Challenges, opportunities & limitations of **new and emerging RT technologies**

Michael Brada

IRPA 13 Glasgow

15 May 2012

Particle RT

IGRT

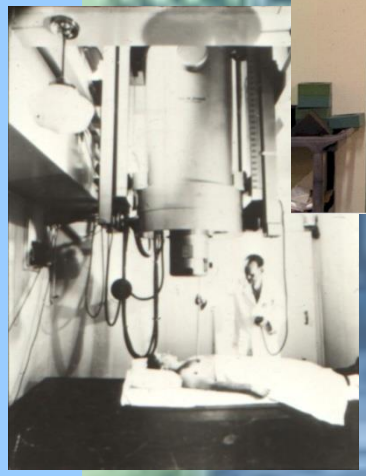
IMRT

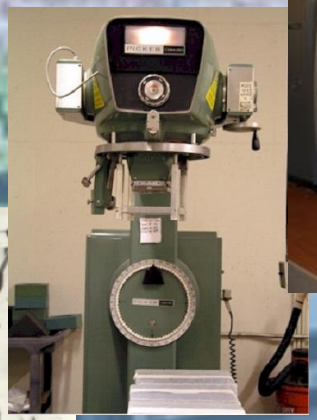
SRT

CRT

RT

DXT





Gamma knife

Tomotherapy

Novalis

Cyberknife

Protons

.....

New radiotherapy technology

Modern technology of radiotherapy delivery

refinements of conformal radiotherapy

conformality

- photons **(IMRT)**
- protons

time factor (4D radiotherapy)

- intrafraction patient and tumour motion
- interfraction changes in tumour & normal tissue

quality assurance

- imaging closer to treatment delivery **(IGRT)**

New and emerging radiotherapy technologies

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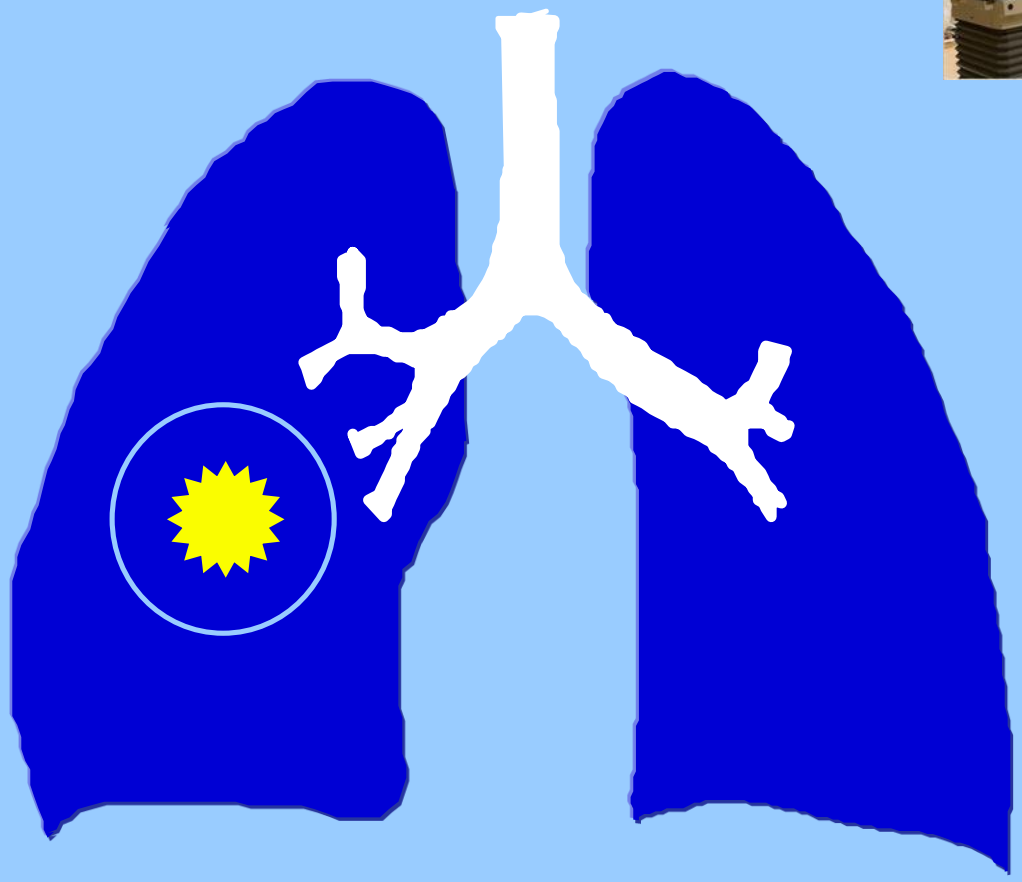
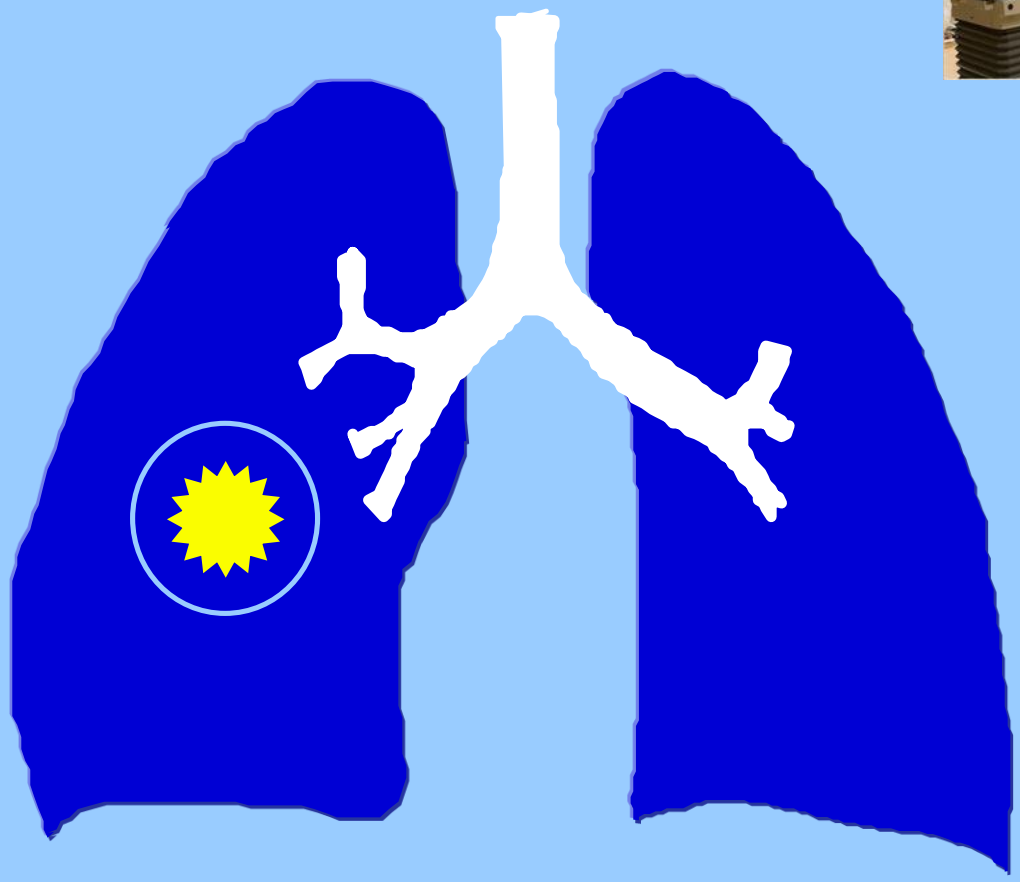
New and emerging radiotherapy technologies

Improvement in therapeutic ratio



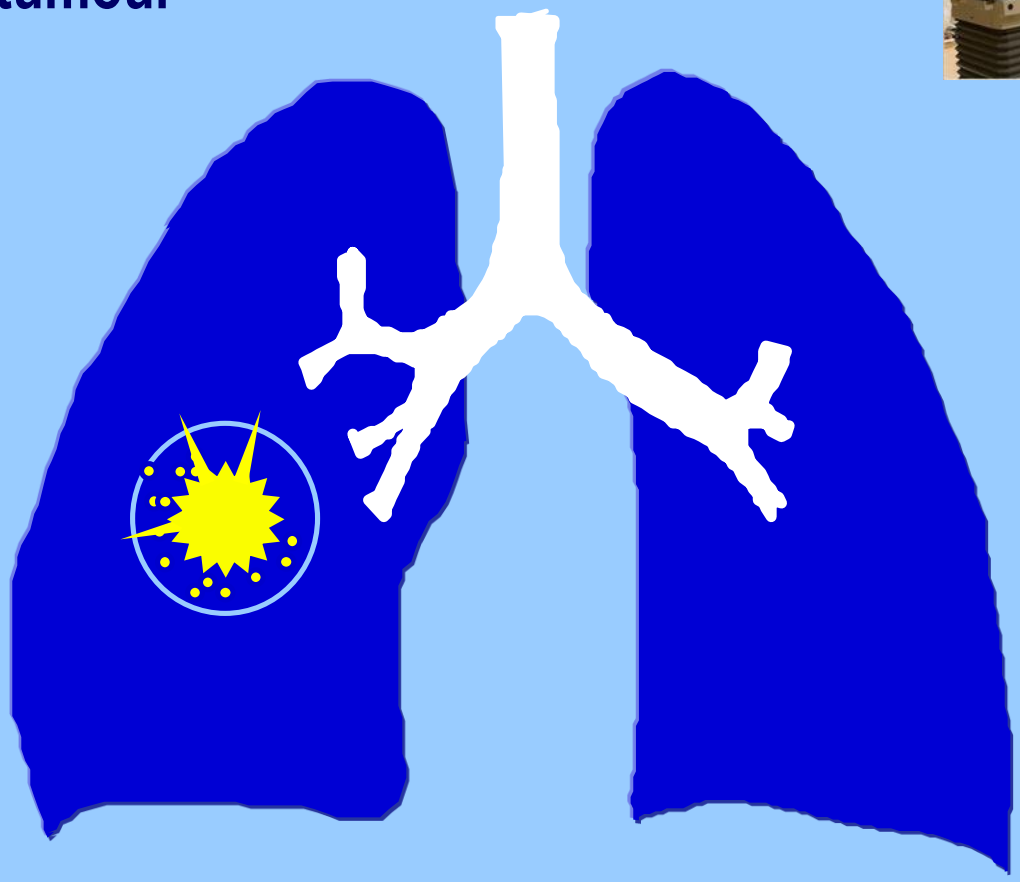
Improving conformality

Improvement in therapeutic ratio



Improving conformality

Improvement in therapeutic ratio
Missing tumour



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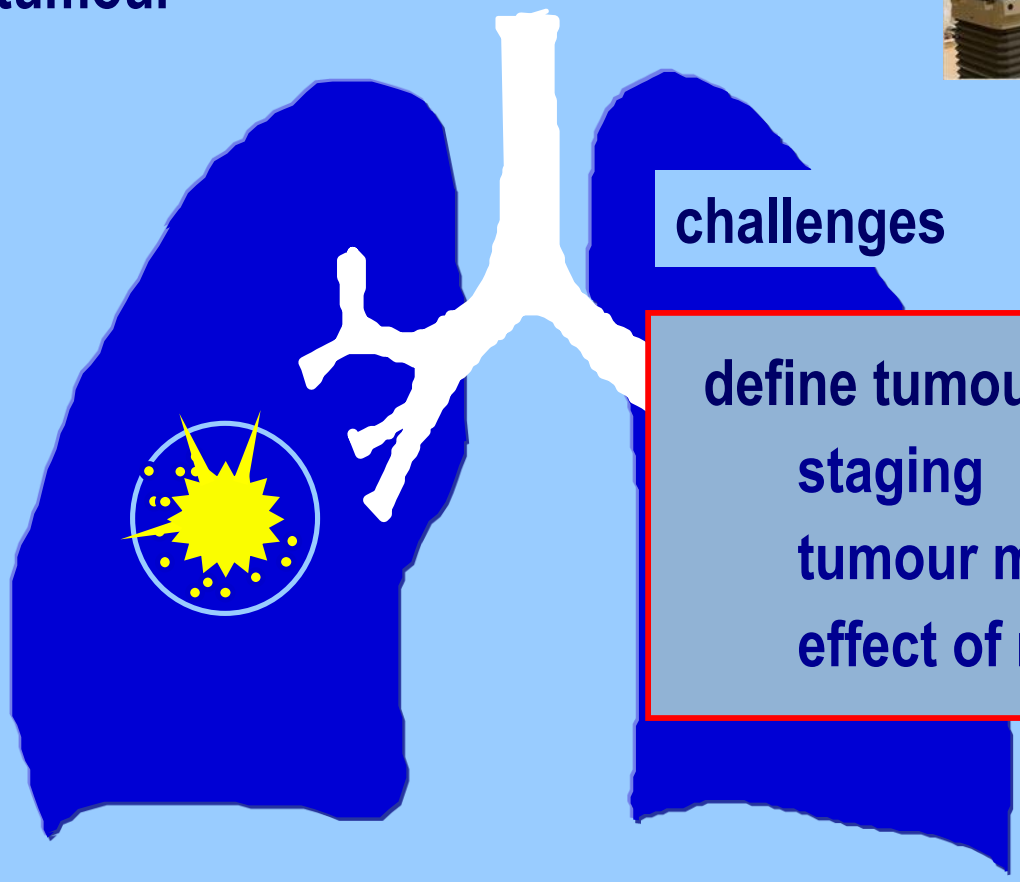


challenges

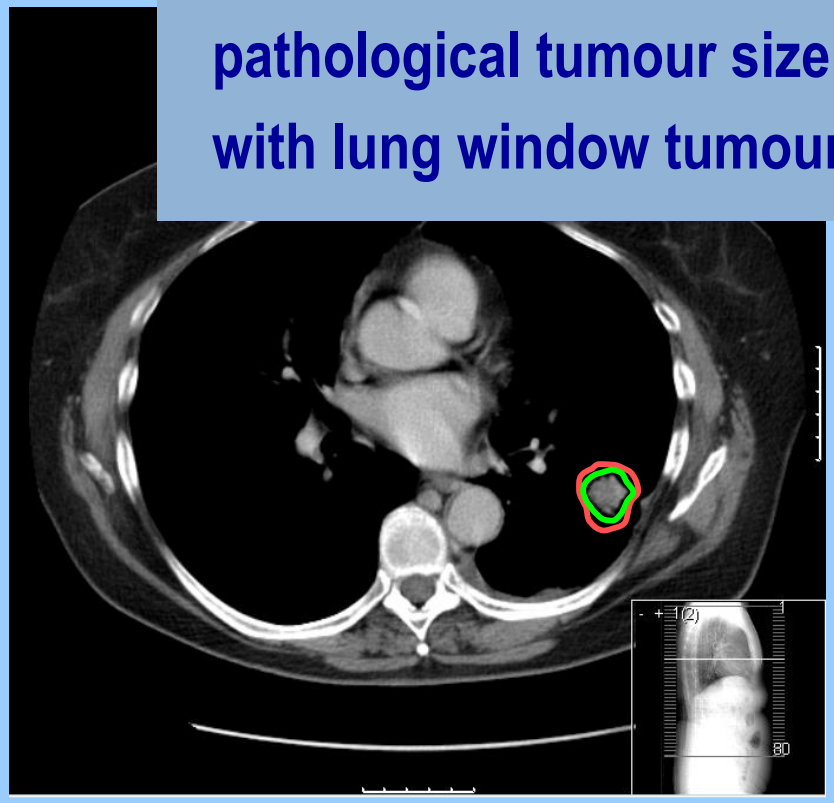
define tumour extent

- staging
- tumour margin
- effect of motion

Improving conformality

CT imaging

pathological tumour size correlated better with lung window tumour size

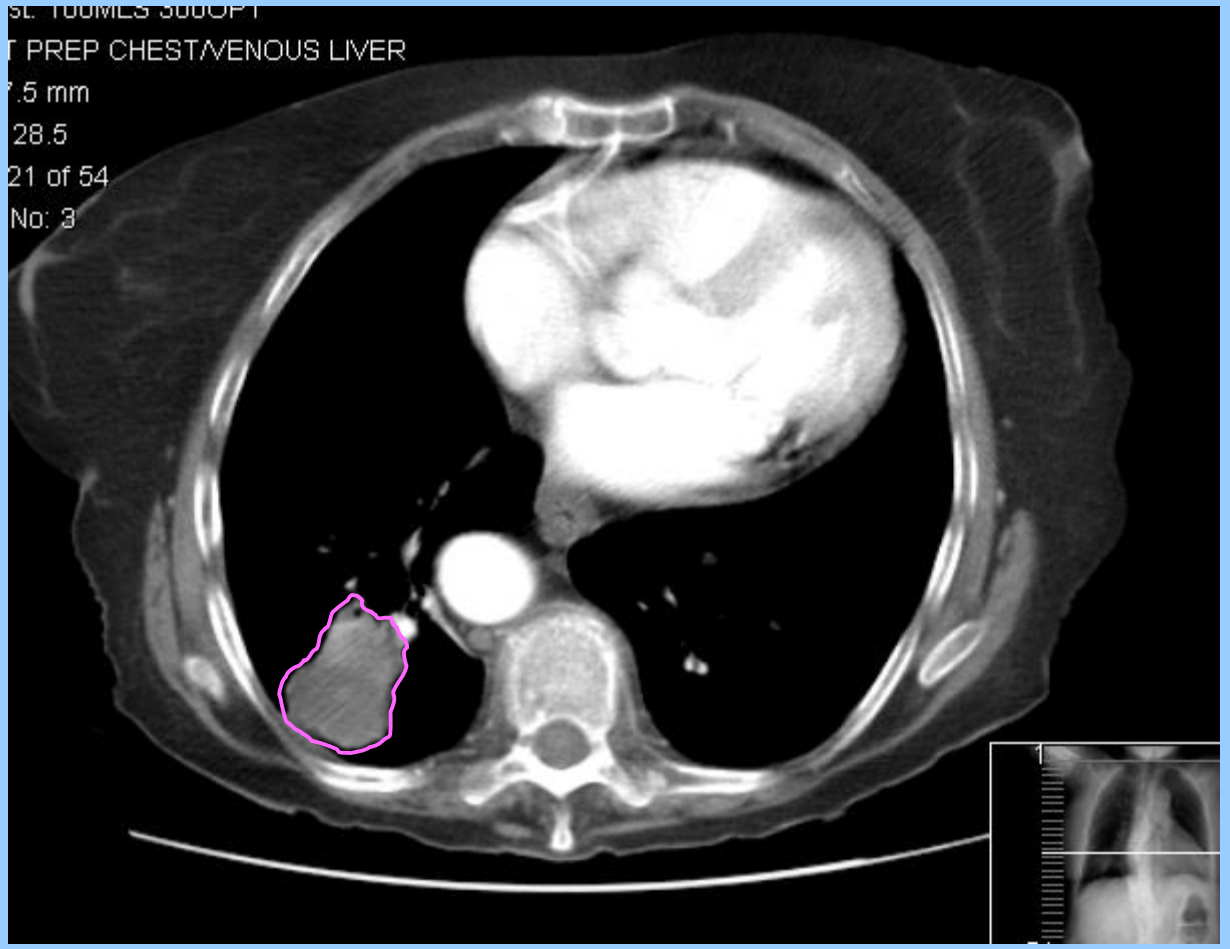


35 patients with T1N0 adenoca
wedge biopsy → lobectomy

Delineation of primary tumour

Grills et al 2007

CT- PET



Delineation of primary tumour

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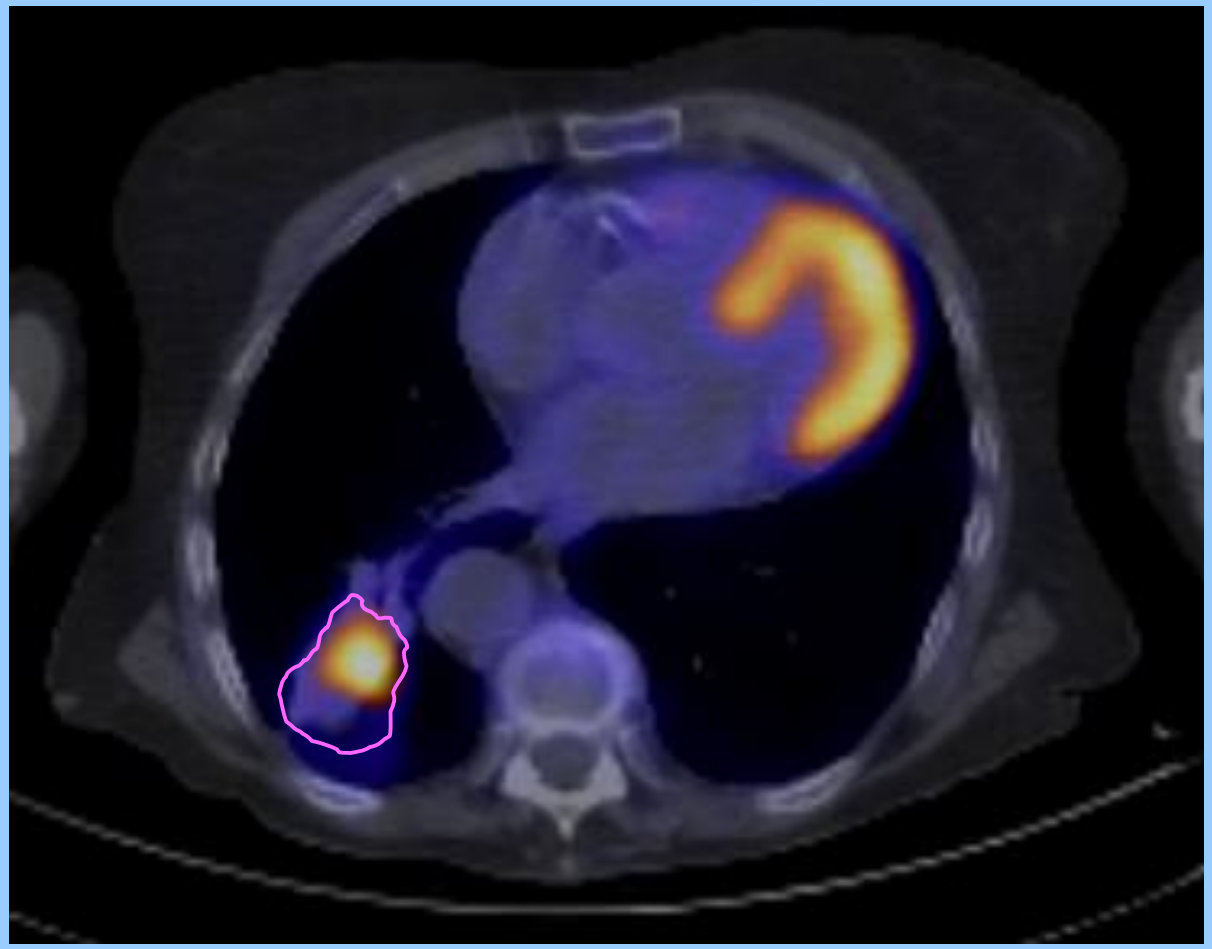

