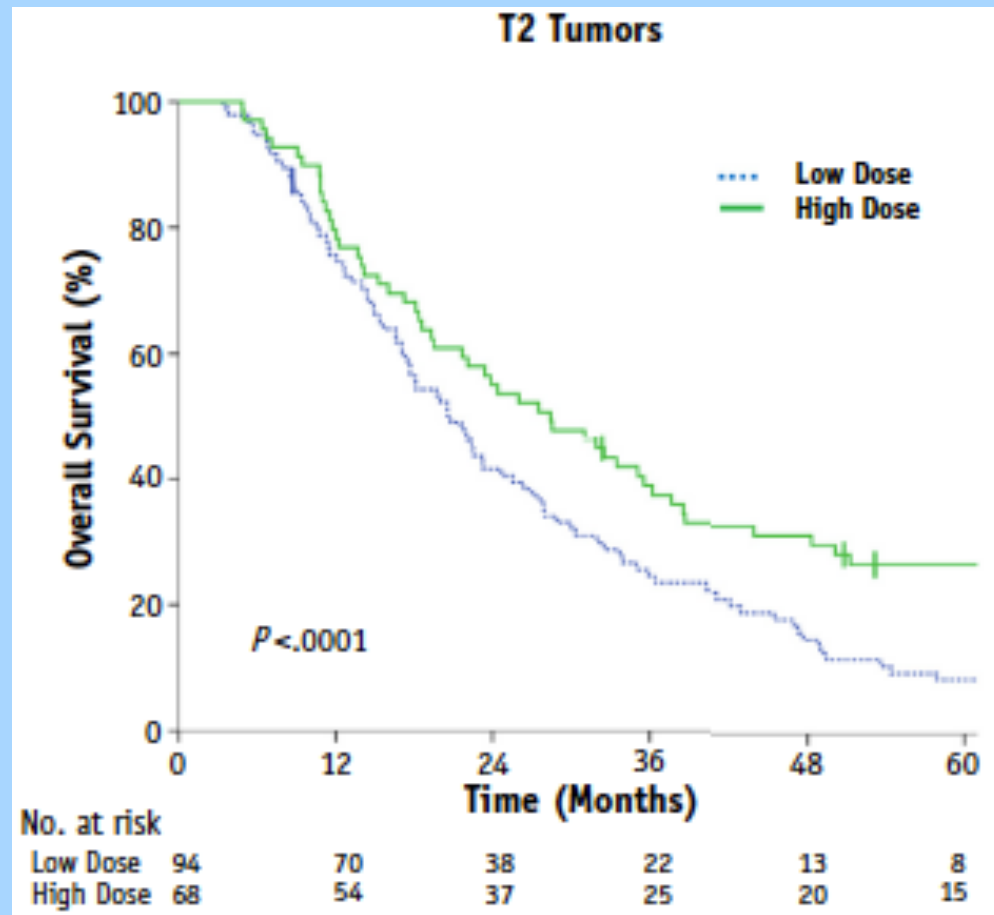
Survival & dose fractionation



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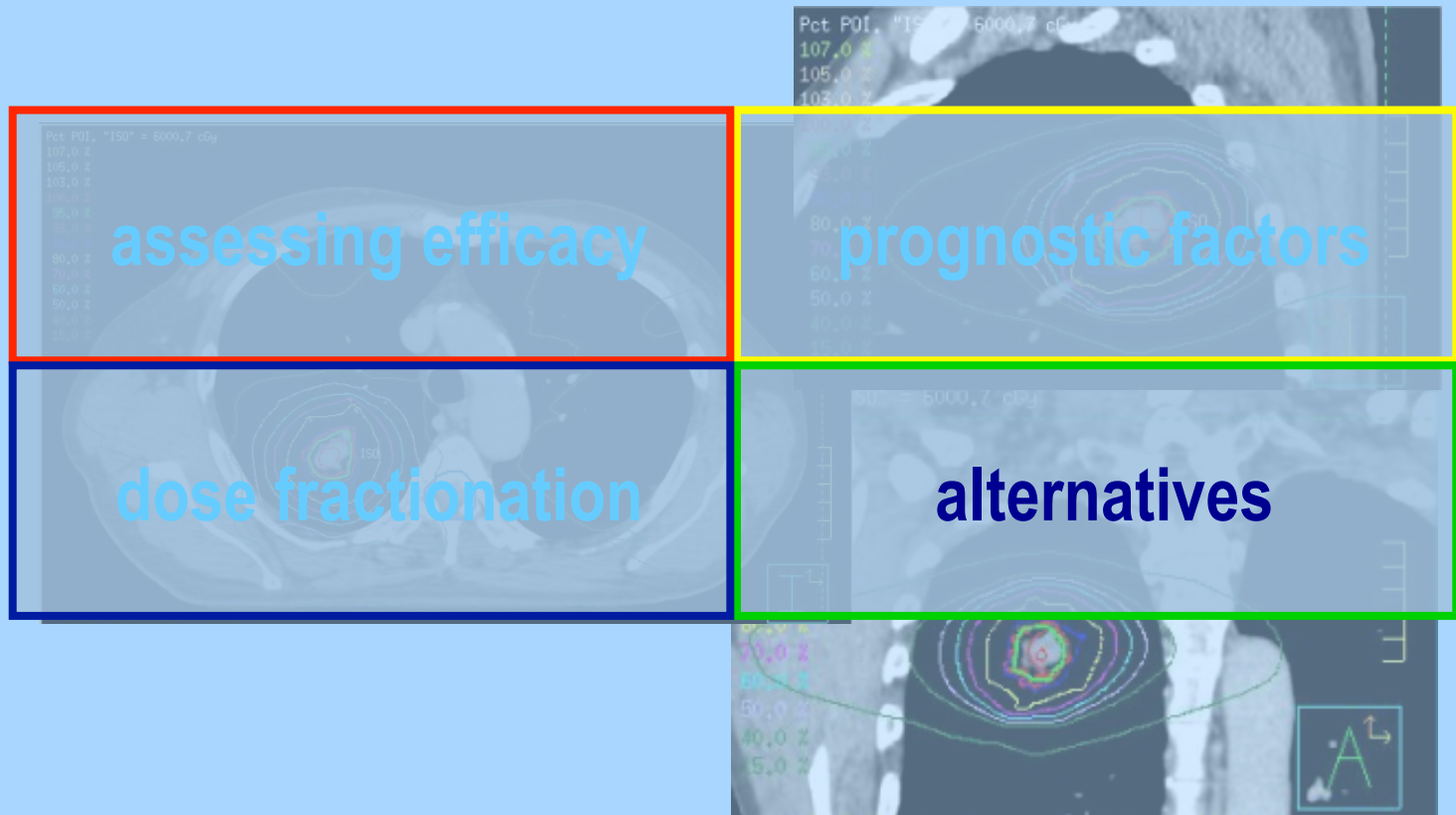
Survival & dose fractionation



495 patients, Stage I NSCLC & SABR, National Cancer Database, us

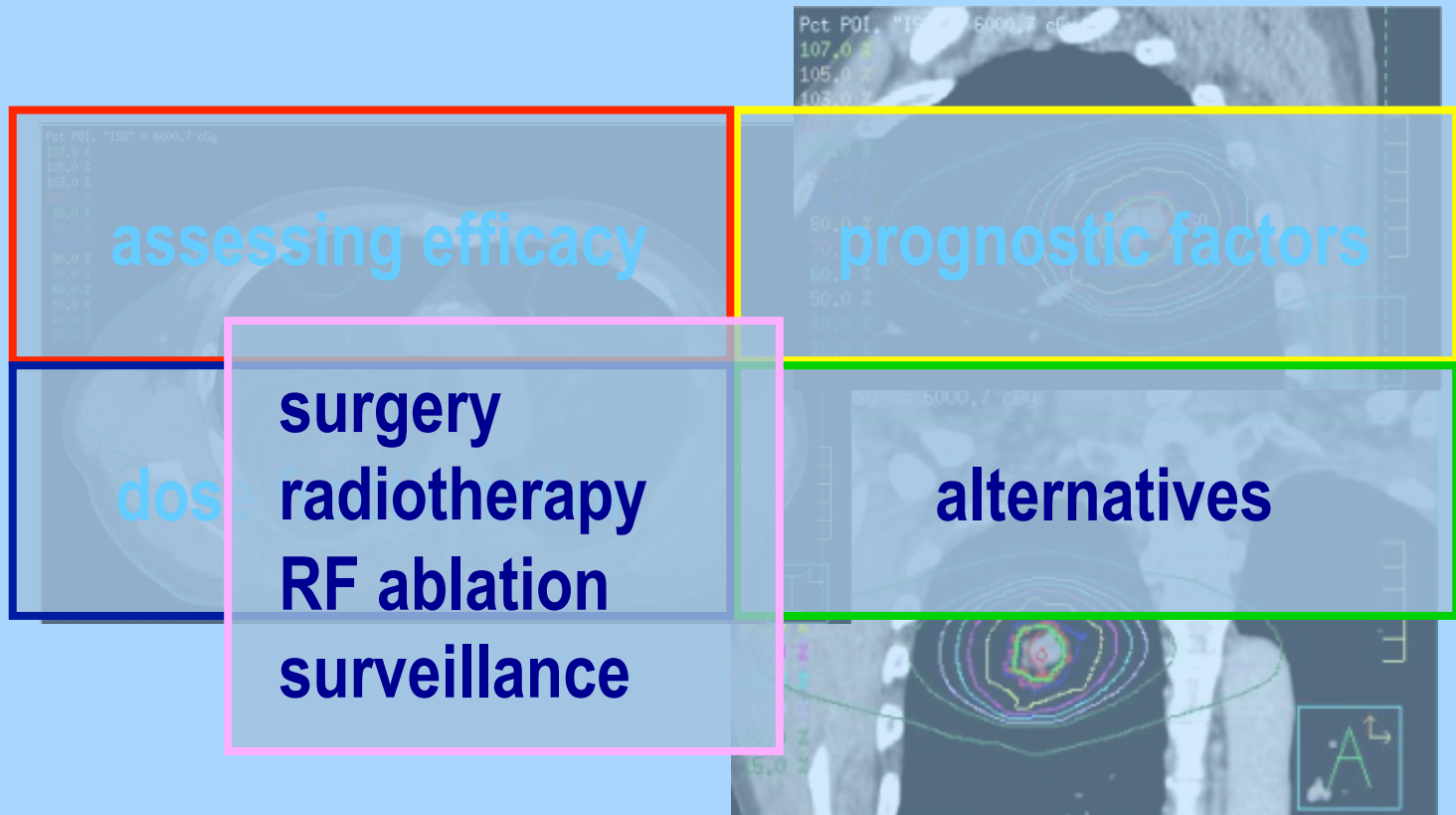
Evaluation of outcome of local treatment in localised NSCLC