Delineation of primary tumour

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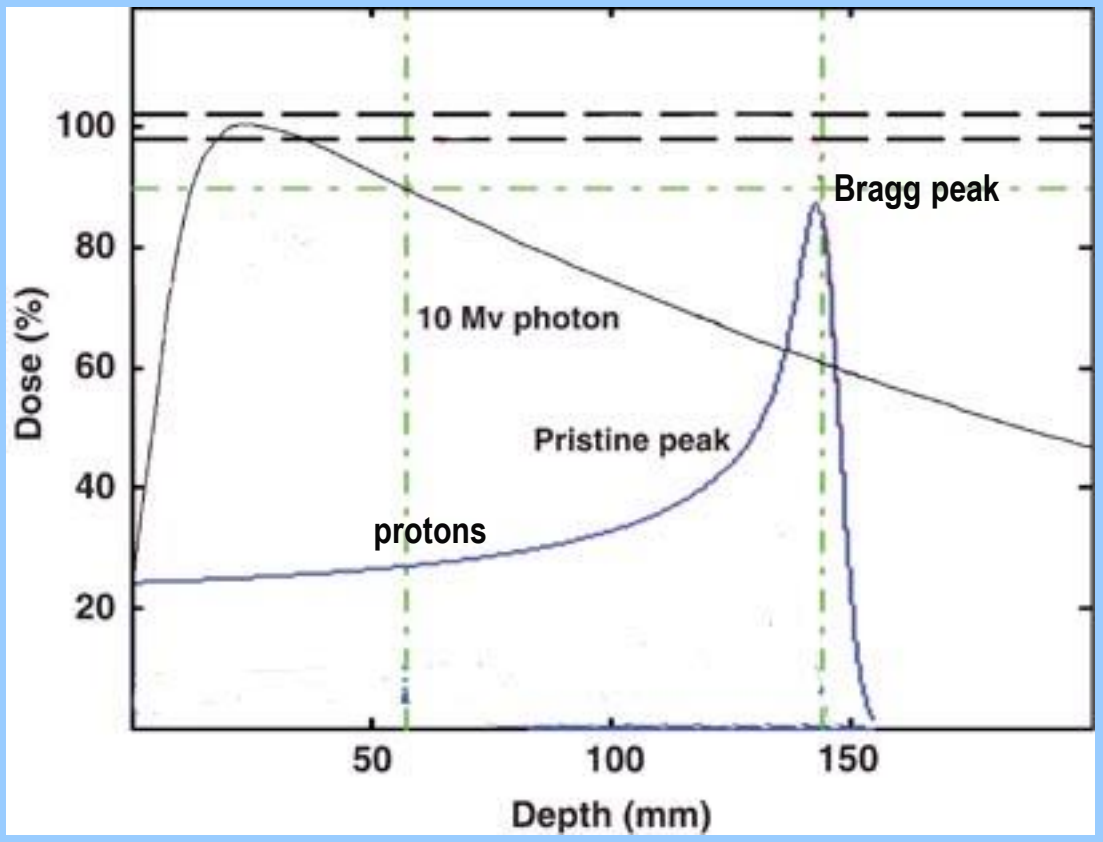
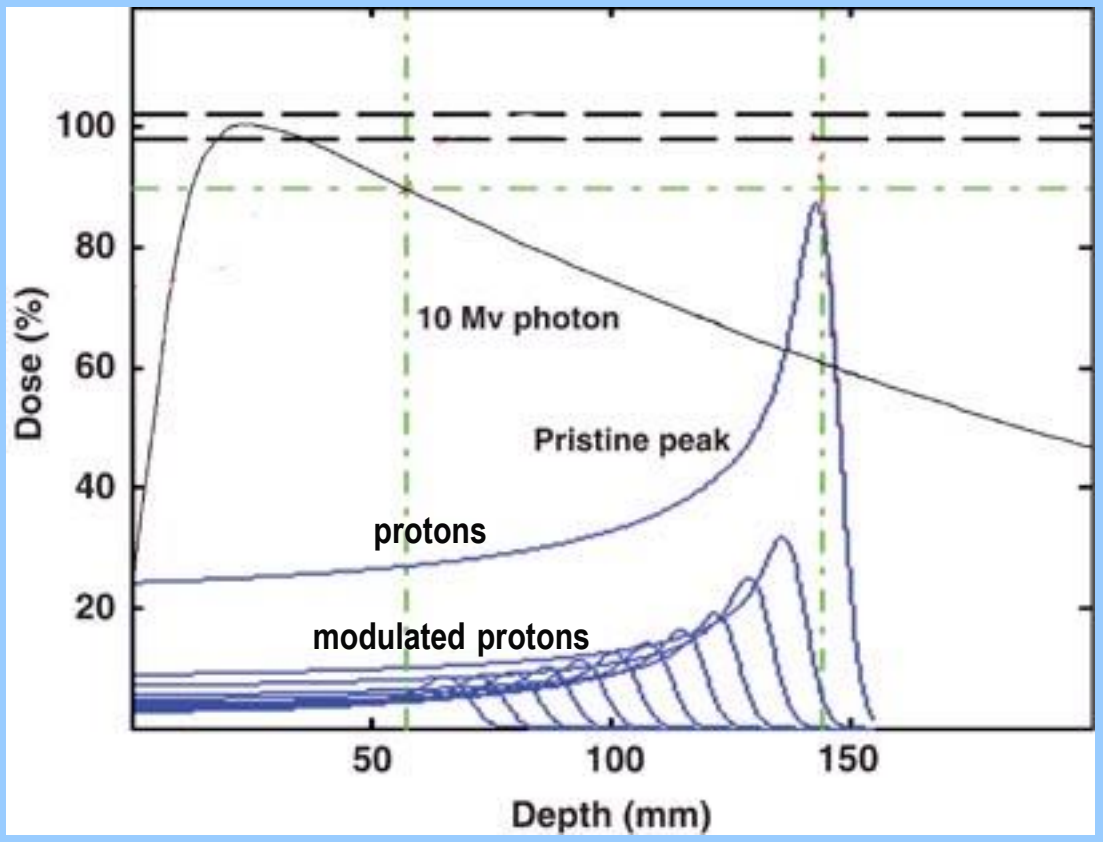
New and emerging radiotherapy technologies



Depth dose distribution of photons and protons



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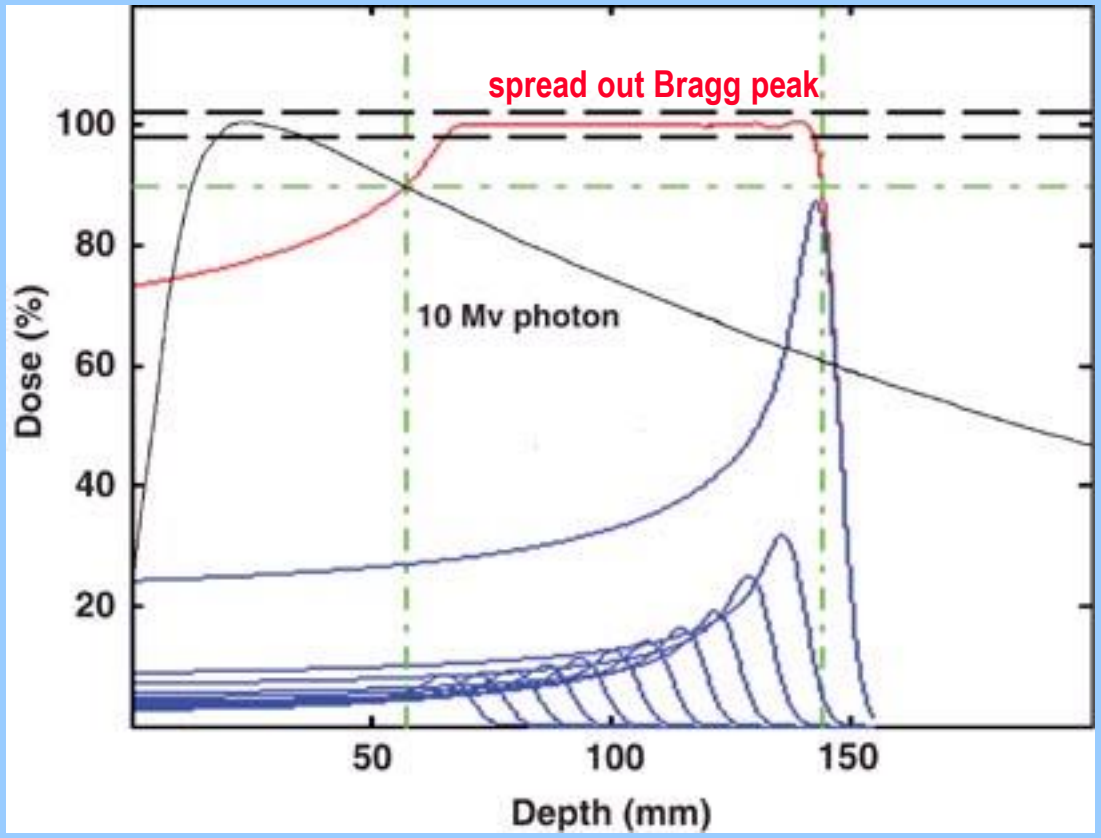

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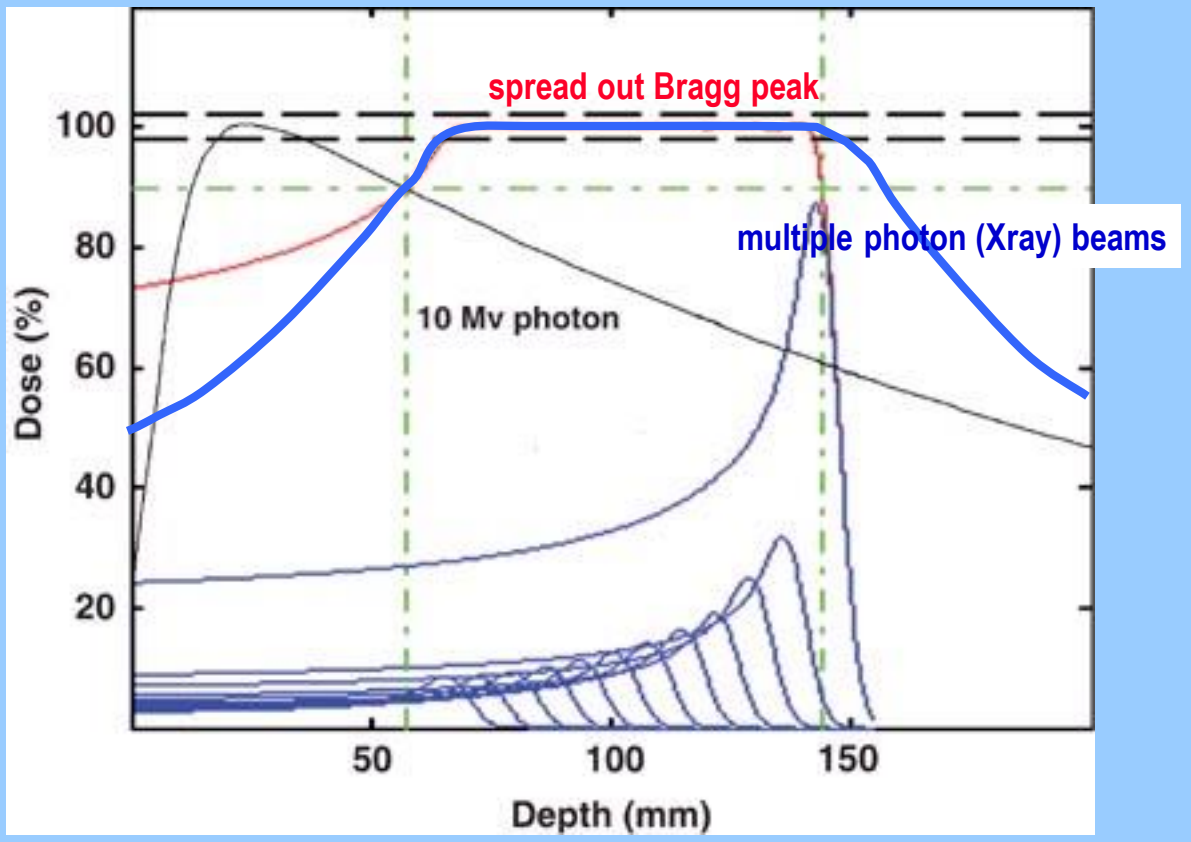
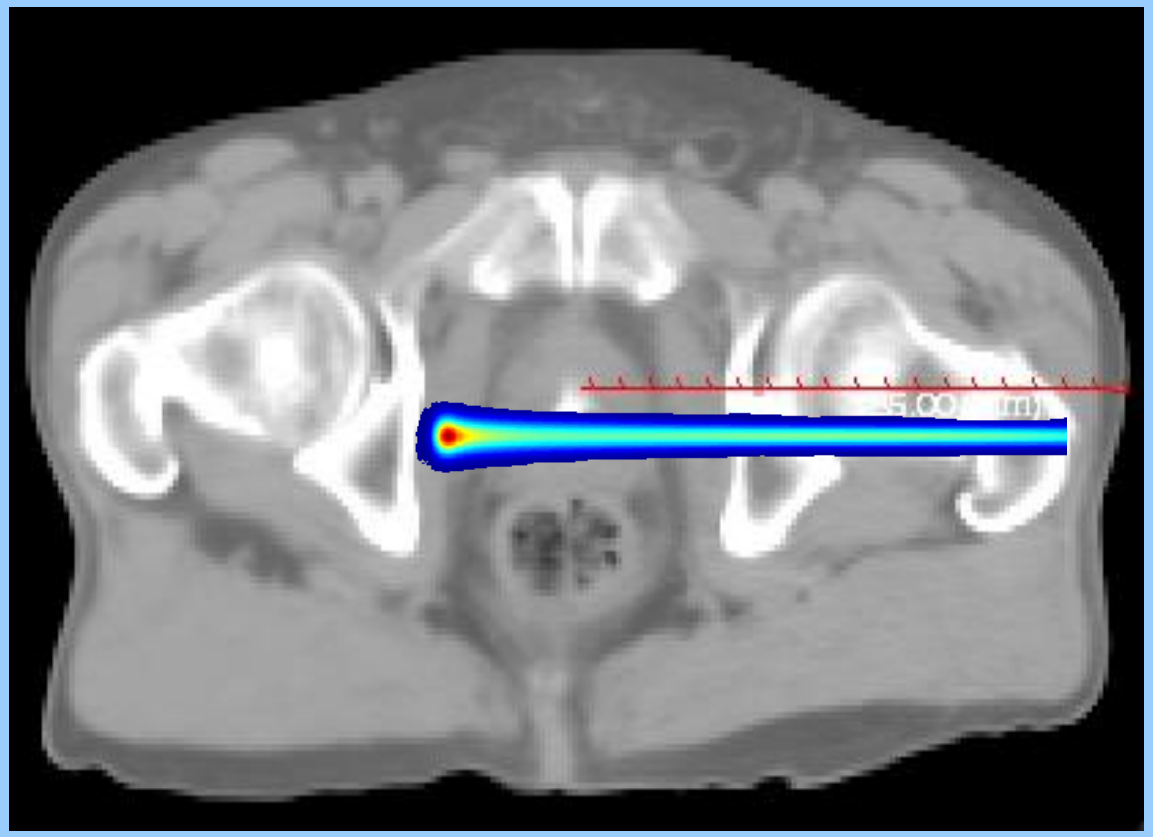


Depth dose distribution of photons and protons

Range uncertainties due to setup

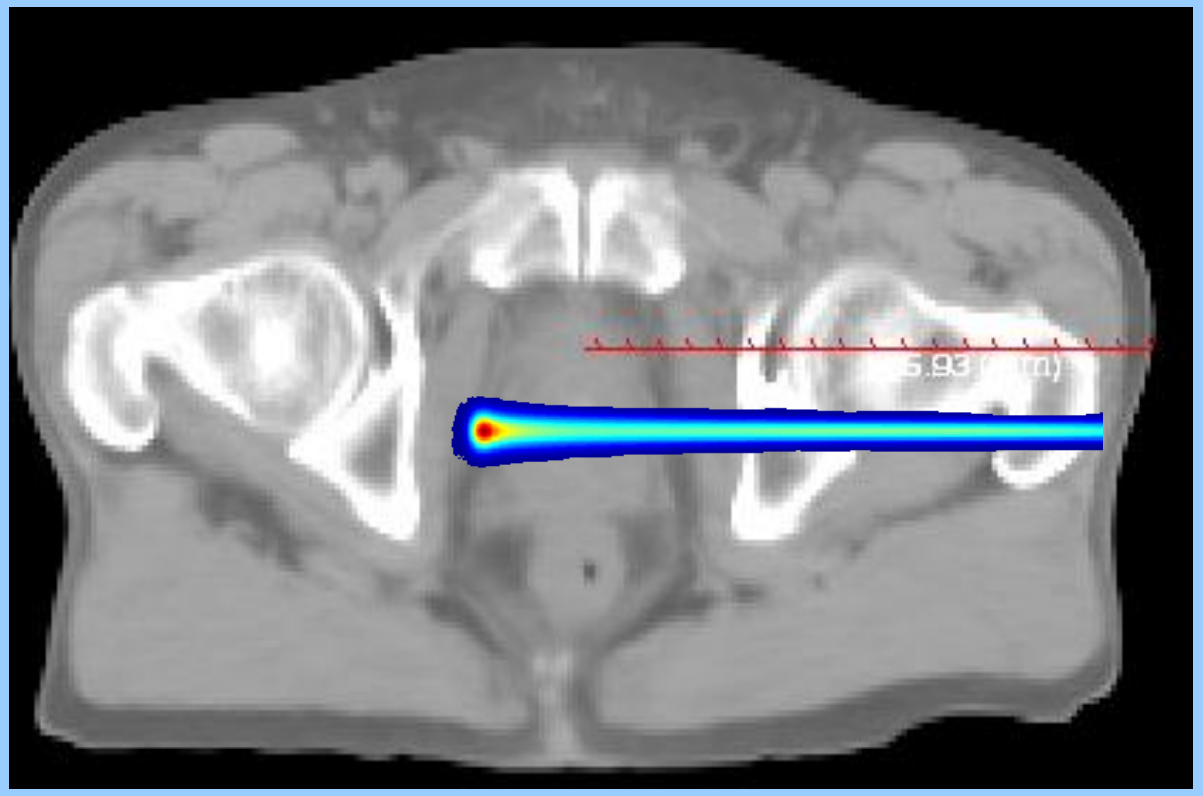


8 Jan

Proton uncertainties

Chen, Rosenthal, et al., IJROBP 48(3):339, 2000

Range uncertainties due to setup



11 Jan

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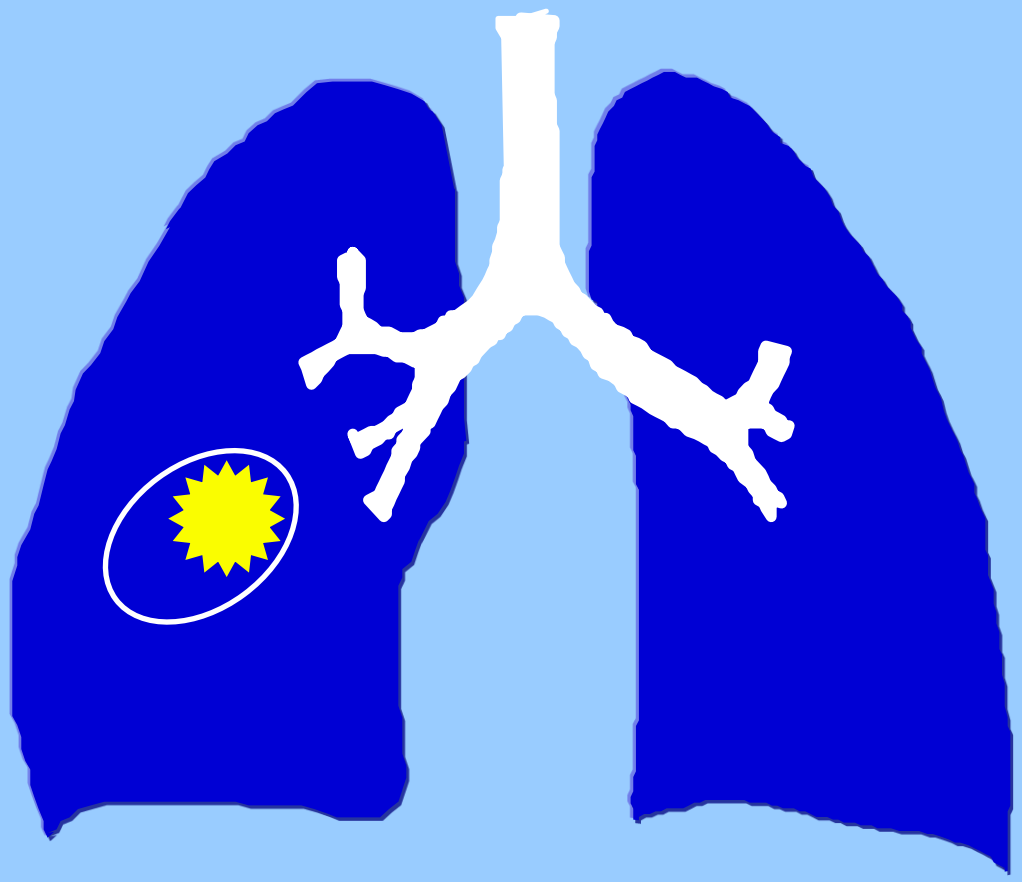
Intrafraction motion



Tumour motion in NSCLC RT

technology intensive

normal unregulated breathing

regular breathing

real time tracking

voluntary breath hold

predictive tracking

imposed breath hold

sedation

gating with free breathing or breath hold

anaesthaesia

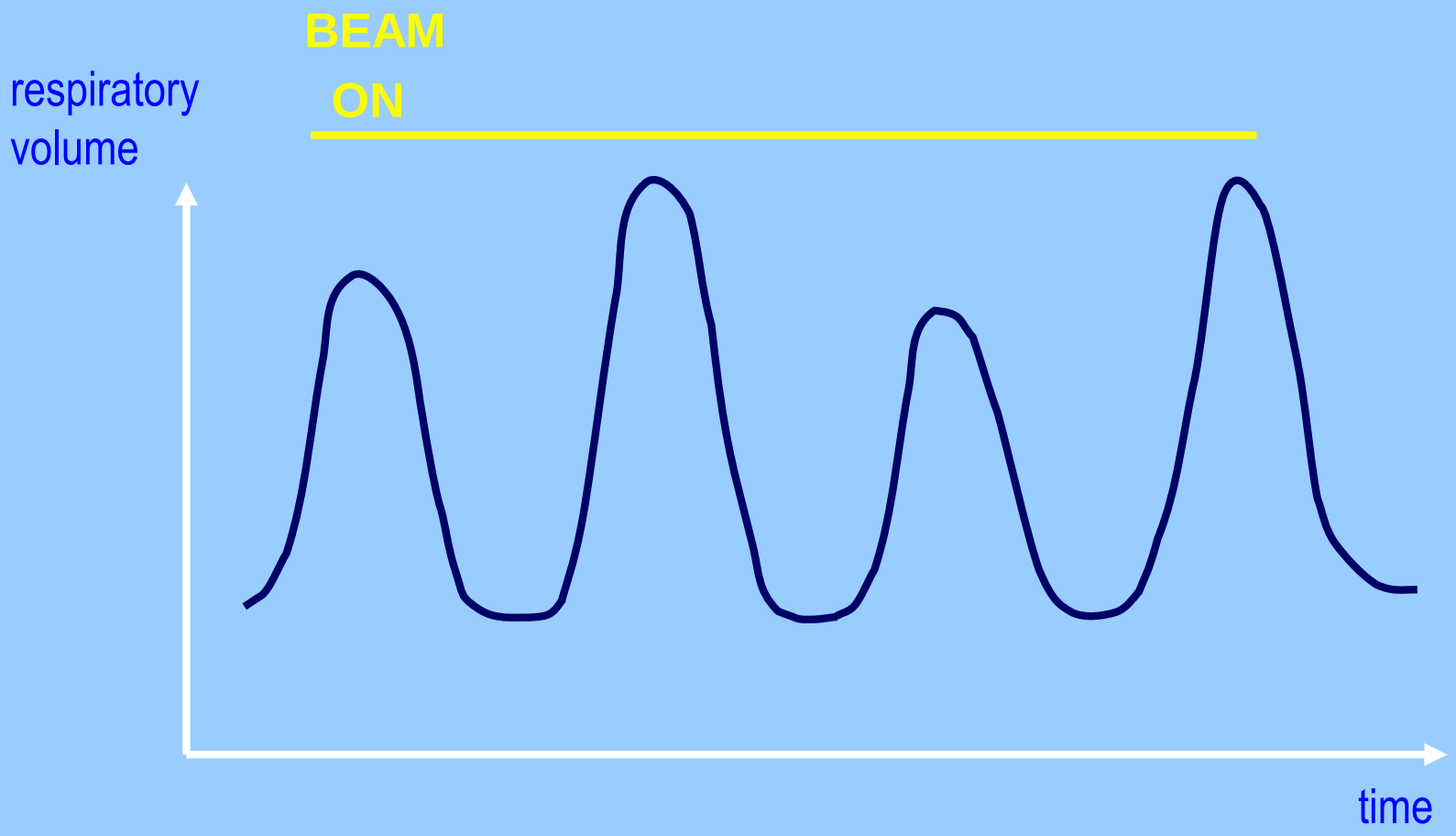
standard fixed delivery

patient intensive

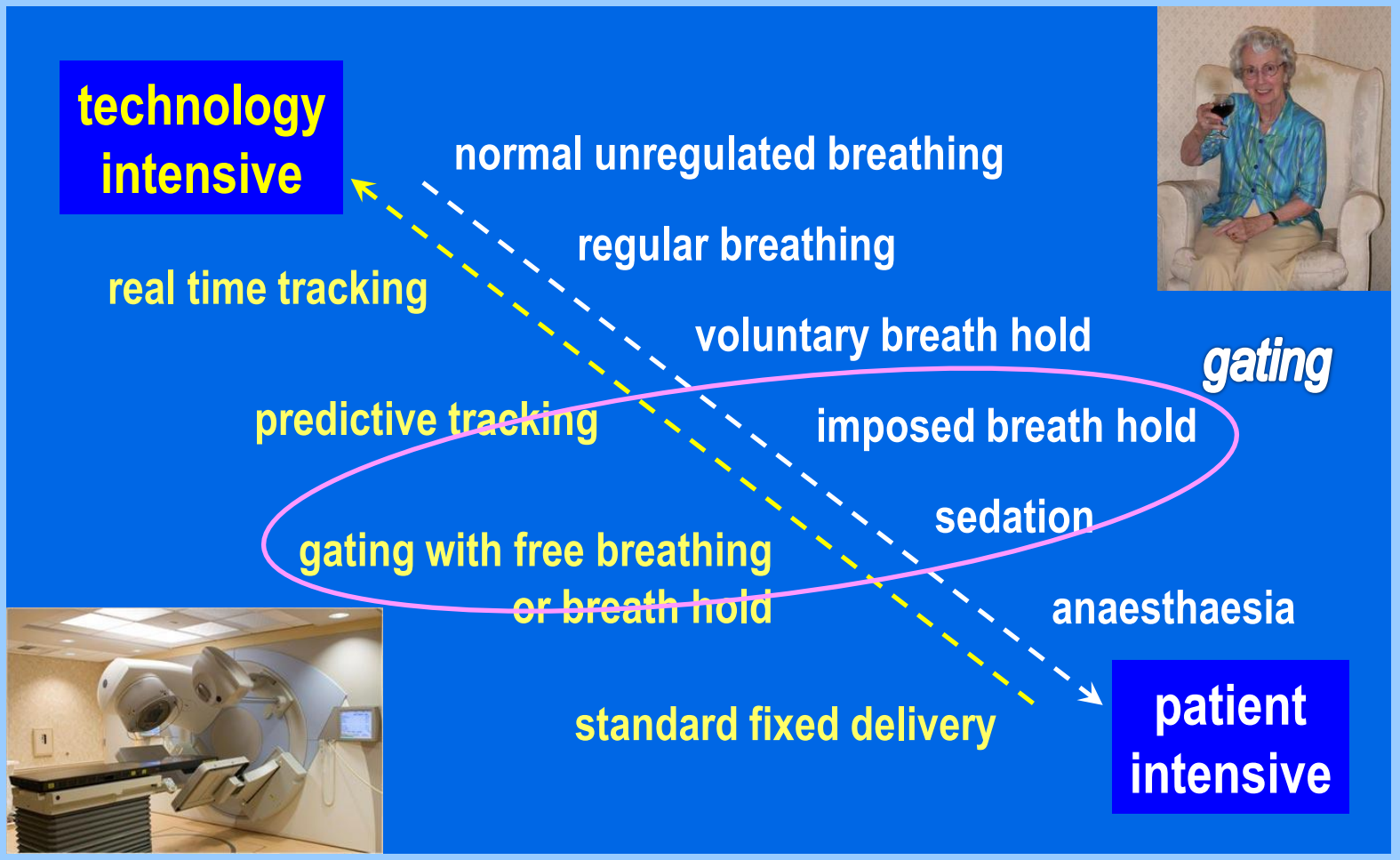
conventional treatment

Solutions to tumour motion in NSCLC RT

Radiotherapy to a moving target – conventional RT

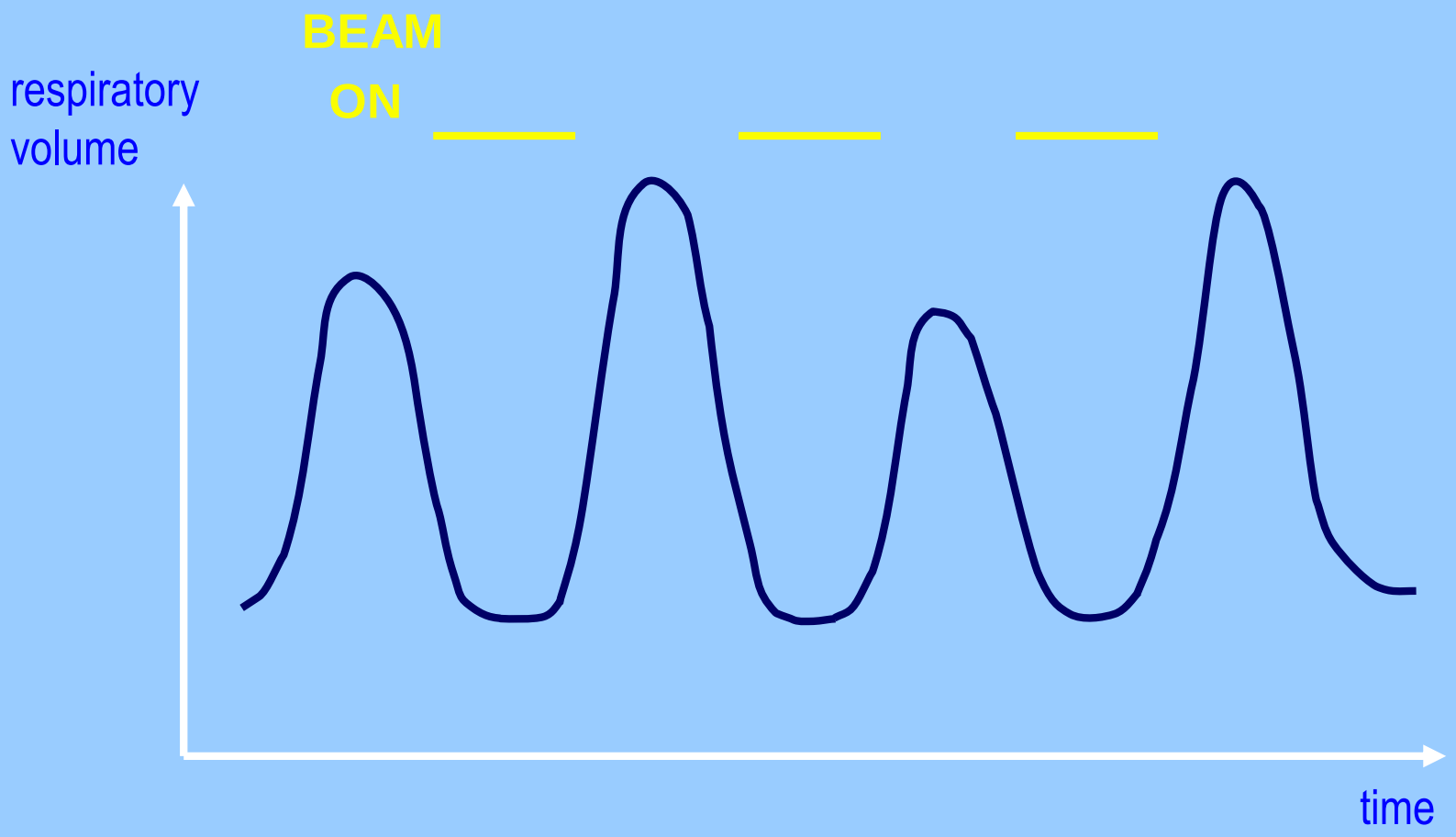


Solutions to tumour motion in NSCLC RT



Solutions to tumour motion in NSCLC RT

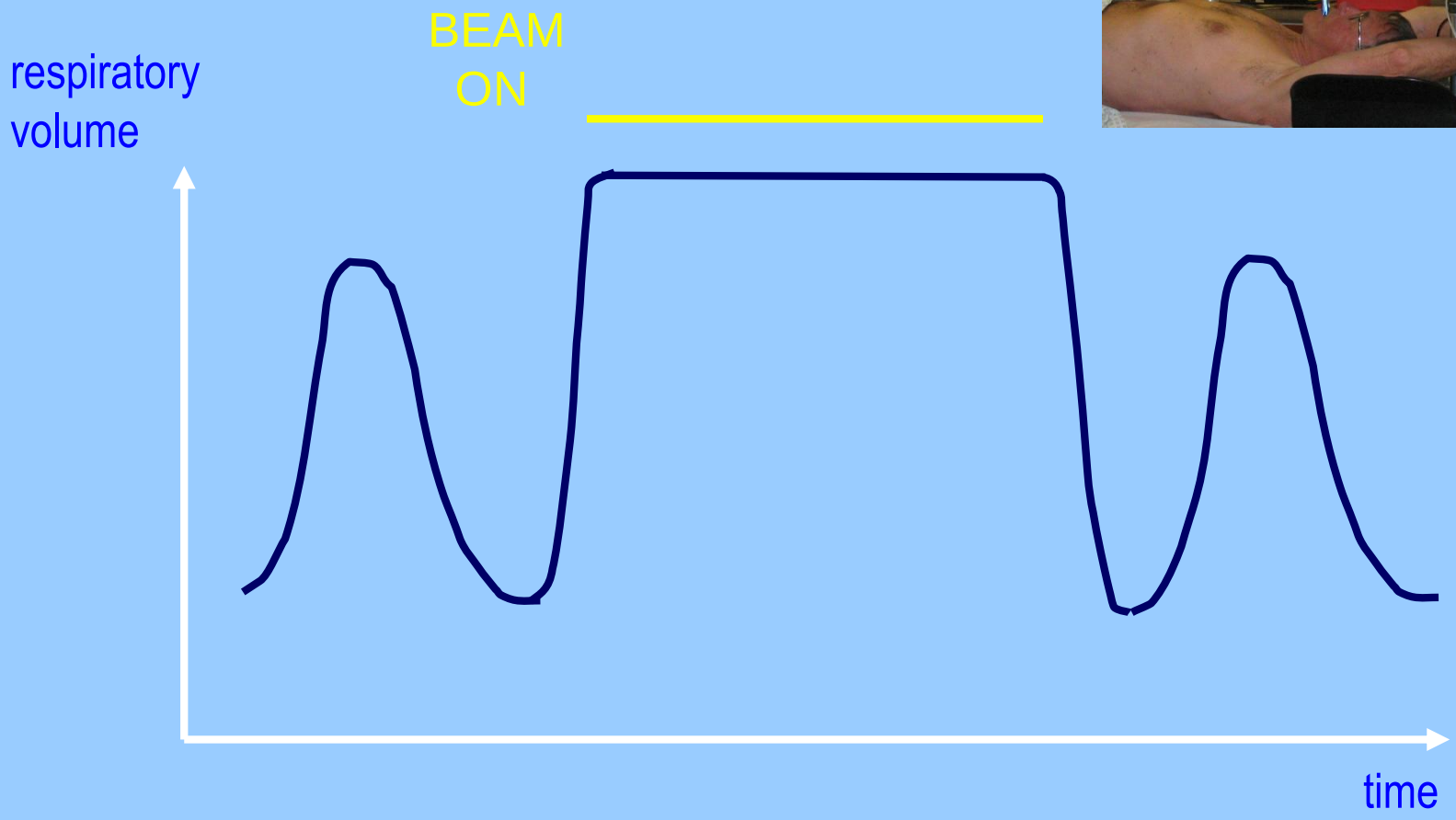
Radiotherapy to a moving target – gating