SABR in localised NSCLC



Evaluation of outcome of local treatment in localised NSCLC

SABR in localised NSCLC



Evaluation of outcome of local treatment in localised NSCLC

Alternative therapies for stage I NSCLC and survival

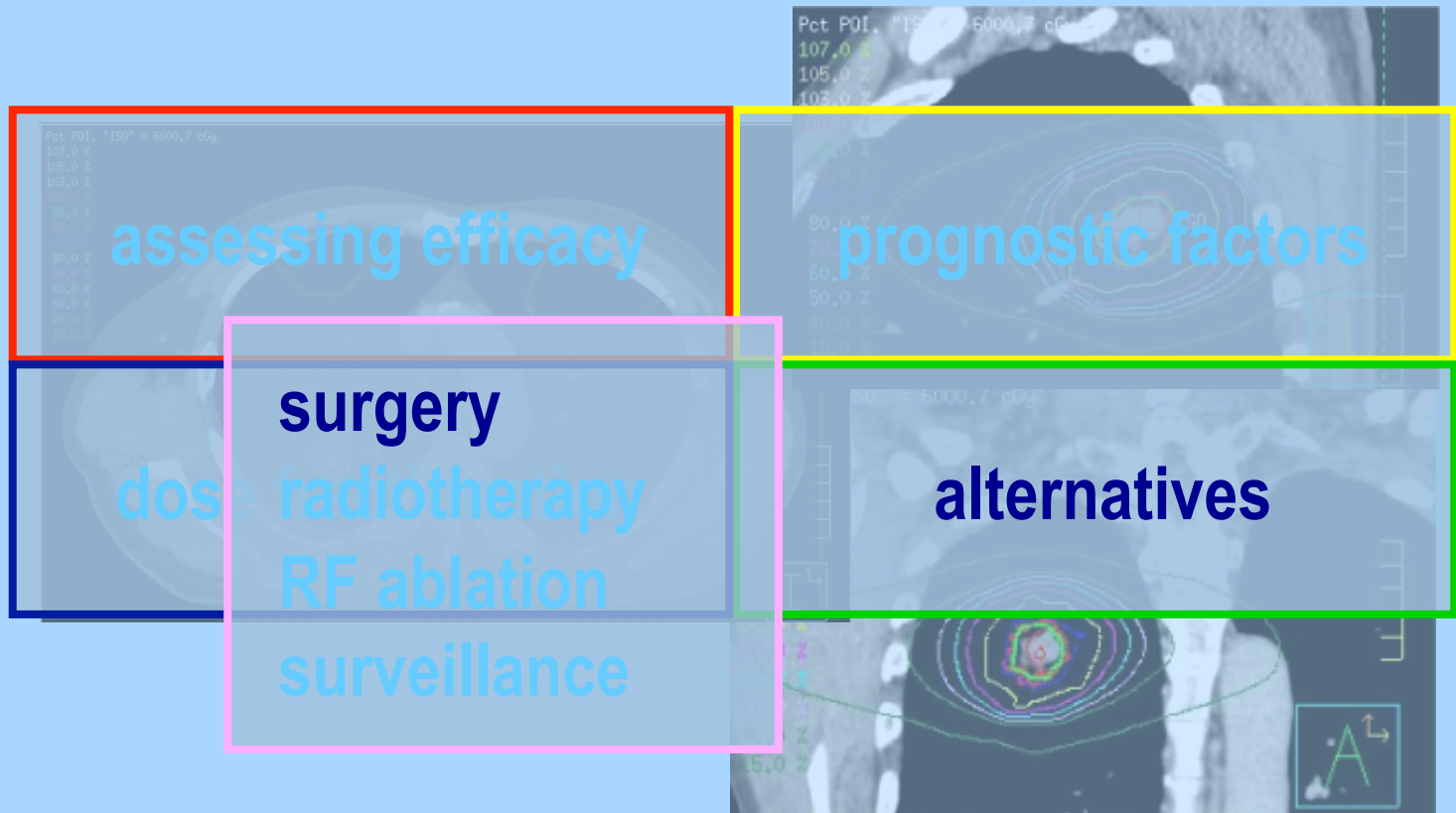
Surgery and SABR have similar outcome

Surgery is superior to SABR

Conventional fractionated RT is inferior to SABR

Radiofrequency ablation and SABR have similar outcome

SABR in localised NSCLC



Evaluation of outcome of local treatment in localised NSCLC

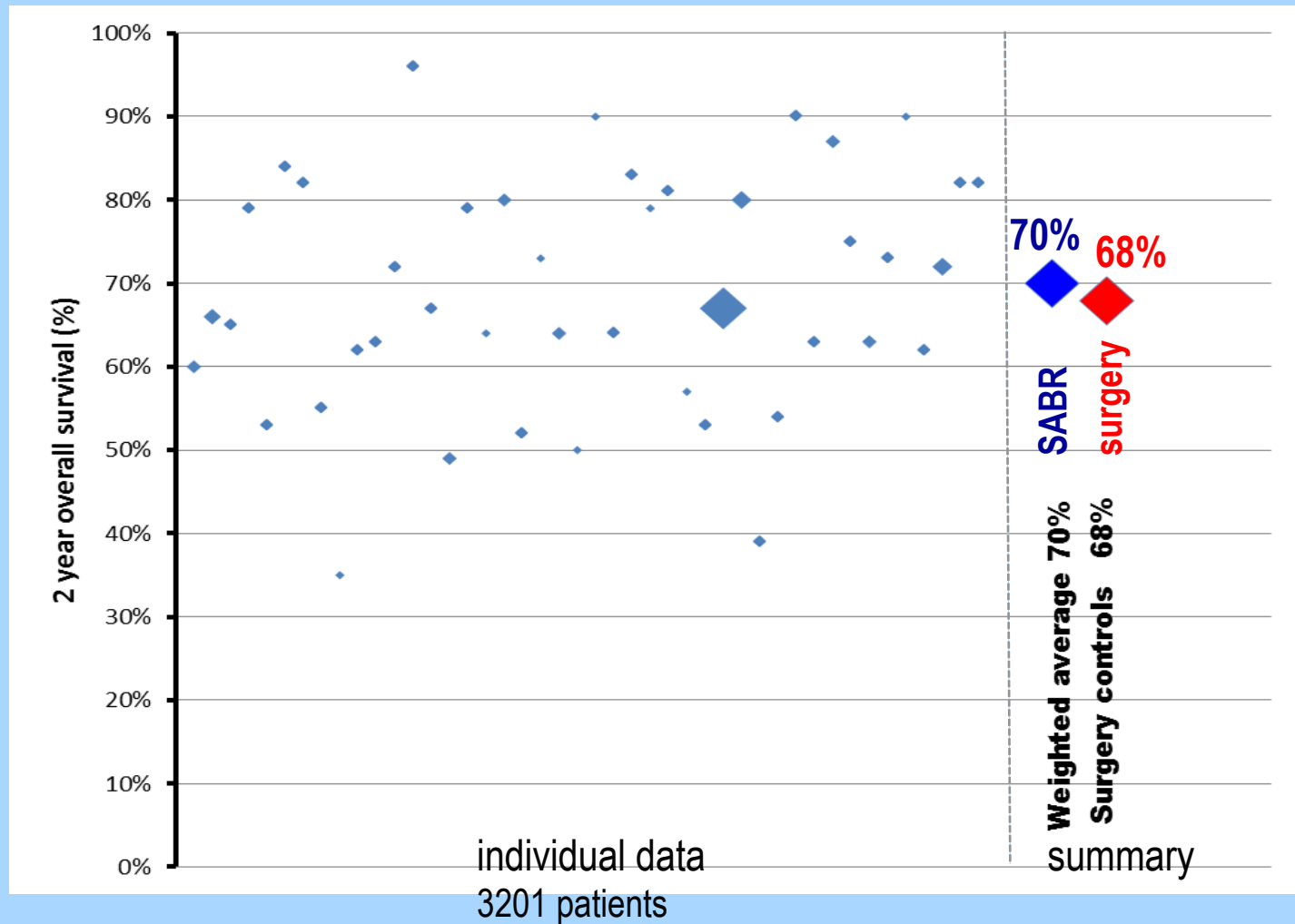
Meta-analysis of published results

January 2006 – June 2012

published SABR studies in early stage NSCLC	data on 2 yr survival & local control no. studies (patients)
systematic review	45 (3201)

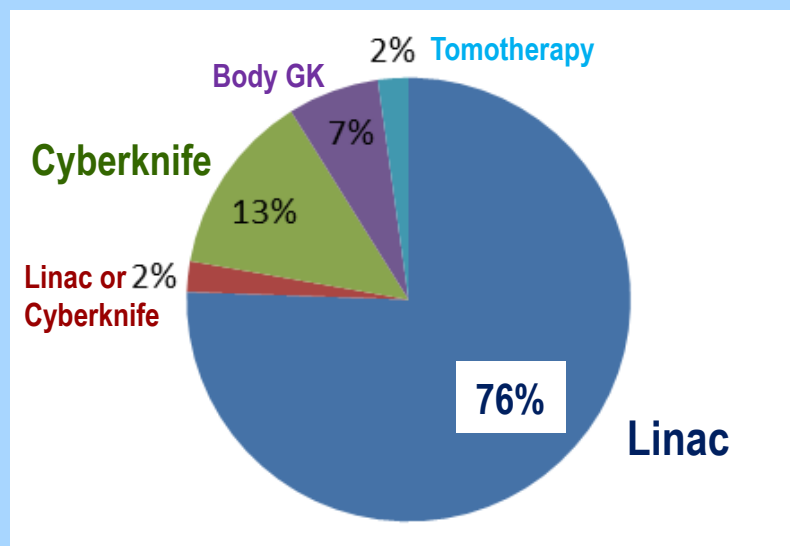
SABR for localised NSCLC

2 year survival

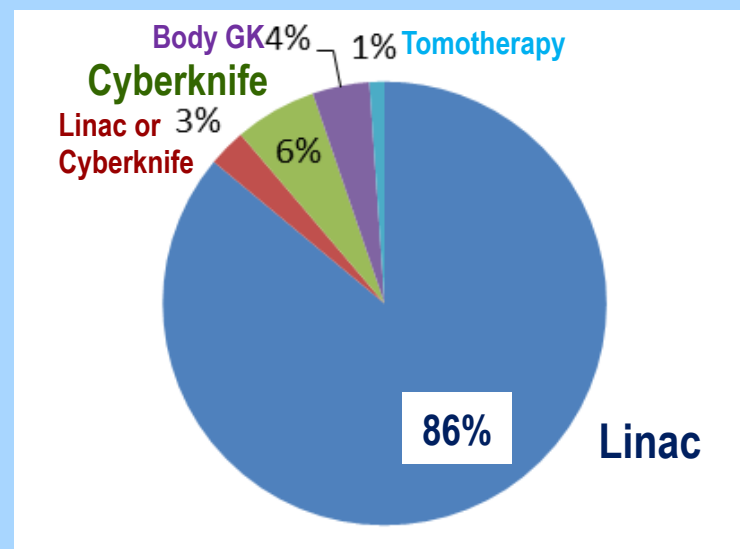


Meta-analysis of SABR for stage I NSCLC

Technology used for delivery of SABR



% reported studies



% patients

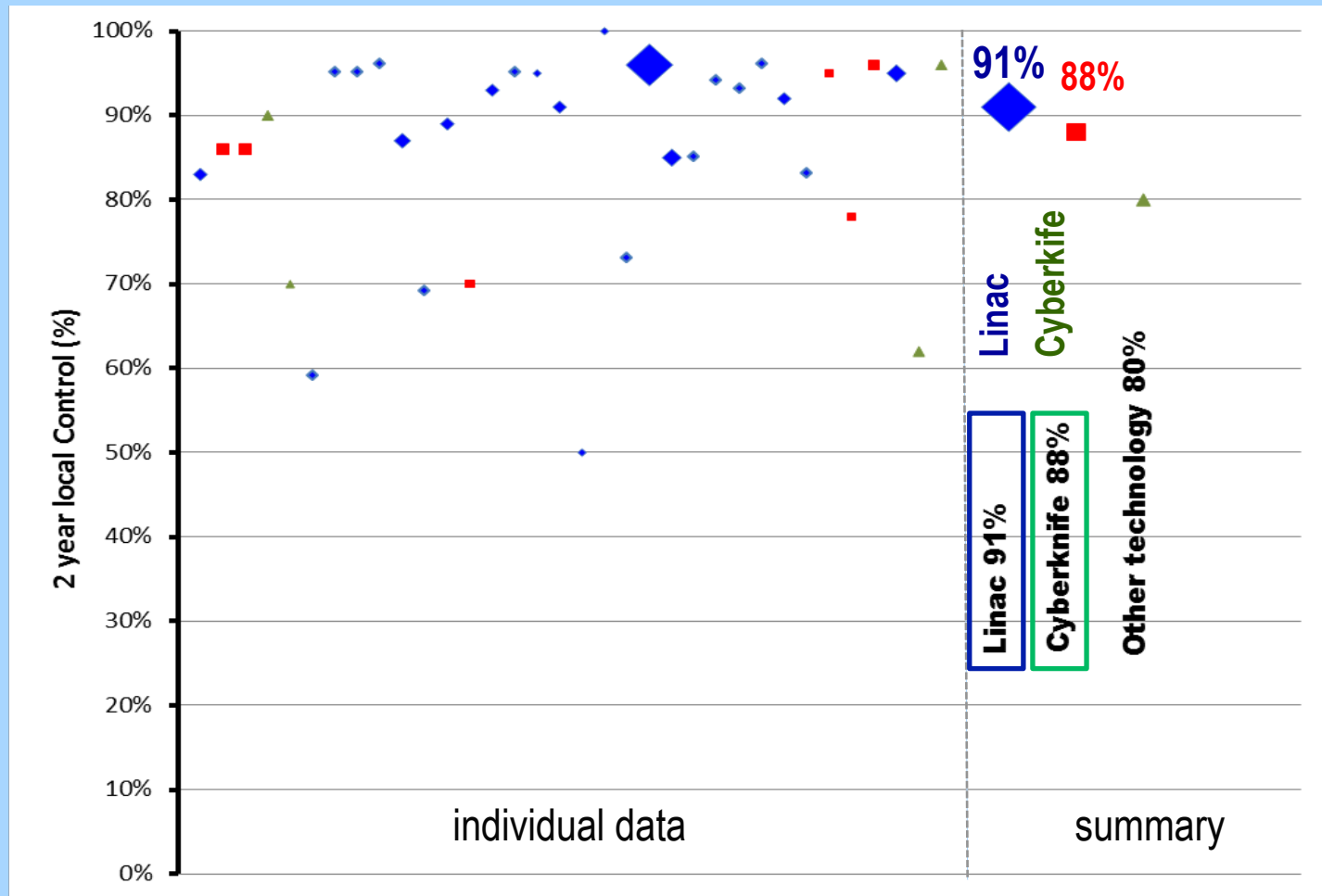
Linac – linear accelerator, GK – gamma knife, Cyberknife – robotic arm mounted small linac

Meta-analysis of SABR for stage I NSCLC

Solda, Lodge, Ashley, Whittington, Goldstraw & Brada 2013; Radiother Oncol, 109, 1-7