Solutions to tumour motion in NSCLC RT

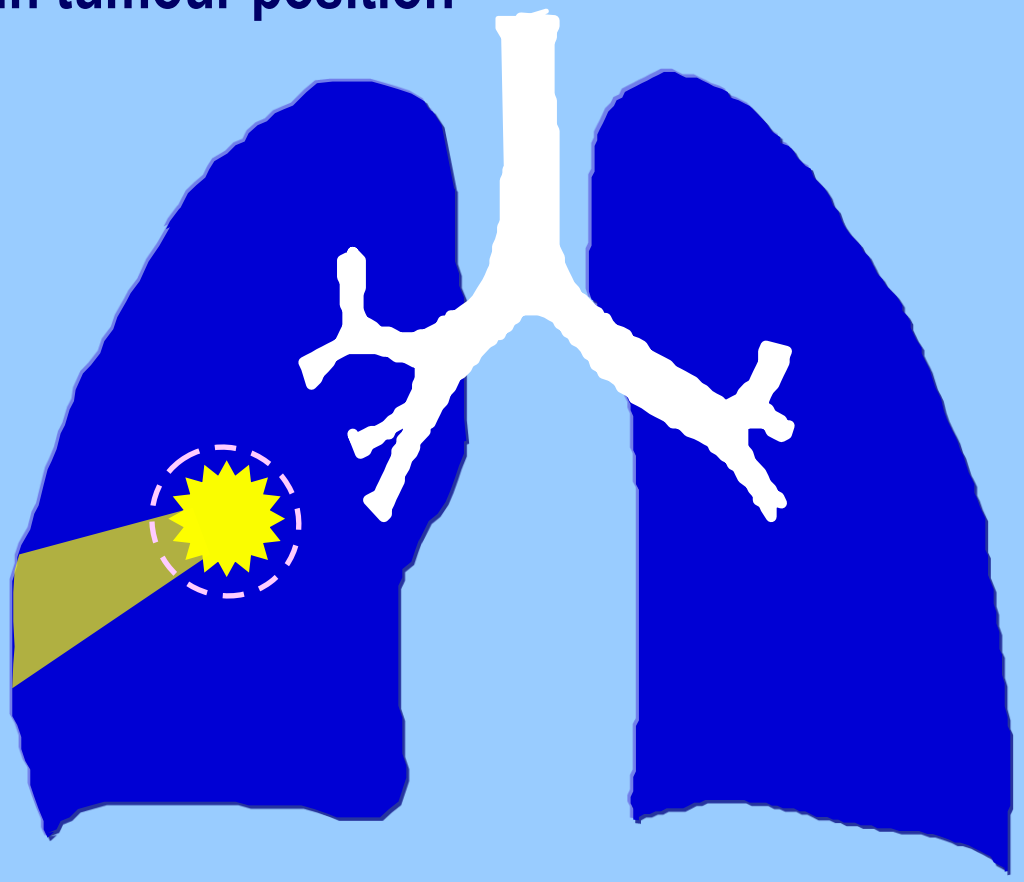
Radiotherapy to a moving target – gating

active breathing control (ABC)



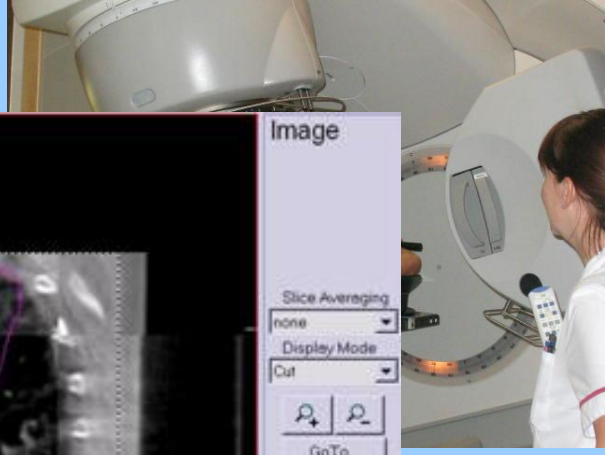
Solutions to tumour motion in NSCLC RT

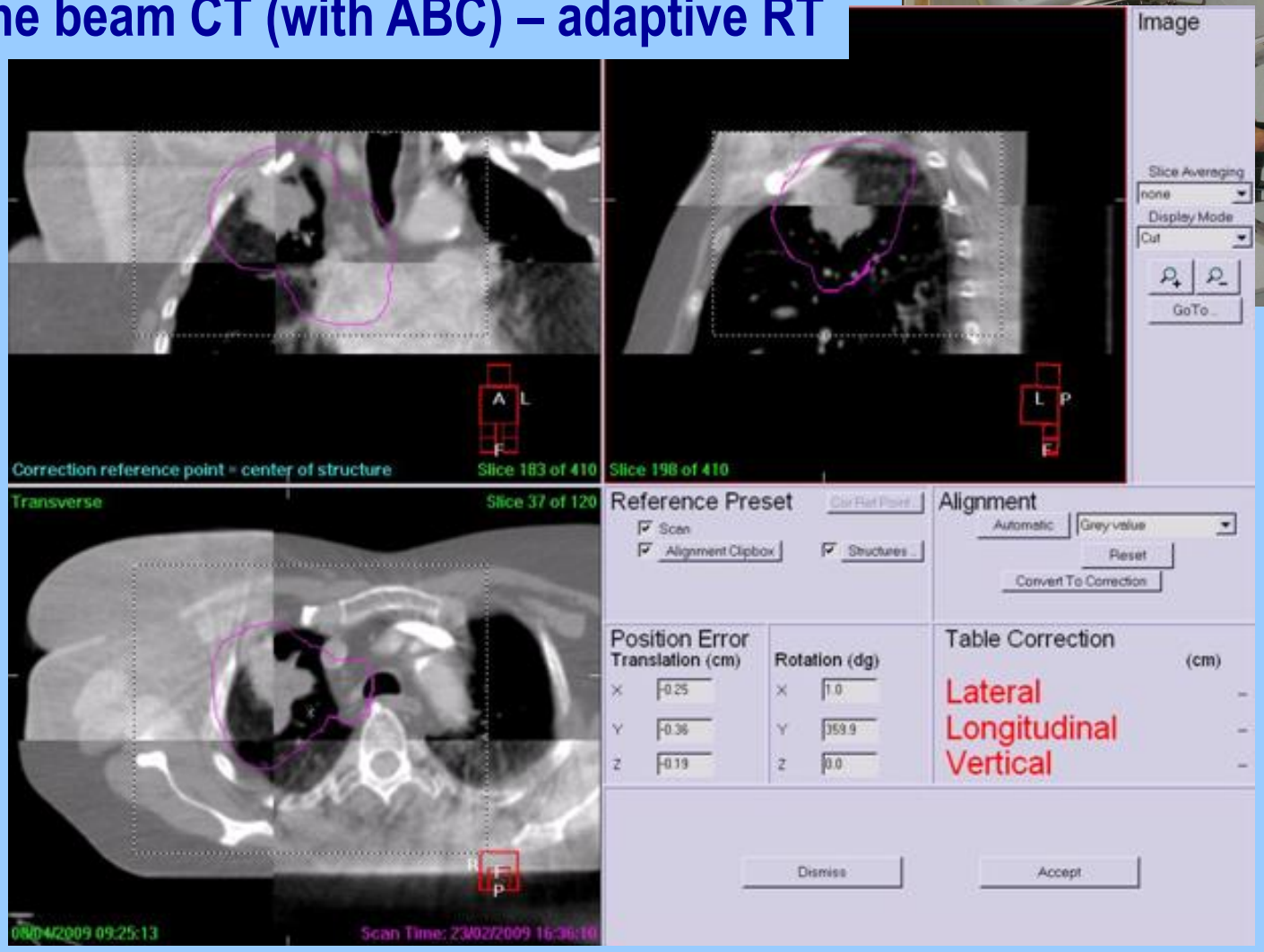
Adaptive radiotherapy
change in tumour position



IGRT in interfraction motion

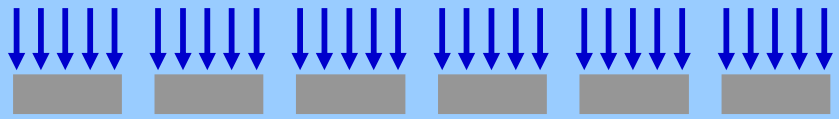
cone beam CT (with ABC) – adaptive RT



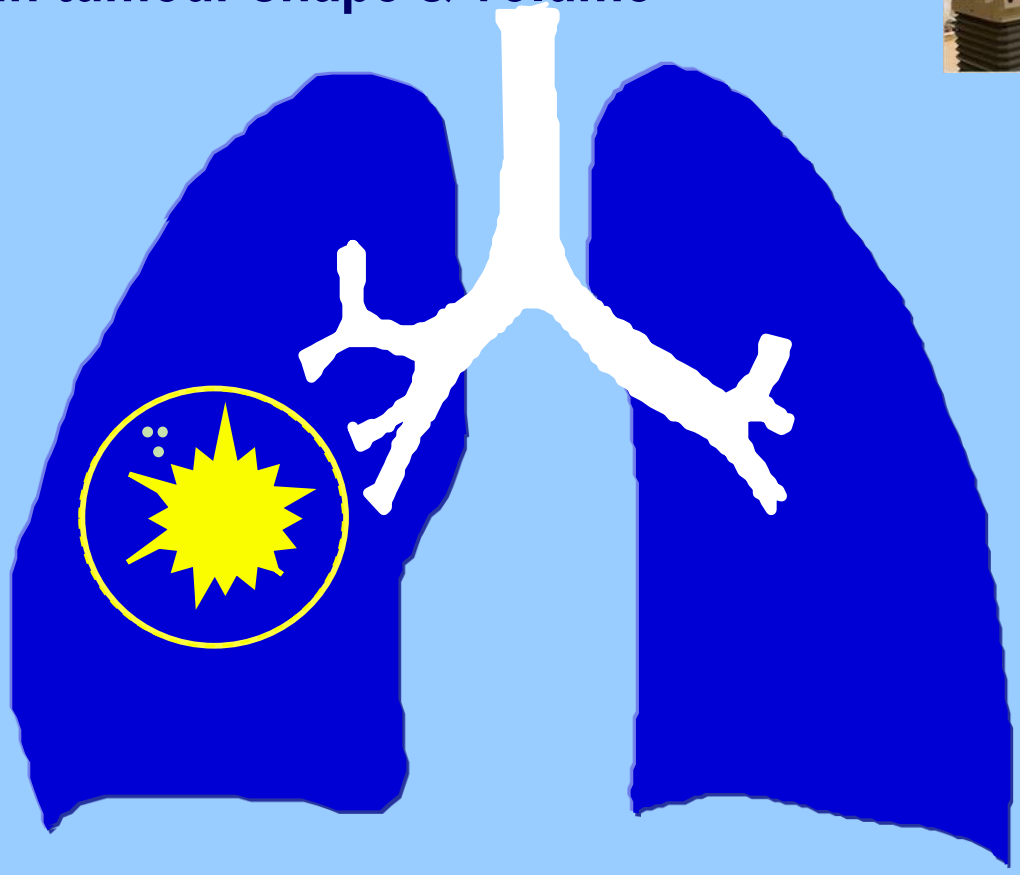


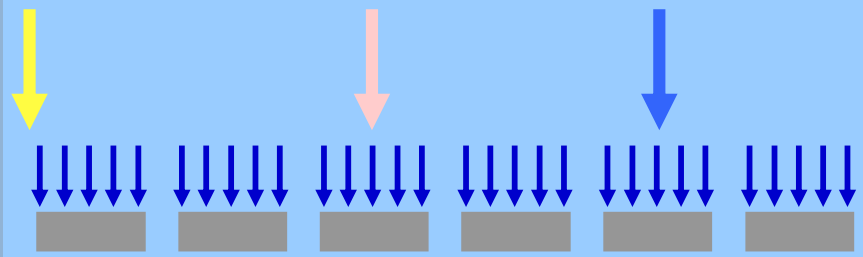
week 3

IGRT in interfraction motion



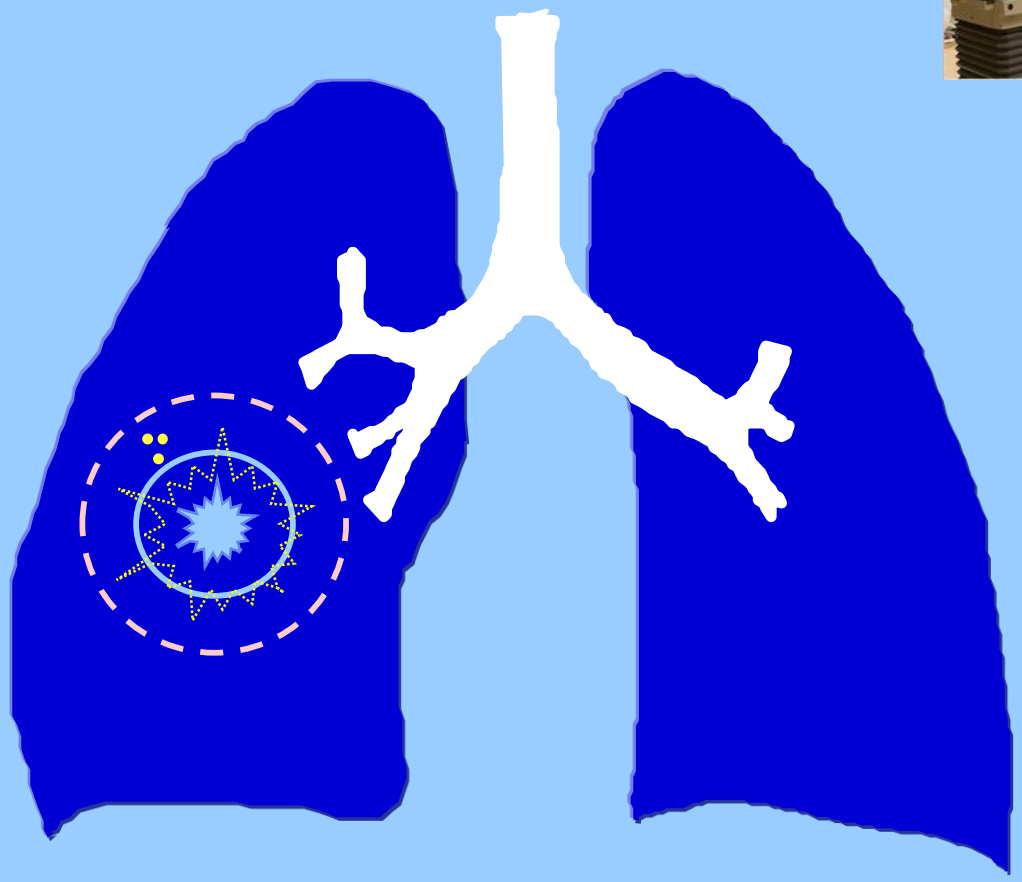
Adaptive radiotherapy
change in tumour shape & volume



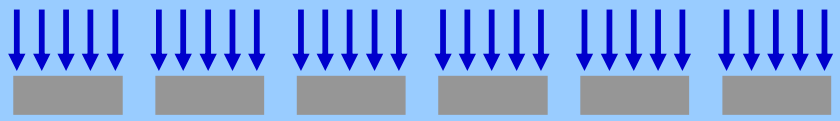


IGRT in interfraction motion

Uncertainties



IGRT in interfraction motion



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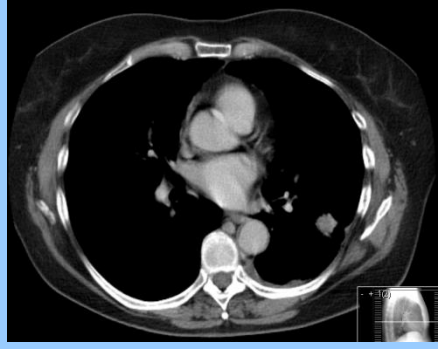
Imaging for radiotherapy