2 year local control

Technology used for delivery of SABR

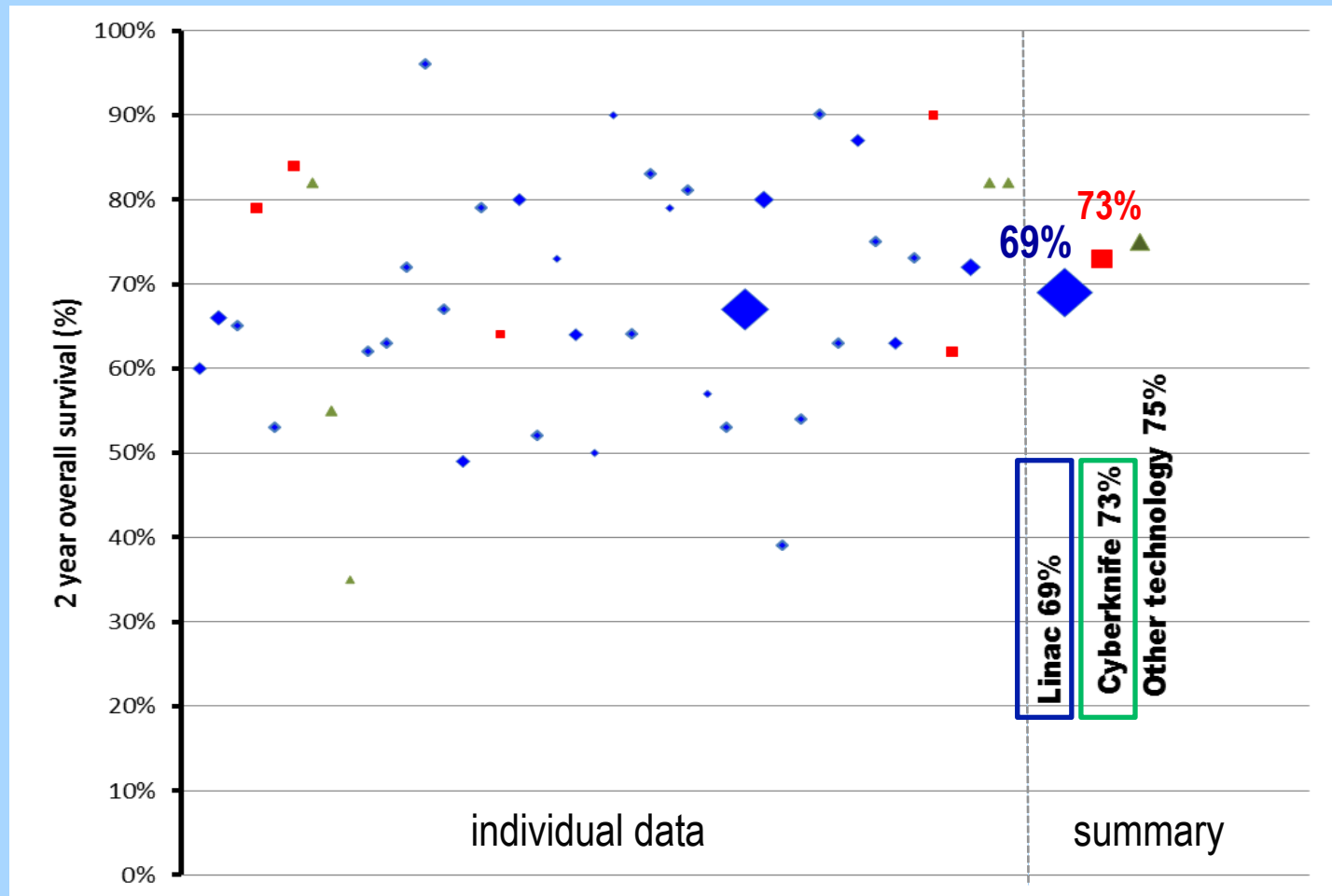


Linac – linear accelerator, Cyberknife – robotic arm mounted small linac

Meta-analysis of SABR for stage I NSCLC

2 year survival

Technology used for delivery of SABR



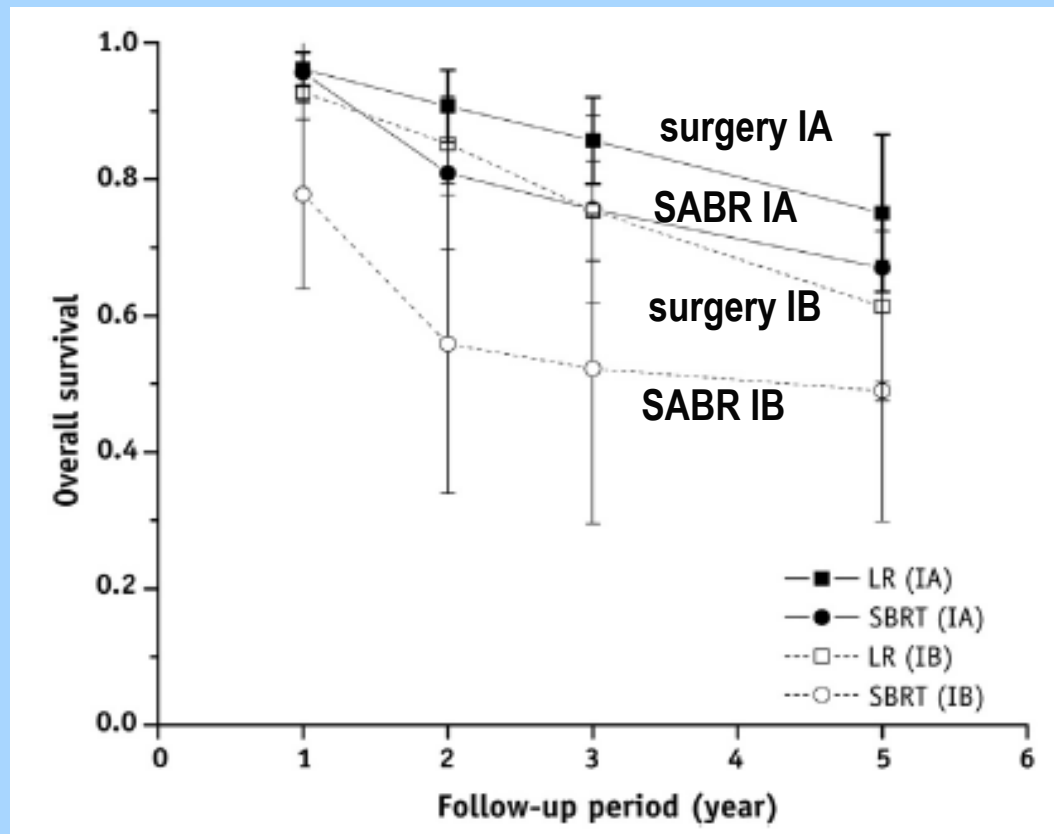
Linac – linear accelerator, Cyberknife – robotic arm mounted small linac