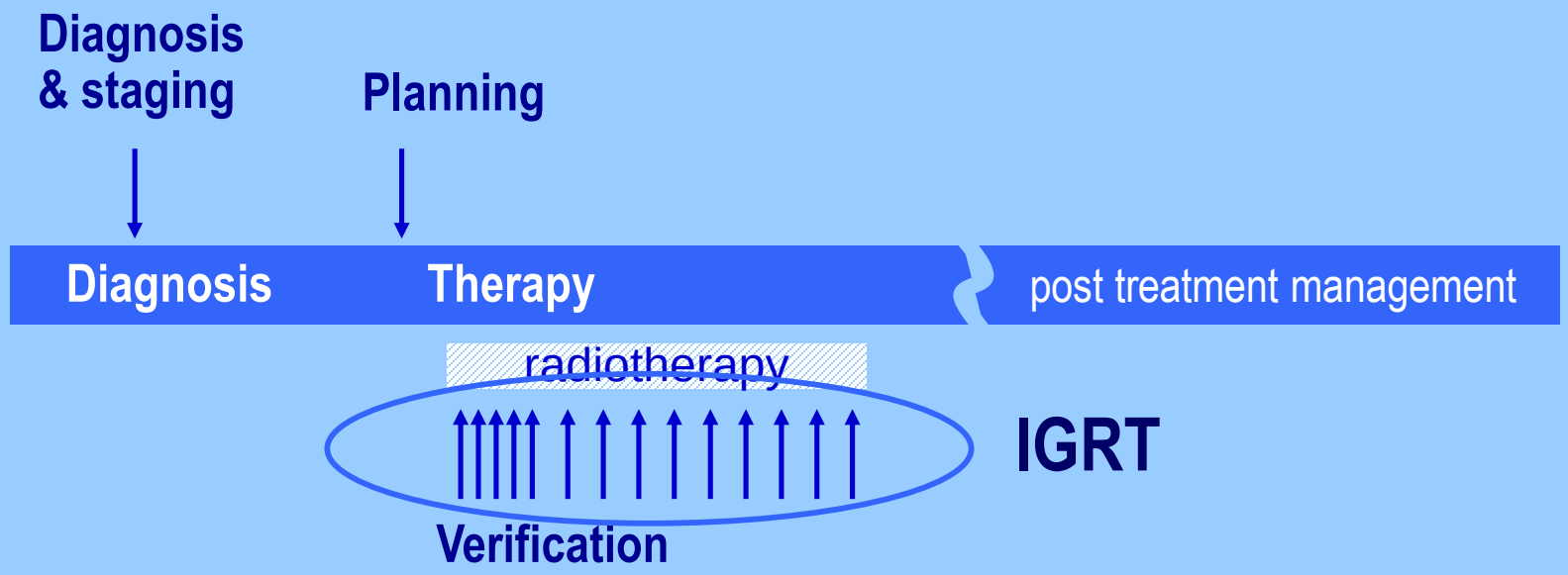


Image guidance in lung cancer radiotherapy

IGRT– image guided radiotherapy

CBCT frequency

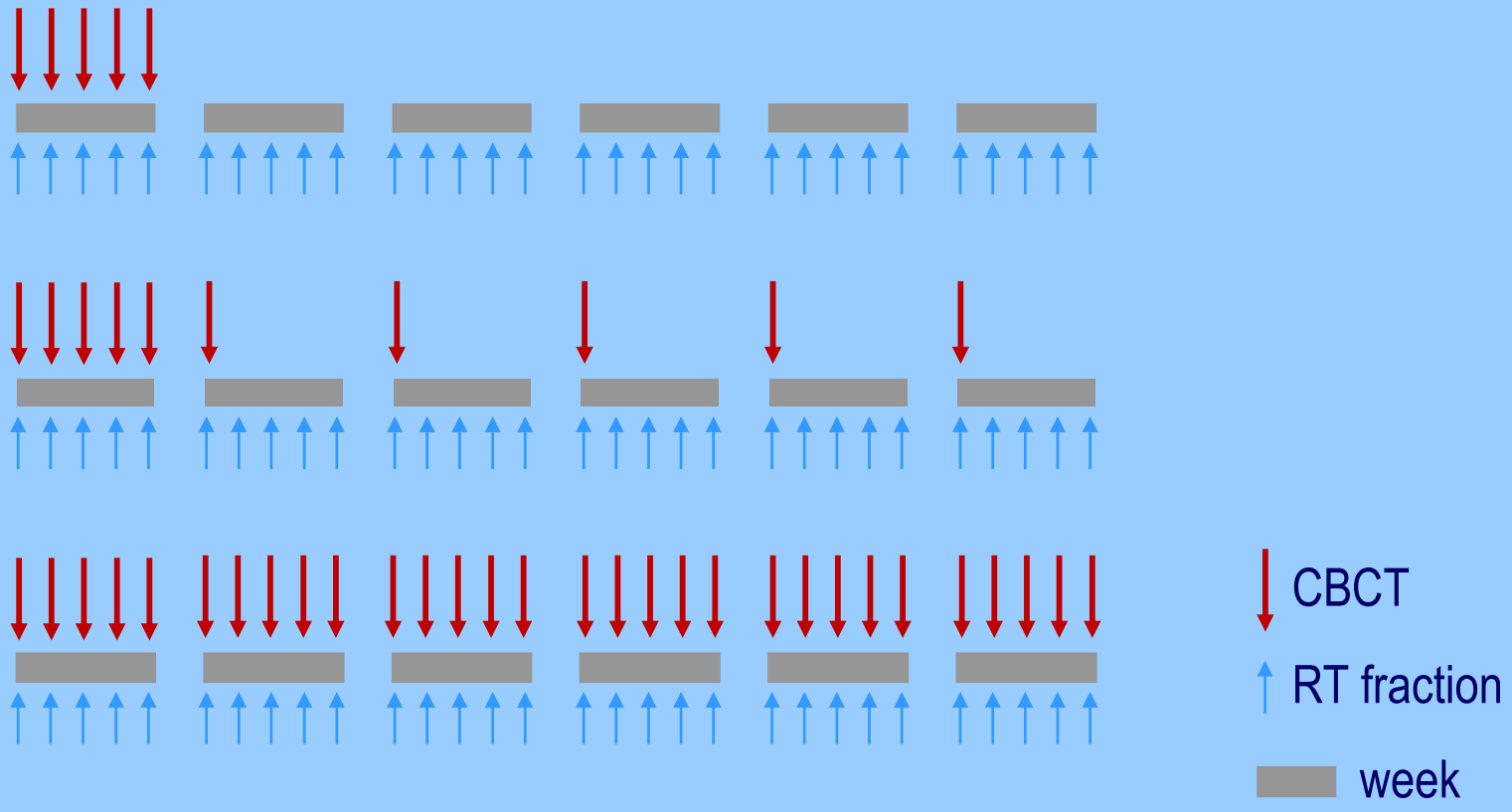


Image guidance in lung cancer radiotherapy

CBCT – cone beam CT

Patient positioning - set up errors
& CBCT frequency

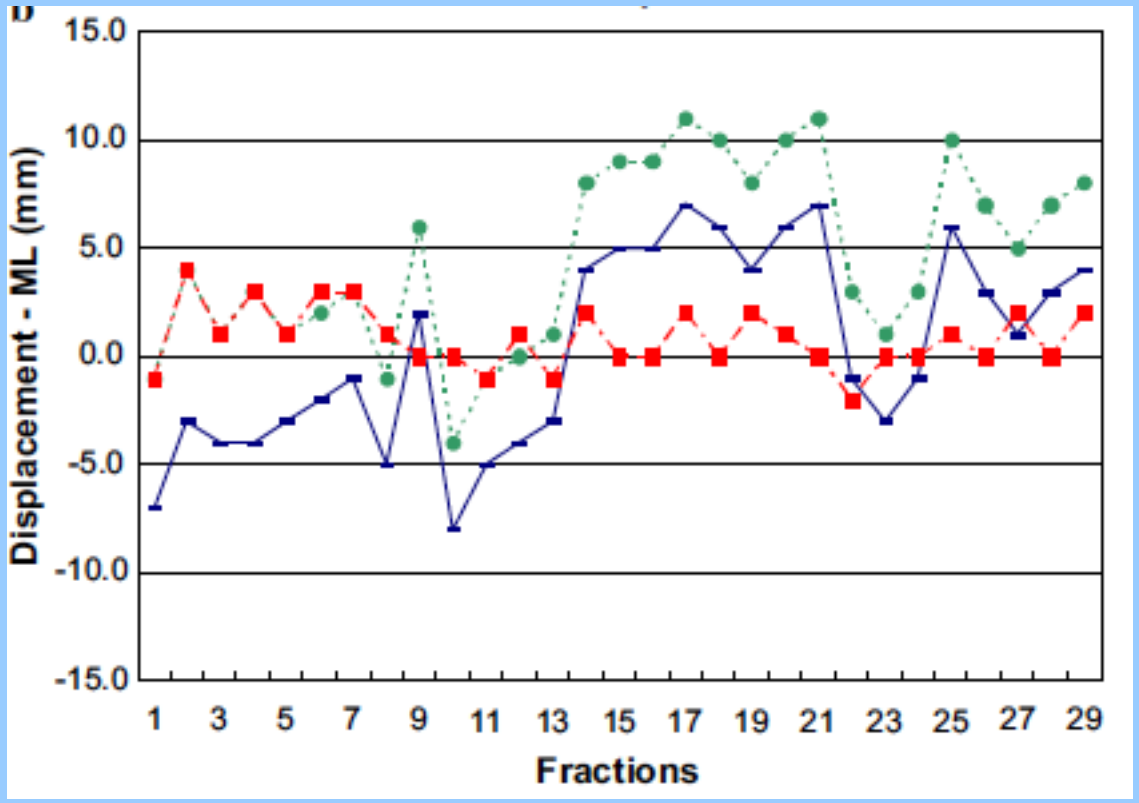


Image guidance
- none
- first 5 days
- daily

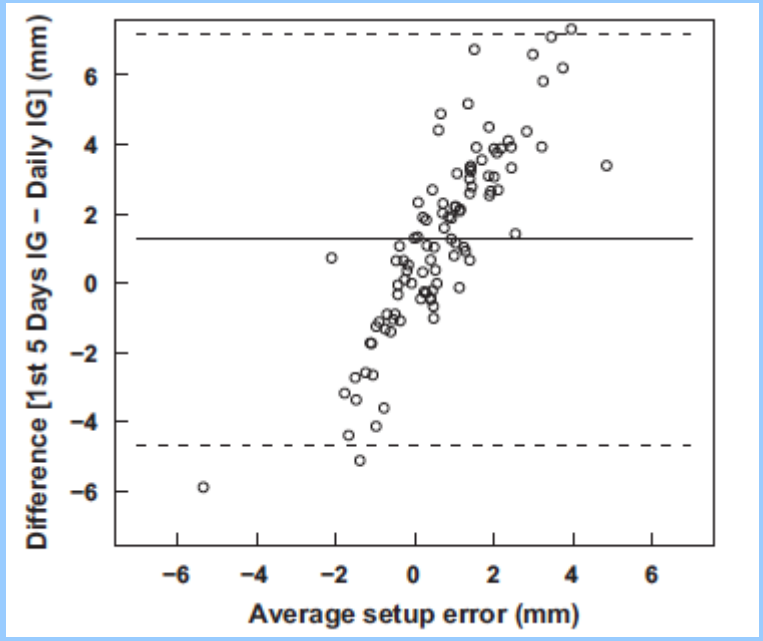
Image guidance in lung cancer radiotherapy

CBCT – cone beam CT
ML – medio-lateral (L-R)

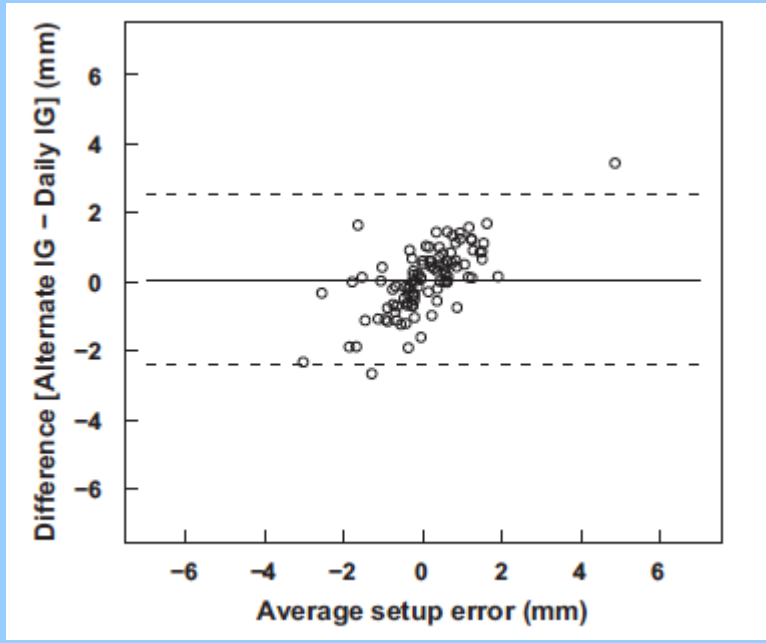
Higgins et al 2011

Patient positioning - set up errors
& CBCT frequency & mean error

first 5 days vs. daily



alternate days vs. daily



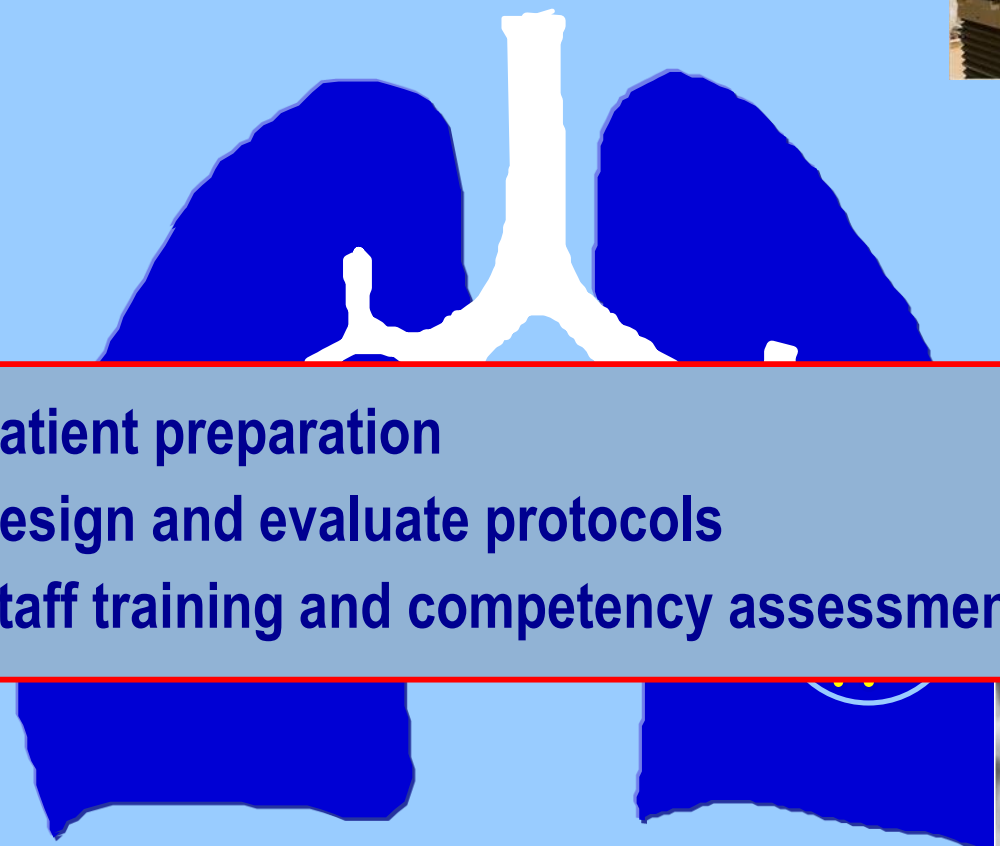
Bland – Altman plots in cranio-caudal plane

Image guidance in lung cancer radiotherapy

CBCT – cone beam CT

Higgins et al 2011

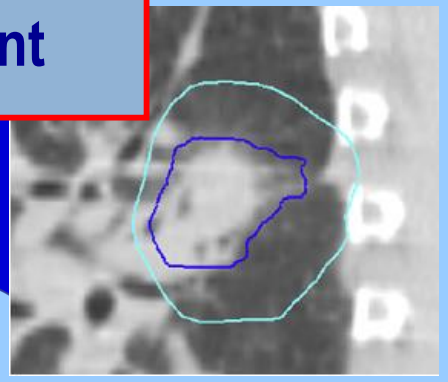
! Strategies to avoid worse outcome !



patient preparation

design and evaluate protocols

staff training and competency assessment



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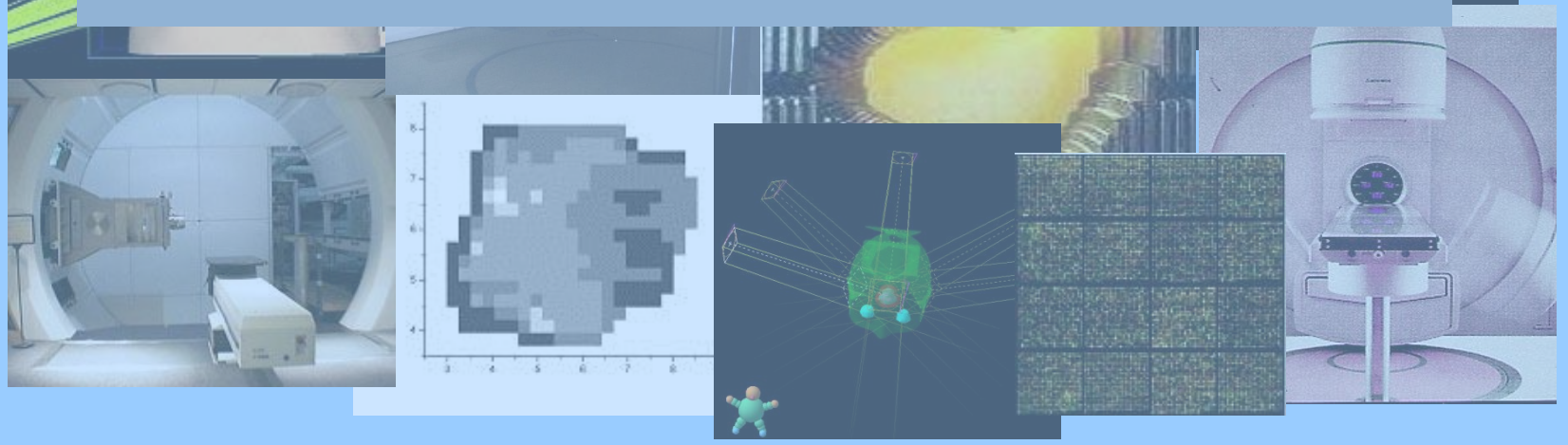
New and emerging radiotherapy technologies

Introduction of technology into clinical practice

driven by:

- clinical need
- technology & commerce

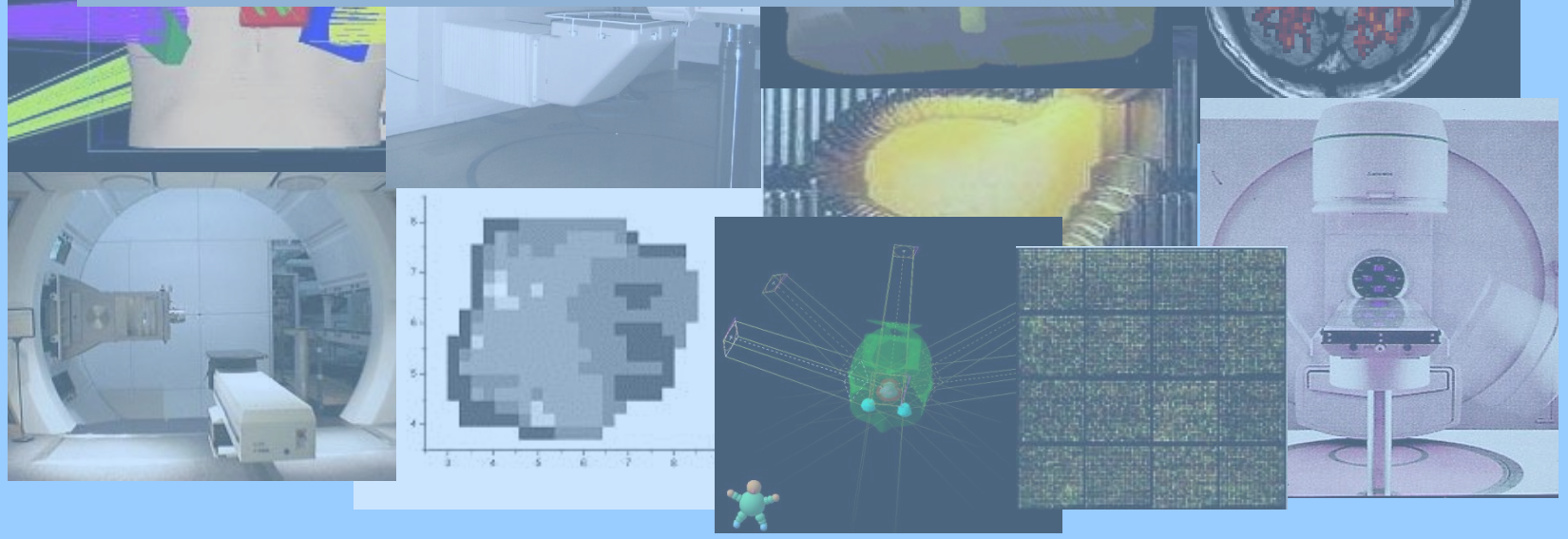


New radiotherapy technology

Introduction of RT technology into clinical practice

benefits radiotherapy process

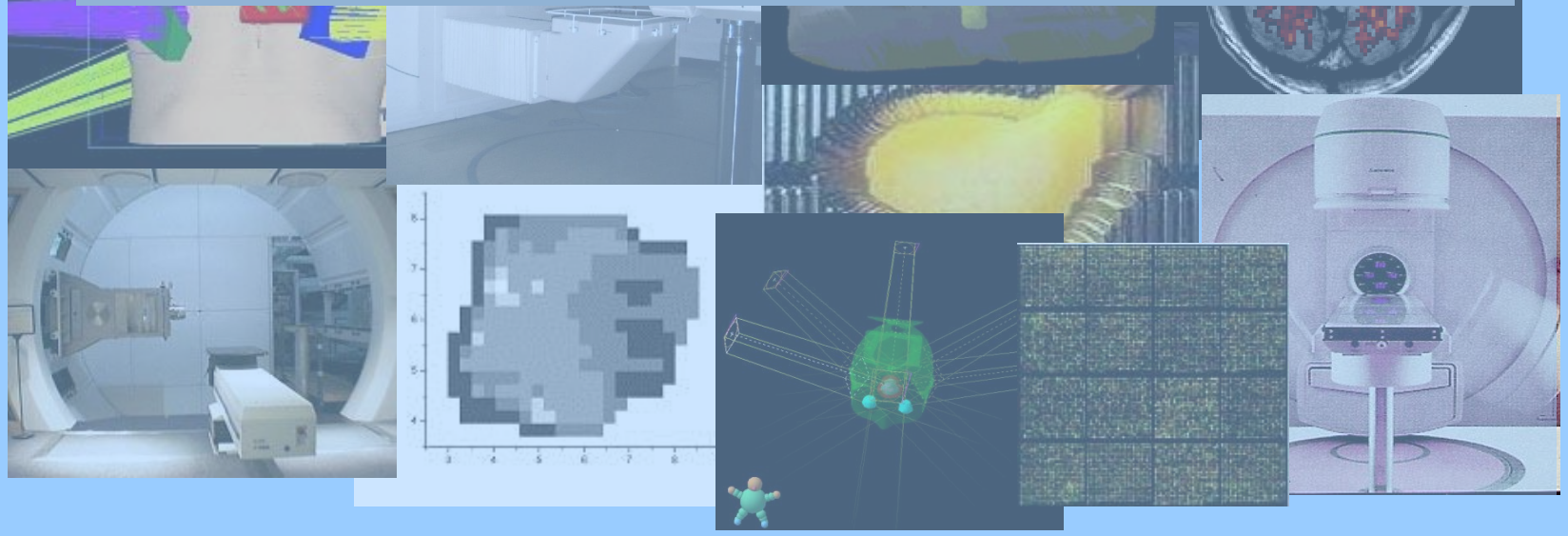
clinical benefit



New radiotherapy technology

Clinical benefit

what would you like new technology to achieve

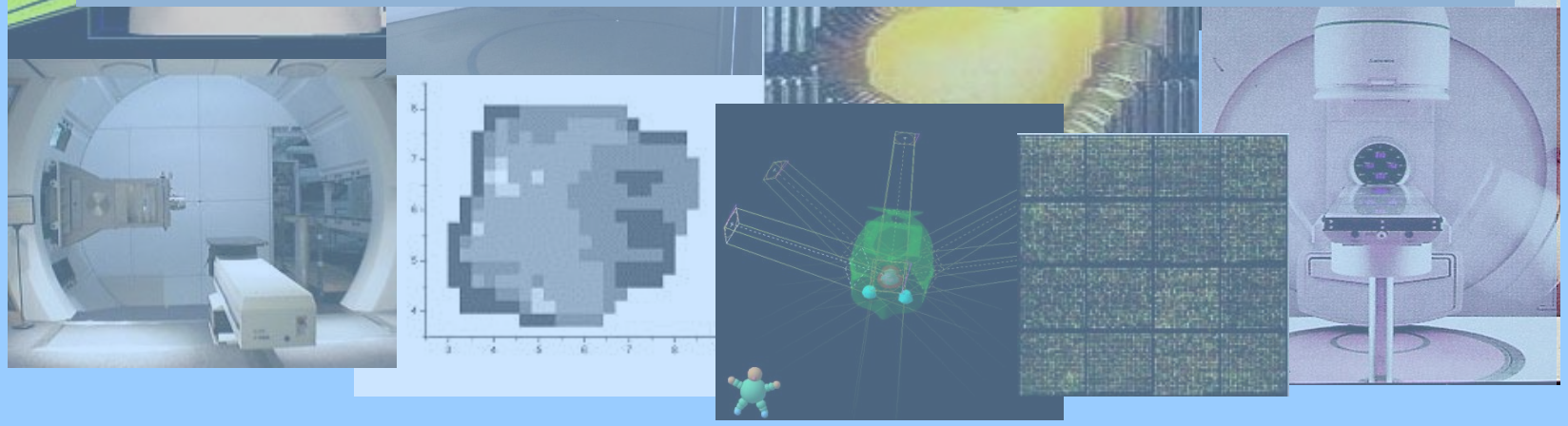


New radiotherapy technology

Clinical benefit - personal

what would you like new technology to achieve

if friend or family need radiotherapy



New radiotherapy technology

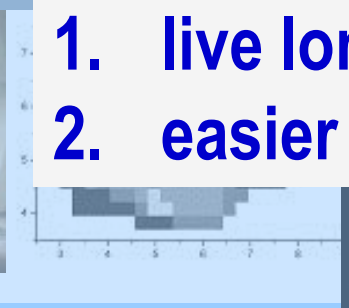
Clinical benefit - personal

what would you like new technology to achieve

if friend or family need radiotherapy

and they have to pay

1. live longer with fewer side effects
2. easier treatment



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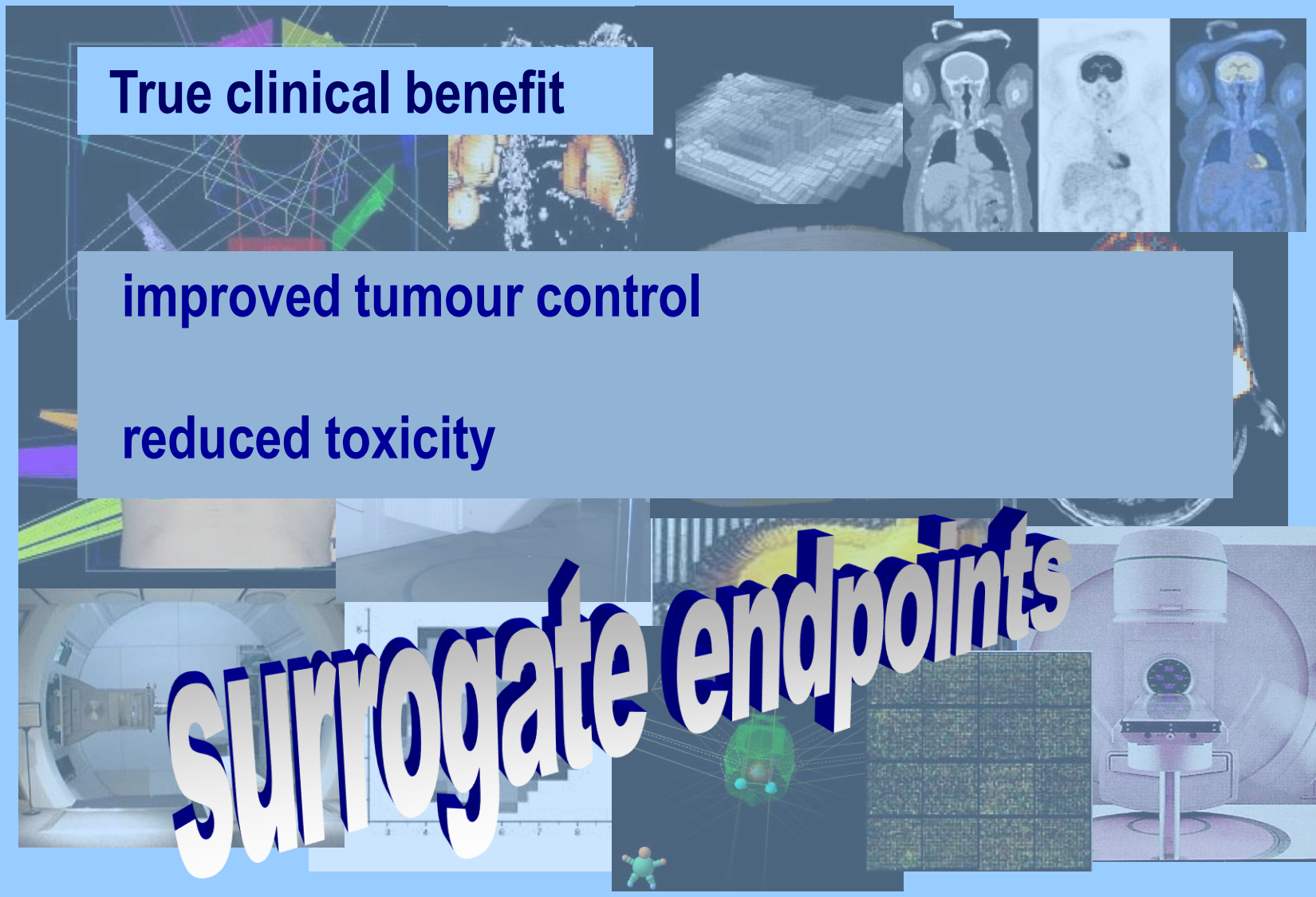


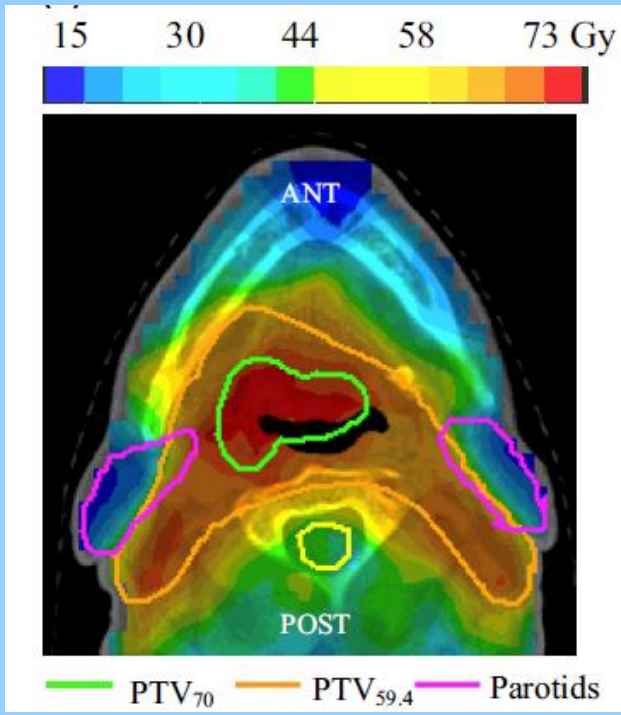
New radiotherapy technology

True clinical benefit

IMRT for parotid sparing

Preserve salivary function

Tumour control …?



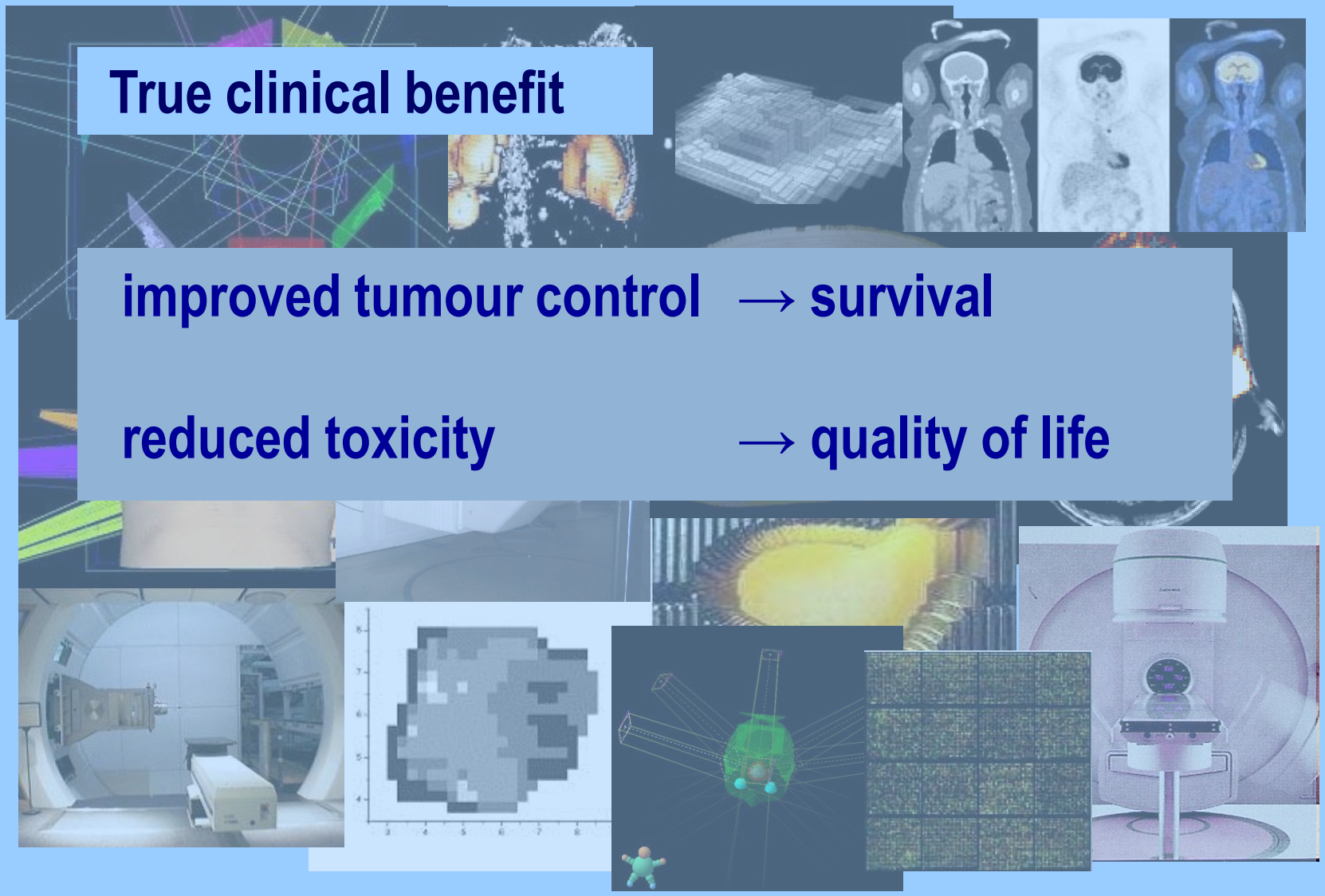
New radiotherapy technology

IMRT - intensity modulated radiotherapy

True clinical benefit

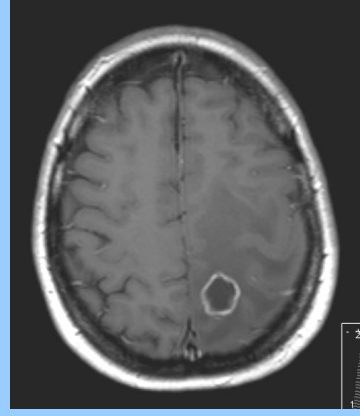
improved tumour control → survival

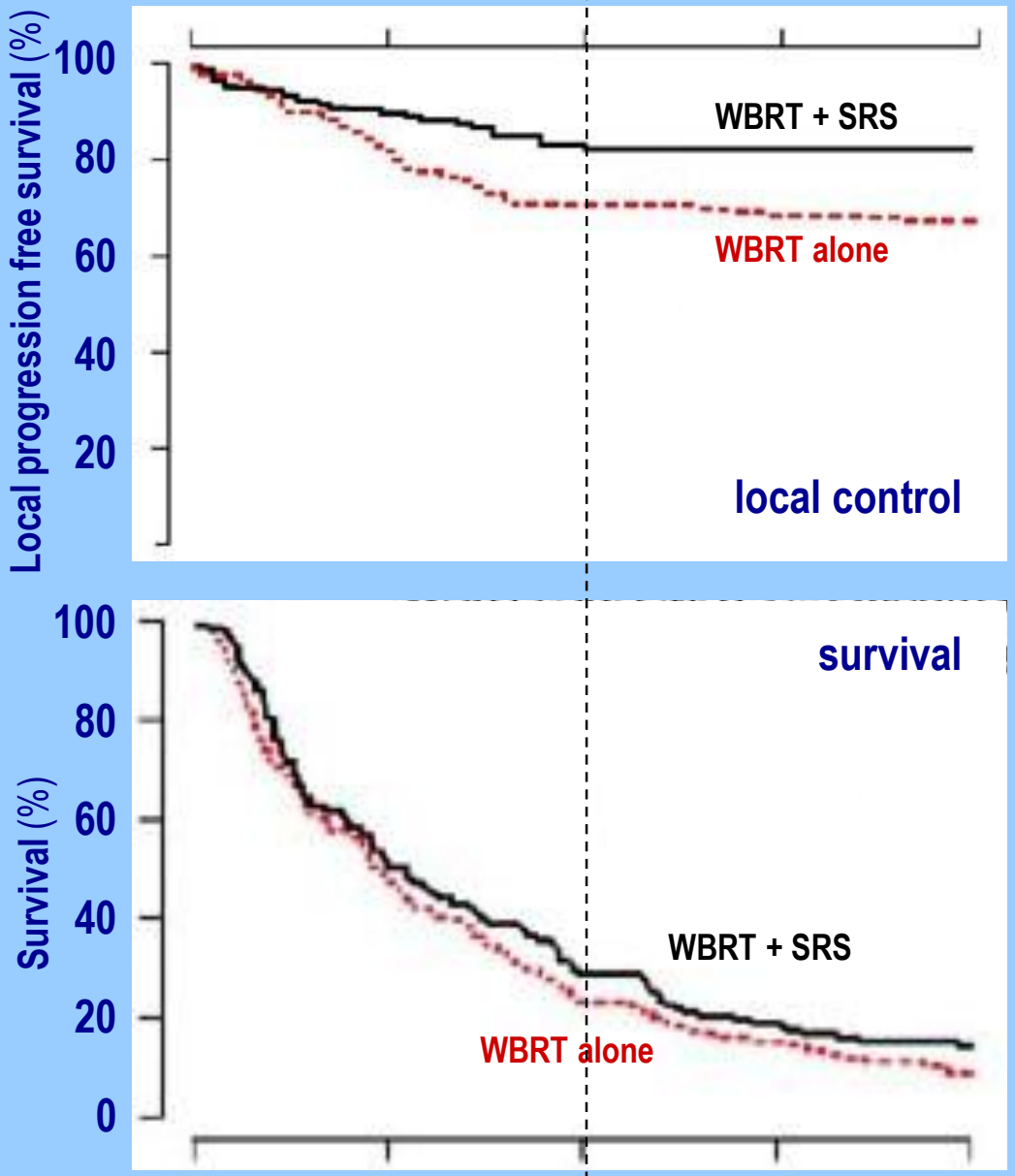
reduced toxicity → quality of life



New radiotherapy technology

Radiosurgery for brain metastases

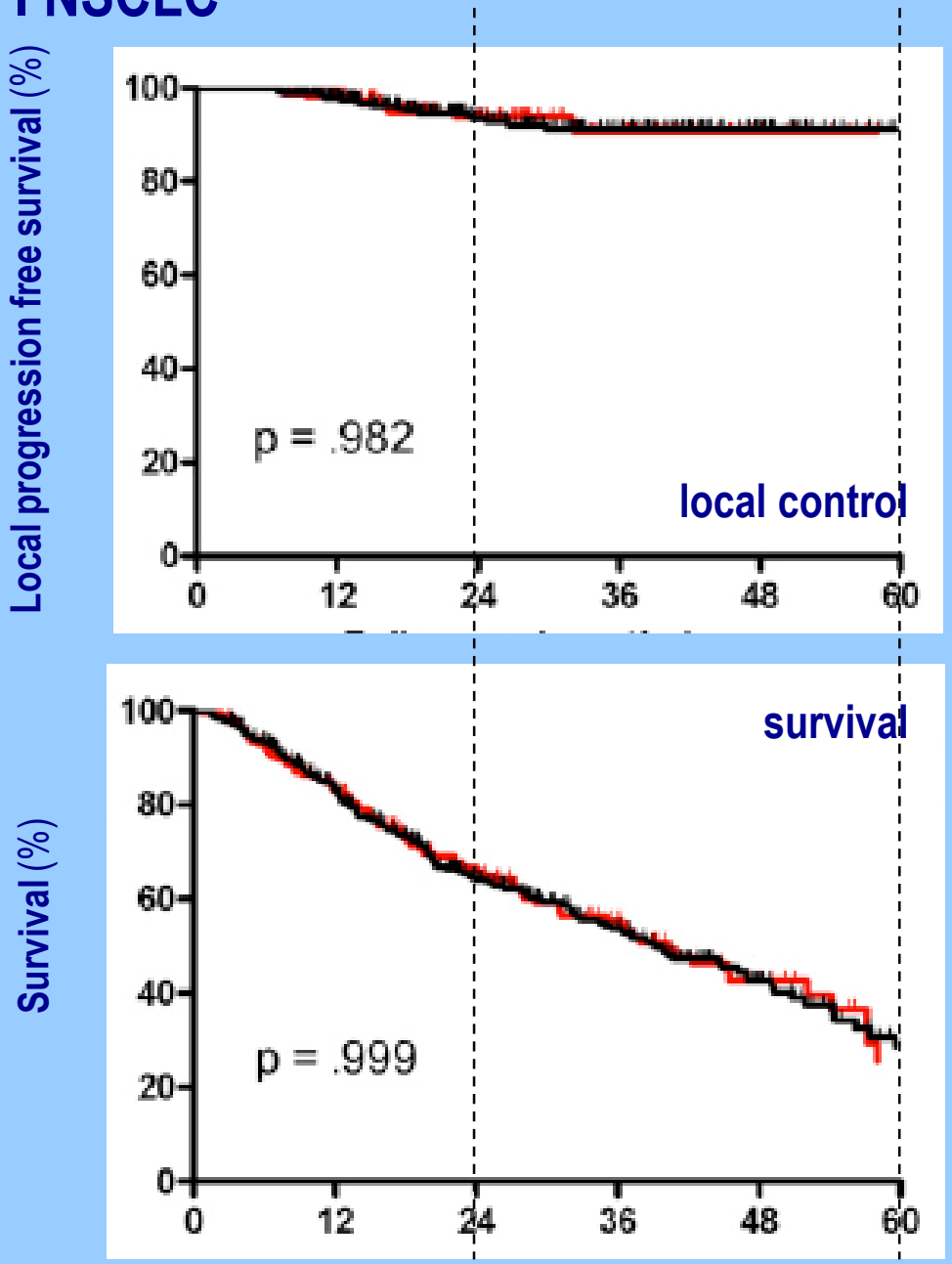




Andrews et al 2004 RTOG 9508

WBRT whole brain RT
SRS stereotactic radiosurgery

SABR for stage I NSCLC



Verstegen et al 2011 VU Amsterdam

SABR – stereotactic ablative body radiotherapy

Introduction of technology into clinical practice

driven by:

technology & commerce

clinical need

- driving forces are difficult to distinguish
- marketing blurs the reality

New radiotherapy technology

Introduction of technology into clinical practice

driven by:

- technology & comm
- clinical

Precise

Focused

Image guided

Intensity modulated

- driving forces difficult to distinguish
- marketing blurs the reality

New radiotherapy technology

Introduction into clinical practice

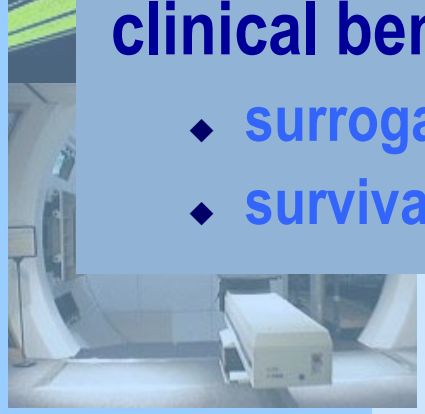
requirements:

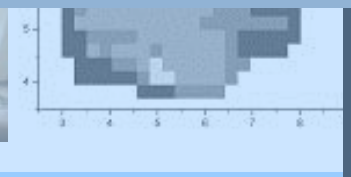
technical benefit in clinical setting

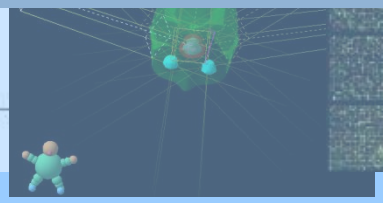
- representative series of patients
- clinically relevant endpoint

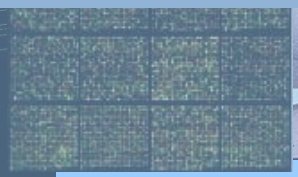
clinical benefit

- surrogate endpoint (tumour control and toxicity)
- survival and quality of life









Evaluating new radiotherapy technology

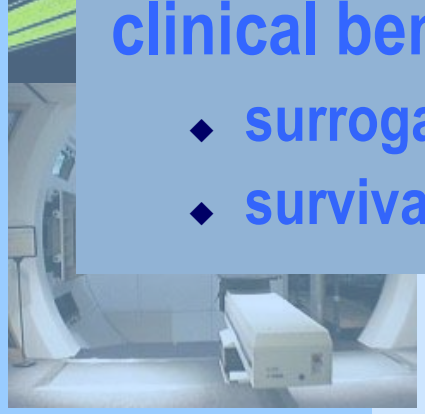
Introduction into clinical practice

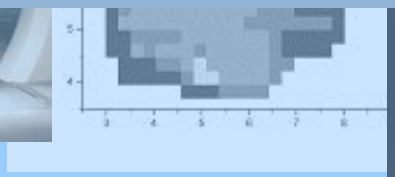
technical benefit in clinical setting

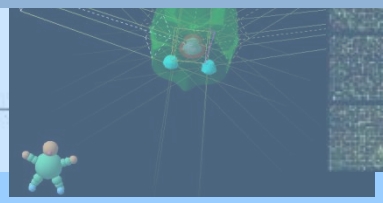
- representative series of patients
- clinically relevant endpoint

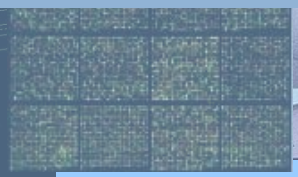
clinical benefit

- surrogate endpoint (tumour control and toxicity)
- survival and quality of life









Evaluating new radiotherapy technology

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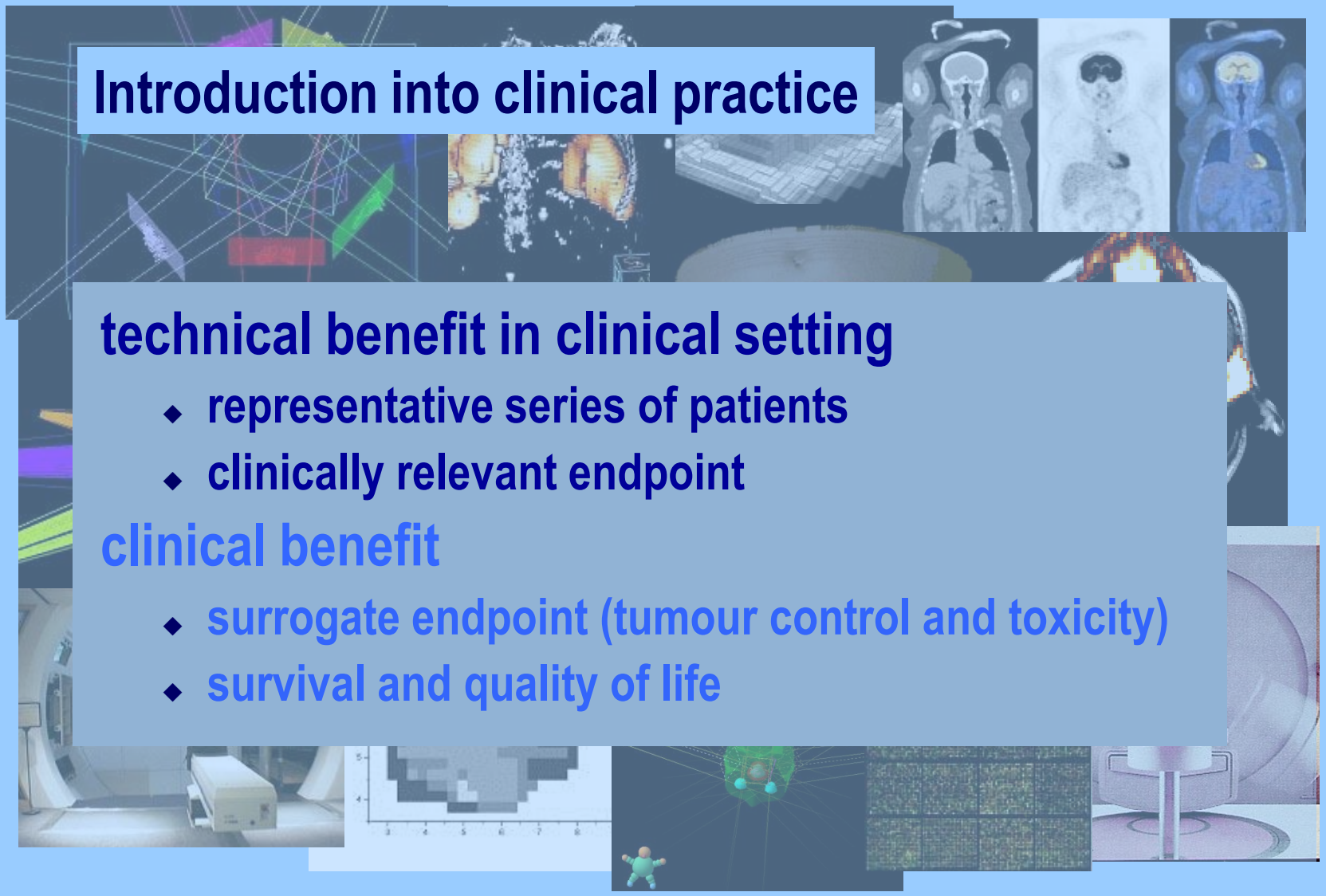

Introduction into clinical practice

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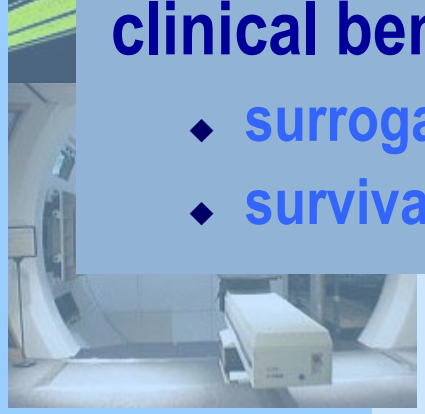

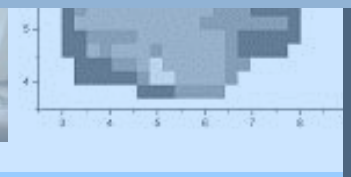

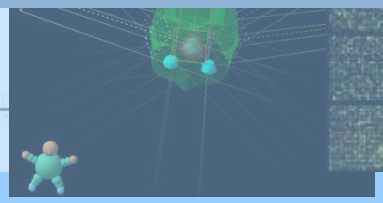

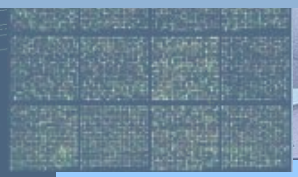

Evaluating new radiotherapy technology

Conventional design

to evaluate

Phase I

Phase II

Phase III

model of drug testing

Evidence based medicine

Conventional design

to evaluate

Phase I	feasibility & toxicity
Phase II	
Phase III	

model of drug testing

Evidence based medicine

Conventional design

to evaluate

Phase I feasibility & toxicity

Phase II initial investigation of activity

no information on comparative efficacy

Phase III

model of drug testing

Evidence based medicine

Conventional design

to evaluate

Phase I	clinical pharmacology & toxicity
Phase II	initial investigation of activity
Phase III	comparative efficacy

model of drug testing

Evidence based medicine

Introduction into clinical practice

technical benefit in clinical setting

- representative series of patients
- clinically relevant endpoint

clinical benefit

- surrogate endpoint (tumour control and toxicity)
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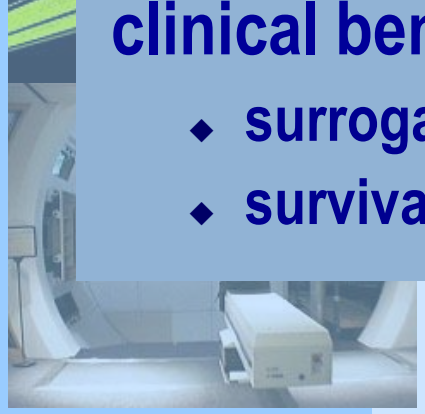
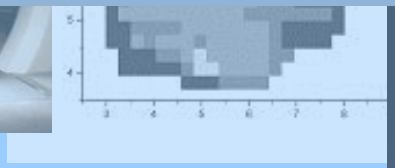
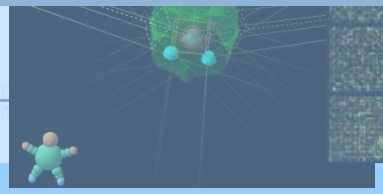
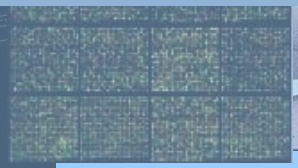








Evaluating new radiotherapy technology

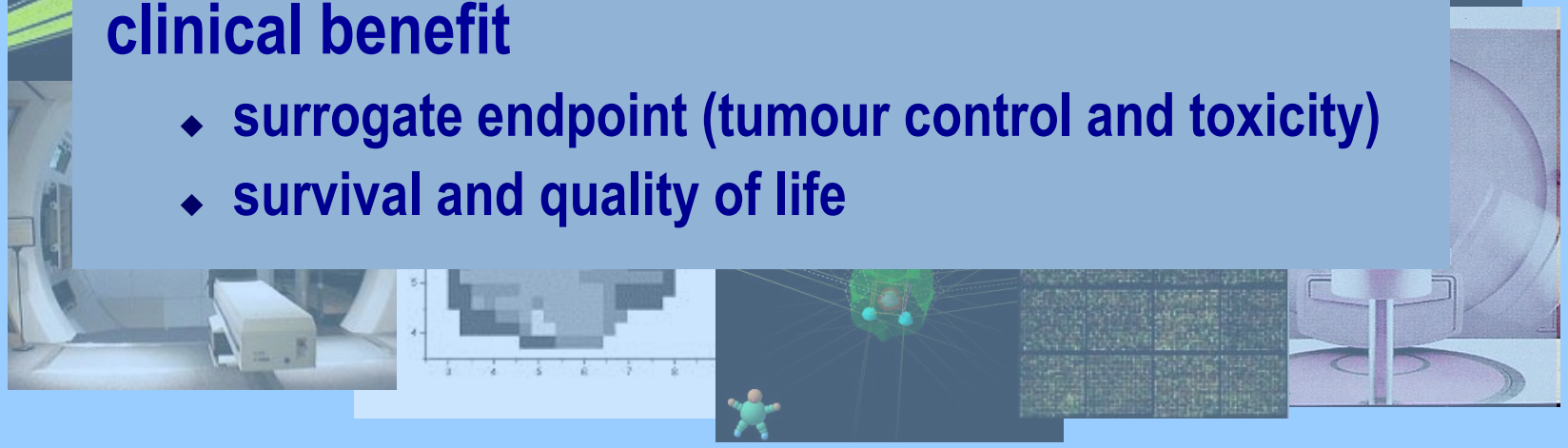
Introduction into clinical practice
Protons

technical benefit in clinical setting

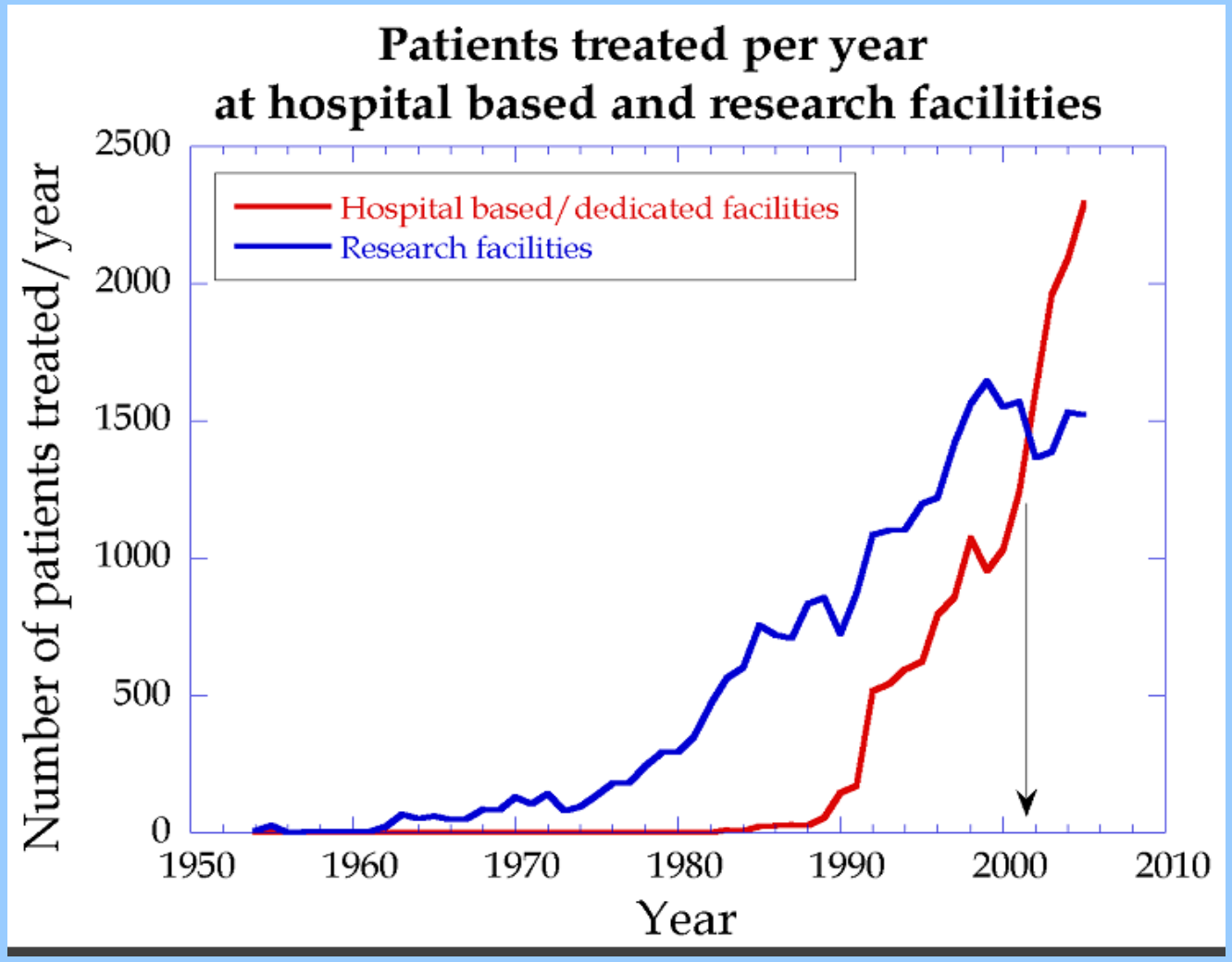
- representative series of patients
- clinically relevant endpoint

clinical benefit

- surrogate endpoint (tumour control and toxicity)
- survival and quality of life



Evaluating new radiotherapy technology



Clinical use of protons

courtesy of Thomas Bortfeld

Clinical evidence for efficacy of protons

Systematic review of published literature

Tumour site	tumour control*	survival*	toxicity*
Head & neck tumours			
Prostate cancer			
Ocular tumours			
Gastrointestinal cancer			
Lung cancer			
CNS tumours			
Sarcomas			
Paediatric tumours			

* benefit compared to best conventional treatment

Protons in other tumours

Brada et al 2007 JCO, 25 (8), 965-70
Brada et al 2009 Cancer Journal 15 (4), 319 -24
DeRusscher et al 2012

Clinical evidence for efficacy of protons

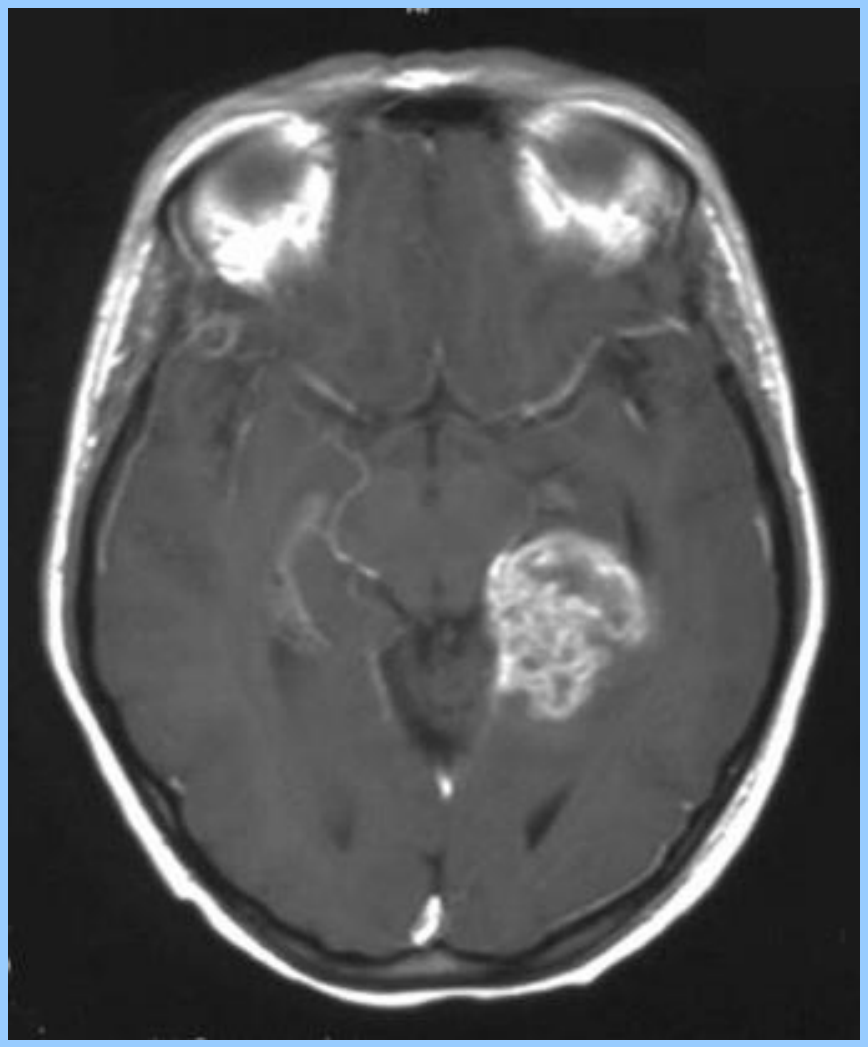
Systematic review of published literature

Tumour site	tumour control*	survival*	toxicity*
Head & neck tumours	✘	✘	✘
Prostate cancer	✘	✘	✘
Ocular tumours	✘	✘	✘
Gastrointestinal cancer	✘	✘	✘
Lung cancer	✘	✘	✘
CNS tumours	✘	✘	✘
Sarcomas	✘	✘	✘
Paediatric tumours	✘	✘	✘

* benefit compared to best conventional treatment

Protons in other tumours

Brada et al 2007 JCO, 25 (8), 965-70
Brada et al 2009 Cancer Journal 15 (4), 319 -24
DeRuysscher et al 2012



NovoTTF

TTF fields – tumour treating fields

Alternating electric fields

Clinical trials

NovoTTF

Alternating electric fields

NovoTTFtrial (NovoCure)