Meta-analysis of SABR for stage I NSCLC

meta-analysis of published studies

40 SABR studies (4850 pts) and 23 surgery studies (7071 patients)

survival

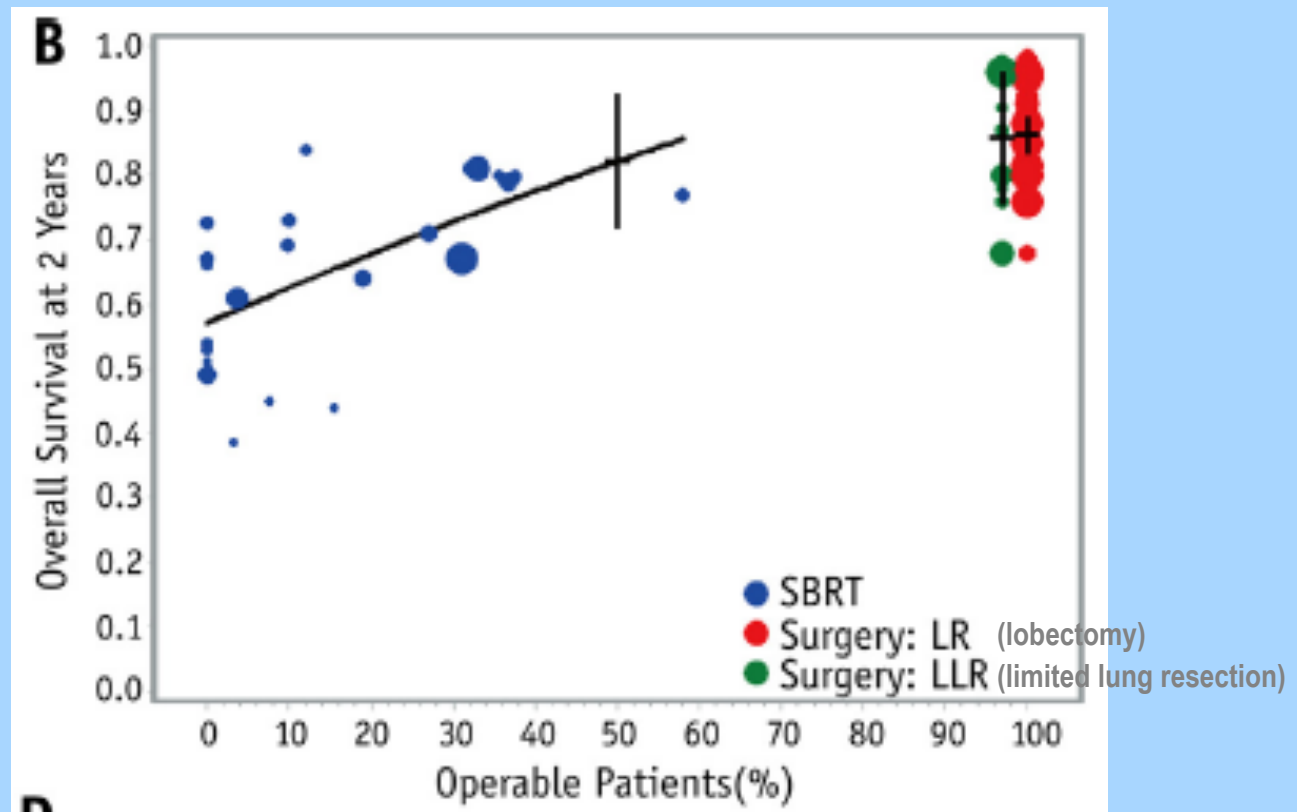


Comparison of surgery & SABR in stage I NSCLC

meta-analysis of published studies

40 SABR studies (4850 pts) and 23 surgery studies (7071 patients)

survival and operability

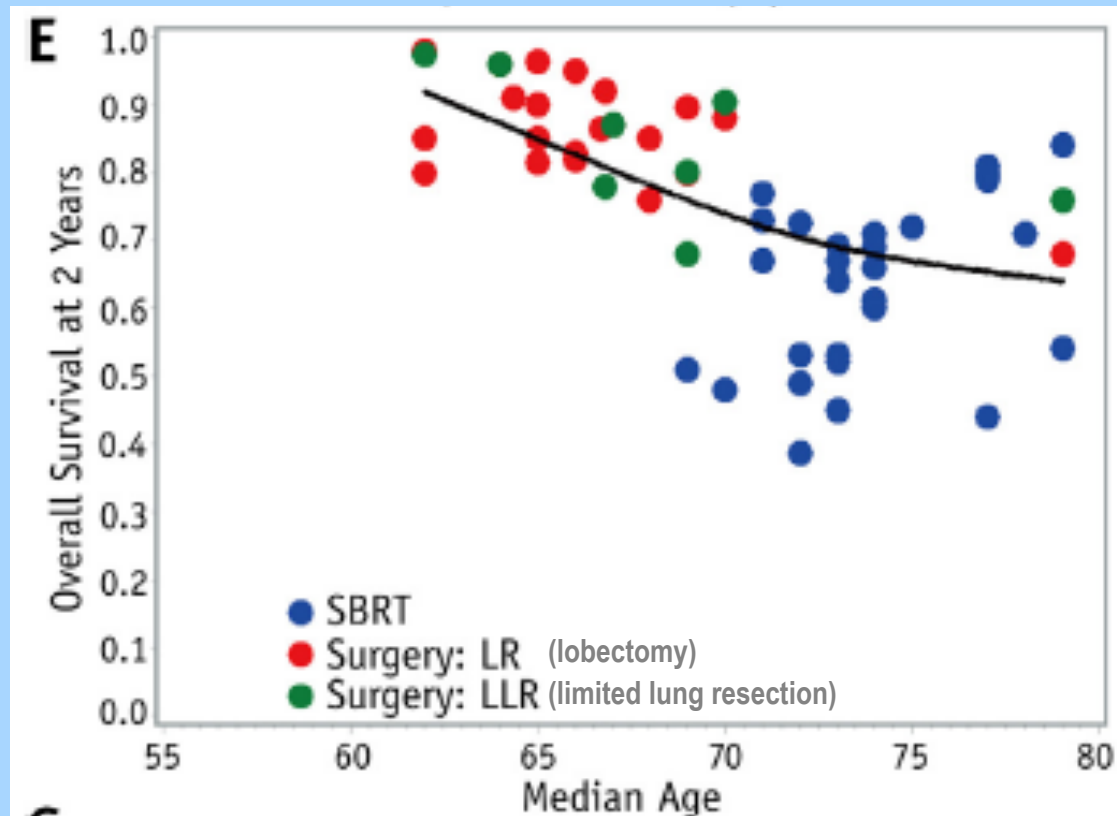


Comparison of surgery & SABR in stage I NSCLC

meta-analysis of published studies

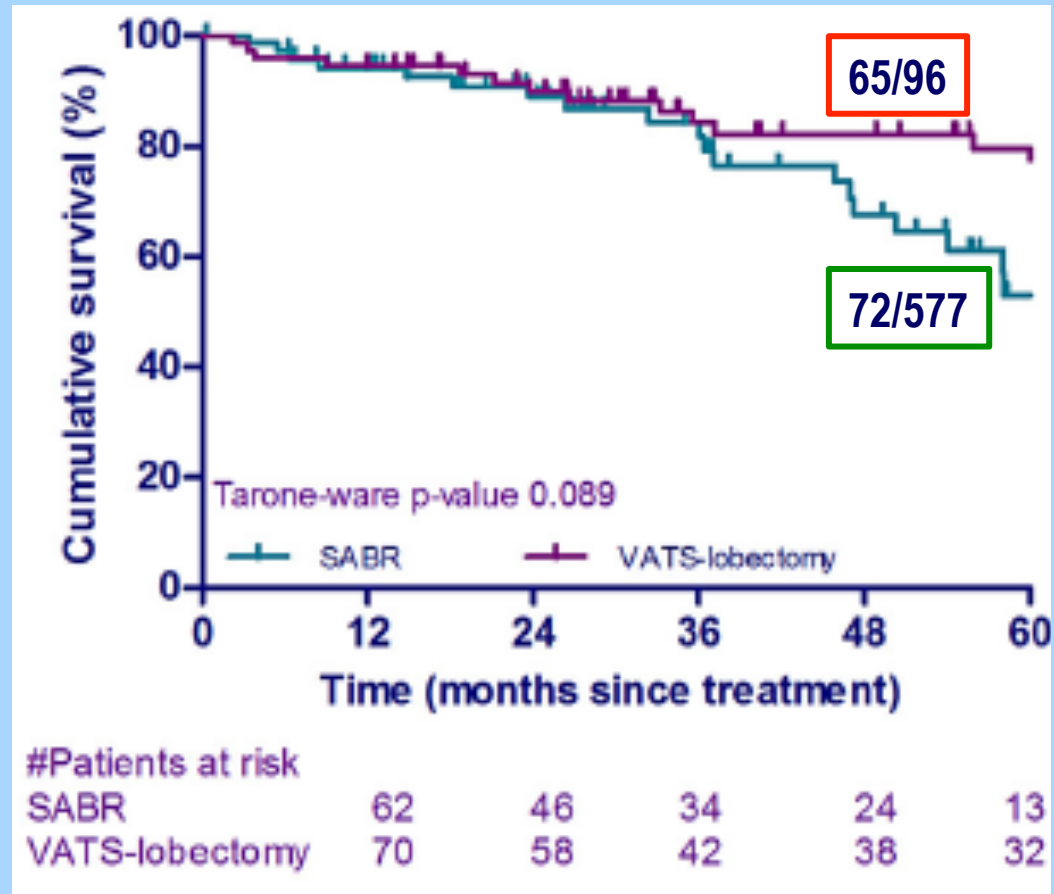
40 SABR studies (4850 pts) and 23 surgery studies (7071 patients)

survival and age



Comparison of surgery & SABR in stage I NSCLC

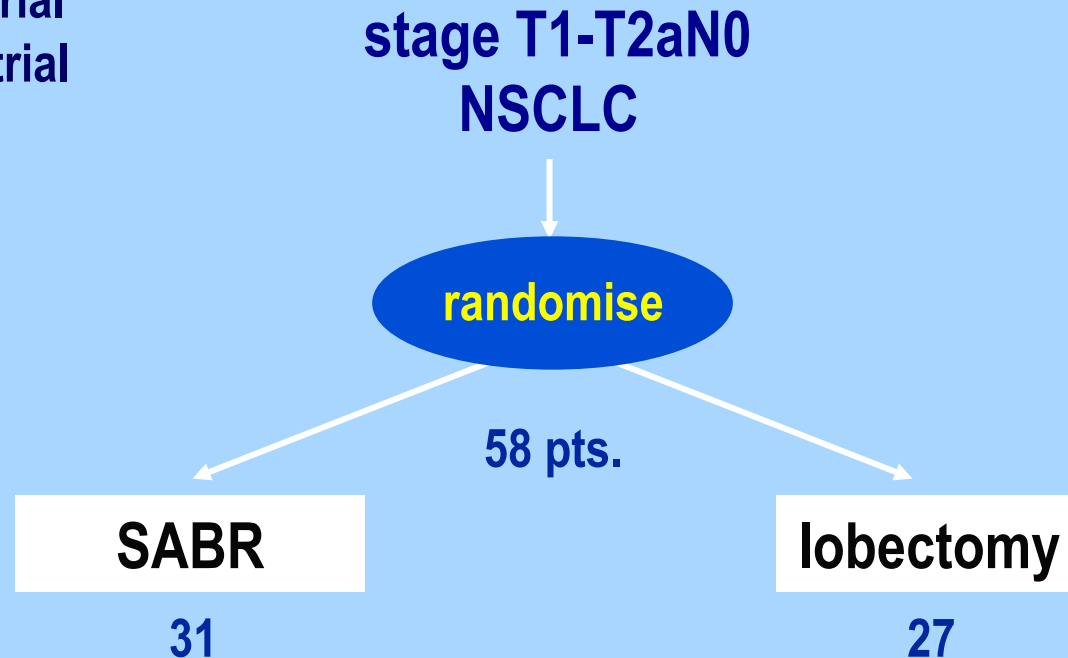
propensity matching VU Amsterdam and EU Rotterdam



Comparison of surgery & SABR in stage I NSCLC

Operable NSCLC

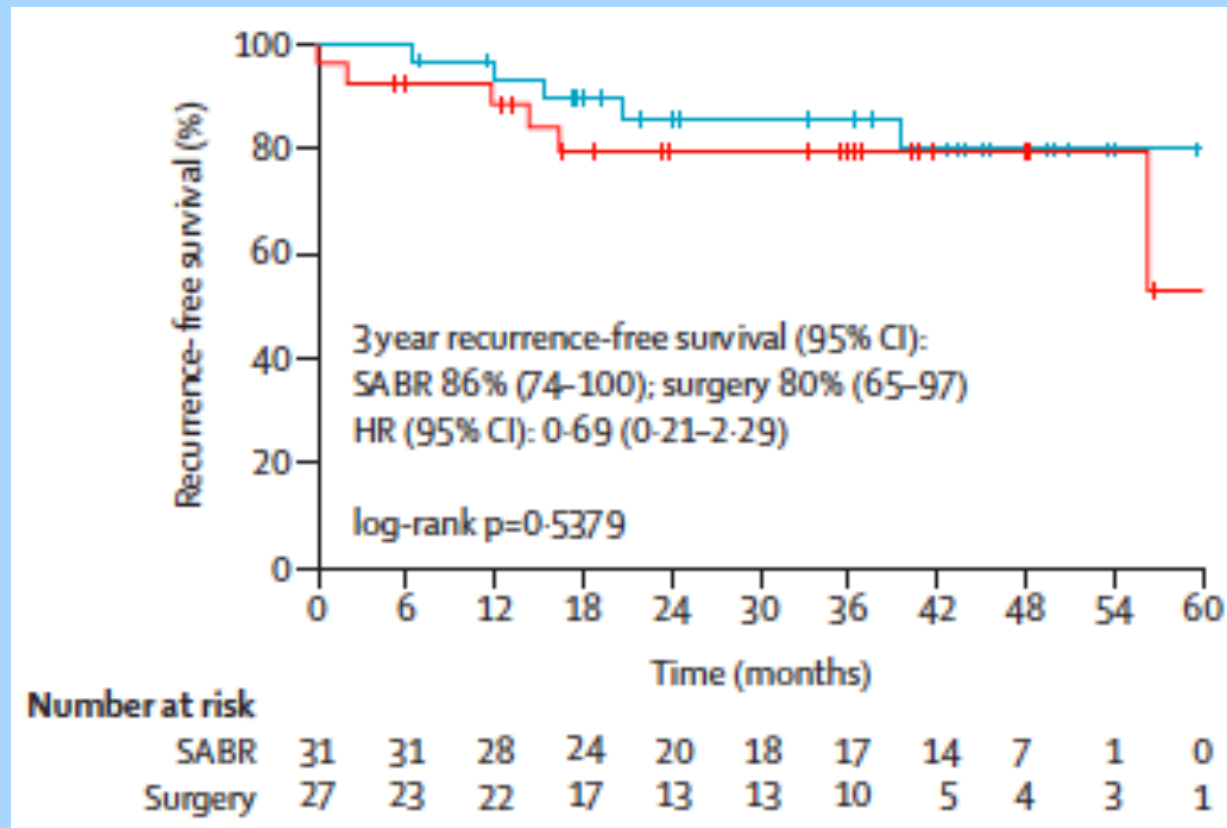
pooled analysis of
STARS trial
ROSEL trial