Recurrent glioblastoma

randomise

NovoTTF
>20 hours/day

120 patients

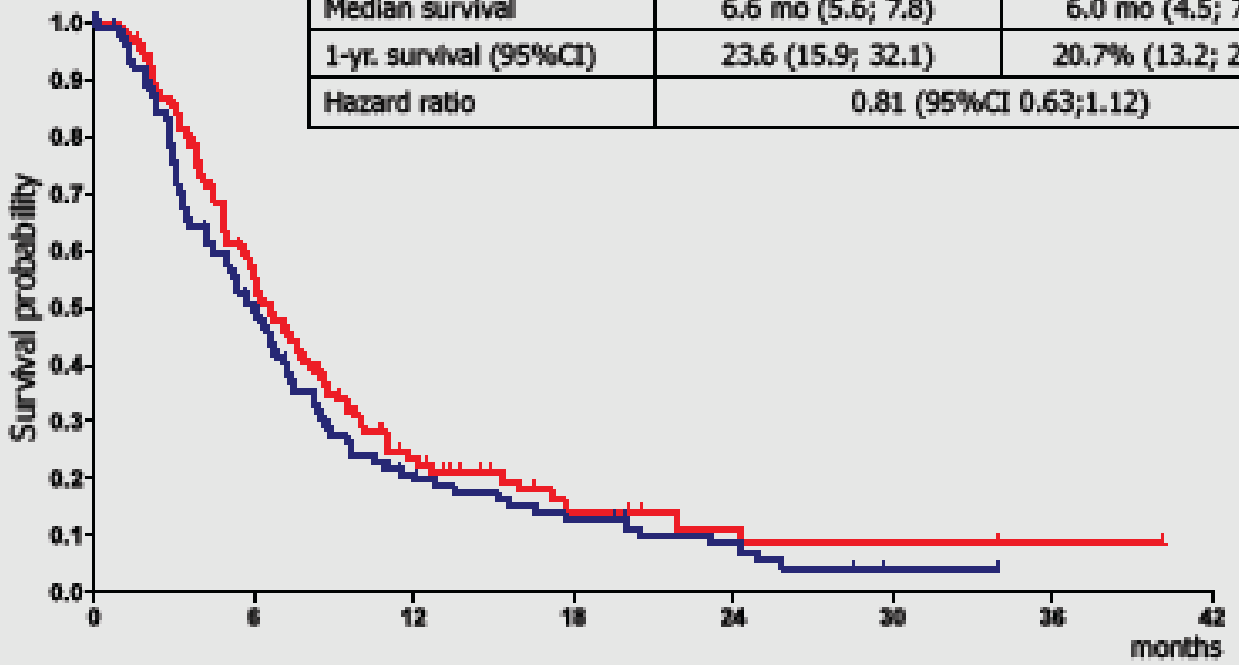
physician choice chemotherapy

117 patients

Alternating electric fields

NovoTTF trial
Survival by intent to treat (ITT) 237 patients

	Novo-TTF	Physicians Choice
Median survival	6.6 mo (5.6; 7.8)	6.0 mo (4.5; 7.1)
1-yr. survival (95%CI)	23.6 (15.9; 32.1)	20.7% (13.2; 29.4)
Hazard ratio	0.81 (95%CI 0.63;1.12)	

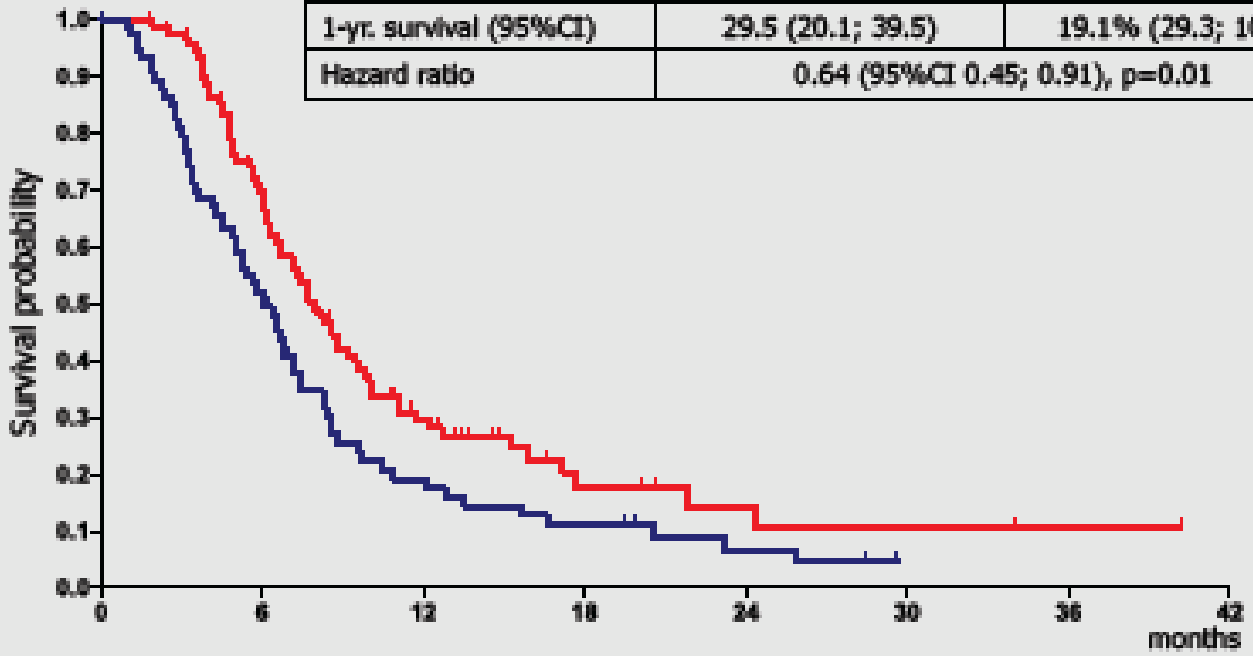


Alternating electric fields

Stupp et al ASCO 2010

NovoTTF trial
Survival by treatment per protocol (TPP) 185 patients

	Novo-TTF	Physicians Choice
Median survival	7.8 mo (6.6; 9.4)	6.1 mo (4.8; 7.1)
1-yr. survival (95%CI)	29.5 (20.1; 39.5)	19.1% (29.3; 10.7)
Hazard ratio	0.64 (95%CI 0.45; 0.91), p=0.01	



Alternating electric fields

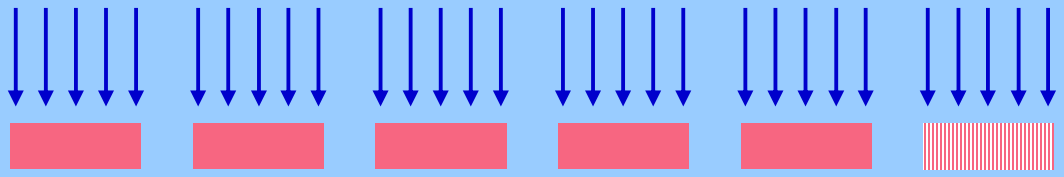
Stupp et al ASCO 2010

Successful Phase III Clinical Trial Results Reported
For NovoCure's Novel Medical Device
For Treatment Of Recurrent Glioblastoma

Alternating electric fields

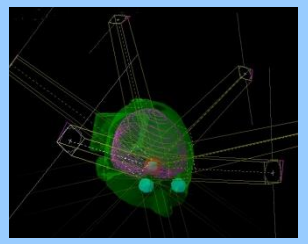
Stereotactic radiotherapy for acoustic neuroma

Fractionated stereotactic radiotherapy

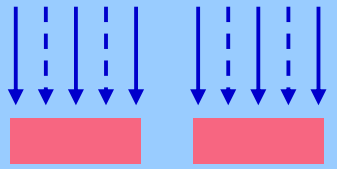


fractions
weeks

45 - 50Gy in 25 - 30 fractions

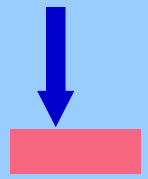


Hypofractionated stereotactic radiotherapy



20 - 30Gy in 6 - 10 fractions

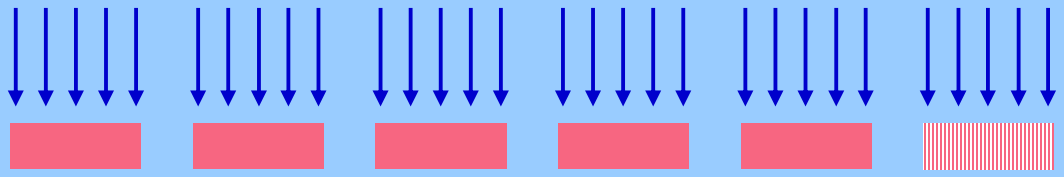
Single fraction radiosurgery



10 - 25Gy in 1 fraction

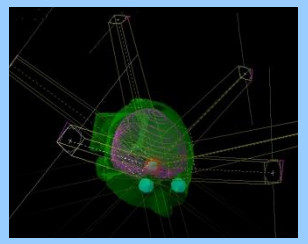
Fractionation in stereotactic radiotherapy

Fractionated stereotactic radiotherapy

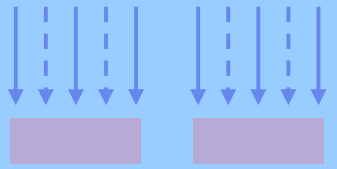


fractions
weeks

45 - 50Gy in 25 - 30 fractions

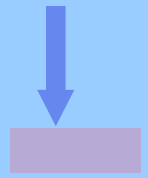


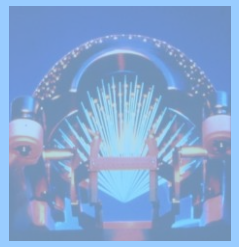
Hypofractionated stereotactic radiotherapy



20 - 30Gy in 6 - 10 fractions

Single fraction radiosurgery

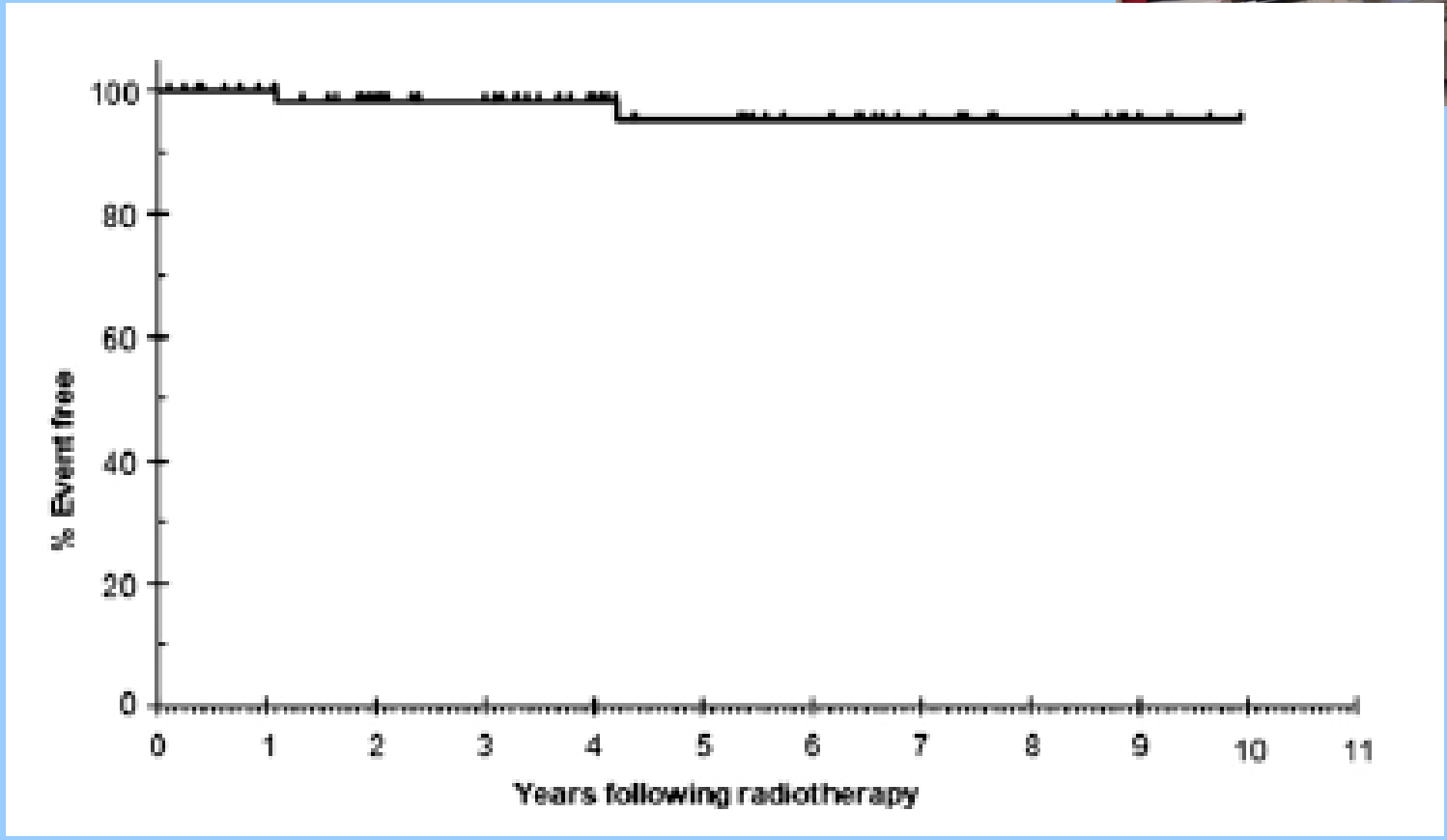




10 - 25Gy in 1 fraction

Fractionation in stereotactic radiotherapy

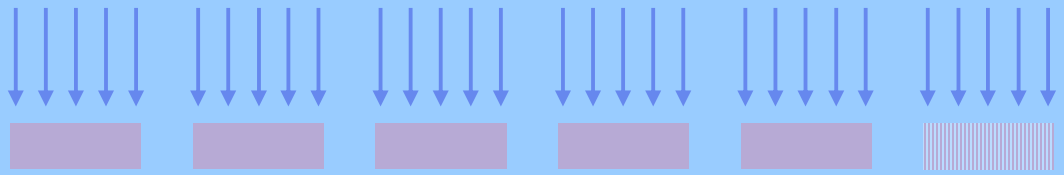
Tumour control



Powell et al 2010 IJROBP
72 patients with acoustic neuroma
Royal Marsden Hospital

Stereotactic RT for acoustic neuroma

Fractionated stereotactic radiotherapy



fractions
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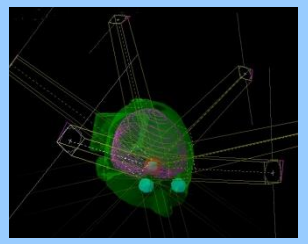
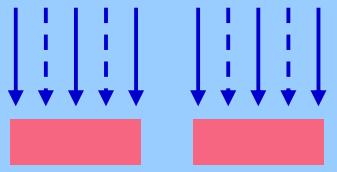
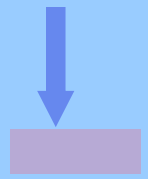


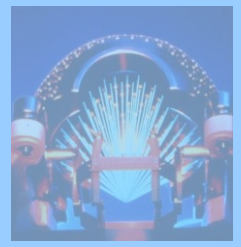
Hypofractionated stereotactic radiotherapy



25Gy in 5 fractions
30Gy in 10 fractions

Single fraction radiosurgery



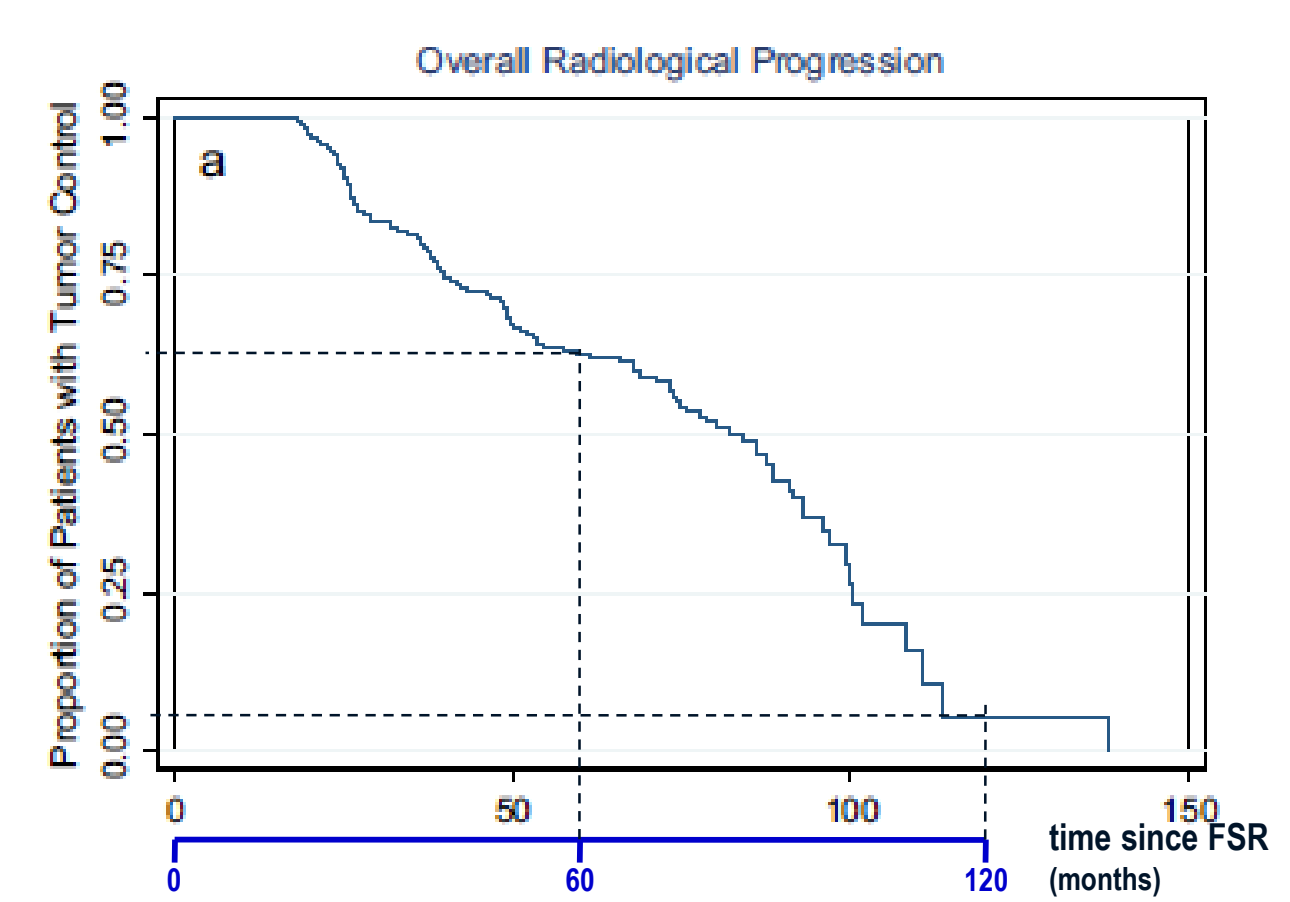


10 - 25Gy in 1 fraction

Fractionation in stereotactic radiotherapy

Kapoor et al 2010, Int J Rad Oncol Biol Phys, Johns Hopkins experience

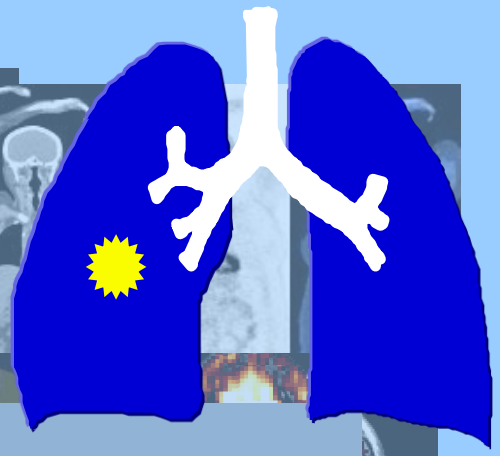
Tumour control



Fractionated s

Kapoor et al 2010, Int J Rad Oncol Biol Phys, Johns Hopkins experience

Introduction into clinical practice



technical benefit in clinical setting

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Evaluating new radiotherapy technology

Risks from introduction into clinical practice

system problems and complexity

- system errors
- demands on under resourced service

individual patient risks

- reliance on image interpretation
- clinical expertise vs technical prowess
- commercial interests & direct to patient marketing

Conventional design

to evaluate

Phase I	clinical pharmacology & toxicity
Phase II	initial investigation of activity
Phase III	comparative efficacy

model of drug testing

Evidence based medicine

Introduction of technology into clinical practice

driven by:

technology & commerce

clinical need

- driving forces are difficult to distinguish
- marketing blurs the reality

New radiotherapy technology

Challenges, opportunities & limitations of **new and emerging RT technologies**

University College Hospital, London
Leaders in Oncology Care, London

mbrada@theloc.com

Michael Brada

IRPA 13 Glasgow
15 May 2012