Comparison of surgery & SABR in stage I NSCLC

Operable NSCLC pooled analysis of STARS & ROSEL trials

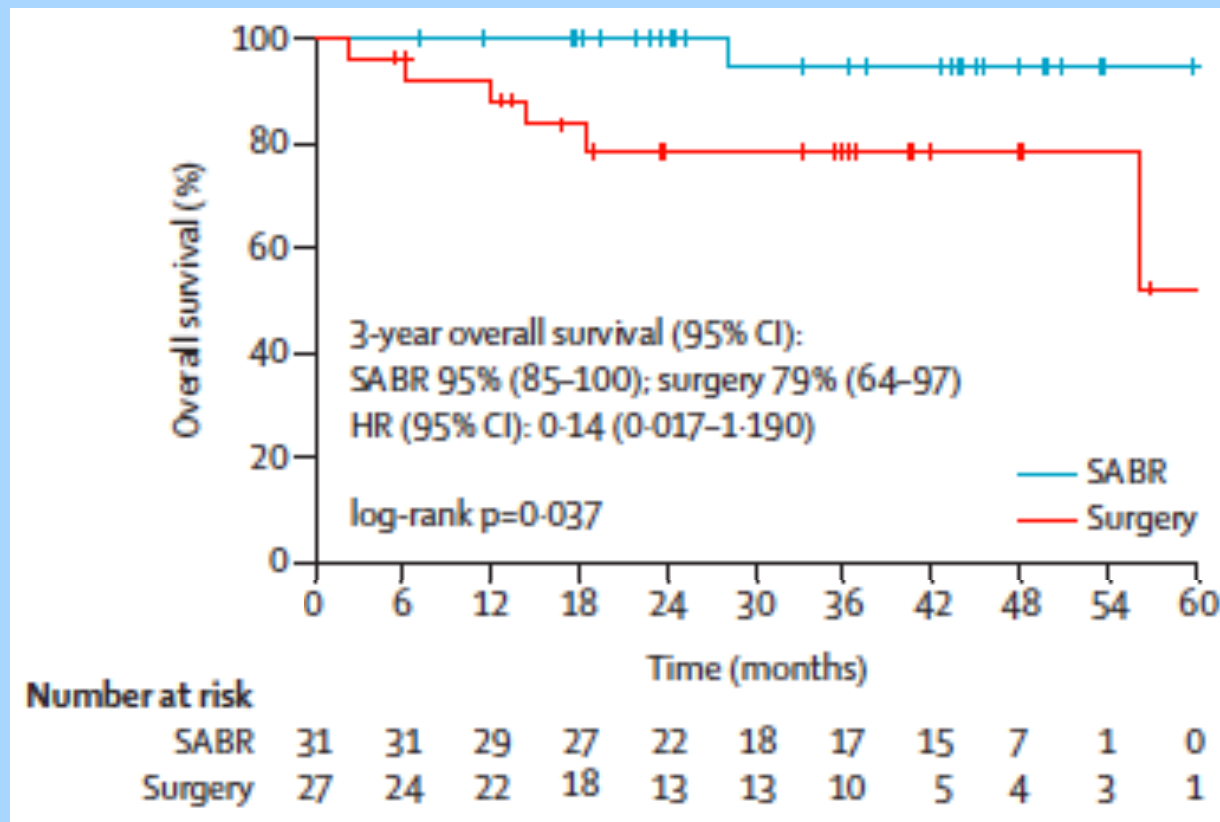
Recurrence-free survival



Comparison of surgery & SABR in stage I NSCLC

Operable NSCLC pooled analysis of STARS & ROSEL trials

Survival

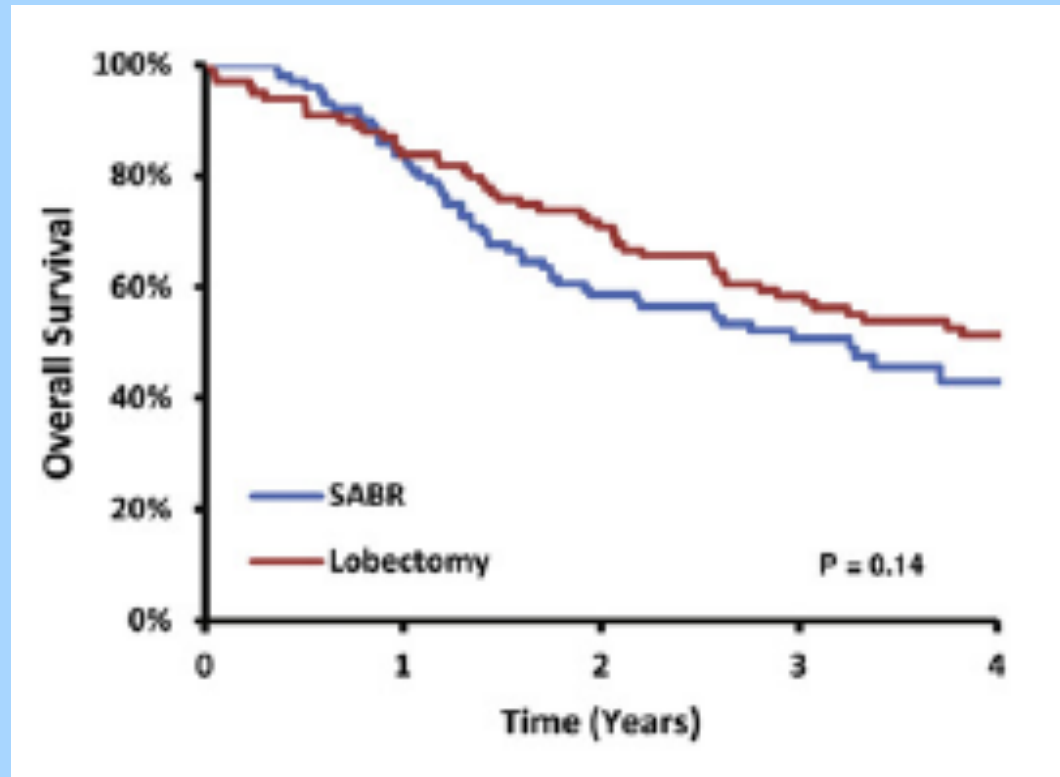


Comparison of surgery & SABR in stage I NSCLC

SEERS - Medicare 2001 – 07

10,923 patients with stage IA & IB NSCLC, aged >65

propensity matched – SABR vs lobectomy

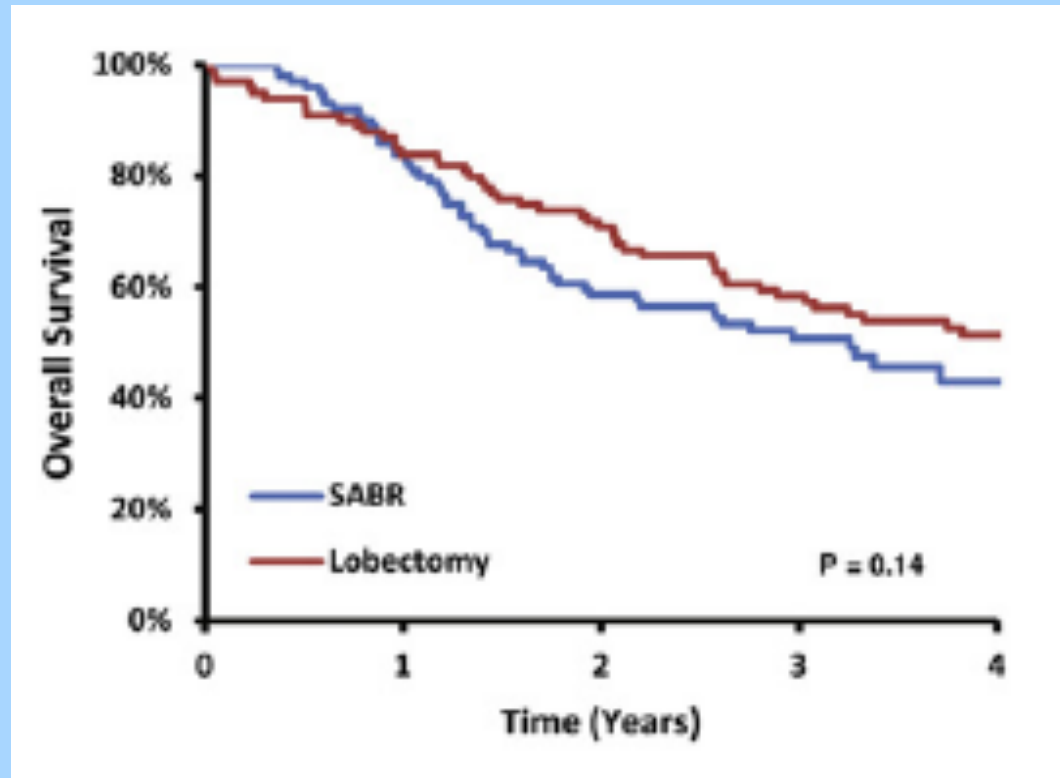


Comparison of surgery & SABR in stage I NSCLC

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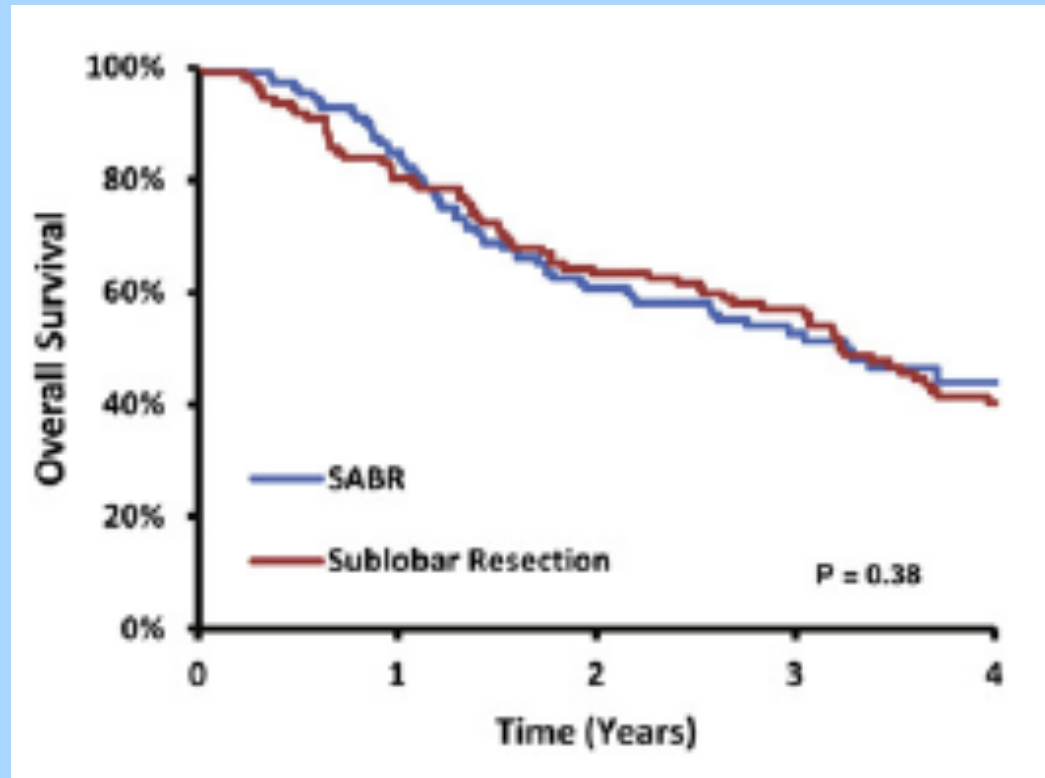


Comparison of surgery & SABR in stage I NSCLC

SEERS - Medicare 2001 – 07

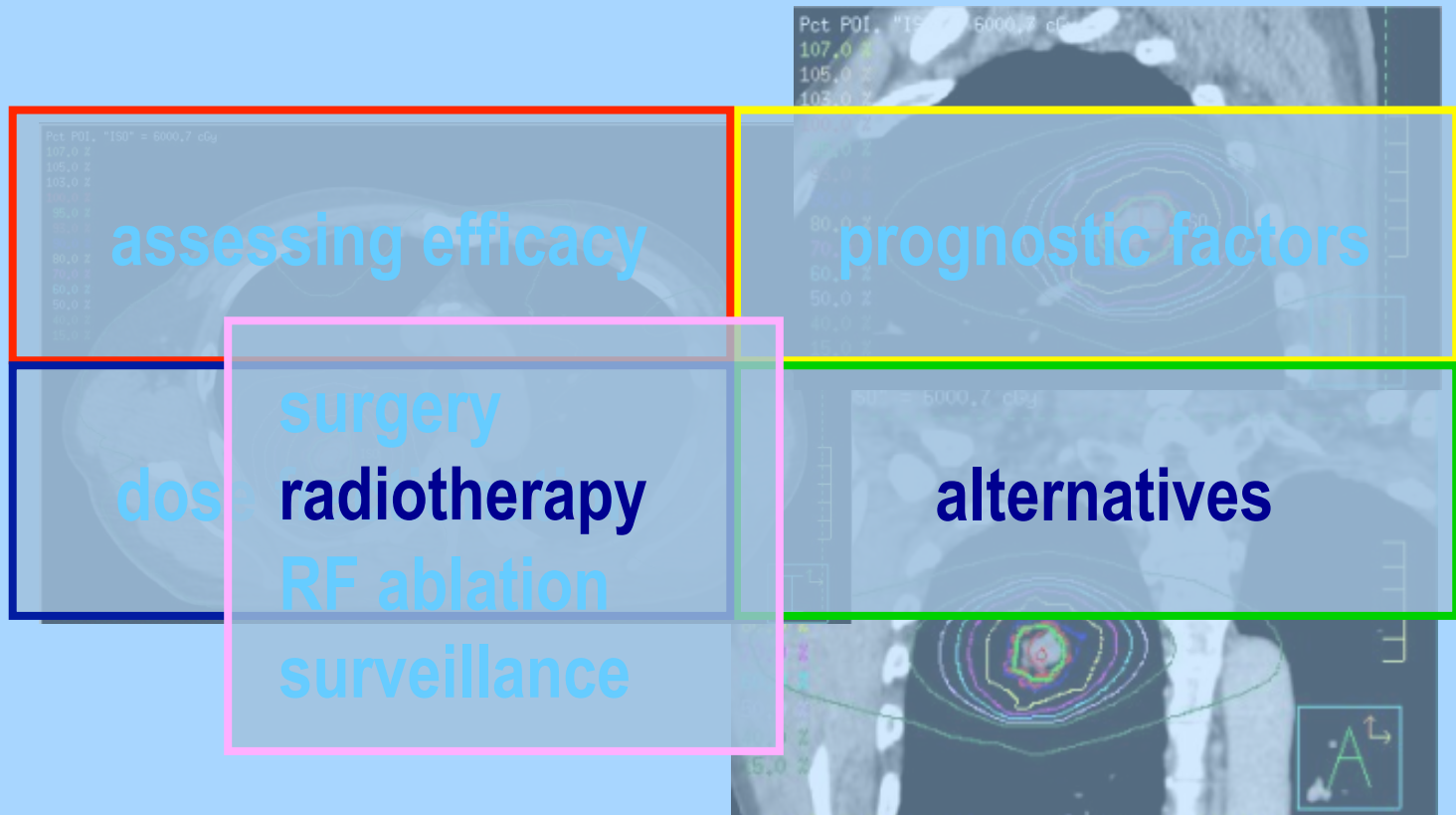
10,923 patients with stage IA & IB NSCLC, aged >65

propensity matched – SABR vs sublobar resection



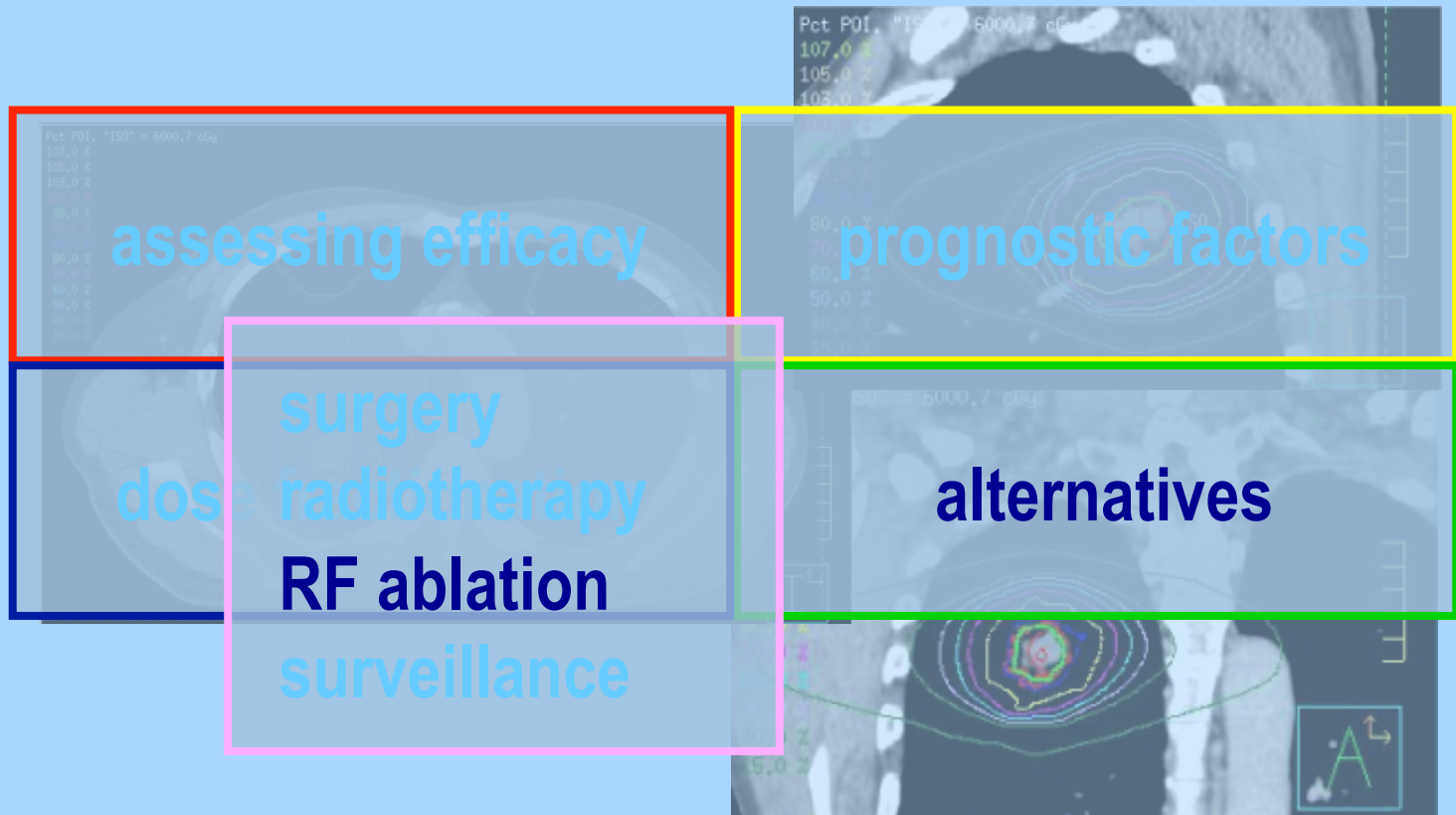
Comparison of surgery & SABR in stage I NSCLC

SABR in localised NSCLC



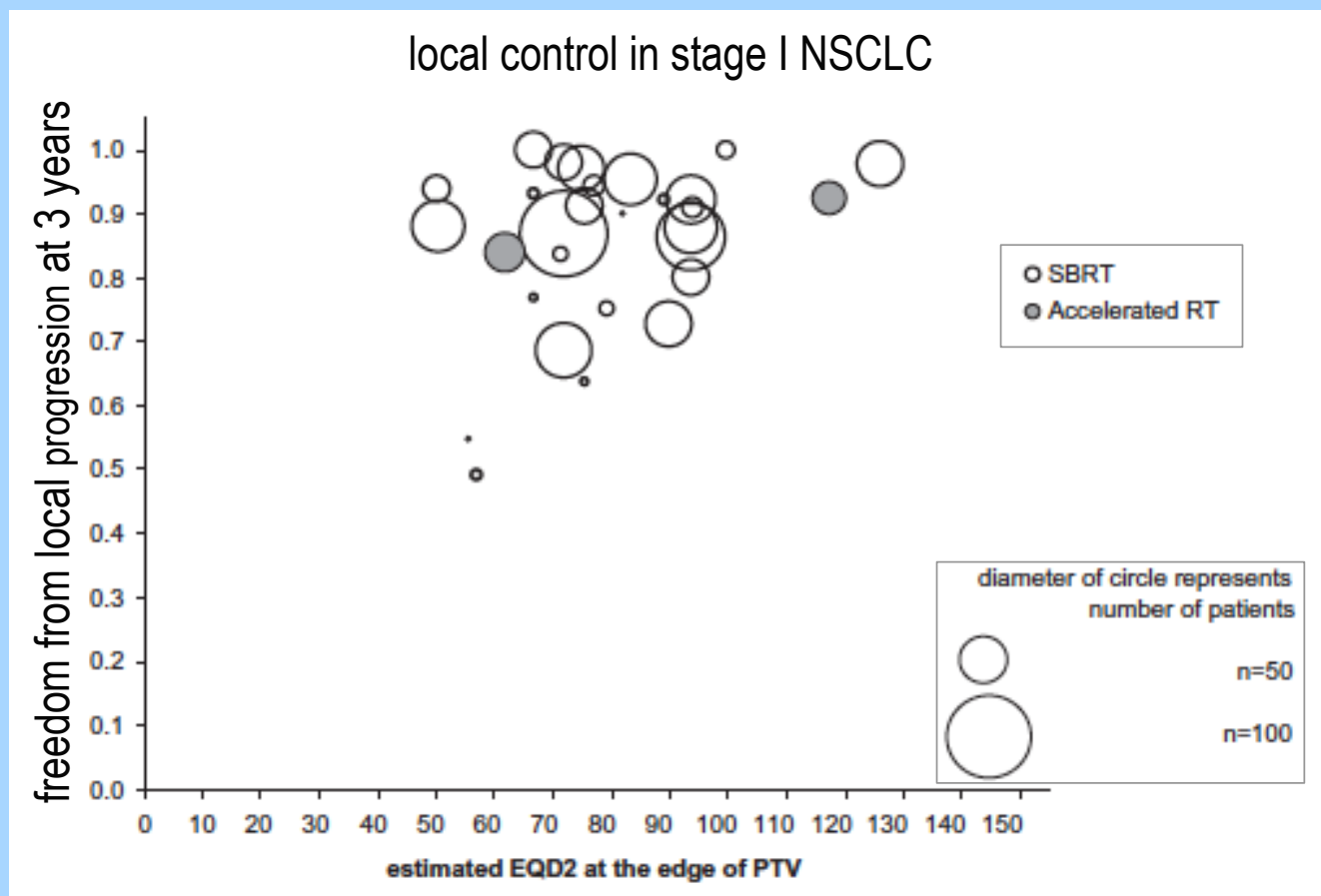
Evaluation of outcome of local treatment in localised NSCLC

SABR in localised NSCLC



Evaluation of outcome of local treatment in localised NSCLC

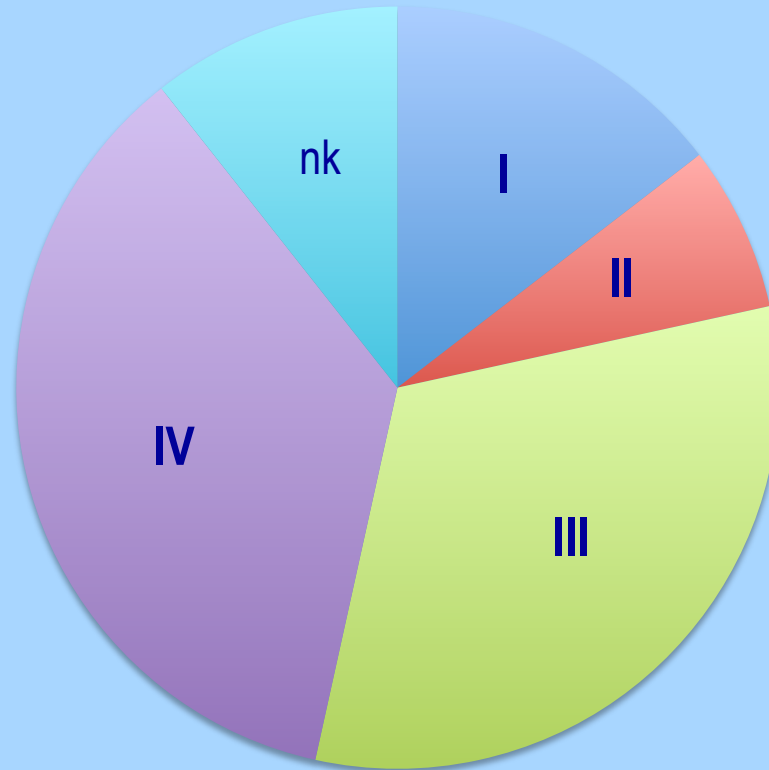
Dose comparison of SABR & accelerated RT



Local control vs dose in SABR

Stage distribution of lung cancer

CR UK cancer statistics - England & Wales 2012



Lung cancer in England and Wales

SABR in localised NSCLC



assessing efficacy



prognostic factors



dose fractionation



alternatives

Evaluation of outcome of local treatment in localised NSCLC

Evaluation of outcome in lung SABR

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